Non-Self-Administered
Prior Authorization Approval Criteria

Effective Date: 04/01/2019

Standard Non-Self-Administered Prior Authorization Guidelines

STANDARD COMMERCIAL DRUG FORMULARY
NON-SELF-ADMINISTERED
PRIOR AUTHORIZATION GUIDELINES

1. **Formulary Agents**
   Drug products that are listed in the Formulary as Prior Authorization (PA) require evaluation, per MedImpact Pharmacy and Therapeutics Committee guidelines, when the member presents a prescription to a network pharmacy. Each request will be reviewed on individual patient need. If the request does not meet the criteria established by the P & T Committee, the request will not be approved and alternative therapy will be recommended.
2. **Non-Formulary Agents**
   Any product not found in the Formulary listing, or any Formulary updates published by MedImpact**,** shall be considered a Non-Formulary drug. Coverage for non-formulary agents may be applied for in advance. When a member gives a prescription order for a non-formulary drug to a pharmacist, the pharmacist will evaluate the patient's drug history and contact the physician to determine if there is a legitimate medical need for a non-formulary drug. Each request will be reviewed on individual patient need. The following basic criteria are used:
   a. The use of Formulary Drug Products is contraindicated in the patient.
   b. The patient has failed an appropriate trial of Formulary or related agents.
   c. The choices available in the Drug Formulary are not suited for the present patient care need, and the drug selected is required for patient safety.
   d. The use of a Formulary drug may provoke an underlying condition, which would be detrimental to patient care.

   If the request does not meet the criteria established by the P & T Committee, the request will not be approved and alternative therapy will be recommended.
3. **Obtaining Coverage**
   Coverage may be obtained by:
   a. Faxing a completed **Prior Authorization Request** to DHMP at (303) 602-2081.
   b. Contacting DHMP Pharmacy Department at (303) 602-2070 and providing all necessary information requested.

   Non-approved requests may be appealed. The prescriber must provide information to support the appeal on the basis of medical necessity.

ABATACEPT - IV (NSA)

Generic	Brand	HICL	GCN	Exception/Other
ABATACEPT/MALTOSE	ORENCIA - IV		26306	

NOTE: For requests for the SQ dosage form of Orencia, please see the Orencia SQ PA Guideline.

GUIDELINES FOR USE

INITIAL CRITERIA (NOTE: FOR RENEWAL CRITERIA SEE BELOW)

1. Does the patient have a diagnosis of moderate to severe rheumatoid arthritis (RA) and meet **ALL** of the following criteria?
   - Therapy is prescribed by or given in consultation with a rheumatologist
   - The patient has had a previous trial of at least one of the following DMARDs (disease-modifying antirheumatic drugs) such as methotrexate, leflunomide, hydroxychloroquine, or sulfasalazine
   - The patient is 18 years of age or older
   - The patient has had a previous trial of the formulary preferred immunomodulators: Enbrel and Humira (**NOTE:** pharmaceutical samples acquired from the prescriber or manufacturer assistance program do not qualify)

   If yes, **approve for 6 months by GPID as follows:**
   - **Approve for 1 month by GPID with a maximum quantity limit of #4 vials (four 250mg vials) for 3 fills AND**
   - **Approve for 5 months by GPID with a maximum quantity limit of #4 vials (four 250mg vials) per month (start date is 1 month after the start of the 1st PA).**
     APPROVAL TEXT: Renewal for moderate to severe rheumatoid arthritis (RA) requires that the patient has experienced or maintained a 20% or greater improvement in tender joint count or swollen joint count while on therapy.

   If no, continue to #2.

CONTINUED ON NEXT PAGE

ABATACEPT - IV (NSA)

INITIAL CRITERIA (CONTINUED)

2. Does the patient have a diagnosis of moderate to severe polyarticular juvenile idiopathic arthritis (PJIA) and meet **ALL** of the following criteria?
   - Therapy is prescribed by or given in consultation with a rheumatologist
   - The patient has had a previous trial of at least one of the following DMARDs (disease-modifying antirheumatic drugs) such as methotrexate, leflunomide, hydroxychloroquine, or sulfasalazine
   - The patient is 6 years of age or older
   - The patient has had a previous trial of the formulary preferred immunomodulators: Enbrel and Humira (**NOTE:** pharmaceutical samples acquired from the prescriber or manufacturer assistance program do not qualify)

   If yes, **approve for 6 months by GPID as follows:**
   - **Approve for 1 month by GPID with a maximum quantity limit of #4 vials (four 250mg vials) for 3 fills AND**
   - **Approve for 5 months by GPID with a maximum quantity limit of #4 vials (four 250mg vials) per month (start date is 1 month after the start of the 1st PA).**
     APPROVAL TEXT: Renewal for moderate to severe polyarticular juvenile idiopathic arthritis (PJIA) requires that the patient has experienced or maintained a 20% or greater improvement in tender joint count or swollen joint count while on therapy.

   If no, continue to #3.

CONTINUED ON NEXT PAGE

ABATACEPT - IV (NSA)

INITIAL CRITERIA (CONTINUED)

3. Does the patient have a diagnosis of psoriatic arthritis (PsA) and meet **ALL** of the following criteria?
   - Therapy is prescribed by or given in consultation with a rheumatologist or dermatologist
   - The patient has had a previous trial of at least one of the following DMARDs (disease-modifying antirheumatic drugs) such as methotrexate, leflunomide, hydroxychloroquine, or sulfasalazine
   - The patient is 18 years of age or older
   - The patient has had a previous trial of any two of the following formulary preferred immunomodulators: Enbrel, Humira, Cosentyx, Stelara, or Otezla (**NOTE:** pharmaceutical samples acquired from the prescriber or manufacturer assistance program do not qualify)

   If yes, **approve for 6 months by GPID as follows:**
   - **Approve for 1 month by GPID with a maximum quantity limit of #4 vials (four 250mg vials) for 3 fills AND**
   - **Approve for 5 months by GPID with a maximum quantity limit of #4 vials (four 250mg vials) per month (start date is 1 month after the start of the 1st PA).**

   APPROVAL TEXT: Renewal for psoriatic arthritis (PsA) requires that the patient has experienced or maintained a 20% or greater improvement in tender joint count or swollen joint count while on therapy.

   If no, do not approve.
   DENIAL TEXT: The guideline named **ABATACEPT - IV (Orencia - IV)** requires a diagnosis of moderate to severe rheumatoid arthritis, moderate to severe polyarticular juvenile idiopathic arthritis, or psoriatic arthritis. In addition, the following criteria must be met:
   For patients with moderate to severe rheumatoid arthritis, approval requires:
   - Therapy is prescribed by or given in consultation with a rheumatologist
   - The patient has had a previous trial of at least one of the following DMARDs (disease-modifying antirheumatic drugs) such as methotrexate, leflunomide, hydroxychloroquine, or sulfasalazine
   - The patient is 18 years of age or older
   - The patient has had a previous trial of the formulary preferred immunomodulators: Enbrel **AND** Humira

   (Initial denial text continued on next page)

CONTINUED ON NEXT PAGE

ABATACEPT - IV (NSA)

INITIAL CRITERIA (CONTINUED)

For patients with moderate to severe polyarticular juvenile idiopathic arthritis, approval requires:

- Therapy is prescribed by or given in consultation with a rheumatologist
- The patient has had a previous trial of at least one of the following DMARDs (disease-modifying antirheumatic drugs) such as methotrexate, leflunomide, hydroxychloroquine, or sulfasalazine
- The patient is 6 years of age or older
- The patient has had a previous trial of the formulary preferred immunomodulators: Enbrel **AND** Humira

For patients with psoriatic arthritis, approval requires:

- Therapy is prescribed by or given in consultation with a rheumatologist or dermatologist
- The patient has had a previous trial of at least one of the following DMARDs (disease-modifying antirheumatic drugs) such as methotrexate, leflunomide, hydroxychloroquine, or sulfasalazine
- The patient is 18 years of age or older
- The patient has had a previous trial of any two of the following formulary preferred immunomodulators: Enbrel, Humira, Cosentyx, Stelara, or Otezla

The use of pharmaceutical samples (from the prescriber or manufacturer assistance program) will not be considered when evaluating the medical condition or prior prescription history for drugs that require prior authorization.

RENEWAL CRITERIA

1. Does the patient have a diagnosis of moderate to severe rheumatoid arthritis (RA), psoriatic arthritis (PsA), or moderate to severe polyarticular juvenile idiopathic arthritis (PJIA) **AND** meet the following criterion?
   - The patient has experienced or maintained a 20% or greater improvement in tender joint count or swollen joint count while on therapy

   If yes, **approve for 12 months by GPID with a quantity limit of #4 vials (four 250mg vials) per month.**
   If no, do not approve.
   DENIAL TEXT: The guideline named **ABATACEPT - IV (ORENCIA - IV)** requires a diagnosis of moderate to severe rheumatoid arthritis, psoriatic arthritis, or moderate to severe polyarticular juvenile idiopathic arthritis for renewal. In addition, the following criterion must be met:
   - The patient has experienced or maintained a 20% or greater improvement in tender joint count or swollen joint count while on therapy

CONTINUED ON NEXT PAGE

ABATACEPT - IV (NSA)

RATIONALE
Ensure appropriate use of abatacept-IV consistent with its FDA approved indications.

FDA APPROVED INDICATIONS
ABATACEPT (Orencia) is a selective T cell costimulation modulator indicated for:

Adult Rheumatoid Arthritis (RA)
Moderately to severely active RA in adults. Orencia may be used as monotherapy or concomitantly with DMARDs other than TNF antagonists.

Polyarticular Juvenile Idiopathic Arthritis (PJIA)
Moderately to severely active polyarticular juvenile idiopathic arthritis in pediatric patients 2 years of age and older. Orencia may be used as monotherapy or concomitantly with methotrexate.

Adult Psoriatic Arthritis (PsA)
ORENCIA is indicated for the treatment of adult patients with active psoriatic arthritis (PsA).

Important Limitations of Use
ABATACEPT (Orencia) should not be given concomitantly with TNF antagonists. Orencia is not recommended for use concomitantly with other biologic rheumatoid arthritis (RA) therapy, such as anakinra.

DOSAGE AND ADMINISTRATION
Adult Rheumatoid Arthritis (RA) and Adult Psoriatic Arthritis (PsA)
ORENCIA IV lyophilized powder should be reconstituted and administered after as a 30-minute intravenous infusion utilizing the weight range-based dosing specified in the Table below. Following the initial intravenous administration, an intravenous infusion should be given at 2 and 4 weeks after the first infusion and every 4 weeks thereafter.

TABLE 1

BODY WEIGHT OF PATIENT	DOSE	NUMBER OF VIALS
Less than 60 kg	500 MG	2
60 to 100 kg	750 MG	3
More than 100 kg	1000 MG	4

Each vial provides 250mg of abatacept for administration

CONTINUED ON NEXT PAGE

ABATACEPT - IV (NSA)

FDA APPROVED INDICATIONS (CONTINUED)

DOSAGE AND ADMINISTRATION

Polyarticular Juvenile Idiopathic Arthritis (PJIA)

ORENCIA should be administered as a 30-minute intravenous infusion based on body weight. Pediatric patients with body weight less than 75 kg should be administered a dose of 10 mg/kg. Pediatric patients with body weight of 75 kg or more should be administered ORENCIA following the adult intravenous dosing regimen (see Table 1 above), not to exceed a maximum dose of 1000 mg. Following the initial administration, ORENCIA should be given at 2 and 4 weeks after the first infusion and every 4 weeks thereafter. Any unused portions in the vials must be immediately discarded.

REFERENCES

- Orencia [Prescribing Information]. Princeton, NJ: E.R. Squibb & Sons, L.L.C. June 2017.

Library	Commercial	NSA
Yes	No	Yes

Part D Effective: N/A
Commercial Effective: 04/01/18

Created: 05/05
Client Approval: 03/18

P&T Approval: 01/18

ADO-TRASTUZUMAB EMTANSINE

Generic	Brand	HICL	GCN	Exception/Other
ADO-TRASTUZUMAB EMTANSINE	KADCYLA	40046		

This drug requires a written request for prior authorization.

GUIDELINES FOR USE

1. Does the patient have a diagnosis of metastatic breast cancer?

   If yes, continue to #2.
   If no, do not approve.
   DENIAL TEXT: Approval requires a diagnosis of metastatic breast cancer that is HER2 positive (defined as IHC 3+ or FISH amplification ratio greater than 2.0) and prior therapy for metastatic disease (such as Perjeta with Herceptin and a taxane (either docetaxel or paclitaxel); or Herceptin with: paclitaxel with or without carboplatin, docetaxel, vinorelbine, or Xeloda) or has developed disease recurrence during or within six months of completing adjuvant therapy. Prior therapies may also require a prior authorization.

2. Is the patient's breast cancer HER2 positive (defined as IHC 3+ or FISH amplification ratio greater than 2.0)?

   If yes, continue to #3.
   If no, do not approve.
   DENIAL TEXT: Approval requires a diagnosis of metastatic breast cancer that is HER2 positive (defined as IHC 3+ or FISH amplification ratio greater than 2.0) and prior therapy for metastatic disease (such as Perjeta with Herceptin and a taxane (either docetaxel or paclitaxel); or Herceptin with: paclitaxel with or without carboplatin, docetaxel, vinorelbine, or Xeloda) or has developed disease recurrence during or within six months of completing adjuvant therapy. Prior therapies may also require a prior authorization.

CONTINUED ON NEXT PAGE

ADO-TRASTUZUMAB EMTANSINE

GUIDELINES FOR USE (CONTINUED)

3. Has the patient received prior therapy for metastatic disease (such as Perjeta with Herceptin and a taxane (either docetaxel or paclitaxel); or Herceptin with: paclitaxel with or without carboplatin, docetaxel, vinorelbine, or Xeloda) or developed disease recurrence during or within six months of completing adjuvant therapy?

   If yes, **approve for 12 months with a fill limit of 12 fills of #2 vials per 21 day supply.**
   APPROVAL TEXT: Please note that this drug has an important FDA safety warning. For more information, please ask your doctor or pharmacist.
   If no, do not approve.
   DENIAL TEXT: Approval requires a diagnosis of metastatic breast cancer that is HER2 positive (defined as IHC 3+ or FISH amplification ratio greater than 2.0) and prior therapy for metastatic disease (such as Perjeta with Herceptin and a taxane (either docetaxel or paclitaxel); or Herceptin with: paclitaxel with or without carboplatin, docetaxel, vinorelbine, or Xeloda) or has developed disease recurrence during or within six months of completing adjuvant therapy. Prior therapies may also require a prior authorization.

RATIONALE
To ensure appropriate use aligned with FDA approved indications and NCCN guidelines.

The recommended dose of Kadcyla is 3.6 mg/kg given as an intravenous infusion every 3 weeks (21-day cycle) until disease progression or unacceptable toxicity. Do not administer Kadcyla at doses greater than 3.6 mg/kg. Do not substitute Kadcyla for or with Herceptin. Administer infusion over 90 minutes for first dose. Patients should be observed during the infusion and for at least 90 minutes following the initial dose for fever, chills, or other infusion related reactions. Subsequent infusions can be administered over 30 minutes if prior infusions were well tolerated. Patients should be observed during the infusion and for at least 30 minutes after infusion.

If a planned dose is delayed or missed, it should be administered as soon as possible; do not wait until the next planned cycle. The schedule of administration should be adjusted to maintain a 3-week interval between doses. The infusion may be administered at the dose and rate the patient tolerated in the most recent infusion. The infusion rate of Kadcyla should be slowed or interrupted if the patient develops an infusion-related reaction. Permanently discontinue Kadcyla for life-threatening infusion related reactions.

Management of increased serum transaminases, hyperbilirubinemia, left ventricular dysfunction, thrombocytopenia, pulmonary toxicity or peripheral neuropathy may require temporary interruption, dose reduction, or treatment discontinuation of Kadcyla. The first dose reduction is to 3mg/kg, followed by a reduction to 2.4mg/kg. Any further reduction should result in discontinuation of treatment.

CONTINUED ON NEXT PAGE

ADO-TRASTUZUMAB EMTANSINE

RATIONALE (CONTINUED)
A reduction in the dose is recommended in the case of hepatotoxicity signaled by increases in serum transaminases and/or hyperbilirubinemia or in the case of Grade 4 thrombocytopenia (platelets < 25,000/mm^3). Temporary discontinuation is recommended for patients experiencing Grade 3 or 4 peripheral neuropathy until resolution to ≤ Grade 2. Permanent discontinuation is advised for patients with serum transaminases > 3 x ULN and concomitant total bilirubin > 2 x ULN; patients diagnosed with nodular regenerative hyperplasia (NRH), interstitial lung disease (ILD), or pneumonitis.

Kadcyla (ado-trastuzumab emtansine) is a HER2-targeted antibody-drug conjugate of Herceptin (trastuzumab) and DM1, a microtubule inhibitor. DM1 is too toxic to deliver directly into a patient's bloodstream, like other chemotherapy drugs. The Herceptin component of Kadcyla targets and delivers DM1 directly into cancer cells, sparing noncancerous cells. Upon binding to sub-domain IV of the HER2 receptor, ado-trastuzumab emtansine undergoes receptor-mediated internalization and subsequent lysosomal degradation, resulting in intracellular release of DM1-containing cytotoxic catabolites. Binding of DM1 to tubulin disrupts microtubule networks in the cell, which results in cell cycle arrest and apoptotic cell death.

Breast cancer is the most common cancer among women and the second leading cause of cancer death. An estimated 232,340 Americans will be diagnosed with breast cancer and another 39,620 will die of it in 2013. The most common risk factors are female gender and increasing age. The five year survival rate for metastatic breast cancer is 15%. In HER2-positive breast cancers, the increased amount of the protein contributes to cancer call growth and survival. Nearly 20% of breast cancers have increased amounts of HER2.

The National Comprehensive Cancer Network (NCCN) guidelines recommend Perjeta (pertuzumab) with Herceptin and a taxane (either docetaxel or paclitaxel) as the preferred first-line therapy for HER2 positive metastatic breast cancer. Other first-line regimens include Herceptin with: paclitaxel ± carboplatin, docetaxel, vinorelbine, or Xeloda (capecitabine). Regimens for Herceptin-exposed HER2-positive disease include:

- Tykerb + Xeloda
- Herceptin + Xeloda
- Herceptin + Tykerb (without cytotoxic therapy)
- Herceptin + other agents

CONTINUED ON NEXT PAGE

ADO-TRASTUZUMAB EMTANSINE

RATIONALE (CONTINUED)
Additional phase III studies may expand upon Kadcyla's initial indication. Kadcyla alone or in combination with Perjeta is being evaluated against Herceptin plus taxane (docetaxel or paclitaxel) in patients with HER2-positive progressive or recurrent locally advanced or previously untreated metastatic breast cancer in the MARIANNE study, with initial results expected in the first half 2014. The TH3RESA study will evaluate Kadcyla with treatment of the physician's choice in patients with metastatic or unresectable locally advanced/recurrent HER2-positive breast cancer previously treated with Herceptin, a taxane, and Tykerb and disease progression after at least two regimens of HER2-directed therapy. Additionally Kadcyla is being studied as adjuvant therapy for HER2-positive breast cancer in the KATHERINE study and for advanced gastric cancer in another trial.

Kadcyla's pivotal trial included in the prescribing information was the EMILIA study; a randomized, multicenter, open-label Phase III trial of 991 patients with HER2-positive, unresectable locally advanced or metastatic breast cancer. Prior taxane and trastuzumab-based therapy was required before trial enrollment. Patients with only prior adjuvant therapy were required to have disease recurrence during or within six months of completing adjuvant therapy. Breast tumor samples were required to show HER2 over expression defined as 3+ IHC or FISH amplification ratio ≥ 2.0 determined at a central laboratory. Patients were randomly allocated (1:1) to receive Tykerb plus Xeloda or Kadcyla. Randomization was stratified by world region (United States, Western Europe other), number of prior chemotherapy regimens for unresectable locally advanced or metastatic disease (0–1, >1) and visceral versus non-visceral disease as determined by the investigators.

Kadcyla was given intravenously at 3.6 mg/kg on Day 1 of a 21-day cycle. Tykerb was administered at 1250 mg/day orally once per day of a 21-day cycle and Xeloda was administered at 1000 mg/m^2 orally twice daily on Days 1−14 of a 21-day cycle. Patients were treated with Kadcyla or Tykerb plus Xeloda until progression of disease, withdrawal of consent, or unacceptable toxicity. At the time of the primary analysis, median time on study drug was 5.7 months for Kadcyla, 4.9 months for Tykerb, and 4.8 months for Xeloda.

The co-primary efficacy endpoints of the study were progression-free survival (PFS) based on tumor response assessments by an independent review committee (IRC), and overall survival (OS). Additional endpoints included PFS (based on investigator tumor response assessments), objective response rate (ORR), duration of response and time to symptom progression.

Patient demographics and baseline tumor characteristics were balanced between treatment arms. The median age was approximately 53 years (range 24-84 years and all but 5 patients were women. Tumor prognostic characteristics including hormone receptor status (positive: 55%, negative: 43%), presence of visceral disease (68%) and non-visceral disease only (33%) and the number of metastatic sites (< 3: 61%, ≥ 3: 37%) were similar in the study arms.

CONTINUED ON NEXT PAGE

ADO-TRASTUZUMAB EMTANSINE

RATIONALE (CONTINUED)
The majority of patients (88%) had received prior systemic treatment in the metastatic setting. All but one patient received Herceptin prior to study entry; approximately 85% of patients received prior Herceptin in the metastatic setting. Over 99% percent of patients had received a taxane, and 61% of patients had received an anthracycline prior to study entry. Overall, patients received a median of 3 systemic agents in the metastatic setting. Among patients with hormone receptor-positive tumors, 44.4% received prior adjuvant hormonal therapy and 44.8% received hormonal therapy for locally advanced/metastatic disease.

Median progression-free survival as assessed by independent review was 9.6 months with Kadcyla versus 6.4 months with Tykerb plus Xeloda (hazard ratio for progression or death from any cause, 0.65; 95% confidence interval [CI], 0.55 to 0.77; P<0.001), and median overall survival at the second interim analysis crossed the stopping boundary for efficacy (30.9 months vs. 25.1 months; hazard ratio for death from any cause, 0.68; 95% CI, 0.55 to 0.85; P<0.001). The objective response rate was higher with Kadcyla (43.6%, vs. 30.8% with Tykerb plus Xeloda; P<0.001); results for all additional secondary end points favored Kadcyla.

A treatment benefit with Kadcyla in terms of PFS and OS was observed in patient subgroups based on stratification factors, key baseline demographic and disease characteristics, and prior treatments. In the subgroup of patients with hormone receptor-negative disease (n=426), the hazard ratios for PFS and OS were 0.56 (95% CI: 0.44, 0.72) and 0.75 (95% CI: 0.54, 1.03), respectively. In the subgroup of patients with hormone receptor-positive disease (n=545), the hazard ratios for PFS and OS were 0.72 (95% CI: 0.58, 0.91) and 0.62 (95% CI: 0.46, 0.85), respectively. In the subgroup of patients with non-measurable disease (n=205), based on IRC assessments, the hazard ratios for PFS and OS were 0.91 (95% CI: 0.59, 1.42) and 0.96 (95% CI: 0.54, 1.68), respectively; in patients with measurable disease the hazard ratios were 0.62 (95% CI: 0.52, 0.75) and 0.65 (95% CI: 0.51, 0.82), respectively. The PFS and OS hazard ratios in patients who were younger than 65 years old (n=853) were 0.62 (95% CI: 0.52, 0.74) and 0.66 (95% CI: 0.52, 0.83), respectively. In patients ≥ 65 years old (n=138), the hazard ratios for PFS and OS were 1.06 (95% CI: 0.68, 1.66) and 1.05 (95% CI: 0.58, 1.91), respectively.

Kadcyla has boxed warnings for hepatotoxicity, cardiac toxicity, and embryo-fetal toxicity. Warnings and precautions include pulmonary toxicity, infusion-related reactions, hypersensitivity reactions, thrombocytopenia, and neurotoxicity. The most common adverse drug reactions (frequency > 25%) with Kadcyla were fatigue, nausea, musculoskeletal pain, thrombocytopenia, headache, increased transaminases, and constipation.

Nursing mothers should discontinue nursing or discontinue Kadcyla taking into consideration the importance of the drug to the mother. Females of reproductive potential should be counseled on pregnancy prevention and planning. These patients are encouraged to participate in the MotHER Pregnancy Registry. Kadcyla is pregnancy category D.

CONTINUED ON NEXT PAGE

ADO-TRASTUZUMAB EMTANSINE

RATIONALE (CONTINUED)
NCCN considers either immunohistochemistry (IHC) or *in situ* hybridization (ISH) tests as an acceptable method for making an initial determination of HER2 tumor status. Breast cancer tumors are classified as HER2 positive if they are scored as 3+ by an IHC method.

FDA APPROVED INDICATIONS
Kadcyla (ado-trastuzumab emtansine) is indicated, as a single agent, for the treatment of patients with HER2-positive, metastatic breast cancer who previously received trastuzumab and a taxane, separately or in combination. Patients should have either:
- Received prior therapy for metastatic disease, or
- Developed disease recurrence during or within six months of completing adjuvant therapy.

REFERENCES

- Kadcyla [Prescribing Information]. South San Francisco, CA: Genentech, Inc.; February 2013.
- Verma S, Miles D, Gianni L, et al. Trastuzumab Emtansine for HER2-Positive Advanced Breast Cancer. N Engl J Med 2012; 367:1783-91.
- National Comprehensive Cancer Network. NCCN Clinical Practice Guidelines in Oncology : Breast Cancer. Version 1.2013. Available at: http://www.nccn.org/professionals/physician_gls/pdf/breast.pdf [Accessed March 4, 2013].
- American Cancer Society. Breast Cancer Detailed Guide. Available at: http://www.cancer.org/cancer/breastcancer [Accessed March 4, 2013].
- A Study of Trastuzumab Emtansine (T-DM1) Plus Pertuzumab/Pertuzumab Placebo Versus Trastuzumab [Herceptin] Plus a Taxane in Patients With Metastatic Breast Cancer (MARIANNE). Available at: http://clinicaltrials.gov/show/NCT01120184 [Accessed March 4, 2013].
- A Study of Trastuzumab Emtansine in Comparison With Treatment of Physician's Choice in Patients With HER2-Positive Breast Cancer Who Have Received at Least Two Prior Regimens of HER2-Directed Therapy (TH3RESA). Available at: http://clinicaltrials.gov/show/NCT01419197 [Accessed March 4, 2013].
- A Study of Trastuzumab Emtansine Versus Trastuzumab as Adjuvant Therapy in Patients With HER2-Positive Breast Cancer Who Have Residual Tumor in the Breast or Axillary Lymph Nodes Following Preoperative Therapy (KATHERINE). Available at: http://clinicaltrials.gov/ct2/show/NCT01772472 [Accessed March 4, 2013].
- A Study of Trastuzumab Emtansine Versus Taxane in Patients With Advanced Gastric Cancer. Available at: http://clinicaltrials.gov/ct2/show/NCT01641939 [Accessed March 4, 2013].

Library	Commercial	NSA
Yes	No	Yes

Part D Effective: N/A
Commercial Effective: 01/01/14
Created: 03/13
Client Approval: 11/13
P&T Approval: 11/13

AFLIBERCEPT (NSA)

Generic	Brand	HICL	GCN	Exception/Other
AFLIBERCEPT	EYLEA		30919	

GUIDELINES FOR USE

1. Is this medication being prescribed by or given in consultation with an ophthalmologist and/or retina specialist?

   If yes, continue to #2.
   If no, do not approve.
   DENIAL TEXT: See the denial text at the end of the guideline.

2. Does the patient have a diagnosis of neovascular (wet) age-related macular degeneration (AMD)?

   If yes, continue to #5.
   If no, continue to #3.

3. Does the patient have a diagnosis of macular edema following retinal vein occlusion (RVO)?

   If yes, continue to #5.
   If no, continue to #4.

4. Does the patient have a diagnosis of diabetic macular edema (DME) **OR** diabetic retinopathy with DME?

   If yes, continue to #5.
   If no, do not approve.
   DENIAL TEXT: See the denial text at the end of the guideline.

5. Is the patient receiving treatment in both eyes at this time?

   If yes, **approve for 12 months by GPID with a quantity not to exceed 0.10mL (#2 vials) per month.**
   If no and one eye is being treated at this time, **approve for 12 months by GPID with a quantity not to exceed 0.05mL (#1 vial) per month.**

DENIAL TEXT: The guideline named **AFLIBERCEPT (Eylea)** requires that the medication is prescribed by or given in consultation with an ophthalmologist and/or retina specialist and the patient has a diagnosis of neovascular (wet) age-related macular degeneration (AMD); macular edema following retinal vein occlusion (RVO); diabetic macular edema (DME); or diabetic retinopathy with DME.

CONTINUED ON NEXT PAGE

AFLIBERCEPT (NSA)

RATIONALE
To ensure appropriate use of Eylea consistent with FDA approved indication.

FDA APPROVED INDICATIONS
Eylea is indicated for the treatment of patients with:
- Neovascular (Wet) Age-Related Macular Degeneration (AMD)
- Macular Edema Following Retinal Vein Occlusion (RVO)
- Diabetic Macular Edema (DME)
- Diabetic Retinopathy (DR) in Patients with DME

DOSAGE AND ADMINISTRATION
Neovascular (Wet) Age-Related Macular Degeneration (AMD)
The recommended dose for Eylea is 2 mg (0.05 mL) administered by intravitreal injection every 4 weeks (approximately every 28 days, monthly) for the first 12 weeks (3 months), followed by 2 mg (0.05 mL) via intravitreal injection once every 8 weeks (2 months). Although Eylea may be dosed as frequently as 2 mg every 4 weeks (approximately every 25 days, monthly), additional efficacy was not demonstrated when Eylea was dosed every 4 weeks compared to every 8 weeks. Some patients may need every 4 week (monthly) dosing after the first 12 weeks (3 months). Although not as effective as the recommended every 8 week dosing regimen, patients may also be treated with one dose every 12 weeks after one year of effective therapy. Patients should be assessed regularly.

Macular Edema Following Retinal Vein Occlusion (RVO)
The recommended dose for Eylea is 2 mg (0.05 mL) administered by intravitreal injection once every 4 weeks (approximately every 25 days, monthly).

Diabetic Macular Edema (DME) and Diabetic Retinopathy (DR) in Patients with DME
The recommended dose for Eylea is 2 mg (0.05 mL) administered by intravitreal injection every 4 weeks (approximately every 28 days, monthly) for the first 5 injections, followed by 2 mg (0.05 mL) via intravitreal injection once every 8 weeks (2 months). Although Eylea may be dosed as frequently as 2 mg every 4 weeks (approximately every 25 days, monthly), additional efficacy was not demonstrated in most patients when Eylea was dosed every 4 weeks compared to every 8 weeks. Some patients may need every 4 week (monthly) dosing after the first 20 weeks (5 months).

REFERENCES
- Eylea [Prescribing Information]. Tarrytown, NY: Regeneron; August 2018.

Library	Commercial	NSA
Yes	No	Yes

Part D Effective: N/A
Commercial Effective: 09/17/18
Created: 04/14
Client Approval: 08/18
P&T Approval: 11/14

ALEMTUZUMAB (NSA)

Generic	Brand	HICL	GCN	Exception/Other
ALEMTUZUMAB	LEMTRADA		36182	

GUIDELINES FOR USE

INITIAL CRITERIA (NOTE: FOR RENEWAL CRITERIA SEE BELOW)

1. Does the patient have a relapsing form of multiple sclerosis (MS) and meets the following criteria?
   - The patient has tried at least two formulary agents that have been FDA approved for the treatment of relapsing forms of multiple sclerosis (MS) (**Please note** that other MS agents also require prior authorization.)

   If yes, **approve for 1 month by GPID for 6mL (five 1.2mL vials) per 5 day supply.**
   If no, do not approve.
   DENIAL TEXT: The guideline named **ALEMTUZUMAB (Lemtrada)** requires that the patient has a relapsing form of multiple sclerosis and that the patient has tried at least two formulary agents that have been FDA approved for the treatment of relapsing form of multiple sclerosis (**Please note** that other multiple sclerosis agents may also require prior authorization).

RENEWAL CRITERIA

1. Does the patient have a relapsing form of multiple sclerosis (MS)?

   If yes, continue to #2.
   If no, do not approve.
   DENIAL TEXT: See the renewal denial text at the end of the guideline.

2. Has the patient already received two courses of Lemtrada (a total of 9.6mL [eight 1.2mL vials] of Lemtrada)?

   If yes, do not approve.
   DENIAL TEXT: See the renewal denial text at the end of the guideline.
   If no, continue to #3.

CONTINUED ON NEXT PAGE

ALEMTUZUMAB (NSA)

RENEWAL CRITERIA (CONTINUED)

3. Have at least 12 months elapsed since receiving the first course of Lemtrada?

   If yes, **approve for lifetime by GPID with one fill count for 3.6mL (three 1.2mL vials) per 3 day supply.** [**Note**: The patient should only be approved for renewal for one fill in a lifetime.]
   If no, do not approve.
   DENIAL TEXT: See the renewal denial text at the end of the guideline.

DENIAL TEXT: The guideline named **ALEMTUZUMAB (Lemtrada)** renewal requires that the patient have a relapsing form of multiple sclerosis. Approval also requires that at least 12 months has elapsed since receiving the first course of Lemtrada. Patients are limited to two courses of therapy in a lifetime with Lemtrada.

RATIONALE
To ensure appropriate utilization of LEMTRADA.

FDA APPROVED INDICATIONS
LEMTRADA is indicated for the treatment of patients with relapsing forms of multiple sclerosis (MS). Because of its safety profile, the use of Lemtrada should be reserved for patients who have had an inadequate response to two or more drugs indicated for the treatment of MS.

The efficacy of Lemtrada was evaluated in two studies, known in the literature as CARE- MS I and CARE-MS II studies, and referred to in the prescribing information as Study 2 and 1, respectively. Both studies were 2-year randomized, open-label, rater-blinded, active comparator (interferon 576 beta-1a 44 micrograms administered subcutaneously three times a week) controlled study in patients with RRMS. Patients had to have at least 2 relapses during the 2 years prior to trial entry and at least 1 relapse during the year prior to trial entry. Subjects randomized to Lemtrada received 12mg, once daily, as an infusion for 5 days for the first treatment course and then 1 year later received a 12 mg, once daily, as an infusion for 3 days for the 2nd course of treatment. In Study 1, both co-primary endpoints were statistically significantly lower for Lemtrada than for Rebif. In Study 2, the annualized relapse rate was statistically significantly lower for Lemtrada than for Rebif. There was no significant difference between Lemtrada and Rebif for the time to confirmed disability progression. Neither study showed a difference for the MRI outcome measure of change in T2 lesion volume.

CONTINUED ON NEXT PAGE

ALEMTUZUMAB (NSA)

FDA APPROVED INDICATIONS (CONTINUED)

DOSING

Lemtrada is administered by intravenous infusion over 4 hours and for 2 annual treatment courses. The first course is 12mg/day for 5 consecutive days. The second course, which follows 12 months after the 1st course, is 12mg/day for 3 consecutive days. Patients should be pre-medicated with high dose corticosteroids (1000mg methylprednisolone or equivalent) immediately prior to receiving the Lemtrada infusion for the first 3 days of each treatment course. It is also recommended that patients be treated with anti-viral prophylaxis for herpetic viral infections on the first day of each treatment course and continue for a minimum of two months following treatment or until CD4+ lymphocyte count is ≥ 200 cells per microliter. Lemtrada should be administered in a setting with personnel and equipment to manage any serious infusion reaction or anaphylaxis.

REFERENCES

- Lemtrada [Prescribing Information]. Genzyme Corporation. Cambridge, MA. November 2014. Available at: http://www.accessdata.fda.gov/drugsatfda_docs/label/2014/103948s5139lbl.pdf [Accessed 12/3/14].
- UpToDate, Inc. Treatment of Relapsing Remitting Multiple Sclerosis. UpToDate [database online]. Waltham, MA. Available at http://www.uptodate.com/contents/treatment-of-relapsing-remitting-multiple-sclerosis-in-adults?source=search_result&search=RRMS&selectedTitle=1%7E20 [Accessed 12/3/14}.

Library	Commercial	NSA
Yes	No	Yes

Part D Effective: N/A
Commercial Effective: 10/01/16
Created: 02/15
Client Approval: 09/16
P&T Approval: 08/16

ALGLUCOSIDASE ALFA

Generic	Brand	HICL	GCN	Exception/Other
ALGLUCOSIDASE ALFA	LUMIZYME MYOZYME	33588		

This drug requires a written request for prior authorization.

GUIDELINES FOR USE

1. Does the patient have a diagnosis of Pompe's disease (acid alpha-glucosidase [GAA] deficiency)?

   If yes, **approve for lifetime by HICL**.
   If no, do not approve.
   DENIAL TEXT: Our guideline for **ALGLUCOSIDASE ALFA** requires a diagnosis of Pompe's disease (acid alpha-glucosidase deficiency).

RATIONALE
Promote appropriate utilization and dosing based on FDA approved indication.

FDA APPROVED INDICATIONS
Lumizyme is a hydrolytic lysosomal glycogen-specific enzyme indicated for patients with Pompe disease (GAA deficiency).

Myozyme is a lysosomal glycogen=specific enzyme indicated for patients with Pompe disease (GAA deficiency).

DOSAGE AND ADMINISTRATION
20 mg per kg body weight administered every 2 weeks as an intravenous infusion

REFERENCES

- Lumizyme [Prescribing Information]. Cambridge, MA:Genzyme Corporation; August 2014.Myozyme [Prescribing Information] , Cambridge, MA:Genzyme Corporation; May 2014.

Library	Commercial	NSA
Yes	No	Yes

Part D Effective: N/A
Commercial Effective: 01/01/15
Created: 08/14
Client Approval: 11/14
P&T Approval: 11/14

ASPARAGINASE

Generic	Brand	HICL	GCN	Exception/Other
ASPARAGINASE	ELSPAR		38750	
ASPARAGINASE (ERWINIA CHRYSAN)	ERWINAZE		30918	
PEGASPARGASE	ONCASPAR		24231	

This drug requires a written request for prior authorization.

GUIDELINES FOR USE

1. Does the patient have a diagnosis of acute lymphoblastic leukemia (ALL)?

   If yes, continue to #2.
   If no, do not approve.
   ERWINAZE DENIAL TEXT: Approval requires a diagnosis of acute lymphoblastic leukemia (ALL) and a hypersensitivity reaction to Elspar or Oncaspar, which may also require prior authorization, or be covered under the medical benefit.
   ELSPAR and ONCASPAR DENIAL TEXT: Approval requires a diagnosis of acute lymphoblastic leukemia (ALL).

2. Is the request for Erwinaze?

   If yes, continue to #3.
   If no, **approve as follows:**
   - **ELSPAR: Approve for 3 months up to #60 vials per month.**
   - **ONCASPAR: Approve for 3 months up to #2 vials per month.**

3. Has the patient developed a hypersensitivity to *E. Coli*-derived asparaginase (for example, Elspar or Oncaspar)?

   If yes, **approve for 3 months up to #60 vials per month.**
   If no, do not approve.
   ERWINAZE DENIAL TEXT: Approval requires a diagnosis of acute lymphoblastic leukemia (ALL) and a hypersensitivity reaction to Elspar or Oncaspar, which may also require prior authorization, or be covered under the medical benefit.

CONTINUED ON NEXT PAGE

ASPARAGINASE

RATIONALE

Promote appropriate utilization and dosing of asparaginase products for their FDA approved indication as a component of a multi-agent chemotherapeutic regimen for the treatment of patients with acute lymphoblastic leukemia (ALL). Require hypersensitivity to *E. coli*-derived asparaginase prior to Erwinaze therapy as per its FDA approved indication. Both Elspar and Oncaspar are derived from *E. coli*. The dosing approved in this prior authorization guideline allows for appropriate dosing of patients with a body surface area (BSA) of 2.0 m^2 or less. Clinical review is required for patients with a BSA above 2.0 m^2.

Elspar is administered either as a single dose of up to 25,000IU/m^2 once weekly for 2 weeks, 600IU/m^2 every other day for 3 to 4 weeks, or daily doses of 1,000 to 20,000IU/m^2 for 10 to 12 days.

Erwinaze is dosed as follows:

- To substitute for a dose of pegaspargase the recommended dose is 25,000 IU/m^2 three times a week (Monday, Wednesday, Friday) for six doses for each planned dose.
- To substitute for a dose of native *E. coli* asparaginase the recommended dose is 25,000 IU/m^2 for each schedule dose of native *E. coli* asparaginase within a treatment.

Oncaspar is dosed 2,500IU/m^2 no more frequently than every 14 days.

FDA APPROVED INDICATIONS

Elspar is indicated in therapy of patients with acute lymphocytic leukemia. This agent is useful primarily in combination with other chemotherapeutic agents in the induction of remissions of the disease in pediatric patients. Elspar should not be used as the sole induction agent unless combination therapy is deemed inappropriate. Elspar is not recommended for maintenance therapy.

Erwinaze is indicated as a component of a multi-agent chemotherapeutic regimen for the treatment of patients with acute lymphoblastic leukemia (ALL) who have developed hypersensitivity to E. coli-derived asparaginase.

Oncaspar is indicated as a component of a multi-agent chemotherapeutic regimen for the treatment of patients with ALL and hypersensitivity to native forms of L-asparaginase.

REFERENCES

- EUSA Pharma (USA), Inc. Erwinaze package insert. Langhorne, PA. November 2011.
- Lundbeck Inc. Elspar package insert. Deerfield, IL. April 2010.
- Sigma-Tau Pharmaceuticals, Inc. Oncaspar package insert. Gaithersburg, MD. May 2011.

Library	Commercial	NSA
Yes	No	Yes

Part D Effective: N/A Created: 12/11
Commercial Effective: 01/01/14 Client Approval: 11/13 P&T Approval: 11/13

ATEZOLIZUMAB (NSA)

Generic	Brand	HICL	GCN	Exception/Other
ATEZOLIZUMAB	TECENTRIQ	43408		ROUTE = INTRAVEN.

GUIDELINES FOR USE

1. Does the patient have a diagnosis of locally advanced or metastatic urothelial carcinoma and meets **ONE** of the following criteria?
   - The patient is not eligible to receive cisplatin-containing chemotherapy **AND** has a tumor that expresses PD-L1 (PD-L1 sustained tumor-infiltrating immune cells [IC] covering 5% or more of the tumor area), as determined by an FDA approved test
   - The patient is not eligible to receive any platinum containing chemotherapy regardless of PD-L1 status
   - The patient has disease progression on or after treatment with a platinum-containing chemotherapy (e.g., cisplatin, carboplatin, oxaliplatin)
   - The patient has disease progression within 12 months of neoadjuvant or adjuvant treatment with a platinum-containing chemotherapy (e.g. cisplatin, carboplatin, oxaliplatin)

   If yes, **approve for 12 months by HICL with a quantity limit of #20mL (1 vial) per 21 days.**
   If no, continue to #2.

2. Does the patient have a diagnosis of metastatic non-small cell lung cancer (NSCLC)?

   If yes, continue to #3.
   If no, do not approve**.**
   DENIAL TEXT: See the denial text at the end of the guideline.

3. Does the patient have an ALK mutation **AND** meet the following criteria?
   - The patient had disease progression on or after treatment with **ALL** of the following:
     - Platinum-containing chemotherapy (e.g., cisplatin, carboplatin, oxaliplatin)
     - ALK-directed therapy [e.g., Xalkori (crizotinib), Zykadia (ceritinib)]

   If yes, **approve for 12 months by HICL with a quantity limit of #20mL (1 vial) per 21 days.**
   If no, continue to #4.

4. Does the patient have an EGFR mutation **AND** meet the following criteria?
   - The patient had disease progression on or after treatment with **ALL** of the following:
     - Platinum-containing chemotherapy (e.g., cisplatin, carboplatin, oxaliplatin)
     - EGFR-directed therapy [e.g., Tarceva (erlotinib), Iressa (gefitinib), Gilotrif (afatinib)]

   If yes, **approve for 12 months by HICL with a quantity limit of #20mL (1 vial) per 21 days.**
   If no, continue to #5.

CONTINUED ON NEXT PAGE

ATEZOLIZUMAB (NSA)

GUIDELINES FOR USE (CONTINUED)

5. Does the patient have disease progression on or after treatment with a platinum-containing chemotherapy (e.g., cisplatin, carboplatin, oxaliplatin)?

   If yes, **approve for 12 months by HICL with a quantity limit of #20mL (1 vial) per 21 days.**
   If no, continue to #6.

6. Does the patient have a diagnosis of a metastatic non-squamous non-small cell lung cancer (NSCLC) and meet the following criteria?
   - The requested medication will be given in combination with bevacizumab, paclitaxel, and carboplatin as a first-line treatment
   - The patient does not have EGFR or ALK genomic tumor aberrations

   If yes, **approve for 12 months by HICL with a quantity limit of #20mL (1 vial) per 21 days.**
   If no, do not approve.
   DENIAL TEXT: The guideline named **ATEZOLIZUMAB (Tecentriq)** requires a diagnosis of locally advanced or metastatic urothelial carcinoma or metastatic non-small cell lung cancer (NSCLC). The following criteria must be met:
   For patients with locally advanced or metastatic urothelial carcinoma, approval requires ONE of the following:
   - The patient is not eligible to receive cisplatin-containing chemotherapy **AND** has a tumor that expresses PD-L1 (PD-L1 sustained tumor-infiltrating immune cells [IC] covering 5% or more of the tumor area), as determined by an FDA approved test
   - The patient is not eligible to receive any platinum containing chemotherapy regardless of PD-L1 status
   - The patient has disease progression on or after treatment with a platinum-containing chemotherapy (e.g., cisplatin, carboplatin, oxaliplatin)
   - The patient has disease progression within 12 months of neoadjuvant or adjuvant treatment with a platinum-containing chemotherapy (e.g. cisplatin, carboplatin, oxaliplatin)

   For patients with metastatic non-small cell lung cancer (NSCLC), approval requires ONE of the following:
   - The requested medication will be given as first line treatment for metastatic non-squamous NSCLS and meet ALL of the following criteria:
     - Prescribed in combination with bevacizumab, paclitaxel, and carboplatin
     - The patient does not have EGFR or ALK genomic tumor aberrations

   (Denial text continued on next page)

CONTINUED ON NEXT PAGE

ATEZOLIZUMAB (NSA)

GUIDELINES FOR USE (CONTINUED)

- The patient has disease progression on or after treatment with ONE of the following:
  - *For patients who have an ALK mutation:* platinum-containing chemotherapy (e.g., cisplatin, carboplatin, oxaliplatin) **AND** ALK-directed therapy [e.g., Xalkori (crizotinib), Zykadia (ceritinib)]
  - *For patients who have an EGFR mutation:* platinum-containing chemotherapy (e.g., cisplatin, carboplatin, oxaliplatin) **AND** EGFR-directed therapy [e.g., Tarceva (erlotinib), Iressa (gefitinib), Gilotrif (afatinib)]
  - *For patients who do not have an ALK or EGFR mutation:* platinum-containing chemotherapy (e.g., cisplatin, carboplatin, oxaliplatin)

RATIONALE

For further information, please refer to the Prescribing Information and/or Drug Monograph for Tecentriq.

REFERENCES

- Tecentriq [Prescribing Information]. Genentech Inc.: South San Francisco, CA; December 2018.

Library	Commercial	NSA
Yes	No	Yes

Part D Effective: N/A
Commercial Effective: 01/01/19
Created: 05/16
Client Approval: 12/18
P&T Approval: 01/19

AVELUMAB (NSA)

Generic	Brand	HICL	GCN	Exception/Other
AVELUMAB	BAVENCIO	44170		

GUIDELINES FOR USE

1. Does the patient have a diagnosis of metastatic Merkel cell carcinoma (MCC) and meet the following criterion?
   - The patient is 12 years or older

   If yes, **approve for 12 months by HICL.**
   If no, continue to #2.

2. Does the patient have a diagnosis of locally advanced or metastatic urothelial carcinoma (UC) and meet **ONE** of the following criteria?
   - The patient has disease progression during or following platinum-containing chemotherapy (e.g., cisplatin, carboplatin, oxaliplatin)
   - The patient has disease progression within 12 months of neoadjuvant or adjuvant treatment with platinum-containing chemotherapy (e.g., cisplatin, carboplatin, oxaliplatin)

   If yes, **approve for 12 months by HICL.**
   If no, do not approve.
   DENIAL TEXT: The guideline named **AVELUMAB (Bavencio)** requires a diagnosis of metastatic Merkel cell carcinoma (MCC), locally advanced urothelial carcinoma, or metastatic urothelial carcinoma. The following criteria must be met:
   For metastatic Merkel Cell Carcinoma, approval requires the following
   - The patient is 12 years or older

   For locally advanced or metastatic urothelial carcinoma, approval requires one of the following:
   - The patient has disease progression during or following platinum-containing chemotherapy (e.g., cisplatin, carboplatin, oxaliplatin)
   - The patient has disease progression within 12 months of neoadjuvant or adjuvant treatment with platinum-containing chemotherapy (e.g., cisplatin, carboplatin, oxaliplatin)

RATIONALE
Promote appropriate utilization of Bavencio (avelumab) based on the FDA approved indication.

CONTINUED ON NEXT PAGE

AVELUMAB (NSA)

FDA APPROVED INDICATIONS

Bavencio is a programmed death ligand-1 (PD-L1) blocking antibody indicated for the treatment of:

- Adult and pediatric patients 12 years and older with metastatic Merkel cell carcinoma (MCC)
- Patients with locally advanced or metastatic urothelial carcinoma (UC) who:
  - Have disease progression during or following platinum-containing chemotherapy
  - Have disease progression within 12 months of neoadjuvant or adjuvant treatment with platinum-containing chemotherapy

These indications are approved under accelerated approval. Continued approval for these indications may be contingent upon verification and description of clinical benefit in confirmatory trials.

DOSAGE AND ADMINISTRATION

Administer 10 mg/kg as an intravenous infusion over 60 minutes every 2 weeks.

Premedicate with acetaminophen and an antihistamine for the first 4 infusions and subsequently as needed.

DOSAGE FORMS

Injection: 200 mg/10 mL (20 mg/mL) solution in single-dose vial.

REFERENCES

- Bavencio [Prescribing Information]. Darmstadt, Germany. Merck KGaA; May 2017.

Library	Commercial	NSA
Yes	No	Yes

Part D Effective: N/A
Commercial Effective: 10/01/17
Created: 04/17
Client Approval: 08/17
P&T Approval: 07/17

AXICABTAGENE CILOLEUCEL (NSA)

Generic	Brand	HICL	GCN	Exception/Other
AXICABTAGENE CILOLEUCEL	YESCARTA	44577		

GUIDELINES FOR USE

1. Does the patient have **ONE** of the following diagnoses?
   - Primary Central Nervous System Lymphoma (PCNSL)
   - Mantle Cell Lymphoma (MCL)
   - Burkitt's Lymphoma

   If yes, do not approve.
   DENIAL TEXT: See the denial text at the end of the guideline.
   If no, continue to #2.

2. Does the patient have **ONE** of the following diagnoses?
   - Diffuse Large B-Cell Lymphoma (DLBCL) not otherwise specified
   - Primary Mediastinal Large B-Cell Lymphoma (PMBCL)
   - High grade B-Cell Lymphoma (e.g.,double-hit or triple-hit lymphoma)
   - Diffuse Large B-Cell Lymphoma (DLBCL) arising from Follicular lymphoma (FL) [i.e., transformed follicular Lymphoma (TFL)]

   If yes, continue to #3.
   If no, do not approve.
   DENIAL TEXT: See the denial text at the end of the guideline.

3. Does the patient meet **ALL** of the following criteria?
   - The patient is 18 years of age or older
   - Treatment is prescribed by a Yescarta-certified hematologist or oncologist
   - Yescarta will be administered at a treatment center that is certified to administer Yescarta
   - The patient has not received a previous trial of Yescarta

   If yes, continue to #4.
   If no, do not approve.
   DENIAL TEXT: See the denial text at the end of the guideline.

CONTINUED ON NEXT PAGE

AXICABTAGENE CILOLEUCEL (NSA)

GUIDELINES FOR USE (CONTINUED)

4. Does the physician attest that the patient meets **ONE** of the following criteria?
   - The patient has had disease progression or relapsed after stem cell transplantation (SCT)
   - The patient has had disease progression or relapsed after two or more lines of systemic therapy

   If yes, **approve 1 fill by HICL.**
   If no, do not approve.
   DENIAL TEXT: See the denial text at the end of the guideline.

   DENIAL TEXT: The guideline named **AXICABTAGENE CILOLEUCEL (Yescarta)** requires that the patient has a diagnosis of diffuse large B-cell lymphoma (DLBCL) not otherwise specified, primary mediastinal large B-cell lymphoma (PMBCL), high grade B-cell lymphoma (e.g.,double-hit or triple-hit lymphoma), or diffuse large B-cell lymphoma (DLBCL) arising from follicular lymphoma (FL) [i.e., transformed follicular lymphoma (TFL)]. **AXICABTAGENE CILOLEUCEL (Yescarta)** is not FDA-approved for the treatment of Primary Central Nervous System Lymphoma (PCNSL), Mantle Cell Lymphoma (MCL), or Burkitt's lymphoma. In addition, the following criteria must be met:
   - The patient is 18 years of age or older
   - Treatment is prescribed by a Yescarta-certified hematologist or oncologist
   - Yescarta will be administered at a treatment center that is certified to administer Yescarta
   - The patient has not had a previous trial of Yescarta
   - Physician attestation of **ONE** of the following criteria:
     - The patient has had disease progression or relapsed after stem cell transplantation (SCT)
     - The patient has had disease progression or relapsed after two or more lines of systemic therapy

---

RATIONALE
Promote appropriate utilization of **YESCARTA** based on FDA approved indication, dosing and clinical trial design.

NOTE: Yescarta is available only through a restricted program under a Risk Evaluation and Mitigation Strategy (REMS) because of the risk of cytokine release syndrome (CRS) and neurological events. Healthcare facilities that dispense and administer Yescarta must be enrolled and comply with the REMS requirements. Certified healthcare facilities must have on-site, immediate access to tocilizumab, and ensure that a minimum of two doses of tocilizumab are available for each patient for infusion within 2 hours after Yescarta infusion, if needed for treatment of CRS.

CONTINUED ON NEXT PAGE

AXICABTAGENE CILOLEUCEL (NSA)

RATIONALE (CONTINUED)

Yescarta is the second gene therapy to be approved by the FDA and was granted Priority Review, Breakthrough Therapy, and Orphan Drug designations. Yescarta is an engineered chimeric antigen receptor (CAR) product that targets CD19, a protein expressed on the surface of B cell leukemia and lymphoma cells. The CAR product is utilized in the process of autologous cell therapy in which a patient's own white blood cells are collected, T cells are isolated, the CAR gene is inserted into the T cells, the T cell colony is expanded, and then the engineered T cells are infused back into the patient. This process results in an expanded number of tumor-specific T cells that circulate throughout the body to target and kill cancer cells.

Diffuse large B-cell lymphoma (DLBCL) is the most common aggressive non-Hodgkin lymphoma (NHL), accounting for three out of every five cases. In the U.S. each year, there are approximately 7,500 patients with refractory DLBCL who are eligible for CAR T therapy. Historically, when treated with the current standard of care, patients with refractory large B-cell lymphoma had a median overall survival of approximately six months, with only 7% attaining a complete response. Currently, patients with large B-cell lymphoma in second or later lines of therapy have poor outcomes and greater unmet need, since nearly half of them either do not respond or relapse shortly after transplant.

FDA APPROVED INDICATIONS

Yescarta is a CD19-directed genetically modified autologous T cell immunotherapy indicated for the treatment of adult patients with relapsed or refractory large B-cell lymphoma after two or more lines of systemic therapy, including diffuse large B-cell lymphoma (DLBCL) not otherwise specified, primary mediastinal large B-cell lymphoma, high grade B-cell lymphoma, and DLBCL arising from follicular lymphoma.

Limitation of Use: Yescarta is not indicated for the treatment of patients with primary central nervous system lymphoma.

DOSAGE AND ADMINISTRATION

- Yescarta is supplied as a frozen cell suspension of genetically modified autologous T cells in one infusion bag labeled for the specific recipient. Yescarta is shipped directly to the cell lab associated with the infusion center and is administered in a certified health care facility.
- Yescarta is for autologous use and is administered by intravenous infusion only.
- Prior to infusion:
  - Verify the patient's identity
  - Premedicate with acetaminophen and an H1-antihistamine
  - Confirm availability of tocilizumab
- Yescarta dosing is based on the number of chimeric antigen receptor (CAR) positive viable T cells.
  - The target Yescarta dose is 2×10^6 CAR-positive viable T cells per kg body weight, with a maximum of 2×10^8 CAR-positive viable T cells.

CONTINUED ON NEXT PAGE

AXICABTAGENE CILOLEUCEL (NSA)

AVAILABLE STRENGTHS

Each single infusion bag of Yescarta contains a suspension of chimeric antigen receptor (CAR)-positive T cells in approximately 68 mL. The target dose is 2×10^6 CAR-positive viable T cells per kg body weight, with a maximum of 2×10^8 CAR-positive viable T cells.

REFERENCES

- Yescarta [Prescribing Information]. Santa Monica, CA: Kite Pharma, Inc. October 2017.
- ClinicalTrials.gov [Internet]. Bethesda (MD): National Library of Medicine (US). Identifier NCT 02348216. A Phase 1-2 Multi-Center Study Evaluating KTE-C19 in Subjects With Refractory Aggressive Non-Hodgkin Lymphoma (ZUMA-1). Available at: https://clinicaltrials.gov/ct2/show/NCT02348216. Accessed October 18, 2017.
- Kite Pharma [Press Release]. Kite's Yescarta (Axicabtagene Ciloleucel) Becomes First CAR T Therapy Approved by the FDA for the Treatment of Adult Patients With Relapsed or Refractory Large B-Cell Lymphoma After Two or More Lines of Systemic Therapy. Available at: http://investors.gilead.com/phoenix.zhtml?c=69964&p=irol-newsArticle_Print&ID=2309672. Accessed October 18, 2017.

Library	Commercial	NSA
Yes	No	Yes

Part D Effective: N/A
Commercial Effective: 01/01/18
Created: 10/17
Client Approval: 12/17
P&T Approval: 10/17

BELINOSTAT (NSA)

Generic	Brand	HICL	GCN	Exception/Other
BELINOSTAT	BELEODAQ	41264		

This drug requires a written request for prior authorization.

GUIDELINES FOR USE

1. Is the requested medication being used for the treatment of a patient with relapsed or refractory peripheral T-cell lymphoma (PTCL)?

   If yes, **approve for 12 months by HICL.**
   If no, do not approve.
   DENIAL TEXT: The guideline for **BELINOSTAT (Belinostat)** requires a diagnosis of relapsed or refractory peripheral T-cell lymphoma (PTCL).

RATIONALE

Promote appropriate utilization of Beleodaq based on FDA approved indication.

There is no consensus regarding the preferred induction chemotherapy for peripheral T-cell lymphoma (PTCL), and patients should be encouraged to participate in clinical trials whenever possible. Most of the treatment regimens that have been studied combine an anthracycline with an alkylating agent. Examples of regimens most commonly considered for the treatment of patients with PTCL not enrolled in clinical trials include:

- CHOP (cyclophosphamide, doxorubicin, vincristine, prednisone) with or without etoposide
- EPOCH (etoposide, prednisone, vincristine, cyclophosphamide, doxorubicin)

DOSAGE

The recommended dosage of Beleodaq is 1,000 mg/m^2 administered over 30 minutes by intravenous infusion once daily on Days 1-5 of a 21-day cycle. Cycles can be repeated every 21 days until disease progression or unacceptable toxicity.

FDA APPROVED INDICATION

Beleodaq is a histone deacetylase inhibitor indicated for the treatment of patients with relapsed or refractory peripheral T-cell lymphoma (PTCL).

This indication is approved under accelerated approval based on tumor response rate and duration of response. An improvement in survival or disease-related symptoms has not been established. Continued approval for this indication may be contingent upon verification and description of clinical benefit in the confirmatory trial.

CONTINUED ON NEXT PAGE

BELINOSTAT

REFERENCES

- Beleodaq [Prescribing Information]. Irvine, CA: Spectrum Pharmaceuticals; July 2014.

Library	Commercial	NSA
Yes	No	Yes

Part D Effective: N/A
Commercial Effective: 10/01/16
Created: 07/14
Client Approval: 09/16
P&T Approval: 08/16

BENRALIZUMAB (NSA)

Generic	Brand	HICL	GCN	Exception/Other
BENRALIZUMAB	FASENRA	44635		

GUIDELINES FOR USE

INITIAL CRITERIA (NOTE: FOR RENEWAL CRITERIA SEE BELOW)

1. Does the patient have a diagnosis of severe eosinophilic asthma and meet **ALL** of the following criteria?
   - The patient is 12 years of age or older
   - The patient has a documented blood eosinophil level of at least 300 cells/mcL or more within the past 6 months
   - The patient is currently adherent to a maximally tolerated dose of an inhaled corticosteroid **AND** at least one other maintenance medication (e.g., a long-acting inhaled beta2-agonist, long-acting muscarinic antagonist, a leukotriene receptor antagonist, theophylline, or oral corticosteroid)
   - The patient has experienced at least 2 or more asthma exacerbations within the past 12 months (exacerbation is defined as an asthma-related event requiring hospitalization, emergency room visit, or systemic corticosteroid burst lasting at least 3 or more days)
   - The patient has **ONE** of the following:
     - o Asthma Control Test (ACT) score of less than 20
     - o Asthma Control Questionnaire (ACQ) score of at least 1.5 or more
     - o Asthma Therapy Assessment Questionnaire (ATAQ) score of at least 1 or more
   - Fasenra will be used as add-on maintenance treatment
   - The patient is NOT being concurrently treated with Xolair, Dupixent, or another anti-IL5 asthma biologic (e.g. Nucala, Cinqair)
   - Fasenra is prescribed by or given in consultation with a physician specializing in pulmonary medicine or allergy medicine

   If yes, **please enter TWO approvals by HICL as follows:**
   - **FIRST APPROVAL: approve for 12 weeks (total fill count of 3) with a quantity limit of 1mL (one 30mg/mL pre-filled syringe) per 28 days.**
   - **SECOND APPROVAL: approve for 40 weeks (total fill count of 5) with a quantity limit of 1mL (one 30mg/mL pre-filled syringe) per 56 days.**

   APPROVAL TEXT: Renewal requires the patient to have experienced a reduction in asthma exacerbations (defined as an asthma-related event requiring hospitalization, emergency room visit, or systemic corticosteroid burst lasting at least 3 days) from baseline AND an improvement in the Asthma Control Test (ACT), Asthma Control Questionnaire (ACQ), or Asthma Therapy Assessment Questionnaire (ATAQ) score from baseline. In addition, if the patient was on maintenance therapy with oral corticosteroids prior to the initiation of Fasenra, then the patient must demonstrate a reduction in the total daily dose of oral corticosteroids for Fasenra renewal.

   If no, do not approve.
   DENIAL TEXT: See the initial denial text at the end of the guideline.

CONTINUED ON NEXT PAGE

BENRALIZUMAB (NSA)

INITIAL CRITERIA (CONTINUED)

INITIAL DENIAL TEXT: The guideline named **BENRALIZUMAB (Fasenra)** requires a diagnosis of severe eosinophilic asthma. In addition, the following criteria must be met:

- The patient is 12 years of age or older
- The patient has a documented blood eosinophil level of at least 300 cells/mcL or more within the past 6 months
- The patient is currently adherent to a maximally tolerated dose of an inhaled corticosteroid **AND** at least one other maintenance medication (e.g., a long-acting inhaled beta2-agonist, long-acting muscarinic antagonist, a leukotriene receptor antagonist, theophylline, or oral corticosteroid)
- The patient has experienced at least 2 or more asthma exacerbations within the past 12 months (exacerbation is defined as an asthma-related event requiring hospitalization, emergency room visit, or systemic corticosteroid burst lasting at least 3 or more days)
- The patient has **ONE** of the following:
  - Asthma Control Test (ACT) score of less than 20
  - Asthma Control Questionnaire (ACQ) score of at least 1.5 or more
  - Asthma Therapy Assessment Questionnaire (ATAQ) score of at least 1 or more
- Fasenra will be used as add-on maintenance treatment
- The patient is NOT being concurrently treated with Xolair, Dupixent, or another anti-IL5 asthma biologic (e.g. Nucala, Cinqair)
- Fasenra is prescribed by or given in consultation with a physician specializing in pulmonary medicine or allergy medicine

RENEWAL CRITERIA

1. Does the patient have a diagnosis of severe asthma **AND** meet the following criteria?
   - The patient has experienced a reduction in asthma exacerbations (defined as an asthma-related event requiring hospitalization, emergency room visit, or systemic corticosteroid burst lasting at least 3 days) from baseline
   - The patient has experienced an improvement in the Asthma Control Test (ACT), Asthma Control Questionnaire (ACQ), **OR** Asthma Therapy Assessment Questionnaire (ATAQ) score from baseline

   If yes, continue to #2.
   If no, do not approve.
   DENIAL TEXT: See the renewal denial text at the end of the guideline.

2. Was the patient treated with a maintenance therapy regimen of oral corticosteroids prior to initiation of Fasenra?

   If yes, continue to #3.
   If no, **approve for 12 months by HICL with a quantity limit of 1mL (one 30mg/mL pre-filled syringe) per 56 days.**

CONTINUED ON NEXT PAGE

BENRALIZUMAB (NSA)

RENEWAL CRITERIA (CONTINUED)

3. Has the patient decreased their total daily dose of oral corticosteroids from baseline?

   If yes, **approve for 12 months by HICL with a quantity limit of 1mL (one 30mg/mL pre-filled syringe) per 56 days.**
   If no, do not approve.
   RENEWAL DENIAL TEXT: The guideline named **BENRALIZUMAB (Fasenra)** requires a diagnosis of severe asthma for renewal. In addition, the following criteria must also be met:
   - The patient has experienced a reduction in asthma exacerbations (defined as an asthma-related event requiring hospitalization, emergency room visit, or systemic corticosteroid burst lasting at least 3 days) from baseline
   - The patient has experienced an improvement in the Asthma Control Test (ACT), Asthma Control Questionnaire (ACQ), or Asthma Therapy Assessment Questionnaire (ATAQ) score from baseline
   - The patient has decreased their total daily oral corticosteroid dose from baseline if the patient was on a maintenance therapy with oral corticosteroids prior to initiation of Fasenra

RATIONALE
For further information, please refer to the Prescribing Information and/or Drug Monograph for Fasenra

REFERENCES
- Fasenra [Prescribing Information]. Wilmington, DE. AstraZeneca Pharmaceutical LP. November 2017.

Library	Commercial	NSA
Yes	No	Yes

Part D Effective: N/A
Commercial Effective: 01/01/19
Created: 02/18
Client Approval: 11/18
P&T Approval: 10/18

BEVACIZUMAB (NSA)

Generic	Brand	HICL	GCN	Exception/Other
BEVACIZUMAB	AVASTIN	25963		

This drug requires a written request for prior authorization.

GUIDELINES FOR USE

1. Does the patient have a diagnosis of metastatic colorectal cancer (mCRC) **AND** meet the following criterion?
   - The requested medication is being used in combination with intravenous 5-fluorouracil based chemotherapy for first or second-line treatment

   If yes, **approve for 12 months by HICL.**
   If no, continue to #2.

2. Does the patient have a diagnosis of metastatic colorectal cancer (mCRC) and meet **ALL** of the following criteria?
   - The requested medication is being used in combination with fluoropyrimidine- irinotecan- (i.e., FOLFIRI) or fluoropyrimidine-oxaliplatin- (i.e., FOLFOX, CapeOx) based chemotherapy as a second-line treatment
   - The patient has progressed on a first-line Avastin-containing regimen

   If yes, **approve for 12 months by HICL.**
   If no, continue to #3.

3. Does the patient have a diagnosis of unresectable, locally advanced, recurrent or metastatic non-squamous non-small cell lung cancer (NSCLC) **AND** meet the following criterion?
   - The requested medication is being used in combination with carboplatin and paclitaxel for first-line treatment

   If yes, **approve for 12 months by HICL.**
   If no, continue to #4.

4. Does the patient have a diagnosis of recurrent glioblastoma (GBM) **AND** is 18 years or older?

   If yes, **approve for 12 months by HICL.**
   If no, continue to #5.

CONTINUED ON NEXT PAGE

BEVACIZUMAB (NSA)

GUIDELINES FOR USE (CONTINUED)

5. Does the patient have a diagnosis of metastatic renal cell carcinoma (RCC) **AND** meet the following criterion?
   - The requested medication is being used in combination with interferon alfa

   If yes, **approve for 12 months by HICL.**
   If no, continue to #6.

6. Is Avastin being used to treat neovascular (wet) macular degeneration **AND** meet the following criterion?
   - The requested medication is prescribed by an ophthalmologist and/or retina specialist

   If yes, **approve for 12 months by HICL, up to one vial per affected eye per month.**
   If no, continue to #7.

7. Does the patient have a diagnosis of persistent, recurrent, or metastatic cervical cancer **AND** meet the following criterion?
   - The requested medication is being used in combination with paclitaxel and cisplatin OR paclitaxel and topotecan

   If yes, **approve for 12 months by HICL.**
   If no, continue to #8.

8. Does the patient have a diagnosis of platinum-resistant recurrent epithelial ovarian, fallopian tube or primary peritoneal cancer and meet **ALL** of the following criteria?
   - The requested medication is being used in combination with paclitaxel, pegylated liposomal doxorubicin, or topotecan
   - The patient has received no more than 2 prior chemotherapy regimens

   If yes, **approve for 12 months by HICL.**
   If no, continue to #9.

CONTINUED ON NEXT PAGE

BEVACIZUMAB (NSA)

GUIDELINES FOR USE (CONTINUED)

9. Does the patient have a diagnosis of platinum-sensitive recurrent epithelial ovarian, fallopian tube or primary peritoneal cancer and meet **ONE** of the following criteria?
   - The requested medication is being used in combination with carboplatin and paclitaxel, **OR**
   - The requested medication is being used in combination with carboplatin and gemcitabine, **OR**
   - The requested medication is being used as a single agent after prior use in combination with one of the carboplatin-containing chemotherapy regimens listed above

   If yes, **approve for 12 months by HICL.**
   If no continue to #10.

10. Does the patient have a diagnosis of stage III or IV epithelial ovarian, fallopian tube, or primary peritoneal cancer and meet **ALL** of the following criteria?
    - The requested medication is being used following initial surgical resection
    - The requested medication is being used in combination with carboplatin and paclitaxel, **OR** as a single agent after prior use in combination with carboplatin and paclitaxel

    If yes, **approve for 12 months by HICL.**
    If no, do not approve.
    DENIAL TEXT: The guideline named **BEVACIZUMAB (Avastin)** requires a diagnosis of **ONE** of the following:
    - **Metastatic colorectal cancer (mCRC)** and meet **ONE** of the following:
      - The requested medication is being used in combination with intravenous 5-fluorouracil based chemotherapy for first or second-line treatment
      - The requested medication is being used in combination with fluoropyrimidine- irinotecan- (i.e., FOLFIRI) or fluoropyrimidine-oxaliplatin- (i.e., FOLFOX, CAPeOX) based chemotherapy as a second-line treatment AND the patient has progressed on a first-line Avastin-containing regimen
    - **Unresectable, locally advanced, recurrent or metastatic non-squamous non-small cell lung cancer (NSCLC)** in combination with carboplatin and paclitaxel for first-line treatment
    - **Recurrent glioblastoma (GBM)** AND patient is 18 years or older
    - **Metastatic renal cell carcinoma (RCC)** in combination with interferon alfa
    - **Neovascular (wet) macular degeneration** and treatment is prescribed by an ophthalmologist and/or retina specialist
    - **Persistent, recurrent, or metastatic cervical cancer**, in combination with paclitaxel and cisplatin OR paclitaxel and topotecan

    (Denial text continued on next page)

CONTINUED ON NEXT PAGE

BEVACIZUMAB (NSA)

GUIDELINES FOR USE (CONTINUED)

- **Platinum-resistant recurrent epithelial ovarian, fallopian tube or primary peritoneal cancer**, in combination with paclitaxel, pegylated liposomal doxorubicin, or topotecan AND patient has received no more than 2 prior chemotherapy regimens
- **Platinum-sensitive recurrent epithelial ovarian, fallopian tube or primary peritoneal cancer,** in combination with carboplatin and paclitaxel, OR with carboplatin and gemcitabine, OR as a single agent after prior use in combination with one of the carboplatin-containing chemotherapy regimens listed above
- **Stage III or IV epithelial ovarian, fallopian tube, or primary peritoneal cancer following initial surgical resection,** in combination with carboplatin and paclitaxel, **OR** as a single agent after prior use in combination with carboplatin and paclitaxel

---

RATIONALE

Ensure appropriate utilization of bevacizumab based on its FDA approved indications.

Avastin is a recombinant humanized monoclonal IgG1 antibody administered intravenously that inhibits tumor angiogenesis through inhibition of VEGF similar to Zaltrap. Due to its structural similarity to Lucentis, ophthalmologists use Avastin as an intravitreal injection for the treatment of diabetic macular edema, diabetic retinopathy, and macular degeneration. Randomized, controlled trials such as the Comparison of Age-Related Macular Degeneration Treatment Trial (CATT) and Inhibition of VEGF in Age-related choroidal Neovascularization (IVAN) trial have demonstrated that Lucentis and Avastin are likely to provide similar efficacy when used for treatment of neovascular (wet) age-related macular degeneration.

FDA APPROVED INDICATIONS

Avastin is a vascular endothelial growth factor-specific angiogenesis inhibitor indicated for the treatment of:

- Metastatic colorectal cancer, with intravenous 5-fluorouracil–based chemotherapy for first- or second-line treatment.
    - Limitation of Use: Avastin is not indicated for adjuvant treatment of colon cancer.
- Metastatic colorectal cancer, with fluoropyrimidine- irinotecan- or fluoropyrimidine-oxaliplatin-based chemotherapy for second-line treatment in patients who have progressed on a first-line Avastin-containing regimen.
    - Limitation of Use: Avastin is not indicated for adjuvant treatment of colon cancer
- Non-squamous non-small cell lung cancer, in combination with carboplatin and paclitaxel for first line treatment of unresectable, locally advanced recurrent or metastatic disease.
- Recurrent glioblastoma in adult patients.

CONTINUED ON NEXT PAGE

BEVACIZUMAB (NSA)

FDA APPROVED INDICATIONS (CONTINUED)

- Metastatic renal cell carcinoma in combination with interferon alfa.
- Cervical cancer, in combination with paclitaxel and cisplatin or paclitaxel and topotecan in persistent, recurrent, or metastatic disease.
- Epithelial ovarian, fallopian tube or primary peritoneal cancer:
  - In combination with carboplatin and paclitaxel, followed by Avastin as a single agent, for stage III or IV disease following initial surgical resection
  - In combination with paclitaxel, pegylated liposomal doxorubicin, or topotecan for platinum-resistant recurrent disease who received no more than 2 prior chemotherapy regimens
  - In combination with carboplatin and paclitaxel or carboplatin and gemcitabine, followed by Avastin as a single agent, for platinum sensitive recurrent disease.

DOSAGE AND ADMINISTRATION
Do not administer Avastin until at least 28 days following surgery and the wound is fully healed.

Metastatic Colorectal Cancer (mCRC): The recommended dose when Avastin is administered in combination with intravenous 5-fluorouracil-based chemotherapy is:
- 5 mg/kg every 2 weeks intravenously in combination with bolus-IFL
- 10 mg/kg every 2 weeks intravenously in combination with FOLFOX4
- 5 mg/kg intravenously every 2 weeks or 7.5 mg/kg intravenously every 3 weeks in combination with fluoropyrimidine-irinotecan- or fluoropyrimidine-oxaliplatin-based chemotherapy in patients who have progressed on a first-line Avastin-containing regimen

Non-Small Cell Lung Cancer (NSCLC): The recommended dose is 15 mg/kg intravenously every 3 weeks in combination with carboplatin and paclitaxel.

Recurrent Glioblastoma (GBM): The recommended dose is 10 mg/kg intravenously every 2 weeks.

Metastatic Renal Cell Carcinoma (mRCC): The recommended dose is 10 mg/kg intravenously every 2 weeks in combination with interferon alfa.

Persistent, Recurrent, or Metastatic Cervical Cancer: The recommended dose of Avastin is 15 mg/kg intravenously every 3 weeks in combination with paclitaxel and cisplatin or in combination with paclitaxel and topotecan.

CONTINUED ON NEXT PAGE

BEVACIZUMAB (NSA)

FDA APPROVED INDICATIONS (CONTINUED)

DOSAGE AND ADMINISTRATION
Epithelial Ovarian, Fallopian Tube or Primary Peritoneal Cancer:

- ***Treatment of Stage III or IV Disease Following Initial Surgical Resection:***
  - The recommended dose is 15 mg/kg intravenously every 3 weeks in combination with carboplatin and paclitaxel for up to 6 cycles, followed by Avastin 15 mg/kg every 3 weeks as a single agent, for a total of up to 22 cycles or until disease progression, whichever occurs earlier.
- ***Platinum Resistant* - Recurrent:**
  - When used in combination with paclitaxel, pegylated liposomal doxorubicin, or topotecan (every week), the recommended dose of Avastin is 10 mg/kg intravenously every 2 weeks.
  - When used in in combination with topotecan (every 3 weeks), the recommended dose of Avastin is 15 mg/kg intravenously every 3 weeks.
- ***Platinum Sensitive* - Recurrent**:
  - When used in in combination with carboplatin and paclitaxel, the recommended dose of Avastin is 15 mg/kg intravenously every 3 weeks for 6 to 8 cycles, followed by Avastin 15 mg/kg every 3 weeks as a single agent until disease progression.
  - When used in in combination with carboplatin and gemcitabine, the recommended dose of Avastin is 15 mg/kg intravenously every 3 weeks for 6 to 10 cycles, followed by Avastin 15 mg/kg every 3 weeks as a single agent until disease progression.

REFERENCES

- Avastin [Prescribing Information]. South San Francisco, CA: Genentech, Inc.; June 2018.
- Comparison of Age-related Macular Degeneration Treatments Trials (CATT) Research Group, Martin DF, Maguire MG, Fine SL, Ying GS, Jaffe GJ, Grunwald JE, Toth C, Redford M, Ferris FL. Ranibizumab and bevacizumab for treatment of neovascular age-related macular degeneration: two-year results. Ophthalmology. 2012 Jul; 119 (7):1388-98.
- IVAN Study Investigators, Chakravarthy U, Harding SP, et al. Ranibizumab versus bevacizumab to treat neovascular age-related macular degeneration: one-year findings from the IVAN randomized trial. Ophthalmology. 2012 Jul;119(7):1399-411.

Library	Commercial	NSA
Yes	No	Yes

Part D Effective: N/A
Commercial Effective: 07/09/18
Created: 02/13
Client Approval: 06/18
P&T Approval: 07/18

BLINATUMOMAB (NSA)

Generic	Brand	HICL	GCN	Exception/Other
BLINATUMOMAB	BLINCYTO	41612		

GUIDELINES FOR USE

INITIAL CRITERIA (NOTE: FOR RENEWAL CRITERIA SEE BELOW)

1. Does the patient have a diagnosis of relapsed or refractory B-cell precursor acute lymphoblastic leukemia (ALL)?

   If yes, **approve for 3 months by HICL with a quantity limit of #28 vials per 42 days with a fill count of 2.**
   APPROVAL TEXT: A prior authorization has been approved for two cycles of Blincyto. For renewal, please document the following:
   - Whether the patient has achieved complete remission (CR) or CR with partial hematological recovery of peripheral blood counts (CPh) after two cycles.
   - Whether the patient has received stem cell transplant after completion of Blincyto therapy.

   If no, continue to #2.

2. Does the patient have a diagnosis of minimal residual disease (MRD)-positive B-cell precursor acute lymphoblastic leukemia (ALL) and meet **ALL** of the following criteria?
   - The patient is in first or second complete remission
   - The patient has minimal residual disease (MRD) greater than or equal to 0.1%

   If yes, **approve for 2 months by HICL with a quantity limit of #28 vials per 42 days with a fill count of 1.**
   APPROVAL TEXT: A prior authorization has been approved for one cycle of Blincyto. For renewal, please document that the patient has achieved undetectable minimal residual disease (MRD) within one cycle of Blincyto treatment and is relapse-free (i.e., hematological or extramedullary relapse, or secondary leukemia).

   If no, do not approve.
   INITIAL DENIAL TEXT: The guideline named **BLINATUMOMAB (Blincyto)** requires a diagnosis of relapsed or refractory B-cell precursor acute lymphoblastic leukemia (ALL) or minimal residual disease (MRD)-positive B-cell precursor acute lymphoblastic leukemia (ALL). In addition, the following criteria must be met.
   For diagnosis of minimal residual disease (MRD) - positive B-cell precursor acute lymphoblastic leukemia (ALL), approval requires:
   - The patient is in first or second complete remission
   - The patient has minimal residual disease (MRD) greater than or equal to 0.1%

CONTINUED ON NEXT PAGE

BLINATUMOMAB (NSA)

GUIDELINES FOR USE (CONTINUED)

RENEWAL CRITERIA

1. Does the patient have a diagnosis of minimal residual disease (MRD)-positive B-cell precursor acute lymphoblastic leukemia (ALL) and meet **ALL** of the following criteria?
   - The patient has achieved undetectable minimal residual disease (MRD) within one cycle of Blincyto treatment
   - The patient is relapse-free (i.e., hematological or extramedullary relapse, or secondary leukemia)

   If yes, **approve for 5 months by HICL with a quantity limit of #28 vials per 42 days with a fill count of 3.**
   If no, continue to #2.

2. Does the patient have a diagnosis of relapsed or refractory B-cell precursor acute lymphoblastic leukemia (ALL) and meet **ALL** of the following criteria?
   - The patient has completed two cycles of induction treatment (cycle 1 and 2) with Blincyto
   - The patient has achieved complete remission (CR) or CR with partial hematological recovery of peripheral blood counts (CPh) after two cycles

   If yes, continue to #3.
   If no, send to clinical pharmacist for review.
   CLINICAL PHARMACIST: Please review initial criteria. If initial criteria were met, an additional cycle may be approved. Please check if initial therapy was interrupted for dose modification, and follow prescribing information regarding dose modification for toxicities due to Blincyto.

3. Has the patient obtained allogeneic hematopoietic stem-cell transplant?

   If yes, do not approve.
   DENIAL TEXT: See the renewal denial text at the end of the guideline.
   If no, continue to #4.

4. Is the requested medication being used for consolidation therapy of cycles 3 - 5?

   If yes, **approve for 5 months by HICL with a quantity limit of #28 vials per 42 days with a fill count of 3.**
   APPROVAL TEXT: An approval has been entered for 3 cycles of Blincyto to complete 3 cycles of consolidation therapy.

   If no, continue to #5.

CONTINUED ON NEXT PAGE

BLINATUMOMAB (NSA)

RENEWAL CRITERIA (CONTINUED)

5. Is the requested medication being used for continued therapy of cycles 6 - 9?

   If yes, **approve for 12 months by HICL with a quantity limit of #28 vials per 84 days with a fill count of 4.**
   APPROVAL TEXT: An approval has been entered for 4 cycles of Blincyto for continued therapy to complete 9 cycles of therapy. This medication has been FDA approved for a total of 9 cycles.

   If no, do not approve.
   DENIAL TEXT: See the renewal denial text at the end of the guideline.

RENEWAL DENIAL TEXT: The guideline named **BLINATUMOMAB (Blincyto)** requires a diagnosis of relapsed or refractory B-cell precursor acute lymphoblastic leukemia (ALL) OR minimal residual disease (MRD)-positive B-cell precursor acute lymphoblastic leukemia (ALL). In addition, the following criteria must be met.
For diagnosis of relapsed or refractory B-cell precursor acute lymphoblastic leukemia (ALL), approval requires:
- The patient has achieved complete remission (CR) or CR with partial hematological recovery of peripheral blood counts (CPh) after two cycles of induction treatment (cycle 1 and 2) with Blincyto
- The patient has not received allogeneic hematopoietic stem-cell transplant

For diagnosis of minimal residual disease (MRD)-positive B-cell precursor acute lymphoblastic leukemia (ALL), approval requires:
- The patient have achieved undetectable minimal residual disease (MRD) within one cycle of Blincyto treatment
- The patient is relapse-free (i.e., hematological or extramedullary relapse, or secondary leukemia)

CONTINUED ON NEXT PAGE

BLINATUMOMAB (NSA)

RATIONALE
To promote appropriate utilization of Blincyto based on FDA approved indication and NCCN guidelines.

FDA APPROVED INDICATION
Blincyto is a bispecific CD19-directed CD3 T-cell engager indicated for the treatment of adults and children with

- B-cell precursor acute lymphoblastic leukemia (ALL) in first or second complete remission with minimal residual disease (MRD) greater than or equal to 0.1%.
  - This indication is approved under accelerated approval based on MRD response rate and hematological relapse-free survival. Continued approval for this indication may be contingent upon verification and description of clinical benefit in the confirmatory trials
- Relapsed or refractory B-cell precursor acute lymphoblastic leukemia (ALL).

DOSAGE & ADMINISTRATION
MRD-Positive B-cell Precursor ALL

- A treatment course consists of 1 cycle of BLINCYTO for induction followed by up to 3 additional cycles for consolidation
- A single cycle of treatment of Blincyto induction or consolidation consists of 28 days of continuous intravenous infusion, followed by a 14- day treatment-free interval (total 42 days)
- The table below shows the recommended dose by patient weight and schedule.

Patient Weight	Induction Cycle 1		Consolidation Cycles 2 - 4	
	Days 1-28	Days 29-42	Days 1-28	Days 29-42
≥45 kg (fixed-dose)	28 mcg/day	14-day treatment-free interval	28 mcg/day	14-day treatment-free interval
<45 kg (BSA-based dose)	15 mcg/m^2/day (not to exceed 28 mcg/day)		15 mcg/m^2/day (not to exceed 28 mcg/day)	

Relapsed or Refractory B-cell Precursor ALL
A treatment course consists of up to 2 cycles for induction followed by 3 additional cycles for consolidation and up to 4 additional cycles of continued therapy.

A single cycle of treatment of Blincyto induction or consolidation consists of 28 days of continuous intravenous infusion, followed by a 14-day treatment-free interval (total 42 days).

A single cycle of treatment of Blincyto continued therapy consists of 28 days of continuous intravenous infusion followed by a 56-day treatment-free interval (total 84 days).

See the table below for the recommended dose by patient weight and schedule. Patients greater than or equal to 45 kg receive a fixed-dose, and for patients less than 45 kg, the dose is calculated using the patient's body surface area (BSA).

CONTINUED ON NEXT PAGE

BLINATUMOMAB (NSA)

FDA APPROVED INDICATION (CONTINUED)

DOSAGE & ADMINISTRATION

Blincyto dosage and schedule for the treatment of Relapsed or Refractory B-cell Precursor ALL

Patient Weight	Induction Cycle 1			Induction Cycle 2	
	Days 1-7	Days 8-28	Days 29-42	Days 1-28	Days 29-42
≥45 kg (fixed-dose)	9 mcg/day	28 mcg/day	14-day treatment-free interval	28 mcg/day	14-day treatment free interval
<45 kg (BSA-based dose)	5 mcg/m^2/day (not to exceed 9 mcg/day)	15 mcg/m^2/day (not to exceed 28 mcg/day)		15 mcg/m^2/day (not to exceed 28 mcg/day)	

Patient Weight	Consolidation Cycle 3 - 5		Continued Therapy Cycle 6 - 9	
	Days 1-28	Days 29-42	Days 1-28	Days 29-84
≥45 kg (fixed-dose)	28 mcg/day	14-day treatment-free interval	28 mcg/day	56-day treatment-free interval
<45 kg (BSA-based dose)	15 mcg/m^2/day (not to exceed 28 mcg/day)		15 mcg/m^2/day (not to exceed 28 mcg/day)	

If the interruption after an adverse event is no longer than 7 days, continue the same cycle to a total of 28 days of infusion inclusive of days before and after the interruption in that cycle. If the interruption after an adverse event is longer than 7 days, start a new cycle.

REFERENCES

- Blincyto [Prescribing Information]. Thousand Oaks, CA: Amgen Inc. March 2018.

Library	Commercial	NSA
Yes	No	Yes

Part D Effective: N/A
Commercial Effective: 07/01/18
Created: 02/15
Client Approval: 05/18
P&T Approval: 04/18

BORTEZOMIB (NSA)

Generic	Brand	HICL	GCN	Exception/Other
BORTEZOMIB	VELCADE, BORTEZOMIB	25202		

This drug requires a written request for prior authorization.

GUIDELINES FOR USE

1. Does the patient have a diagnosis of multiple myeloma?

   If yes, **approve for 12 months by HICL.**
   If no, continue to #2.

2. Does the patient have a diagnosis of mantle cell lymphoma?

   If yes, continue to #3.
   If no, do not approve.
   DENIAL TEXT: See the denial text at the end of the guideline.

3. Has the patient received at least one prior therapy for mantle cell lymphoma?

   If yes, **approve for 12 months by HICL.**
   If no, **approve Velcade for 12 months by NDC 63020-0049-01. (Note: If the request is for bortezomib by Fresenius Kabi, do not approve since this is indicated for mantle cell lymphoma ONLY in patients who have received at least 1 prior therapy)**

DENIAL TEXT: The guideline named **BORTEZOMIB** requires a diagnosis of multiple myeloma or mantle cell lymphoma. In addition, the following criterion must be met:
For bortezomib (manufactured by Fresenius Kabi), approval requires the patient has received at least one prior therapy for mantle cell lymphoma.

RATIONALE
Ensure appropriate utilization of bortezomib based on FDA approved indication.

FDA APPROVED INDICATIONS
Velcade (Millennium) is a proteasome inhibitor indicated for:
- Treatment of patients with multiple myeloma
- Treatment of patients with mantle cell lymphoma

Bortezomib (Fresenius Kabi) is a proteasome inhibitor indicated for:
- Treatment of patients with multiple myeloma
- Treatment of patients with mantle cell lymphoma who have received at least 1 prior therapy

CONTINUED ON NEXT PAGE

BORTEZOMIB (NSA)

REFERENCES

- Velcade [Prescribing Information]. Cambridge, MA: Millennium Pharmaceuticals; June 2017.
- Bortezomib [Prescribing Information]. Lake Zurich, IL: Fresenius Kabi; November 2017.

Library	Commercial	NSA
Yes	No	Yes

Part D Effective: N/A
Commercial Effective: 01/29/18

Created: 11/12
Client Approval: 01/18

P&T Approval: 01/18

BOTULINUM NEUROTOXIN (NSA)

Generic	Brand	HICL	GCN	Exception/Other
ONABOTULINUM TOXIN A	BOTOX	04867		BRAND ≠ BOTOX COSMETIC
ABOBOTULINUM TOXIN A	DYSPORT	36477		
RIMABOTULINUM TOXIN B	MYOBLOC	21869		
INCOBOTULINUM TOXIN A	XEOMIN	36687		

**** Please use the criteria for the specific drug requested ****

GUIDELINES FOR USE

BOTOX

1. Is the request for the improvement of appearance of glabellar lines in the face (for example wrinkles)?

   If yes, do not approve.
   BOTOX DENIAL TEXT: See the denial text at the end of the guideline.
   If no, continue to #2.

CONTINUED ON NEXT PAGE

BOTULINUM NEUROTOXIN (NSA)

GUIDELINES FOR USE - BOTOX (CONTINUED)

2. Does the patient have **ONE** of the following conditions **AND** meet the associated criteria?
   - For the treatment of overactive bladder (OAB) approval requires:
     - Patient is 18 years of age or older
     - Patient had a trial or is contraindicated to an anticholinergic medication (such as oxybutynin, Ditropan XL, Detrol, Detrol LA, Enablex, Toviaz, VESIcare, or Sanctura)
   - For the treatment of urinary incontinence approval requires:
     - Patient is 18 years of age or older
     - Detrusor overactivity associated with a neurologic condition [e.g., spinal cord injury (SCI), multiple sclerosis (MS)]
     - Patient had a trial or is contraindicated to an anticholinergic medication (such as oxybutynin, Ditropan XL, Detrol, Detrol LA, Enablex, Toviaz, VESIcare, or Sanctura)
   - For the prophylaxis of headaches in patients with chronic migraine (≥15 days per month with headache lasting 4 hours a day or longer) approval requires:
     - Patient is 18 years of age or older
     - The patient has had a previous trial of any **TWO** of the following prophylactic migraine treatments: Valproic acid/divalproex sodium, topiramate, propranolol, timolol, amitriptyline, venlafaxine, atenolol, nadolol, lisinopril, candesartan, clonidine, guanfacine, carbamazepine, nebivolol, pindolol, or cyproheptadine
   - For the treatment of upper or lower limb spasticity requires that the patient is 18 years of age or older
   - For the treatment of cervical dystonia (spasmodic torticollis or involuntary contracting of the neck muscles) requires that the patient is 18 years of age or older
   - For the treatment of severe axillary hyperhidrosis (excessive underarm sweating) requires that the patient is 18 years of age or older
   - For the treatment of blepharospasm (involuntary forcible closure of the eyelid) requires that the patient is 12 years of age or older
   - For the treatment of strabismus (crossed-eye) requires that the patient is 12 years of age or older

   If yes, **approve for 12 months by GPID with the following quantity limits: up to #4 of the 100-unit vials or #1 of the 200-unit vial every 3 months.**
   If no, do not approve.
   BOTOX DENIAL TEXT: See the denial text at the end of the guideline.

CONTINUED ON NEXT PAGE

BOTULINUM NEUROTOXIN (NSA)

GUIDELINES FOR USE - BOTOX (CONTINUED)

BOTOX DENIAL TEXT: The guideline named **BOTULINUM NEUROTOXIN (Botox)** requires one of the following non-cosmetic conditions: treatment of overactive bladder (OAB), treatment of urinary incontinence, prophylaxis of headaches in chronic migraine (at least 15 days per month with headache lasting 4 hours a day or longer), treatment of upper or lower limb spasticity, treatment of cervical dystonia (spasmodic torticollis or involuntary contracting of the neck muscles), treatment of severe axillary hyperhidrosis (excessive underarm sweating), treatment of blepharospasm (involuntary forcible closure of the eyelid), or treatment of strabismus (crossed-eye). In addition, the following criteria must also be met:

For the treatment of overactive bladder (OAB), approval requires:

- Patient is 18 years of age or older
- A trial or contraindication to an anticholinergic medication (such as oxybutynin, Ditropan XL, Detrol, Detrol LA, Enablex, Toviaz, VESIcare, or Sanctura)

For the treatment of urinary incontinence, approval requires:

- Patient is 18 years of age or older
- Detrusor overactivity associated with a neurologic condition [e.g., spinal cord injury (SCI), multiple sclerosis (MS)]
- A trial or contraindication to an anticholinergic medication (such as oxybutynin, Ditropan XL, Detrol, Detrol LA, Enablex, Toviaz, VESIcare, or Sanctura)

For the prophylaxis of headaches in patients with chronic migraine (at least 15 days per month with headache lasting 4 hours a day or longer), approval requires:

- Patient is 18 years of age or older
- The patient has had a previous trial of any **TWO** of the following prophylactic migraine treatments: Valproic acid/divalproex sodium, topiramate, propranolol, timolol, amitriptyline, venlafaxine, atenolol, nadolol, lisinopril, candesartan, clonidine, guanfacine, carbamazepine, nebivolol, pindolol, or cyproheptadine

For the treatment of spasticity, cervical dystonia and severe axillary hyperhidrosis, approval requires:

- Patient is 18 years of age or older

For the treatment of blepharospasm and strabismus, approval requires:

- Patient is 12 years of age or older

This medication will not be approved for the improvement of appearance of glabellar lines in the face (for example wrinkles).

CONTINUED ON NEXT PAGE

BOTULINUM NEUROTOXIN (NSA)

GUIDELINES FOR USE (CONTINUED)

DYSPORT

1. Is the request for the improvement of appearance of glabellar lines in the face (for example wrinkles)?

   If yes, do not approve.
   DYSPORT DENIAL TEXT: See the denial text at the end of the guideline.
   If no, continue to #2.

2. Is the request for the treatment of cervical dystonia (spasmodic torticollis or involuntary contracting of the neck muscles) **AND** the patient is at least 18 years or older?

   If yes, **approve for 12 months by GPID with a quantity limit of up to #2 vials every 3 months.**
   If no, continue to #3.

3. Is the request for the treatment of upper limb spasticity **AND** the patient is at least 18 years or older?

   If yes, **approve for 12 months by GPID with a quantity limit of up to #2 vials every 3 months.**
   If no, continue to #4.

4. Is the request for the treatment of lower limb spasticity in a pediatric patient 2 years of age or older?

   If yes, **approve for 12 months by GPID with a quantity limit of up to #2 vials every 3 months.**
   If no, do not approve.
   DYSPORT DENIAL TEXT: The guideline named **BOTULINUM NEUROTOXIN (Dysport)** requires a non-cosmetic diagnosis of cervical dystonia also called spasmodic torticollis (involuntary contracting of the neck muscles) in a patient at least 18 years or older, upper limb spasticity in a patient at least 18 years or older, or lower limb spasticity in a pediatric patient 2 years of age or older. This medication will not be approved for the improvement of appearance of glabellar lines in the face (for example wrinkles).

CONTINUED ON NEXT PAGE

BOTULINUM NEUROTOXIN (NSA)

GUIDELINES FOR USE (CONTINUED)

MYOBLOC

1. Is the request for the improvement of appearance of glabellar lines in the face (for example wrinkles)?

   If yes, do not approve.
   MYOBLOC DENIAL TEXT: See the denial text at the end of the guideline.
   If no, continue to #2.

2. Is the request for the treatment of cervical dystonia (spasmodic torticollis or involuntary contracting of the neck muscles) **AND** the patient is at least 18 years or older?

   If yes, **approve for 12 months by GPID with the following quantity limits: up to #2 of the 2,500-unit vials, #1 of the 5,000-unit vial, or #1 of the 10,000-unit vial every 3 months.**
   If no, do not approve.
   MYOBLOC DENIAL TEXT: The guideline named **BOTULINUM NEUROTOXIN (Myobloc)** requires a non-cosmetic diagnosis of cervical dystonia also called spasmodic torticollis (involuntary contracting of the neck muscles) and the patient is at least 18 years or older. This medication will not be approved for the improvement of appearance of glabellar lines in the face (for example wrinkles).

XEOMIN

1. Is the request for the improvement of appearance of glabellar lines in the face (for example wrinkles)?

   If yes, do not approve.
   XEOMIN DENIAL TEXT: See the denial text at the end of the guideline.
   If no, continue to #2.

2. Does the patient have a diagnosis of chronic sialorrhea (hypersalivation) **AND** the patient is at least 18 years or older?

   If yes, **approve for 12 months or length of therapy (whichever is less) by GPID with the following quantity limits: up to #2 of the 50-unit vials or #1 of the 100-units vials every 4 months.**
   If no, continue to #3.

CONTINUED ON NEXT PAGE

BOTULINUM NEUROTOXIN (NSA)

GUIDELINES FOR USE - XEOMIN (CONTINUED)

3. Does the patient have **ONE** of the following conditions **AND** meets the associated criteria?
   - For the treatment of cervical dystonia (spasmodic torticollis or involuntary contracting of the neck muscles) **AND** the patient is 18 years of age or older
   - For the treatment of blepharospasm (involuntary forcible closure of the eyelid) approval requires **ALL** of the following:
     - Patient is 18 years of age or older
     - Patient has had a previous trial of Botox (onabotulinum toxin A)
   - For the treatment of upper limb spasticity **AND** the patient is at least 18 years or older

   If yes, **approve for 12 months or length of therapy (whichever is less) by GPID with the following quantity limits: up to #3 of the 50-unit vials or #2 of the 100 or 200-unit vials every 3 months.**

   If no, do not approve. **If the request is for blepharospasm, please enter a proactive authorization for Botox for 12 months or length of therapy (whichever is less) by GPID with the following quantity limits: up to #4 of the 100-unit vials or #1 of the 200-unit vial every 3 months.**
   XEOMIN DENIAL TEXT: The guideline named **BOTULINUM NEUROTOXIN (Xeomin)** requires a non-cosmetic diagnosis such as chronic sialorrhea (hypersalivation), cervical dystonia (spasmodic torticollis or involuntary contracting of the neck muscles), blepharospasm (involuntary forcible closure of the eyelid), or upper limb spasticity. In addition, the patient must be 18 years of age or older and the following criteria must also be met:
   For the treatment of blepharospasm, approval requires:
   - A previous trial of Botox (onabotulinum toxin A). A prior authorization has been entered for Botox.

   This medication will not be approved for the improvement of appearance of glabellar lines in the face (for example wrinkles).

CONTINUED ON NEXT PAGE

BOTULINUM NEUROTOXIN (NSA)

RATIONALE
To ensure botulinum neurotoxin is used for a non-cosmetic FDA-approved indication.

FDA APPROVED INDICATIONS
BOTOX is an acetylcholine release inhibitor and a neuromuscular blocking agent indicated for:
- Treatment of overactive bladder (OAB) with symptoms of urge urinary incontinence, urgency, and frequency, in adults who have an inadequate response to or are intolerant of an anticholinergic medication
- Treatment of urinary incontinence due to detrusor overactivity associated with a neurologic condition [e.g., spinal cord injury (SCI), multiple sclerosis (MS)] in adults who have an inadequate response to or are intolerant of an anticholinergic medication
- Prophylaxis of headaches in adult patients with chronic migraine (≥15 days per month with headache lasting 4 hours a day or longer)
- Treatment of upper or lower limb spasticity in adult patients, to decrease the severity of increased muscle tone in elbow flexors (biceps), wrist flexors (flexor carpi radialis and flexor carpi ulnaris), finger flexors (flexor digitorum profundus and flexor digitorum sublimis), and thumb flexors (adductor pollicis and flexor pollicis longus)
- Treatment of lower limb spasticity in adult patients to decrease the severity of increased muscle tone in ankle and toe flexors (gastrocnemius, soleus, tibialis posterior, flexor hallucis longus, and flexor digitorum longus)
- Treatment of cervical dystonia in adult patients, to reduce the severity of abnormal head position and neck pain
- Treatment of severe primary axillary hyperhidrosis that is inadequately managed by topical agents in adult patients
- Treatment of strabismus and blepharospasm associated with dystonia including benign essential blepharospasm or VII nerve disorders in patients ≥12 years of age and above

Important limitations: Safety and effectiveness of Botox have not been established for:
- Prophylaxis of episodic migraine (14 headache days or fewer per month) in seven placebo-controlled studies
- Treatment of upper or lower limb muscle groups
- Treatment of spasticity in pediatric patients under age 18 years
- Improving upper extremity functional abilities, or range of motion at a joint affected by a fixed contracture. Treatment with Botox is not intended to substitute for usual standard of care rehabilitation regimens
- Treatment of axillary hyperhidrosis in pediatric patients under age 18
- Hyperhidrosis in other body areas. Weakness of hand muscles and blepharoptosis may occur in patients who receive Botox for palmar hyperhidrosis and facial hyperhidrosis, respectively. Patients should be evaluated for potential causes of secondary hyperhidrosis (e.g., hyperthyroidism) to avoid symptomatic treatment of hyperhidrosis without the diagnosis and/or treatment of the underlying disease

CONTINUED ON NEXT PAGE

BOTULINUM NEUROTOXIN (NSA)

FDA APPROVED INDICATIONS (CONTINUED)

DYSPORT is indicated for
- The treatment of adults with cervical dystonia
- The temporary improvement in the appearance of moderate to severe glabellar lines associated with procerus and corrugator muscle activity in adult patients < 65 years of age.
- The treatment of upper limb spasticity in adults
- The treatment of lower limb spasticity in pediatric patients 2 years of age and older

MYOBLOC is indicated for:
Treatment of adults with cervical dystonia to reduce the severity of abnormal head position and neck pain associated with cervical dystonia.

XEOMIN is approved for:
- Treatment of chronic sialorrhea in adult patients
- Treatment of adults with cervical dystonia, in both botulinum toxin-naïve and previously treated patients.
- Treatment of blepharospasm in adults previously treated with onabotulinum toxin A (Botox).
- Treatment of upper limb spasticity in adult patients
- Temporary improvement in the appearance of moderate to severe glabellar lines with corrugator and/or procerus muscle activity in adult patients

DOSAGE AND ADMINISTRATION
BOTOX
- In treating adults for one or more indications, the maximum cimulative dose should not exceed a 400 Units administered in a 3 month interval
- The potency Units of BOTOX (onabotulinumtoxinA) for injection are specific to the preparation and assay method utilized. They are not interchangeable with other preparations of botulinum toxin products and, therefore, units of biological activity of BOTOX cannot be compared to nor converted into units of any other botulinum toxin products assessed with any other specific assay method
- **Overactive Bladder:** The recommended dose is 100 Units, and is the maximum recommended dose. The recommended dilution is 100 Units/10 mL with preservative-free 0.9% Sodium Chloride Injection
- **Urinary incontinence:** The recommended dose is 200 Units per treatment, and should not be exceeded
- **Chronic migraine:** The recommended dilution is 200 Units/4 mL or 100 Units/2 mL, with a final concentration of 5 Units per 0.1 mL. The recommended dose for treating chronic migraine is 155 Units administered intramuscularly using a sterile 30-gauge, 0.5 inch needle as 0.1 mL (5 Units) injections per each site. Injections should be divided across 7 specific head/neck muscle areas

CONTINUED ON NEXT PAGE

BOTULINUM NEUROTOXIN (NSA)

FDA APPROVED INDICATIONS (CONTINUED)

DOSAGE AND ADMINISTRATION
BOTOX

- **Upper and lower limb spasticity:** The recommended dilution is 200 Units/4 mL or 100 Units/2 mL with preservative-free 0.9% Sodium Chloride Injection, USP. The lowest recommended starting dose should be used, and no more than 50 Units per site should generally be administered. Repeat treatment may be administered when the effect of a previous injection has diminished, but no sooner than 12 weeks after the previous injection. The recommended dose for treating upper limb spasticity ranges from 75 Units to 400 Units divided among selected muscles at a given treatment session. The recommended dose for treating lower limb spasticity is 300 Units to 400 Units divided among 5 muscles (gastrocnemius, soleus, tibialis posterior, flexor hallucis longus and flexor digitorum longus)
- **Cervical dystonia:** The mean BOTOX dose administered to patients was 236 Units (25th to 75th percentile range of 198 Units to 300 Units). The BOTOX dose was divided among the affected muscles. The initial dose for a patient without prior use of BOTOX should be at a lower dose, with subsequent dosing adjusted based on individual response. Limiting the total dose injected into the sternocleidomastoid muscle to 100 Units or less may decrease the occurrence of dysphagia. The recommended dilution is 200 Units/2 mL, 200 Units/4 mL, 100 Units/1 mL, or 100 Units/2 mL with preservative-free 0.9% Sodium Chloride Injection, USP, depending on volume and number of injection sites desired to achieve treatment objectives
- **Primary axillary hyperhidrosis:** The recommended dose is 50 Units per axilla. The recommended dilution is 100 Units/4 mL with preservative-free 0.9% Sodium Chloride Injection, USP
- **Blepharospasm**: The initial recommended dose is 1.25 Units-2.5 Units (0.05 mL to 0.1 mL volume at each site) injected into the medial and lateral pre-tarsal orbicularis oculi of the upper lid and into the lateral pre-tarsal orbicularis oculi of the lower lid. The recommended dilution to achieve 1.25 Units is 100 Units/8 mL; for 2.5 Units it is 100 Units/4 mL
- **Strabismus:** The volume of BOTOX injected for treatment of strabismus should be between 0.05-0.15 mL per muscle. The recommended dilution to achieve 1.25 Units is 100 Units/8 mL; for 2.5 Units it is 100 Units/4 mL

CONTINUED ON NEXT PAGE

BOTULINUM NEUROTOXIN (NSA)

FDA APPROVED INDICATIONS (CONTINUED)

DOSAGE AND ADMINISTRATION
DYSPORT
Once reconstituted, store in original container in a refrigerator at 2°C to 8°C (36°F to 46°F) and use within 24 hours. Do not freeze after reconstitution. Protect from light. Reconstitution instructions are specific for the 300 Unit and 500 Unit vials. Reconstituted DYSPORT® is intended for intramuscular injection only. After reconstitution, DYSPORT® should be used for only one injection session and for only one patient.

- **Cervical Dystonia**
  Initial dose is 500 Units given intramuscularly as a divided dose among the affected muscles. Re-treatment every 12 weeks or longer, as necessary, based on return of clinical symptoms with doses administered between 250 Units and 1000 Units to optimize clinical benefit. Re-treatment should not occur in intervals of less than 12 weeks. Titrate in 250 Unit steps according to patient's response.
- **Spasticity in Adults**
  Select dose based on muscles affected, severity of muscle spasticity, prior response and adverse reaction history following treatment with DYSPORT® or other botulinum toxin A. Dosing for upper limb spasticity: between 500 Units and 1000 Units. Dosing for lower limb spasticity: up to 1500 Units. The maximum recommended total dose per treatment session (upper and lower limb combined) in adults is 1500 Units. Re-treatment, based on return of clinical symptoms, should not occur in intervals of less than 12 weeks.
- **Pediatric Lower Limb Spasticity**
  Select dose based on the affected muscle, severity of spasticity, and treatment history with botulinum toxins. Dosing is based on Units/kg; recommended total DYSPORT® dose per treatment session is 10 to 15 Units/kg per limb. Total dose per treatment session must not exceed 15 Units/kg for unilateral lower limb injections, 30 Units/kg for bilateral injections, or 1000 units, whichever is lower. Re-treatment, based on return of clinical symptoms, should not occur in intervals of less than 12 weeks.

CONTINUED ON NEXT PAGE

BOTULINUM NEUROTOXIN (NSA)

FDA APPROVED INDICATIONS (CONTINUED)

DOSAGE AND ADMINISTRATION
MYOBLOC
The recommended initial dose of MYOBLOC for patients with a prior history of tolerating botulinum toxin injections is 2,500 to 5,000 Units divided among affected muscles. Patients without a prior history of tolerating botulinum toxin injections should receive a lower initial dose. Subsequent dosing should be optimized according to the patient's individual response. MYOBLOC should be administered by physicians familiar and experienced in the assessment and management of patients with Cervical Dystonia (CD). The method described for performing the potency assay is specific to Solstice Neurosciences' manufacture of MYOBLOC. Due to differences in the specific details of this assay such as the vehicle, dilution scheme and laboratory protocols for various potency assays, Units of biological activity of MYOBLOC cannot be compared to or converted into units of any other botulinum toxin or any toxin assessed with any other specific assay method. Therefore, differences in species' sensitivities to different botulinum neurotoxin serotypes preclude extrapolation of animal dose activity relationships to human dose estimates. The duration of effect in patients responding to MYOBLOC treatment has been observed in studies to be between 12 and 16 weeks at doses of 5,000 Units or 10,000 Units.

XEOMIN
Reconstituted Xeomin is intended for intramuscular injection only or intra-salivary gland injection. Use for only one injection session and for only one patient. Instructions are specific for 50 units, 100 units, and 200 unit vials. Store in a refrigerator (2°C to 8°C) and use within 24 hours.
The optimum dose, frequency, and number of injection sites in the treated muscle(s) should be based on severity and prior treatment response; individualize dosing for each patient:
- **Upper Limb Spasticity in Adults**: The recommended total dose is up to 400 Units no sooner than every 12 weeks
- **Cervical Dystonia**: The recommended initial total dose is 120 Units per treatment session
- **Blepharospasm**: base initial dosing on previous dosing for onabotulinumtoxinA (Botox); if not known, the recommended starting dose is 1.25 Units-2.5 Units per injection site
- **Chronic Sialorrhea**: The recommended total dose is 100Units per treatment session consisting of 30 Units perparotid gland and 20 Units per submandibular gland, no sooner than every 16 weeks

REFERENCES
- Botox [Prescribing Information]. Irvine, CA: Allergan. May 2018.
- Dysport [Prescribing Information]. Basking Ridge, NJ Ispen: Biopharmaceuticals, Inc.; June 2017.
- Myobloc [Prescribing Information] South San Francisco, CA: Solstice Neurosciences, Inc.; January 2012.
- Xeomin [Prescribing Information]. Greensboro, NC: Merz Pharmaceuticals, LLC; July 2018.

CONTINUED ON NEXT PAGE

BOTULINUM NEUROTOXIN (NSA)

Library	Commercial	NSA
Yes	No	Yes

Part D Effective: N/A
Commercial Effective: 10/01/18

Created: 01/10
Client Approval: 09/18

P&T Approval: 07/18

BRENTUXIMAB (NSA)

Generic	Brand	HICL	GCN	Exception/Other
BRENTUXIMAB VEDOTIN	ADCETRIS	37879		

This drug requires a written request for prior authorization.

GUIDELINES FOR USE

1. Is the patient 18 years of age or older?

   If yes, continue to #2.
   If no, do not approve.
   DENIAL TEXT: See the denial text at the end of the guideline.

2. Does the patient have a diagnosis of classical Hodgkin lymphoma and meet **ONE** of the following criteria?
   - Has failed an autologous hematopoietic stem cell transplant (auto-HSCT)
   - Has failed at least two multi-agent chemotherapy regimens (potential regimens include but are not limited to: ABVD [doxorubicin, bleomycin, vinblastine, dacarbazine], Stanford V [doxorubicin, vinblastine, mechlorethamine, etoposide, vincristine, bleomycin, prednisone], BEACOPP [bleomycin, etoposide, doxorubicin, cyclophosphamide, vincristine, procarbazine, prednisone])

   If yes, **approve for 12 months with a quantity limit of #4 vials per 21 days.**
   If no, continue to #3.

3. Does the patient have a diagnosis of classical Hodgkin lymphoma and is considered high risk for relapse or disease progression post-auto-HSCT, as defined according to status following frontline therapy: refractory, relapse within 12 months, or relapse ≥12 months with extranodal disease?

   If yes, continue to #4.
   If no, continue to #5.

4. Did the patient obtain a complete remission (CR), partial remission (PR), or stable disease (SD) to most recent pre-auto-HSCT salvage therapy?

   If yes, **approve for 12 months with a quantity limit of #4 vials per 21 days.**
   If no, do not approve.
   DENIAL TEXT: See the denial text at the end of the guideline.

CONTINUED ON NEXT PAGE

BRENTUXIMAB (NSA)

GUIDELINES FOR USE (CONTINUED)

5. Does the patient have a diagnosis of relapsed systemic anaplastic large cell lymphoma (sALCL) and meet the following criterion?
   - Has failed at least one multi-agent chemotherapy regimen (potential regimens include but are not limited to: CHOP [cyclophosphamide, doxorubicin, vincristine, prednisone] or CHOEP [cyclophosphamide, doxorubicin, vincristine, etoposide, prednisone])

   If yes, **approve for 12 months with a quantity limit of #4 vials per 21 days.**
   If no, continue to #6.

6. Does the patient have a diagnosis of systemic anaplastic large cell lymphoma (sALCL) OR other CD30-expressing peripheral T-cell lymphomas (PTCL), including angioimmunoblastic T-cell lymphoma and PTCL not otherwise specified, and meet ALL of the following criteria?
   - The patient has not received treatment for sALCL or other CD30-expressing PTCL
   - The requested medication will be used in combination with cyclophosphamide, doxorubicin, and prednisone

   If yes, **approve for 12 months with a total fill count of 8 and a quantity limit of #4 vials per 21 days.**
   If no, continue to #7.

7. Does the patient have a diagnosis of primary cutaneous anaplastic large cell lymphoma (pcALCL) or CD30-expressing mycosis fungoides (MF) **AND** meet the following criterion?
   - The patient has received prior systemic therapy

   If yes, **approve for 12 months with a quantity limit of #4 vials per 21 days.**
   If no, continue to #8.

8. Does the patient have a diagnosis of Stage III or IV classical Hodgkin lymphoma (cHL) and meet **ALL** of the following criteria?
   - The requested medication will be used in combination with doxorubicin, vinblastine, and dacarbazine
   - The patient has not received treatment for Stage III or IV classical Hodgkin lymphoma (cHL)

   If yes, **approve for 12 months with a total fill count of 12 and a quantity limit of #3 vials per 14 days.**
   If no, do not approve.
   DENIAL TEXT: See the denial text at the end of the guideline.

CONTINUED ON NEXT PAGE

BRENTUXIMAB (NSA)

GUIDELINES FOR USE (CONTINUED)

DENIAL TEXT: The guideline named **BRENTUXIMAB (Adcetris)** requires a diagnosis of classical Hodgkin lymphoma, Stage III or IV classical Hodgkin lymphoma (cHL), systemic anaplastic large cell lymphoma (sALCL) or other CD30-expressing peripheral T-cell lymphomas (PTCL), primary cutaneous anaplastic large cell lymphoma (pcALCL), or CD30-expressing mycosis fungoides (MF). In addition, the patient must be 18 years of age or older. The following criteria must also be met:

For the diagnosis of classical Hodgkin lymphoma, approval requires ONE of the following:

- The patient has failed autologous hematopoietic stem cell transplant (auto-HSCT)
- The patient has failed at least two multi-agent chemotherapy regimens (potential regimens include but are not limited to: ABVD [doxorubicin, bleomycin, vinblastine, dacarbazine], Stanford V [doxorubicin, vinblastine, mechlorethamine, etoposide, vincristine, bleomycin, prednisone], BEACOPP [bleomycin, etoposide, doxorubicin, cyclophosphamide, vincristine, procarbazine, prednisone])
- The patient is considered high risk of relapse or disease progression post-auto-HSCT **AND** the patient has obtained complete remission (CR), partial remission (PR), or stable disease (SD) to most recent pre-auto-HSCT salvage therapy

For the diagnosis of relapsed systemic anaplastic large cell lymphoma (sALCL), approval requires:

- The patient has failed at least one multi-agent chemotherapy regimen (potential regimens include but are not limited to: CHOP [cyclophosphamide, doxorubicin, vincristine, prednisone] or CHOEP [cyclophosphamide, doxorubicin, vincristine, etoposide, prednisone])

For the diagnosis of systemic anaplastic large cell lymphoma (sALCL) or other CD30-expressing peripheral T-cell lymphomas (PTCL), including angioimmunoblastic T-cell lymphoma and PTCL not otherwise specified, approval requires:

- The patient has not received treatment for sALCL or other CD30-expressing PTCL
- The requested medication will be used in combination with cyclophosphamide, doxorubicin, and prednisone

For the diagnosis of primary cutaneous anaplastic large cell lymphoma (pcALCL) or CD30-expressing mycosis fungoides (MF), approval requires:

- The patient has received prior systemic therapy

For the diagnosis of Stage III or IV classical Hodgkin lymphoma (cHL), approval requires:

- The requested medication will be used in combination with doxorubicin, vinblastine, and dacarbazine
- The patient has not received treatment for Stage III or IV classical Hodgkin lymphoma (cHL)

CONTINUED ON NEXT PAGE

BRENTUXIMAB (NSA)

RATIONALE

For further information, please refer to the Prescribing Information and/or Drug Monograph for Adcetris.

REFERENCES

- Adcetris [Prescribing Information]. Bothell, WA: Seattle Genetics, Inc.; November 2018.

Library	Commercial	NSA
Yes	No	Yes

Part D Effective: N/A
Commercial Effective: 12/10/18
Created: 09/11
Client Approval: 11/18
P&T Approval: 01/19

BUPRENORPHINE EXTENDED-RELEASE (NSA)

Generic	Brand	HICL	GCN	Exception/Other
BUPRENORPHINE EXTENDED-RELEASE	SUBLOCADE		44186 44187	

GUIDELINES FOR USE

1. Does the patient have a diagnosis of moderate to severe opioid use disorder and meet the following criterion?
   - The patient previously initiated treatment with a transmucosal buprenorphine-containing product, which was followed by dose adjustment for a minimum of 7 days

   If yes, continue to #2.
   If no, do not approve.
   DENIAL TEXT: The guideline named **BUPRENORPHINE EXTENDED-RELEASE (Sublocade)** requires a diagnosis of moderate to severe opioid use disorder. In addition, the following must be met:
   - The patient previously initiated treatment with a transmucosal buprenorphine-containing product, which was followed by dose adjustment for a minimum of 7 days

2. Is the patient new to Sublocade treatment?

   If yes, **please enter TWO approvals by GPID as follows:**
   - **FIRST APPROVAL: approve GPID 44186 for 2 months with a quantity limit of #1.5mL (#1 300mg/1.5mL syringe) per 30 days.**
   - **SECOND APPROVAL: approve for 10 months, please enter a start date 2 MONTHS AFTER the START date of the first approval for the requested strength with a quantity limit as follows:**
     - **GPID 44187: #0.5mL (#1 100mg/0.5mL syringe) per 30 days.**
     - **GPID 44186: #1.5mL (#1 300mg/1.5mL syringe) per 30 days.**

   If no, **approve by GPID for 12 months for the requested strength with the associated quantity limit as follows:**
   - **GPID 44187: 0.5mL (#1 100mg/0.5mL syringe) per 30 days.**
   - **GPID 44186: 1.5mL (#1 300mg/1.5mL syringe) per 30 days.**

CONTINUED ON NEXT PAGE

BUPRENORPHINE EXTENDED-RELEASE (NSA)

RATIONALE

For further information, please refer to the Prescribing Information and/or Drug Monograph for Sublocade.

REFERENCES

- Sublocade [Prescribing Information]. North Chesterfield, VA: Invidor, Inc. March 2018.

Library	Commercial	NSA
Yes	No	Yes

Part D Effective: N/A
Commercial Effective: 11/19/18
Created: 05/18
Client Approval: 11/18
P&T Approval: 04/18

BUPRENORPHINE IMPLANT (NSA)

Generic	Brand	HICL	GCN	Exception/Other
BUPRENORPHINE	PROBUPHINE	01762		ROUTE= IMPLANT

GUIDELINES FOR USE

1. Has the patient previously received one Probuphine treatment course in **each** arm (for a maximum of **two** 6-month treatment courses)?

   If yes, do not approve.
   DENIAL TEXT: See the denial text at the end of the guideline.
   If no, continue to #2.

2. Does the patient have a diagnosis of opioid addiction/dependence and meets the following criteria?
   - The patient has achieved and sustained clinical stability on low to moderate doses of transmucosal buprenorphine (defined as 8 mg per day or less of Subutex/Suboxone or its transmucosal buprenorphine product equivalent for a minimum of 3 months without any need for supplemental dosing or adjustments).
     - Examples of acceptable doses of transmucosal buprenorphine include:
       - Subutex (buprenorphine) sublingual tablet (or its generic equivalent): 8mg or less
       - Suboxone (buprenorphine/naloxone) sublingual tablet (or its generic equivalent): 8mg/2 mg or less
       - Bunavail (buprenorphine/naloxone) buccal film: 4.2 mg/0.7 mg or less
       - Zubsolv (buprenorphine/naloxone) sublingual tablets: 5.7 mg/1.4 mg or less
   - Therapy is prescribed by a physician certified with the Probuphine REMS program to prescribe, insert, and remove Probuphine implants as confirmed by checking probuphinerems.com.

   If yes, **approve for 6 months by GPID with a quantity limit of #4 implantable rods.**
   If no, do not approve.
   DENIAL TEXT: See the denial text at the end of the guideline.

DENIAL TEXT: The guideline named **BUPRENORPHINE IMPLANT (Probuphine)** requires that the following criteria must also be met.
- The patient has not previously received one Probuphine treatment course in each arm (for a maximum of **two** 6-month treatment courses)
- The patient has achieved and sustained clinical stability on low to moderate doses of transmucosal buprenorphine (defined as 8 mg per day or less of Subutex/Suboxone or its transmucosal buprenorphine product equivalent for a minimum of 3 months without any need for supplemental dosing or adjustments)
- Therapy is prescribed by a physician certified with the Probuphine REMS program to prescribe, insert, and remove Probuphine implants as confirmed by checking probuphinerems.com

CONTINUED ON NEXT PAGE

BUPRENORPHINE IMPLANT (NSA)

RATIONALE

Under the Drug Addiction Treatment Act (DATA) codified at 21 United States Code (U.S.C.) 823(g), use of this product in the treatment of opioid dependence is limited to physicians who meet certain qualifying requirements, and who have notified the Secretary of Health and Human Services (HHS) of their intent to prescribe or dispense this product for the treatment of opioid dependence and have been assigned a unique identification number that must be included on every prescription.

Probuphine implants should be used only in patients who are opioid tolerant.
Each dose consists of four Probuphine implants inserted subdermally in the inner side of the upper arm. Probuphine subdermal implants are intended to be in place for 6 months of treatment. Remove Probuphine implants by the end of the sixth month.

New implants may be inserted subdermally in an area of the inner side of either upper arm that has not been previously used at the time of removal, if continued treatment is desired. If new implants are not inserted on the same day as the removal of implants, maintain patients on their previous dosage of transmucosal buprenorphine (i.e., the dose from which they were transferred to Probuphine treatment) prior to additional Probuphine treatment.

After one insertion in each arm, most patients should be transitioned back to a transmucosal buprenorphine-containing product for continued treatment. There is no experience with inserting additional implants into other sites in the arm to recommend an approach to a second insertion into a previously used arm. Neither re-insertion into previously used administration sites, nor into sites other than the upper arm, has been studied.

FDA APPROVED INDICATIONS

Indicated for the maintenance treatment of opioid dependence in patients who have achieved and sustained prolonged clinical stability on low-to-moderate doses of a transmucosal buprenorphine-containing product (i.e., doses of no more than 8 mg per day of Subutex or Suboxone sublingual tablet or generic equivalent). Probuphine should be used as part of a complete treatment program to include counseling and psychosocial support. Probuphine is not appropriate for new entrants to treatment and patients who have not achieved and sustained prolonged clinical stability, while being maintained on buprenorphine 8 mg per day or less of a Subutex or Suboxone sublingual tablet or generic equivalent.

DOSING

Four Probuphine implants are inserted subdermally in the upper arm for 6 months of treatment and are removed by the end of the sixth month. Probuphine implants should **not** be used for additional treatment cycles after one insertion in each upper arm. Probuphine implants must be inserted and removed by trained Healthcare Providers only.

CONTINUED ON NEXT PAGE

BUPRENORPHINE IMPLANT (NSA)

REFERENCES

- Probuphine [Prescribing Information]. Braeburn Pharmaceuticals, Inc. Princeton, NJ. May 2016.

Library	Commercial	NSA
Yes	No	Yes

Part D Effective: N/A
Commercial Effective: 10/01/2016
Created: 06/20/2016
Client Approval: 09/16
P&T Approval: 08/16

BUROSUMAB-TWZA (NSA)

Generic	Brand	HICL	GCN	Exception/Other
BUROSUMAB-TWZA	CRYSVITA	44867		

GUIDELINES FOR USE

INITIAL CRITERIA (NOTE: FOR RENEWAL CRITERIA SEE BELOW)

1. Does the patient have a diagnosis of X-linked hypophosphatemia (XLH) confirmed by **ONE** of the following criteria?
   - Physician attestation of XLH symptoms (e.g., osteomalacia, excessive fractures, bowed legs, impaired growth) and **ONE** of the following:
     - The patient has a serum phosphate level of < 3.2 mg/dL in pediatric patients or <2.5 mg/dL in adults **with** normal vitamin D levels
     - The patient has shown hyperexpression of FGF23 protein on assay
     - The patient possesses family history of XLH
   - Genotyping confirmation of the *PHEX* mutation causative of XLH

   If yes, continue to #2.
   If no, do not approve.
   DENIAL TEXT: See the initial denial text at the end of the guideline.

2. Does the patient meet **ALL** of the following criteria?
   - The patient is 1 year of age or older
   - The patient is not on concurrent oral phosphate salt or active vitamin D analog supplementation
   - The medication is prescribed by or in consultation with an endocrinologist, nephrologist, orthopedic surgeon, or medical geneticist

   If yes, **approve for 6 months by HICL with a quantity limit of #3 vials per 14 days.**
   APPROVAL TEXT: Renewal authorization requires verification of normalized phosphate levels as defined by reference range for age.

   If no, do not approve.
   DENIAL TEXT: See the initial denial text at the end of the guideline.

CONTINUED ON NEXT PAGE

BUROSUMAB-TWZA (NSA)

INITIAL CRITERIA (CONTINUED)

INITIAL DENIAL TEXT: The guideline named **BUROSUMAB (Crysvita)** requires a diagnosis of X-linked hypophosphatemia. In addition, the following criteria must be met:

- The diagnosis of XLH is confirmed by **ONE** of the following:
  - Physician attestation of XLH symptoms (e.g., osteomalacia, excessive fractures, bowed legs, impaired growth) and ONE of the following:
    - The patient has a serum phosphate level of < 3.2 mg/dL in pediatric patients or <2.5 mg/dL in adults **with** normal vitamin D levels
    - The patient has shown hyperexpression of FGF23 protein on assay
    - The patient possesses family history of XLH
  - Genotyping confirmation of the *PHEX* mutation causative of XLH
- The patient is 1 year of age or older
- The patient is not on concurrent oral phosphate salt or active vitamin D analog supplementation
- The medication is prescribed by or in consultation with an endocrinologist, nephrologist, orthopedic surgeon, or medical geneticist

RENEWAL CRITERIA

1. Does the patient have a diagnosis of X-linked hypophosphatemia (XLH) and has the patient attained normalized blood phosphate levels as defined by reference range for age?

   If yes, **approve for 12 months by HICL with a quantity limit of #3 vials per 14 days.**
   If no, do not approve.
   RENEWAL DENIAL TEXT: The guideline named **BUROSUMAB (Crysvita)** requires the diagnosis of X-linked hypophosphatemia (XLH) and the patient has attained normalized blood phosphate levels as defined by reference range for age for renewal.

RATIONALE

To promote appropriate utilization of CRYSVITA (burosumab) based on FDA approved indication and dosing.

FDA APPROVED INDICATIONS

Crysvita is indicated for the treatment of X-linked hypophosphatemia (XLH) in adult and pediatric patients 1 year of age and older.

CONTINUED ON NEXT PAGE

BUROSUMAB-TWZA (NSA)

FDA APPROVED INDICATIONS (CONTINUED)

DOSAGE & ADMINISTRATION
Crysvita is administered by subcutaneous injection and should be administered by a healthcare provider. Discontinue oral phosphate and active vitamin D analogs 1 week prior to initiation of treatment. Fasting serum phosphorus concentration should be below the reference range for age prior to initiation of treatment.

Pediatric Patients with X-linked Hypophosphatemia (1 to less than 18 years of age)
The recommended starting dose regimen is 0.8 mg/kg of body weight, rounded to the nearest 10 mg, administered every two weeks. The minimum starting dose is 10 mg up to a maximum dose of 90 mg.

After initiation of treatment with Crysvita, measure fasting serum phosphorus every 4 weeks for the first 3 months of treatment, and thereafter as appropriate. If serum phosphorus is above the lower limit of the reference range for age and below 5 mg/dL, continue treatment with the same dose. Follow dose adjustment schedule in package insert to maintain serum phosphorus within the reference range for age.

Adult Patients with X-linked Hypophosphatemia (18 years of age and older)
The recommended dose regimen in adults is 1 mg/kg body weight, rounded to the nearest 10 mg up to a maximum dose of 90 mg, administered every four weeks.

After initiation of treatment with Crysvita, assess fasting serum phosphorus on a monthly basis, measured 2 weeks post-dose, for the first 3 months of treatment, and thereafter as appropriate. If serum phosphorus is within the normal range, continue with the same dose.

REFERENCES

- Crysvita [Prescribing Information]. Novato, CA: Ultragenyx Pharmaceutical Inc. April 2018.

Library	Commercial	NSA
Yes	No	Yes

Part D Effective: N/A
Commercial Effective: 10/01/18
Created: 08/18
Client Approval: 09/18
P&T Approval: 07/18

CANAKINUMAB (NSA)

Generic	Brand	HICL	GCN	Exception/Other
CANAKINUMAB/PF	ILARIS	36497		

This drug requires a written request for prior authorization.

GUIDELINES FOR USE

1. Dose the patient have a diagnosis of Active Systemic Juvenile Idiopathic Arthritis (SJIA) and meet **ALL** of the following criteria?
   - Prescribed by or supervised by a rheumatologist
   - The patient is 2 years of age or older

   If yes, **approve for 12 months by HICL with a quantity limit of #2 vials (300mg) per 28 days.**
   If no, continue to #2.

2. Does the patient have a diagnosis of Cryopyrin-Associated Periodic Syndromes (CAPS) such as Familial Cold Autoinflammatory Syndrome (FCAS) or Muckle-Wells Syndrome (MWS) and meet **ALL** of the following criteria?
   - Prescribed by or supervised by a rheumatologist
   - The patient is 4 years of age or older

   If yes, **approve for 12 months by HICL with a quantity limit of #1 vial (150mg) per 56 days.**
   If no, continue to #3.

3. Does the patient have a diagnosis of one of the following periodic fever syndromes?
   - Tumor Necrosis Factor Receptor Associated Periodic Syndrome (TRAPS)
   - Hyperimmunoglobulin D Syndrome (HIDS)/Mevalonate Kinase Deficiency (MKD)
   - Familial Mediterranean Fever (FMF)

   If yes, **approve for 12 months by HICL with a quantity limit of #2 vials (300mg) per 28 days.**
   If no, do not approve.
   DENIAL TEXT: See the denial text at the end of the guideline.

CONTINUED ON NEXT PAGE

CANAKINUMAB (NSA)

GUIDELINES FOR USE (CONTINUED)

DENIAL TEXT: The guideline named **CANAKINUMAB (Ilaris)** requires a diagnosis of Active Systemic Juvenile Idiopathic Arthritis (SJIA), Cryopyrin-Associated Periodic Syndromes such as Familial Cold Autoinflammatory Syndrome (FCAS) or Muckle-Wells Syndrome (MWS), Tumor Necrosis Factor Receptor Associated Periodic Syndrome (TRAPS), Hyperimmunoglobulin D Syndrome (HIDS)/Mevalonate Kinase Deficiency (MKD), or Familial Mediterranean Fever (FMF). In addition, the following criteria must also be met.

For patients with active systemic juvenile idiopathic arthritis (SJIA), approval requires all of the following criteria:

- Prescribed by or supervised by a rheumatologist
- The patient is 2 years of age or older

For patients with Cryopyrin-Associated Periodic Syndromes (CAPS) such as Familial Cold Autoinflammatory Syndrome (FCAS) or Muckle-Wells Syndrome (MWS), approval requires all of the following criteria:

- Prescribed by or supervised by a rheumatologist
- The patient is 4 years of age or older

RATIONALE

Ensure appropriate use for canakinumab.

FDA APPROVED INDICATIONS

Ilaris is an interleukin-1β blocker indicated for the treatment of:

Periodic Fever Syndromes:

- Cryopyrin-Associated Periodic Syndromes (CAPS), in adults and children 4 years of age and older including:
  - Familial Cold Autoinflammatory Syndrome (FCAS)
  - Muckle-Wells Syndrome (MWS)
- Tumor Necrosis Factor Receptor Associated Periodic Syndrome (TRAPS) in adult and pediatric patients
- Hyperimmunoglobulin D Syndrome (HIDS)/Mevalonate Kinase Deficiency (MKD) in adult and pediatric patients
- Familial Mediterranean Fever (FMF) in adult and pediatric patients

Active Systemic Juvenile Idiopathic Arthritis (SJIA) in patients aged 2 years and older

CONTINUED ON NEXT PAGE

CANAKINUMAB (NSA)

FDA APPROVED INDICATIONS (CONTINUED)

DOSAGE AND ADMINISTRATION
Injection for subcutaneous use only.

Indication	Dosage
CAPS	Body weight > 40 kg: 150 mg every 8 weeks Body weight ≥ 15 kg and ≤ 40 kg: 2 mg/kg every 8 weeks – dose can be increased to 3 mg/kg every 8 weeks for children with an inadequate response
TRAPS, HIDS/MKD, FMF	Body weight > 40 kg: 150 mg every 4 weeks – dose can be increased to 300 mg every 4 weeks if clinical response is not adequate Body weight ≤ 40 kg: 2 mg/kg every 4 weeks – dose can be increased to 4 mg/kg every 4 weeks if the clinical response is not adequate
SJIA	Body weight ≥ 7.5 kg: 4 mg/kg (with a maximum of 300 mg) every 4 weeks

REFERENCES

- Novartis Pharmaceuticals Corporation. Ilaris [prescribing information]. East Hanover, NJ. September 2016.

Library	Commercial	NSA
Yes	No	Yes

Part D Effective: N/A
Commercial Effective: 01/01/17
Created: 08/13
Client Approval: 12/16
P&T Approval: 11/16

CARFILZOMIB (NSA)

Generic	Brand	HICL	GCN	Exception/Other
CARFILZOMIB	KYPROLIS	39338		

This drug requires a written request for prior authorization.

GUIDELINES FOR USE

1. Does the patient have a diagnosis of multiple myeloma (MM) and meets **ONE** of the following criteria?
   - The patient has tried or has a contraindication to at least one prior multiple myeloma therapy and will be using Kyprolis as a single agent
   - The patient has tried one to three lines of multiple myeloma therapy and will be using Kyprolis in combination with Revlimid (lenalidomide) and dexamethasone
   - The patient has tried one to three lines of multiple myeloma therapy and will be using Kyprolis in combination with dexamethasone

   If yes, **approve for 12 months by HICL.**
   If no, do not approve.
   DENIAL TEXT: The guideline named **CARFILZOMIB (Kyprolis)** requires a diagnosis of multiple myeloma and that the patient meets **ONE** of the following criteria:
   - The patient has tried or has a contraindication to at least one prior multiple myeloma therapy and will be using Kyprolis as a single agent
   - The patient has tried one to three lines of multiple myeloma therapy and will be using Kyprolis in combination with Revlimid (lenalidomide) and dexamethasone
   - The patient has tried one to three lines of multiple myeloma therapy and will be using Kyprolis in combination with dexamethasone

RATIONALE
Ensure appropriate utilization of carfilzomib based on FDA approved indication.

FDA APPROVED INDICATIONS
Kyprolis is a proteasome inhibitor that is indicated for:

- **Combination Therapy**
  - In combination with dexamethasone or with lenalidomide plus dexamethasone for the treatment of patients with relapsed or refractory multiple myeloma who have received one to three lines of therapy

- **Monotherapy**
  - As a single agent for the treatment of patients with relapsed or refractory multiple myeloma who have received one or more lines of therapy

CONTINUED ON NEXT PAGE

CARFILZOMIB (NSA)

FDA APPROVED INDICATIONS (CONTINUED)

DOSING

Please note that doses may be modified based on toxicity. See the carfilzomib, lenalidomide, and dexamethasone prescribing Information respectively for dosing adjustment recommendations.

Combination Therapy

Administer Kyprolis intravenously as a 10-minute infusion on two consecutive days, each week for three weeks followed by a 12-day rest period. Each 28-day period is considered one treatment cycle. The recommended starting dose of Kyprolis is 20 mg/m^2 in Cycle 1 on Days 1 and 2. If tolerated, escalate to a target dose of 27 mg/m^2 on Day 8 of Cycle 1. From Cycle 13, omit the Day 8 and 9 doses of Kyprolis. Discontinue Kyprolis after Cycle 18. Lenalidomide 25 mg is taken orally on Days 1–21 and dexamethasone 40 mg by mouth or intravenously on Days 1, 8, 15, and 22 of the 28-day cycles. Continue treatment until disease progression or unacceptable toxicity occurs. Refer to the lenalidomide and dexamethasone prescribing information for other concomitant medications, such as the use of anticoagulant and antacid prophylaxis that may be required with those agents.

Table 1: Kyprolis in Combination with Lenalidomide and Dexamethasone

	Cycle 1										
	Week 1			Week 2			Week 3			Week 4	
	Day 1	Day 2	Days 3–7	Day 8	Day 9	Days 10–14	Day 15	Day 16	Days 17–21	Day 22	Days 23-28
Kyprolis (mg/m^2):	20	20	-	27	27	-	27	27	-	-	-
Dexamethasone	40 mg	-	-	40 mg	-	-	40 mg	-	-	40 mg	-
Lenalidomide	25 mg daily									-	-
	Cycles 2 to 12										
	Week 1			Week 2			Week 3			Week 4	
	Day 1	Day 2	Days 3–7	Day 8	Day 9	Days 10–14	Day 15	Day 16	Days 17–21	Day 22	Days 23-28
Kyprolis (mg/m^2):	27	27	-	27	27	-	27	27	-	-	-
Dexamethasone	40 mg	-	-	40 mg	-	-	40 mg	-	-	40 mg	-
Lenalidomide	25 mg daily									-	-
	Cycles 13 on[a]										
	Week 1			Week 2			Week 3			Week 4	
	Day 1	Day 2	Days 3–7	Day 8	Day 9	Days 10–14	Day 15	Day 16	Days 17–21	Day 22	Days 23-28
Kyprolis (mg/m^2):	27	27	-	-	-	-	27	27	-	-	-
Dexamethasone	40 mg	-	-	40 mg	-	-	40 mg	-	-	40 mg	-
Lenalidomide	25 mg daily										

[a] Kyprolis is administered through Cycle 18, lenalidomide and dexamethasone continue thereafter.

CONTINUED ON NEXT PAGE

CARFILZOMIB (NSA)

FDA APPROVED INDICATIONS (CONTINUED)

Monotherapy
Administer Kyprolis intravenously as a 10-minute infusion on two consecutive days, each week for three weeks followed by a 12-day rest period. Each 28-day period is considered one treatment cycle. The recommended starting dose of Kyprolis is 20 mg/m^2 in Cycle 1 on Days 1 and 2. If tolerated, escalate to a target dose of 27 mg/m^2 on Day 8 of Cycle 1. From Cycle 13, omit the Day 8 and 9 doses of Kyprolis. Continue treatment until disease progression or unacceptable toxicity occurs.

Table 2: Kyprolis Monotherapy

	Cycle 1									
	Week 1			Week 2			Week 3			Week 4
	Day 1	Day 2	Days 3–7	Day 8	Day 9	Days 10–14	Day 15	Day 16	Days 17–21	Days 22–28
Kyprolis (mg/m^2):	20	20	-	27	27	-	27	27	-	-
	Cycles 2 to 12									
	Week 1			Week 2			Week 3			Week 4
	Day 1	Day 2	Days 3–7	Day 8	Day 9	Days 10–14	Day 15	Day 16	Days 17–21	Days 22–28
Kyprolis (mg/m^2):	27	27	-	27	27	-	27	27	-	-
	Cycles 13 on									
	Week 1			Week 2			Week 3			Week 4
	Day 1	Day 2	Days 3–7	Day 8	Day 9	Days 10–14	Day 15	Day 16	Days 17–21	Days 22–28
Kyprolis (mg/m^2):	27	27	-	-	-	-	27	27	-	-

REFERENCES

- Kyprolis [Prescribing Information]. Thousand Oaks, CA: Onyx Pharmaceuticals; June 2018.

Library	Commercial	NSA
Yes	No	Yes

Part D Effective: N/A
Commercial Effective: 09/01/18
Created: 11/12
Client Approval: 08/18
P&T Approval: 08/16

CEMIPLIMAB-RWLC (NSA)

Generic	Brand	HICL	GCN	Exception/Other
CEMIPLIMAB-RWLC	LIBTAYO	45284		

This drug requires a written request for prior authorization.

GUIDELINES FOR USE

1. Does the patient have a diagnosis of metastatic or locally advanced cutaneous squamous cell carcinoma (CSCC) and meet the following criterion?
   - The patient is not a candidate for curative surgery or curative radiation

   If yes, **approve for 12 months by HICL with a quantity limit of 7mL (1 vial) per 21 days.**
   If no, do not approve.
   DENIAL TEXT: The guideline named **CEMIPLIMAB-RWLC (Libtayo)** requires a diagnosis of metastatic or locally advanced cutaneous squamous cell carcinoma (CSCC) in patients who are not candidates for curative surgery or curative radiation.

RATIONALE

For further information, please refer to the Prescribing Information and/or Drug Monograph for Libtayo.

REFERENCES

- Libtayo [Prescribing Information]. Tarrytown, NY: Regeneron Pharmaceuticals, Inc.; September 2018.

Library	Commercial	NSA
Yes	No	Yes

Part D Effective: N/A
Commercial Effective: 01/01/19
Created: 11/18
Client Approval: 11/18
P&T Approval: 10/18

CERLIPONASE ALFA (NSA)

Generic	Brand	HICL	GCN	Exception/Other
CERLIPONASE ALFA	BRINEURA	44258		

GUIDELINES FOR USE

INITIAL CRITERIA (NOTE: FOR RENEWAL CRITERIA SEE BELOW)

1. Does the patient meet **ALL** of the following criteria?
   - A diagnosis of late infantile neuronal ceroid lipofuscinosis type 2 (CLN2), also known as tripeptidyl peptidase 1 (TPP1) deficiency confirmed by TPP1 enzyme deficiency test or TPP1/CLN2 genotyping
   - The patient is ambulatory and experiencing symptoms (e.g., instability, intermittent falls, requires assistance to walk, or can crawl only)
   - The patient has a documented CLN2 Clinical Rating Scale Score of 3 to 5, with a minimum score of 1 in each of the motor and language domains
   - The patient is 3 years of age or older
   - The medication is prescribed by or given in consultation with a neurologist or pediatric CLN2 specialist

   If yes, **approve for 6 months with a quantity limit of #2 kits per 28 days.**
   If no, do not approve.
   DENIAL TEXT: The guideline named **CERLIPONASE ALFA (Brineura)** requires the following criteria must be met:
   - A diagnosis of late infantile neuronal ceroid lipofuscinosis type 2 (CLN2), also known as tripeptidyl peptidase 1 (TPP1) deficiency confirmed by TPP1 enzyme deficiency test or TPP1/CLN2 genotyping
   - The patient is ambulatory and experiencing symptoms (e.g., instability, intermittent falls, requires assistance to walk, or can crawl only)
   - The patient has a documented CLN2 Clinical Rating Scale Score of 3 to 5, with a minimum score of 1 in each of the motor and language domains
   - The patient is 3 years of age or older
   - The medication is prescribed by or given in consultation with a neurologist or pediatric CLN2 specialist

CONTINUED ON NEXT PAGE

CERLIPONASE ALFA (NSA)

GUIDELINES FOR USE (CONTINUED)

RENEWAL CRITERIA

1. Does the patient meet **ALL** of the following criteria?
   - Patient has improved or maintained baseline motor function (e.g., ambulation, walking, crawling) or demonstrated a less-than-expected decline in motor function (e.g., ambulation, walking or crawling) from baseline
   - CLN2 motor score must be at least 1 (e.g., patient is not bedridden or immobile)

   If yes, **approve for 12 months with a quantity limit of #2 kits per 28 days.**
   If no, do not approve.
   DENIAL TEXT: The guideline named **CERLIPONASE ALFA (Brineura)** requires for renewal the following criteria to be met:
   - Patient has improved or maintained baseline motor function (e.g., ambulation, walking, crawling) or demonstrated a less-than-expected decline in motor function (e.g., ambulation, walking or crawling) from baseline
   - CLN2 motor score must be at least 1 (e.g., patient is not bedridden or immobile)

RATIONALE
Promote appropriate utilization of **CERLIPONASE ALFA** based on FDA approved indication and dosing.

FDA APPROVED INDICATIONS
Brineura is indicated to slow the loss of ambulation in symptomatic pediatric patients 3 years of age and older with late infantile neuronal ceroid lipofuscinosis type 2 (CLN2), also known as tripeptidyl peptidase 1 (TPP1) deficiency.

DOSAGE AND ADMINISTRATION
The recommended dosage of Brineura in pediatric patients 3 years of age and older is 300 mg administered once every other week by intraventricular infusion. Administer Brineura first followed by infusion of the Intraventricular Electrolytes each at an infusion rate of 2.5 mL/hr. The complete Brineura infusion, including the required infusion of Intraventricular Electrolytes, is approximately 4.5 hours. Pre-treatment of patients with antihistamines with or without antipyretics or corticosteroids is recommended 30 to 60 minutes prior to the start of infusion.

AVAILABLE STRENGTHS
Injection: Brineura 150 mg/5 mL (30 mg/mL) solution, two single-dose vials per carton co-packaged with Intraventricular Electrolytes Injection 5 mL in a single-dose vial.

CONTINUED ON NEXT PAGE

CERLIPONASE ALFA (NSA)

FDA APPROVED INDICATIONS (CONTINUED)

CLN2 Disease Clinical Rating Scale
The CLN2 Disease Clinical Rating Scale is a standardized means of quantitatively assessing disease progression and tracks loss of function in 2 main functional domains: motor and language. Each domain is scored from 0 to 3 as described below in table 1. The scores of the two domains sum up to a total score of six, with 0 representing a complete loss of function, while a score of six represents normal function.

Table 1: CLN2 Disease Clinical Rating Scale

Motor function	Language function
3 **Normal** Grossly normal gait. No prominent ataxia, no pathologic falls.	3 **Normal** Apparently normal language. Intelligible and grossly age-appropriate. No decline noted yet.
2 **Clumsy, falls** Independent gait, as defined by ability to walk without support for 10 steps. Will have obvious instability, and may have intermittent falls.	2 **Abnormal** Language has become recognizably abnormal; some intelligible words; may form short sentences to convey concepts, requests, or needs.
1 **No unaided walking** Requires assistance to walk, or can crawl only.	1 **Minimal** Hardly understandable. Few intelligible words.
0 **Immobile** Can no longer walk or crawl.	0 **Unintelligible** No intelligible words or vocalizations.

REFERENCES

- Brineura [Prescribing Information]. Novato, CA: BioMarin Pharmaceutical Inc. April 2017.
- CLN2Connection. Natural History: CLN2 disease follows a devastatingly rapid course—symptoms and functional loss compound with age. Available at: http://www.cln2connection.com/overview/natural-history. Accessed April 28, 2017.

Library	Commercial	NSA
Yes	No	Yes

Part D Effective: N/A
Commercial Effective: 10/01/17
Created: 08/17
Client Approval: 08/17
P&T Approval: 07/17

CETUXIMAB (NSA)

Generic	Brand	HICL	GCN	Exception/Other
CETUXIMAB	ERBITUX	25947		

This drug requires a written request for prior authorization.

GUIDELINES FOR USE

1. Does the patient have a diagnosis of metastatic colorectal cancer (mCRC) and meet **ALL** of the following criteria?
   - Patient's cancer is wild type KRAS (no mutation) as determined by FDA approved tests
   - Patient's cancer is epidermal growth factor receptor (EGFR)-expressing as determined by FDA approved tests

   If yes, continue to #2.
   If no, continue to #3.

2. Does the patient meet **ONE** of the following criteria?
   - The requested medication is being used in combination with FOLFIRI (irinotecan, 5-fluorouracil, leucovorin) for first-line treatment
   - The requested medication is being used in combination with irinotecan in patients who are refractory to irinotecan-based chemotherapy
   - The requested medication is being used as a single agent AND the patient has failed oxaliplatin-based and irinotecan-based chemotherapy unless patient is intolerant to irinotecan

   If yes, **approve for 12 months by HICL.**
   If no, do not approve.
   DENIAL TEXT: See the denial text at the end of the guideline.

3. Does the patient have a diagnosis of locally or regionally advanced squamous cell carcinoma of the head and neck **AND** meet the following criterion?
   - The requested medication will be used in combination with radiation therapy

   If yes, **approve for 12 months by HICL.**
   If no, continue to #4.

4. Does the patient have a diagnosis of recurrent locoregional disease or metastatic squamous cell carcinoma of the head and neck **AND** meet the following criterion?
   - The requested medication is being used in combination with platinum-based therapy (such as cisplatin, carboplatin, or oxaliplatin) and 5-fluorouracil (5-FU) as first-line treatment

   If yes, **approve for 12 months by HICL.**
   If no, continue to #5.

CONTINUED ON NEXT PAGE

CETUXIMAB (NSA)

GUIDELINES FOR USE (CONTINUED)

5. Does the patient have a diagnosis of recurrent or metastatic squamous cell carcinoma of the head and neck and meet **ALL** of the following criteria?
   - The requested medication will be used as a single agent
   - The patient has failed prior platinum-based therapy (such as cisplatin, carboplatin, or oxaliplatin)

   If yes, **approve for 12 months by HICL.**
   If no, do not approve.
   DENIAL TEXT: See the denial text at the end of the guideline.

DENIAL TEXT: The guideline named **CETUXIMAB (Erbitux)** requires a diagnosis of metastatic colorectal cancer (mCRC), locally or regionally advanced squamous cell carcinoma of the head and neck, recurrent locoregional disease or metastatic squamous cell carcinoma of the head and neck, OR recurrent or metastatic squamous cell carcinoma of the head and neck. In addition, the following criteria must be met:

For the diagnosis of metastatic colorectal cancer (mCRC), approval requires:
- Patient's cancer is wild type KRAS (no mutation) as determined by FDA approved tests
- Patient's cancer is epidermal growth factor receptor (EGFR)-expressing as determined by FDA approved tests
- In addition, **ONE** of the following must be met:
  - The requested medication is being used in combination with FOLFIRI (irinotecan, 5-fluorouracil, leucovorin) for first-line treatment
  - The requested medication is being used in combination with irinotecan in patients who are refractory to irinotecan-based chemotherapy
  - The requested medication is being used as a single agent AND the patient has failed oxaliplatin-based and irinotecan-based chemotherapy unless patient is intolerant to irinotecan

For the diagnosis of locally or regionally advanced squamous cell carcinoma of the head and neck, approval requires:
- The requested medication will be used in combination with radiation therapy

For the diagnosis of recurrent locoregional disease or metastatic squamous cell carcinoma of the head and neck, approval requires:
- The requested medication is being used in combination with platinum-based therapy (such as cisplatin, carboplatin, or oxaliplatin) and 5-fluorouracil (5-FU) as first-line treatment

For the diagnosis of recurrent or metastatic squamous cell carcinoma of the head and neck, approval requires:
- The requested medication will be used as a single agent
- The patient has failed prior platinum-based therapy (such as cisplatin, carboplatin, or oxaliplatin)

CONTINUED ON NEXT PAGE

CETUXIMAB (NSA)

RATIONALE
To ensure appropriate use of Erbitux consistent with FDA approved indications.

FDA APPROVED INDICATIONS
Erbitux is an epidermal growth factor receptor (EGFR) antagonist indicated for treatment of:

Head and Neck Cancer
- Locally or regionally advanced squamous cell carcinoma of the head and neck in combination with radiation therapy.
- Recurrent locoregional disease or metastatic squamous cell carcinoma of the head and neck in combination with platinum-based therapy with 5-FU.
- Recurrent or metastatic squamous cell carcinoma of the head and neck progressing after platinum-based therapy.

Colorectal Cancer
K-Ras mutation-negative (wild-type), EGFR-expressing, metastatic colorectal cancer as determined by FDA-approved tests:
- in combination with FOLFIRI for first-line treatment,
- in combination with irinotecan in patients who are refractory to
- irinotecan-based chemotherapy,
- as a single agent in patients who have failed oxaliplatin- and irinotecan-based chemotherapy or who are intolerant to irinotecan.

DOSAGE AND ADMINISTRATION
- Do not administer Erbitux as an intravenous push or bolus
- Administer via infusion pump or syringe pump. Do not exceed an infusion rate of 10 mg/min
- Premedicate with an H1 antagonist
- Administer 400 mg/m2 initial dose as a 120-minute intravenous infusion followed by 250 mg/m2 weekly infused over 60 minutes
- Initiate Erbitux one week prior to initiation of radiation therapy. Complete Erbitux administration 1 hour prior to platinum-based therapy with 5-FU and FOLFIRI
- Reduce the infusion rate by 50% for NCI CTC Grade 1 or 2 infusion reactions and non-serious NCI CTC Grade 3 infusion reaction
- Permanently discontinue for serious infusion reactions

Withhold infusion for severe, persistent acneiform rash. Reduce dose for recurrent, severe rash

REFERENCES
- Erbitux [Prescribing Information]. Princeton, NJ: Bristol-Myers Squibb, November 2017.

CONTINUED ON NEXT PAGE

CETUXIMAB (NSA)

Library	Commercial	NSA
Yes	No	Yes

Part D Effective: N/A
Commercial Effective: 03/12/18

Created: 02/13
Client Approval: 02/18

P&T Approval: 02/13

COPANLISIB (NSA)

Generic	Brand	HICL	GCN	Exception/Other
COPANLISIB	ALIQOPA	44503		

GUIDELINES FOR USE

1. Does the patient have a diagnosis of relapsed follicular lymphoma (FL) and meet the following criteria?
   - The patient is 18 years of age or older
   - The patient has received at least two prior systemic therapies for follicular lymphoma (FL)

   If yes, **approve for 12 months by HICL with a quantity limit of #3 vials per 28 days.**
   If no, do not approve.
   DENIAL TEXT: The guideline named **COPANLISIB (Aliqopa)** requires that the following criteria be met:
   - A diagnosis of relapsed follicular lymphoma (FL)
   - The patient is 18 years of age or older
   - The patient has received at least two prior systemic therapies for follicular lymphoma (FL)

RATIONALE
Promote appropriate utilization of COPANLISIB based on FDA approved indication and dosing.

FDA APPROVED INDICATION
ALIQOPA is indicated for the treatment of adult patients with relapsed follicular lymphoma (FL) who have received at least two prior systemic therapies.

DOSAGE AND ADMINISTRATION
ALIQOPA is administered as a 1-hour intravenous infusion of a 60 mg dose, on Days 1, 8, and 15 of a 28-day treatment cycle on an intermittent schedule (three weeks on and one week off), until disease progression or unacceptable toxicity.

AVAILABLE STRENGTHS
Injection: supplied as a sterile lyophilized solid, white to slightly yellowish in appearance, in a single-dose vial for reconstitution and further dilution. After reconstitution, the solution is colorless to slightly yellowish. Each vial contains 60 mg of ALIQOPA free base.

REFERENCES
- Aliqopa [Prescribing Information]. Bayer HealthCare Pharmaceuticals Inc.: Whippany, NJ. August 2017.

CONTINUED ON NEXT PAGE

COPANLISIB (NSA)

Library	Commercial	NSA
Yes	No	Yes

Part D Effective: N/A
Commercial Effective: 01/01/18
Created: 09/17
Client Approval: 12/17
P&T Approval: 10/17

CORTICOTROPIN (NSA)

Generic	Brand	HICL	GCN	Exception/Other
CORTICOTROPIN	H.P. ACTHAR GEL	02830		ROUTE = INJECTION

This drug requires a written request for prior authorization.

GUIDELINES FOR USE

1. Is the patient less than two years old and diagnosed with infantile spasms?

   If yes, **approve for 28 days with a maximum of #8 vials (each 5mL vial contains 400 units).**
   If no, do not approve.
   DENIAL TEXT: The guideline named **CORTICOTROPIN (H.P. Acthar Gel)** requires a diagnosis of infantile spasms in patients less than 2 years of age. For all other FDA indications, consider the use of IV corticosteroids.
   FDA approved indications include: infantile spasm, acute multiple sclerosis, psoriatic arthritis, rheumatoid arthritis including juvenile rheumatoid arthritis, ankylosing spondylitis, systemic lupus erythematosus or systemic dermatomyositis (polymyositis), severe erythema multiforme, Stevens-Johnson syndrome, serum sickness, severe acute and chronic allergic and inflammatory processes involving the eye and its adnexa (such as keratitis, iritis, iridocyclitis, diffuse posterior uveitis and choroiditis, optic neuritis, chorioretinitis, and anterior segment inflammation), symptomatic sarcoidosis, or to induce a diuresis or a remission of proteinuria in the nephrotic syndrome without uremia of the idiopathic type, or that due to lupus erythematosus.

RATIONALE
Ensure appropriate therapeutic use of this long acting corticotropin formulation.

The recommended regimen for use in infantile spasms is a daily dose of 150 units/m^2 (divided into twice daily intramuscular injections of 75 units/ m^2) then a gradual taper over a 2-week period. A suggested taper schedule is 30 units/ m^2 every morning for 3 days, 15 units/ m^2 every morning for 3 days, 10 units/ m^2 every morning for 3 days, and then 10 units/ m^2 every other morning for 6 days.

8 vials per 28 days supply based on dosage of 150 units/m^2/day with an estimate of 0.7m^2 body surface area, estimated maximum for a child less than 40 pounds (two years old).

The American Academy of Neurology guidelines for treatment of infantile spasms state that response is usually within 2 weeks and current clinical data is insufficient to determine optimum dosage and duration.

CONTINUED ON NEXT PAGE

CORTICOTROPIN (NSA)

RATIONALE (CONTINUED)

Questcor states that the H.P. Acthar Gel vial expires 28 days after initial puncture, when stored under ideal conditions (per USP standard guidelines).

FDA APPROVED INDICATIONS
Acthar Gel is indicated for the treatment of infantile spasms, for acute exacerbations of multiple sclerosis, and for numerous other diseases and disorders. (See below).

INFANTILE SPASMS: Monotherapy for the treatment of infantile spasms in infants and children under 2 years of age.

MULTIPLE SCLEROSIS: Treatment of acute exacerbations of multiple sclerosis in adults. Controlled clinical trials have shown H.P. Acthar Gel to be effective in speeding the resolution of acute exacerbations of multiple sclerosis. However, there is no evidence that it affects the ultimate outcome or natural history of the disease.

RHEUMATIC DISORDERS: As adjunctive therapy for short-term administration (to tide the patient over an acute episode or exacerbation) in: psoriatic arthritis, rheumatoid arthritis, including juvenile rheumatoid arthritis (selected cases may require low-dose maintenance therapy), and ankylosing spondylitis.

COLLAGEN DISEASES: During an exacerbation or as maintenance therapy in selected cases of systemic lupus erythematosus or systemic dermatomyositis (polymyositis).

DERMATOLOGIC DISEASES: Severe erythema multiforme (Stevens-Johnson syndrome).

ALLERGIC STATES: Serum sickness.

OPHTHALMIC DISEASES: Severe acute and chronic allergic and inflammatory processes involving the eye and its adnexa such as: keratitis, iritis, iridocyclitis, diffuse posterior uveitis and choroiditis, optic neuritis, chorioretinitis, and anterior segment inflammation.

RESPIRATORY DISEASES: Symptomatic sarcoidosis.

EDEMATOUS STATE: To induce a diuresis or a remission of proteinuria in the nephrotic syndrome without uremia of the idiopathic type or that due to lupus erythematosus.

CONTINUED ON NEXT PAGE

CORTICOTROPIN (NSA)

REFERENCES

- Amphastar Pharmaceuticals, Inc. Cortrosyn package insert. Rancho Cucamonga, CA. September 2005.
- Baram TZ, Mitchell WG et al. High-dose corticotropin (ACTH) versus prednisone for infantile spasms; a prospective, randomized, blinded study. Pediatrics 1996; 97:375–379.
- CDC child growth charts (birth to 36 months for boys and girls). Last modified 4/20/2001. Accessible online at http://www.cdc.gov/growthcharts/data/set2clinical/cj41l067.pdf [Accessed June 28, 2011].
- Gettig J, Cummings J, and Matuszewski K. H.P. Acthar Gel and Cosyntropin Review. Pharmacy and Therapeutics 2009; 34 (5): 250-252.
- Mackay MT, Weiss, SK, Adams-Webber, T et al. Practice Parameter: Medical Treatment of Infantile Spasms Report of the American Academy of Neurology and the Child Neurology Society. Neurology 2004; 62:1668–1681. Accessible online at http://www.neurology.org/content/62/10/1668.full.pdf [Accessed June 28, 2011].
- Questcor Pharmaceuticals, Inc. HP Acthar Gel package insert. Hayward, CA. June 2011.
- Micromedex® Healthcare Series [database online]. Greenwood Village, Colo: Thomson Healthcare. Available at: http://www.thomsonhc.com/micromedex2/librarian. [Accessed: June 28, 2011].
- Riikonen R. A long-term follow-up study of 214 children with the syndrome of infantile spasms. Neuropediatrics. 1982; 13:14–23.

Library	Commercial	NSA
Yes	No	Yes

Part D Effective: N/A
Commercial Effective: 10/01/17
Created: 11/07
Client Approval: 08/17
P&T Approval: 07/17

DARATUMUMAB (NSA)

Generic	Brand	HICL	GCN	Exception/Other
DARATUMUMAB	DARZALEX	42814		

This drug requires a written request for prior authorization.

GUIDELINES FOR USE

1. Does the patient have a diagnosis of multiple myeloma and meet **ALL** of the following criteria?
   - The patient has received at least three prior lines of therapy, including agents from **BOTH** of the following drug classes:
     - Proteasome inhibitors (PI): bortezomib (Velcade), carfilzomib (Kyprolis), ixazomib (Ninlaro)
     - Immunomodulatory agents: lenalidomide (Revlimid), pomalidomide (Pomalyst), thalidomide (Thalomid)
   - The requested medication will be used as monotherapy (not in combination with a proteasome inhibitor or immunomodulatory agent)

   If yes, **approve for 12 months by HICL.**
   If no, continue to #2.

2. Does the patient have a diagnosis of multiple myeloma and meet **ALL** of the following criteria?
   - The patient is refractory to both a proteasome inhibitor (PI) (bortezomib (Velcade), carfilzomib (Kyprolis), or ixazomib (Ninlaro)) **AND** an immunomodulatory agent (lenalidomide (Revlimid), pomalidomide (Pomalyst), or thalidomide (Thalomid))
   - The requested medication will be used as monotherapy (not in combination with a proteasome inhibitor or immunomodulatory agent)

   If yes, **approve for 12 months by HICL.**
   If no, continue to #3.

3. Does the patient have a diagnosis of multiple myeloma and meet **ALL** of the following criteria?
   - The patient has received at least one prior line of therapy
   - The requested medication will be used in combination with lenalidomide and dexamethasone **OR** in combination with bortezomib and dexamethasone

   If yes, **approve for 12 months by HICL.**
   If no, continue to #4.

CONTINUED ON NEXT PAGE

DARATUMUMAB (NSA)

GUIDELINES FOR USE (CONTINUED)

4. Does the patient have a diagnosis of multiple myeloma and meet **ALL** of the following criteria?
   - The patient has received at least two prior lines of therapy, including lenalidomide and a proteasome inhibitor (PI) (bortezomib (Velcade), carfilzomib (Kyprolis), ixazomib (Ninlaro))
   - The requested medication will be used in combination with pomalidomide and dexamethasone

   If yes, **approve for 12 months by HICL.**
   If no, continue to #5.

5. Does the patient have a newly diagnosed multiple myeloma and meet **ALL** of the following criteria?
   - The patient is ineligible for autologous stem cell transplant
   - The requested medication will be used in combination with bortezomib (Velcade), melphalan and prednisone [VMP]

   If yes, **approve for 12 months by HICL.**
   If no, do not approve.
   DENIAL TEXT: The guideline named **DARATUMUMAB (Darzalex)** requires a diagnosis of multiple myeloma and that the patient meets **ONE** of the following criteria:
   - The patient has received at least three prior lines of therapy, including a proteasome inhibitor (PI) and an immunomodulatory agent **AND** will receive daratumumab as monotherapy
   - The patient is refractory to both a proteasome inhibitor (PI) and an immunomodulatory agent **AND** will receive daratumumab as monotherapy
   - The patient has received at least one prior line of therapy **AND** will receive daratumumab in combination with lenalidomide and dexamethasone **OR** in combination with bortezomib and dexamethasone
   - The patient has received at least two prior lines of therapy, including lenalidomide and a proteasome inhibitor (PI) **AND** will receive daratumumab in combination with pomalidomide and dexamethasone
   - The patient is newly diagnosed with multiple myeloma, ineligible for autologous stem cell transplant, **AND** will receive daratumumab in combination with bortezomib, melphalan and prednisone

   Proteasome inhibitors include: bortezomib, carfilzomib, or ixazomib; immunomodulatory agents include: lenalidomide, pomalidomide, or thalidomide.

CONTINUED ON NEXT PAGE

DARATUMUMAB (NSA)

RATIONALE
To ensure appropriate use of daratumumab (Darzalex) consistent with FDA-approved indications.

FDA-APPROVED INDICATIONS
Daratumumab (Darzalex) is a human CD38-directed monoclonal antibody indicated:

- In combination with bortezomib (Velcade), melphalan, and prednisone for the treatment of patients who are newly diagnosed with multiple myeloma who are ineligible for autologous stem cell transplant.
- In combination with lenalidomide and dexamethasone, or bortezomib and dexamethasone, for the treatment of patients with multiple myeloma who have received at least one prior therapy.
- In combination with pomalidomide and dexamethasone for the treatment of patients with multiple myeloma who have received at least two prior therapies including lenalidomide and a proteasome inhibitor.
- As monotherapy, for the treatment of patients with multiple myeloma who have received at least three prior lines of therapy including a proteasome inhibitor (PI) and an immunomodulatory agent or who are double-refractory to a PI and an immunomodulatory agent.

DOSAGE AND ADMINISTRATION
Pre-medicate with corticosteroids, antipyretics and antihistamines.

Dilute and administer as an intravenous infusion. See prescribing information for dilution volume and rate titration.

Darzalex should be administered by a healthcare professional, with immediate access to emergency equipment and appropriate medical support to manage infusion reactions if they occur.

The recommended dose is 16mg/kg actual body weight.

Table 1. Darzalex dosing schedule for monotherapy and in combination with lenalidomide or pomalidomide and low-dose dexamethasone (4-week cycle dosing regimen)

Schedule	Weeks
Weekly	Weeks 1 to 8 (total of 8 doses)
Every two weeks	Weeks 9 to 24 (total of 8 doses)
Every four weeks	Week 25 onwards until disease progression

Table 2. Darzalex dosing schedule in combination with bortezomib and dexamethasone (3-week cycle dosing regimen)

Schedule	Weeks
Weekly	Weeks 1 to 9 (total of 9 doses)
Every three weeks	Weeks 10 to 24 (total of 5 doses)
Every four weeks	Week 25 onwards until disease progression

CONTINUED ON NEXT PAGE

DARATUMUMAB (NSA)

FDA-APPROVED INDICATIONS (CONTINUED)

DOSAGE AND ADMINISTRATION

Table 3. Darzalex dosing schedule in combination with bortezomib (Velcade), melphalan and prednisone ([VMP], 6-week cycle dosing regimen)

Schedule	Weeks
Weekly	Weeks 1 to 6 (total of 6 doses)
Every three weeks	Weeks 7 to 54 (total of 16 doses)
Every four weeks	Week 55 onwards until disease progression

Administer post-infusion medication as follows to reduce the risk of delayed infusion reactions for patients receiving daratumumab as monotherapy. Consider in other patients.

- Oral corticosteroid (20mg methylprednisolone or equivalent dose of a corticosteroid in accordance with local standards) on the first and second day after all infusions.

REFERENCES

- Darzalex [Prescribing Information]. Horsham, PA: Janssen Biotech, Inc.; May 2018.

Library	Commercial	NSA
Yes	No	Yes

Part D Effective: N/A
Commercial Effective: 06/15/18
Created: 12/15
Client Approval: 05/18
P&T Approval: 07/18

DAUNORUBICIN/CYTARABINE LIPOSOME (NSA)

Generic	Brand	HICL	GCN	Exception/Other
DAUNORUBICIN/ CYTARABINE LIPOSOME	VYXEOS	44461		ROUTE = INTRAVEN.

GUIDELINES FOR USE

1. Does the patient have a diagnosis of acute myeloid leukemia (AML) and meet **ALL** of the following criteria?
   - The patient has newly diagnosed therapy-related acute myeloid leukemia (t-AML) **OR** AML with myelodysplasia-related changes (AML-MRC)
   - The patient is 18 years of age or older

   If yes, **approve for 12 months by HICL.**
   If no, do not approve.
   DENIAL TEXT: The guideline named **DAUNORUBICIN/CYTARABINE LIPOSOME (Vyxeos)** requires a new diagnosis of therapy-related acute myeloid leukemia or acute myeloid leukemia with myelodysplasia-related changes in adult patients.

RATIONALE
Promote appropriate utilization of DAUNORUBICIN/CYTARABINE LIPOSOME based on FDA approved indication.

DOSAGE
VYXEOS is a liposome available as a single-dose vial for reconstitution. VYXEOS is administered via intravenous infusion over 90 minutes. A full VYXEOS course consists of 1-2 cycles of Induction and up to 2 cycles of Consolidation:

- First Induction Cycle: (daunorubicin 44 mg/m^2 and cytarabine 100 mg/m^2) liposome days 1, 3, and 5
- Second Induction Cycle: (daunorubicin 44 mg/m^2 and cytarabine 100 mg/m^2) liposome days 1 and 3 [administered 2 to 5 weeks after the first induction cycle, only for those patients failing to achieve a response with the first induction cycle]
- Consolidation Cycle: (daunorubicin 29 mg/m^2 and cytarabine 65 mg/m^2) liposome days 1 and 3

For patients who do not achieve remission with the first induction cycle, a second induction cycle may be administered 2 to 5 weeks after the first if there was no unacceptable toxicity with VYXEOS. Administer the first consolidation cycle 5 to 8 weeks after the start of the last induction.

For hypersensitivity reactions of any grade/severity, interrupt VYXEOS infusion immediately and manage symptoms. Reduce the rate of infusion or discontinue treatment. Discontinue VYXEOS in patients who exhibit impaired cardiac function unless the benefit of continuing treatment outweighs the risk.

CONTINUED ON NEXT PAGE

DAUNORUBICIN/CYTARABINE LIPOSOME (NSA)

FDA APPROVED INDICATION

VYXEOS is indicated for the treatment of adults with newly-diagnosed therapy-related acute myeloid leukemia or acute myeloid leukemia with myelodysplasia-related changes.

REFERENCES

- Vyxeos [Prescribing Information]. Palo Alto, CA: Jazz Pharmaceuticals, Inc. August 2017.

Library	Commercial	NSA
No	No	Yes

Part D Effective: N/A
Commercial Effective: 01/01/18
Created: 08/17
Client Approval: 12/17
P&T Approval: 10/17

DENOSUMAB-PROLIA (NSA)

Generic	Brand	HICL	GCN	Exception/Other
DENOSUMAB	PROLIA		28656	

GUIDELINES FOR USE

1. Does the patient have osteoporosis **AND** meet **ONE** of the following criteria?
   - Unable to use oral therapy (upper GI problems - unable to tolerate oral medication, lower GI problems - unable to absorb oral medications, trouble remembering to take oral medications or coordinating an oral bisphosphonate with other oral medications or their daily routine)
   - Meets **BOTH** of the following criteria:
     - o High risk for fractures defined as **ONE** of the following:
       - History of osteoporotic fracture(s)
       - 2 or more risk factors for fracture (e.g., history of multiple recent low trauma fractures, BMD T-score -2.5 or less, corticosteroid use, or use of GnRH analogs such as nafarelin, etc.)
       - Pre-treatment FRAX score ≥ 20% for any major fracture OR ≥ 3% for hip fracture
     - o Previous trial of, or a contraindication to bisphosphonates (e.g., Reclast, Fosamax, Actonel, or Boniva)

   If yes, **approve for 2 fills by GPID for #1mL (#1 pre-filled syringe) per fill with an end date of 12 months.**
   If no, continue to #2.

2. Is the patient receiving adjuvant aromatase inhibitor therapy for breast cancer and meet **ALL** of the following criteria?
   - High risk for fractures defined as **ONE** of the following:
     - o History of osteoporotic fracture(s)
     - o 2 or more risk factors for fracture (e.g., history of multiple recent low trauma fractures, BMD T-score -2.5 or less, corticosteroid use, or use of GnRH analogs such as nafarelin, etc.)
     - o Pre-treatment FRAX score ≥ 20% for any major fracture OR ≥ 3% for hip fracture
   - Previous trial of, or a contraindication to bisphosphonates (e.g., Reclast, Fosamax, Actonel, or Boniva)

   If yes, **approve for 2 fills by GPID for #1mL (#1 pre-filled syringe) per fill with an end date of 12 months.**
   If no, continue to #3.

CONTINUED ON NEXT PAGE

DENOSUMAB-PROLIA (NSA)

GUIDELINES FOR USE (CONTINUED)

3. Is the patient receiving androgen deprivation therapy for non-metastatic prostate cancer and meet **ALL** of the following criteria?
   - High risk for fractures defined as **ONE** of the following:
     - o History of osteoporotic fracture(s)
     - o 2 or more risk factors for fracture (e.g., history of multiple recent low trauma fractures, BMD T-score -2.5 or less, corticosteroid use, or use of GnRH analogs such as nafarelin, etc.)
     - o Pre-treatment FRAX score ≥ 20% for any major fracture OR ≥ 3% for hip fracture
   - Previous trial of, or a contraindication to bisphosphonates (e.g., Reclast, Fosamax, Actonel, or Boniva)

   If yes, **approve 2 fills by GPID for #1mL (#1 pre-filled syringe) per fill with an end date of 12 months.**
   If no, do not approve.
   DENIAL TEXT: See the denial text at the end of the guideline.

DENIAL TEXT: The guideline named **DENOSUMAB (Prolia)** requires that the patient have a diagnosis of osteoporosis, that the patient is receiving androgen deprivation therapy for non-metastatic prostate cancer, or that the patient is receiving adjuvant aromatase inhibitor therapy for breast cancer. In addition, the following criteria must be met:

For osteoporosis, approval requires one of the following:

- Unable to use oral therapy (upper GI problems - unable to tolerate oral medication, lower GI problems - unable to absorb oral medications, trouble remembering to take oral medications or coordinating an oral bisphosphonate with other oral medications or their daily routine)
- Meets **BOTH** of the following criteria:
- o High risk for fractures defined as **ONE** of the following:
  - History of osteoporotic fracture(s)
  - 2 or more risk factors for fracture (e.g., history of multiple recent low trauma fractures, BMD T-score -2.5 or less, corticosteroid use, or use of GnRH analogs such as nafarelin, etc.)
  - Pre-treatment FRAX score ≥ 20% for any major fracture OR ≥ 3% for hip fracture
- o Previous trial of, or a contraindication to bisphosphonates (e.g., Reclast, Fosamax, Actonel, or Boniva)

(Denial text continued on next page)

CONTINUED ON NEXT PAGE

DENOSUMAB-PROLIA (NSA)

GUIDELINES FOR USE (CONTINUED)

For breast cancer, approval requires all of the following:

- High risk for fractures defined as **ONE** of the following:
  - History of osteoporotic fracture(s)
  - 2 or more risk factors for fracture (e.g., history of multiple recent low trauma fractures, BMD T-score -2.5 or less, corticosteroid use, or use of GnRH analogs such as nafarelin, etc.)
  - Pre-treatment FRAX score ≥ 20% for any major fracture OR ≥ 3% for hip fracture
- Previous trial of, or a contraindication to bisphosphonates (e.g., Reclast, Fosamax, Actonel, or Boniva)

For prostate cancer, approval requires all of the following:

- High risk for fractures defined as **ONE** of the following:
  - History of osteoporotic fracture(s)
  - 2 or more risk factors for fracture (e.g., history of multiple recent low trauma fractures, BMD T-score -2.5 or less, corticosteroid use, or use of GnRH analogs such as nafarelin, etc.)
  - Pre-treatment FRAX score ≥ 20% for any major fracture OR ≥ 3% for hip fracture
- Previous trial of, or a contraindication to bisphosphonates (e.g., Reclast, Fosamax, Actonel, or Boniva)

RATIONALE

To ensure appropriate use of denosumab based on FDA and Compendia approved indication and dosing.

Prolia Dosing:

- Prolia should be administered by a healthcare professional
- Administer 60 mg every 6 months as a subcutaneous injection in the upper arm, upper thigh, or abdomen
- Instruct patients to take calcium 1000 mg daily and at least 400 IU vitamin D daily

Per American Association of Clinical Endocrinologists and American College of Endocrinology (AACE/ACE) medical guidelines for clinical practice for the diagnosis and treatment of postmenopausal osteoporosis, alendronate, risedronate, zoledronic acid, and denosumab are first line therapy for postmenopausal women with osteoporosis. The Endocrine Society guidelines for the treatment of osteoporosis in men indicate bisphosphonates and denosumab as appropriate therapy for treatment.

National Comprehensive Cancer Network (NCCN) state the use of a bisphosphonate is generally the preferred intervention to improve bone mineral density for female patients receiving aromatase inhibitors. The NCCN also state denosumab, zoledronic acid, or alendronate are recommended for male patients receiving androgen replacement therapy when absolute fracture risk warrants drug therapy.

CONTINUED ON NEXT PAGE

DENOSUMAB-PROLIA (NSA)

FDA APPROVED INDICATIONS

Prolia is a RANK ligand (RANKL) inhibitor indicated for:

- Treatment of postmenopausal women with osteoporosis at high risk for fracture.
- Treatment to increase bone mass in men with osteoporosis at high risk for fracture.
- Treatment to increase bone mass in men at high risk for fracture receiving androgen deprivation therapy for non-metastatic prostate cancer.
- Treatment to increase bone mass in women at high risk for fracture receiving adjuvant aromatase inhibitor therapy for breast cancer.

REFERENCES

- Amgen. Prolia package insert. Thousand Oaks, CA. January 2017.
- Truven Health Analytics. Monograph Name. DRUGDEX® System [database online]. Greenwood Village, CO. Available at: http://www.micromedexsolutions.com/. [Accessed: April 13, 2017].
- National Comprehensive Cancer Network. Prostate Cancer. Version 1.2015. Accessed online October 16, 2015 at: http://www.nccn.org/professionals/physician_gls/pdf/prostate.pdf
- National Comprehensive Cancer Network. Breast Cancer. Version 3.2015. Accessed online October 16, 2015 at: http://www.nccn.org/professionals/physician_gls/pdf/breast.pdf
- Endocrine Society Clinical Guidelines: Osteoporosis in Men. Accessed online April 13, 2017 at: www.endocrine.org
- American Association of Clinical Endocrinologists and American College of Endocrinology (AACE/ACE) medical guidelines for clinical practice for the diagnosis and treatment of postmenopausal osteoporosis. Accessed online April 13, 2017 at: www.aace.com

Library	Commercial	NSA
Yes	No	Yes

Part D Effective: N/A
Commercial Effective: 07/01/17

Created: 07/10
Client Approval: 05/17

P&T Approval: 04/17

DENOSUMAB-XGEVA (NSA)

Generic	Brand	HICL	GCN	Exception/Other
DENOSUMAB	XGEVA		29261	

This drug requires a written request for prior authorization.

GUIDELINES FOR USE

1. Does the patient have a diagnosis of multiple myeloma OR bone metastases from a solid tumor **AND** meet the following criterion?
   - Xgeva is being used to prevent skeletal-related events (e.g., bone fractures or bone pain requiring radiation)

   If yes, **approve for 12 months by GPID for #1 (1.7mL) vial per 28 days.**
   If no, continue to #2.

2. Does the patient have a diagnosis of giant cell tumor of bone that is unresectable or where surgical resection is likely to result in severe morbidity?

   If yes, **approve and enter two authorizations as follows:**
   - **Approve for 1 month by GPID for #3 (5.1mL) vials per 28 days.**
   - **Approve for 11 months by GPID for #1 (1.7mL) vial per 28 days with a start date after the end date of the first authorization.**

   If no, continue to #3.

3. Does the patient have a diagnosis of hypercalcemia of malignancy **AND** meet the following criterion?
   - The patient is refractory to bisphosphonate therapy (e.g., Fosamax, Actonel, or Boniva)

   If yes, **approve and enter two authorizations as follows:**
   - **Approve for 1 month by GPID for #3 (5.1mL) vials per 28 days.**
   - **Approve for 11 months by GPID for #1 (1.7mL) vial per 28 days with a start date after the end date of the first authorization.**

   If no, do not approve.
   DENIAL TEXT: The guideline named **DENOSUMAB (Xgeva)** requires that ONE of the following criteria is met:
   - Diagnosis of multiple myeloma OR bone metastases from solid tumors AND the requested medication is being used to prevent skeletal-related events (e.g., bone fractures or bone pain requiring radiation)
   - Diagnosis of giant cell tumor of bone that is unresectable or where surgical resection is likely to result in severe morbidity
   - Diagnosis of hypercalcemia of malignancy that is refractory to bisphosphonate therapy (e.g., Fosamax, Actonel, or Boniva)

CONTINUED ON NEXT PAGE

DENOSUMAB-XGEVA (NSA)

RATIONALE
To ensure appropriate use of denosumab based on FDA approved indication and dosing.

FDA APPROVED INDICATIONS
Xgeva is a RANK ligand (RANKL) inhibitor indicated for:
- Prevention of skeletal-related events in patients with multiple myeloma and bone metastases from solid tumors
- Treatment of adults and skeletally mature adolescents with giant cell tumor of bone that is unresectable or where surgical resection is likely to result in severe morbidity
- Treatment of hypercalcemia of malignancy refractory to bisphosphonate therapy

DOSAGE AND ADMINISTRATION
Xgeva is intended for subcutaneous route only and should not be administered intravenously, intramuscularly, or intradermally.

- Multiple Myeloma and Bone Metastasis from Solid Tumors: Administer 120 mg every 4 weeks as a subcutaneous injection in the upper arm, upper thigh, or abdomen. Administer calcium and vitamin D as necessary to treat or prevent hypocalcemia
- Giant Cell Tumor of Bone: Administer 120 mg every 4 weeks with additional 120 mg doses on Days 8 and 15 of the first month of therapy. Administer subcutaneously in the upper arm, upper thigh, or abdomen. Administer calcium and vitamin D as necessary to treat or prevent hypocalcemia
- Hypercalcemia of Malignancy: Administer 120 mg every 4 weeks with additional 120 mg doses on Days 8 and 15 of the first month of therapy. Administer subcutaneously in the upper arm, upper thigh, or abdomen.

REFERENCES
- Amgen. Xgeva package insert. Thousand Oaks, CA. January, 2018.

Library	Commercial	NSA
Yes	No	Yes

Part D Effective: N/A
Commercial Effective: 01/29/18
Created: 11/07
Client Approval: 01/18
P&T Approval: 01/18

DINUTUXIMAB

Generic	Brand	HICL	GCN	Exception/Other
DINUTUXIMAB	UNITUXIN	42038		

GUIDELINES FOR USE

1. Does the patient have a diagnosis of high-risk neuroblastoma and meets all the following criteria?
   - Patient is 17 years of age or younger
   - Patient has received an autologous stem cell transplant
   - Patient achieved at least a partial response to chemotherapy given prior to autologous stem cell transplant
   - Patient has not undergone 5 cycles of dinutuximab in the past

   If yes, continue to #2.
   If no, do not approve.
   DENIAL TEXT: See the denial text at the end of the guideline.

2. Will the patient be receiving dinutuximab concurrently with isotretinoin and either Leukine (GM-CSF) or Proleukin (IL-2)?

   If yes, **approve for 12 months by HICL with a fill limit of up to 5 fills.**
   If no, do not approve.
   DENIAL TEXT: See the denial text at the end of the guideline.

DENIAL TEXT: Our guideline for **DINUTUXIMAB** requires a diagnosis of high-risk neuroblastoma. In addition, the following criteria must be met:
- Patient is 17 years of age or younger
- Patient has received an autologous stem cell transplant
- Patient achieved a partial response to chemotherapy given prior to autologous stem cell transplant
- Patient has not undergone 5 cycles of dinutuximab in the past
- Dinutuximab will be used concurrently with isotretinoin and either Leukine or Proleukin

CONTINUED ON NEXT PAGE

DINUTUXIMAB

RATIONALE
Promote appropriate utilization of dinutuximab based on FDA approved indication and dosing.

Unituxin is the first FDA approved medication for the treatment of high-risk neuroblastomas after initial treatment with first-line multi-agent, multimodality therapy, which consists of induction chemotherapy, surgical resection accompanied with radiation, and myeloablative consolidation chemotherapy followed with an autologous stem cell transplant. Following these initial therapies, the prior standard of care was to initiate oral 13-cis-retinoic acid also known as the generic drug isotretinoin, to eradicate residual disease. Unituxin is approved to be given in combination with isotretinoin, IL-2 (marketed as Proleukin [aldesleukin]), and GM-CSF (available as the brand Leukine [sargramostim]) following the initial therapy.

Patients at the highest risk for disease progression and mortality (high-risk neuroblastomas) are those who are older than 18 months of age and have disseminated disease or those with localized disease with unfavorable markers such as MYCN amplification.

FDA APPROVED INDICATION
Unituxin is a GD2-binding monoclonal antibody indicated, in combination with granulocyte-macrophage colony-stimulating factor (GM-CSF), interleukin-2 (IL-2), and 13-cis-retinoic acid (RA), for the treatment of pediatric patients with high-risk neuroblastoma who achieve at least a partial response to prior first-line multiagent, multimodality therapy.

DOSAGE
The recommended daily dose of dinutuximab is 17.5 mg/m2/day as an intravenous infusion over 10 to 20 hours for four consecutive days for a maximum of 5 cycles.

Unituxin is to be used in a regimen containing isotretinoin and either Leukine or Proleukin depending on the cycle. Cycles 1, 3, and 5 are 24 days in duration and Unituxin is given in combination with GM-CSF and RA (see Table 1). Cycles 2 and 4 are 32 days in duration and Unituxin is given in combination with IL-2 and RA (see Table 2).

CONTINUED ON NEXT PAGE

DINUTUXIMAB

DOSAGE (CONTINUED)

Table 1: Dosing Regimen for Cycles 1, 3, and 5 *(from Unituxin Prescribing Information)*

Cycle Day	1	2	3	4	5	6	7	8	9	10	11	12	13	14	15-24
GM-CSF[1]	X	X	X	X	X	X	X	X	X	X	X	X	X	X	
Unituxin[2]				X	X	X	X								
RA[3]											X	X	X	X	X

[1] GM-CSF: 250 µg/m^2/day, administered by either subcutaneous injection (recommended) or IV infusion administered over 2 hours.
[2] Unituxin: 17.5 mg/m^2/day, administered by diluted IV infusion over 10–20 hours.
[3] RA: for >12 kg body weight, 80 mg/m^2 orally twice daily for a total dose of 160 mg/m^2/day; for ≤12 kg body weight, 2.67 mg/kg orally twice daily for a total daily dose of 5.33 mg/kg/day (round dose up to nearest 10 mg).

Table 2: Dosing Regimen for Cycles 2 and 4 *(from Unituxin Prescribing Information)*

Cycle Day	1	2	3	4	5	6	7	8	9	10	11	12-14	15-28	29-32
IL-2[1]	X	X	X	X				X	X	X	X			
Unituxin[2]								X	X	X	X			
RA[3]													X	

[1] IL-2: 3 MIU/m^2/day administered by continuous IV infusion over 96 hours on Days 1-4 and 4.5 MIU/m^2/day on Days 8-11.
[2] Unituxin: 17.5 mg/m^2/day, administered by diluted IV infusion over 10-20 hours.
[3] RA: for >12 kg body weight, 80 mg/m^2 orally twice daily for a total dose of 160 mg/m^2/day; for ≤12 kg body weight, 2.67 mg/kg orally twice daily for a total daily dose of 5.33 mg/kg/day (round dose up to nearest 10 mg).

HOW SUPPLIED

Dinutuximab is supplied in a carton containing one 17.5 mg/5 mL single use vial (NDC 66302-0014-01)

REFERENCES

- Unituxin [Prescribing Information]. United Therapeutics Corp.: Silver Spring, MD. March 2015.
- National Cancer Institution. Neuroblastoma Treatment. Cancer.gov, Available at http://www.cancer.gov/types/neuroblastoma/hp/neuroblastoma-treatment-pdq#section/_214

Library	Commercial	NSA
Yes	No	Yes

Part D Effective: N/A
Commercial Effective: 10/01/15
Created: 07/15
Client Approval: 08/15
P&T Approval: 08/15

DURVALUMAB (NSA)

Generic	Brand	HICL	GCN	Exception/Other
DURVALUMAB	IMFINZI	44230		ROUTE = INTRAVEN.

GUIDELINES FOR USE

1. Does the patient have a diagnosis of locally advanced or metastatic urothelial carcinoma and meet **ONE** of the following criteria?
   - The patient has disease progression on or after treatment with platinum-containing chemotherapy (e.g., cisplatin, carboplatin, oxaliplatin) **OR**
   - The patient has disease progression within 12 months of neoadjuvant or adjuvant treatment with platinum-containing chemotherapy (e.g., cisplatin, carboplatin, oxaliplatin)

   If yes, **approve for 12 months by HICL.**
   If no, continue to #2.

2. Does the patient have a diagnosis of unresectable Stage III non-small cell lung cancer (NSCLC) **AND** meet the following criterion?
   - The patient's disease has not progressed following concurrent platinum-based chemotherapy (e.g., cisplatin, carboplatin, oxaliplatin) and radiation therapy

   If yes, **approve for 12 months by HICL.**
   If no, do not approve.
   DENIAL TEXT: The guideline named **DURVALUMAB (Imfinzi)** requires a diagnosis of locally advanced or metastatic urothelial carcinoma OR unresectable Stage III non-small cell lung cancer (NSCLC). In addition, the following criteria must be met:
   For the diagnosis of locally advanced or metastatic urothelial carcinoma, approval requires ONE of the following:
   - The patient has disease progression on or after treatment with platinum-containing chemotherapy (e.g., cisplatin, carboplatin, oxaliplatin) **OR**
   - The patient has disease progression within 12 months of neoadjuvant or adjuvant treatment with platinum-containing chemotherapy (e.g., cisplatin, carboplatin, oxaliplatin)

   For the diagnosis of unresectable Stage III non-small cell lung cancer (NSCLC), approval requires:
   - The patient's disease has not progressed following concurrent platinum-based chemotherapy (e.g., cisplatin, carboplatin, oxaliplatin) and radiation therapy

CONTINUED ON NEXT PAGE

DURVALUMAB (NSA)

RATIONALE
Promote appropriate utilization of Imfinzi based on FDA approved indication.

FDA APPROVED INDICATIONS
Imfinzi is a programmed death-ligand 1 (PD-L1) blocking antibody indicated for the treatment of patients with:

- Locally advanced or metastatic urothelial carcinoma who:
  - Have disease progression during or following platinum-containing chemotherapy.
  - Have disease progression within 12 months of neoadjuvant or adjuvant treatment with platinum-containing chemotherapy.
  - This indication is approved under accelerated approval based on tumor response rate and duration of response. Continued approval for this indication may be contingent upon verification and description of clinical benefit in confirmatory trials.
- Unresectable Stage III non-small cell lung cancer (NSCLC) whose disease has not progressed following concurrent platinum-based chemotherapy and radiation therapy

DOSAGE AND ADMINISTRATION
Urothelial Carcinoma: The recommended dose of Imfinzi is 10 mg/kg via intravenous infusion over 60 minutes every 2 weeks until disease progression or unacceptable toxicity occurs.

NSCLC: The recommended dose of Imfinzi is 10 mg/kg via intravenous infusion over 60 minutes every 2 weeks until disease progression or unacceptable toxicity, or a maximum of 12 months.

No dose reductions are recommended for adverse reactions. Withhold or discontinue Imfinzi to manage adverse reactions.

REFERENCES
- Imfinzi [Prescribing Information]. AstraZeneca Pharmaceuticals: Wilmington, DE; February 2018.

Library	Commercial	NSA
Yes	No	Yes

Part D Effective: N/A
Commercial Effective: 03/12/18
Created: 08/17
Client Approval: 02/18
P&T Approval: 04/18

ECALLANTIDE (NSA)

Generic	Brand	HICL	GCN	Exception/Other
ECALLANTIDE	KALBITOR	36797		

This drug requires a written request for prior authorization.

GUIDELINES FOR USE

1. Does the patient have a diagnosis of hereditary angioedema and meet **ALL** of the following criteria?
   - Diagnosis is confirmed via complement testing
   - The medication is being used for treatment of acute attacks of hereditary angioedema
   - The patient is 12 years of age or older
   - The medication is prescribed by or given in consultation with an allergist/immunologist or hematologist
   - The medication will be administered by a healthcare professional with appropriate medical support to manage anaphylaxis and/or angioedema

   If yes, **approve for 12 months (up to 12 fills) by HICL with a quantity limit of 12mL per fill.**
   APPROVAL TEXT: Please note that this drug has an important FDA safety warning. For more information, please ask your doctor or pharmacist.

   If no, do not approve.
   DENIAL TEXT: The guideline named **ECALLANTIDE (Kalbitor)** requires a diagnosis of hereditary angioedema. In addition, all of the following criteria must be met:
   - Diagnosis is confirmed via complement testing
   - The medication is being used for treatment of acute attacks of hereditary angioedema
   - The patient is 12 years of age or older
   - The medication is prescribed by or given in consultation with an allergist/immunologist or hematologist
   - The medication will be administered by a healthcare professional with appropriate medical support to manage anaphylaxis and/or angioedema

CONTINUED ON NEXT PAGE

ECALLANTIDE (NSA)

RATIONALE
Ensure appropriate use of Kalbitor (ecallantide) based on FDA-approved indication and dosing/administration.

FDA APPROVED INDICATIONS
Kalbitor (ecallantide) is indicated for treatment of acute attacks of hereditary angioedema in patients 12 years of age and older.

DOSING & ADMINISTRATION
The recommended dose of Kalbitor (ecallantide) is 30mg (3 mL) administered subcutaneously in three 10 mg (1 mL) injections. If the attack persists, an additional dose of 30 mg may be administered within a 24-hour period.

Kalbitor (ecallantide) should only be administered by a healthcare professional with appropriate medical support to manage anaphylaxis and hereditary angioedema.

BOXED WARNING FOR ECALLANTIDE:
Anaphylaxis has been reported after administration of Kalbitor (ecallantide). Because of the risk of anaphylaxis, Kalbitor (ecallantide) should only be administered by a healthcare professional with appropriate medical support to manage anaphylaxis and hereditary angioedema. Healthcare professionals should be aware of the similarity of symptoms between hypersensitivity reactions and hereditary angioedema and patients should be monitored closely. Do not administer Kalbitor (ecallantide) to patients with known clinical hypersensitivity to Kalbitor (ecallantide).

REFERENCES

- Kalbitor [Prescribing Information]. Dyax Corp.: Burlington, MA. March 2015.

Library	Commercial	NSA
Yes	No	Yes

Part D Effective: N/A
Commercial Effective: 03/18/19
Created: 11/13
Client Approval: 03/19
P&T Approval: 07/18

ECULIZUMAB (NSA)

Generic	Brand	HICL	GCN	Exception/Other
ECULIZUMAB	SOLIRIS	34618		

This drug requires a written request for prior authorization.

GUIDELINES FOR USE

1. Does the patient have a diagnosis of Shiga toxin E. coli related hemolytic uremic syndrome (STEC-HUS)?

   If yes, do not approve.
   DENIAL TEXT: See the denial text at the end of the guideline.

   If no, continue to #2.

2. Does the patient have **ONE** of the following diagnoses?
   - Paroxysmal nocturnal hemoglobinuria (PNH)
   - Atypical hemolytic uremic syndrome (aHUS)

   If yes, **approve for 12 months by HICL.**
   APPROVAL TEXT: Please note that this drug has an important FDA safety warning. For more information please ask your doctor or pharmacist.

   If no, continue to #3.

3. Does the patient have a diagnosis of generalized Myasthenia gravis (gMG) and meet **ALL** of the following criteria?
   - The patient is 18 years of age or older
   - The patient's diagnosis is confirmed by a positive Anti-acetylcholine receptor (AchR) antibody test

   If yes, **approve for 12 months by HICL.**
   APPROVAL TEXT: Please note that this drug has an important FDA safety warning. For more information please ask your doctor or pharmacist.

   If no, do not approve.
   DENIAL TEXT: See the denial text at the end of the guideline.

CONTINUED ON NEXT PAGE

ECULIZUMAB (NSA)

GUIDELINES FOR USE (CONTINUED)

DENIAL TEXT: The guideline named **ECULIZUMAB (Soliris)** requires a diagnosis of paroxysmal nocturnal hemoglobinuria (PNH), atypical hemolytic uremic syndrome (aHUS), or generalized Myasthenia gravis (gMG). The following criteria must also be met:

- Eculizumab (Soliris) is NOT being used for Shiga toxin E. coli related hemolytic uremic syndrome (STEC-HUS)

For patients with generalized Myasthenia gravis (gMG), approval requires:

- The patient is 18 years of age or older
- The patient's diagnosis is confirmed by a positive Anti-acetylcholine receptor (AchR) antibody test

RATIONALE

To ensure appropriate use of Soliris based on FDA approved indication and prescribing information.

FDA APPROVED INDICATIONS

Soliris is indicated for paroxysmal nocturnal hemoglobinuria (PNH) to reduce hemolysis, atypical hemolytic uremic syndrome (aHUS) to inhibit complement-mediated thrombotic microangiopathy, and the treatment of adult patients with generalized Myasthenia Gravis (gMG) who are anti-acetylcholine receptor (AchR) antibody positive.

FDA APPROVED INDICATIONS (CONTINUED)

Limitation of Use: Soliris is not indicated for the treatment of patients with Shiga toxin E. coli related hemolytic uremic syndrome (STEC-HUS).

DOSAGE AND ADMINISTRATION

- Healthcare professionals who prescribe Soliris must enroll in the Soliris REMS.
- Vaccinate patients according to current ACIP guidelines to reduce the risk of serious infection.

PNH recommended dosing regimen (for patients 18 years of age and older):

600 mg IV weekly for the first 4 weeks, followed by
900 mg IV for the fifth dose one week later, then
900 mg IV every 2 weeks thereafter

Soliris therapy should be administered at the recommended dosage regimen time points or within two days of these time points.

aHUS recommended dosing regimen (for patients 18 years of age and older

900 mg IV weekly for the first 4 weeks, followed by
1200 mg IV for the fifth dose one week later, then
1200 mg IV every 2 weeks thereafter

CONTINUED ON NEXT PAGE

ECULIZUMAB (NSA)

FDA APPROVED INDICATIONS (CONTINUED)

DOSAGE AND ADMINISTRATION
For patients less than 18 years of age, Soliris should be dosed for aHUS as follows:

Table 1: Dosing Recommendations in Patients Less than 18 years of Age:

Patient Body Weight	Induction	Maintenance
40 kg and over	900 mg weekly x 4 doses	1200 mg at week 5; then 1200 mg every 2 weeks
30 kg to less than 40 kg	600 mg weekly x 2 doses	900 mg at week 3; then 900 mg every 2 weeks
20 kg to less than 30 kg	500 mg weekly x 2 doses	600 mg at week 3; then 600 mg every 2 weeks
10 kg to less than 20 kg	600 mg weekly x 1 dose	300 mg at week 3; then 300 mg every 2 weeks
5 kg to less than 10 kg	300 mg weekly x 1 dose	300 mg at week 3; then 300 mg every 3 weeks

Soliris therapy should be administered at the recommended dosage regimen time points or within two days of these time points.

gMG recommended dosing regimen (for patients 18 years of age and older)
900 mg IV weekly for the first 4 weeks, followed by
1200 mg IV for the fifth dose one week later, then
1200 mg IV every 2 weeks thereafter

Soliris therapy should be administered at the recommended dosage regimen time points or within two days of these time points.

DOSAGE FORMS
Injection: 300 mg single-dose vials each containing 30 mL of 10 mg/mL sterile, colorless, preservative-free eculizumab solution.

CONTINUED ON NEXT PAGE

ECULIZUMAB (NSA)

FDA APPROVED INDICATIONS (CONTINUED)

BOXED WARNING

Soliris contains a black box warning regarding life-threatening and fatal meningococcal infections that have occurred in patients treated with Soliris. The warning advises prescribers to comply with the most current Advisory Committee on Immunization Practices (ACIP) recommendations for meningococcal vaccination in patients with complement deficiencies. Patients should be immunized with a meningococcal vaccine at least 2 weeks prior to administering the first dose of Soliris, unless the risks of delaying Soliris therapy outweigh the risks of developing a meningococcal infection. Patients should be monitored for early signs of meningococcal infections and evaluated immediately if infection is suspected. Soliris is only available through a restricted program under a Risk Evaluation and Mitigation Strategy (REMS). Under the Soliris REMS prescribers must enroll in the program. Enrollment in REMS and other information are available at 1-888-SOLIRIS.

REFERENCES

- Soliris [Prescribing Information]. New Haven, CT: Alexion Pharm.; October 2017.

Library	Commercial	NSA
Yes	No	Yes

Part D Effective: N/A
Commercial Effective: 01/01/18
Created: 08/13
Client Approval: 12/17
P&T Approval: 10/17

EDARAVONE (NSA)

Generic	Brand	HICL	GCN	Exception/Other
EDARAVONE	RADICAVA	44252		

GUIDELINES FOR USE

INITIAL CRITERIA (NOTE: FOR RENEWAL CRITERIA SEE BELOW)

1. Does the patient have a diagnosis of amyotrophic lateral sclerosis (ALS) and meet **ALL** the following?
   - The patient is currently taking riluzole (Rilutek) or has previously tried riluzole (Rilutek)
   - Requested medication is prescribed by or given in consultation with a neurologist or ALS specialist at a ALS Specialty Center or Care Clinic
   - Duration of disease (from onset of symptoms) is less than 2 years
   - Normal Respiratory Function defined as a Forced Vital Capacity (FVC) greater than 80%
   - Mild to moderate ALS disease defined by scores of 2 or higher in all 12 items of the ALSFRS (e.g., speech, salivation, swallowing, handwriting, cutting food, dressing and hygiene, turning in bed, walking, climbing stairs, dyspnea, respiratory insufficiency)

   If yes, **please enter TWO approvals by HICL as follows (total approval duration is 6 months):**
   - **FIRST APPROVAL: approve for 1 month for 1 fill with a quantity limit of #2800mL (twenty-eight 30mg/100mL single-dose bags)**
   - **SECOND APPROVAL: approve for 5 months with a quantity limit of #2000mL (twenty 30mg/100mL single dose bags) per 28 days (Please enter a start date after the end date of the first approval).**

   If no, do not approve.
   DENIAL TEXT: The guideline named **EDARAVONE (Radicava)** requires a diagnosis of amyotrophic lateral sclerosis (ALS) and the following criteria to be met:
   - The patient is currently taking riluzole (Rilutek) or has previously tried riluzole (Rilutek)
   - Requested medication is prescribed by or given in consultation with a neurologist or ALS specialist at a ALS Specialty Center or Care Clinic
   - Duration of disease (from onset of symptoms) is less than 2 years
   - Normal Respiratory Function defined as a Forced Vital Capacity (FVC) greater than 80%
   - Mild to moderate ALS disease defined by scores of 2 or higher in all 12 items of the ALSFRS (e.g., speech, salivation, swallowing, handwriting, cutting food, dressing and hygiene, turning in bed, walking, climbing stairs, dyspnea, respiratory insufficiency)

CONTINUED ON NEXT PAGE

EDARAVONE (NSA)

GUIDELINES FOR USE (CONTINUED)

RENEWAL CRITERIA

1. Does the patient meet **ALL** of the following criteria?
   - Patient has improved or maintained baseline functional ability or demonstrated a less-than-expected decline in functional ability from baseline as measured by functional assessments (e.g., ALSFRS)
   - Patient does not require invasive ventilation
   - Patient has maintained a score of 2 or greater in all 12 items of the ALSFRS-R

   If yes, **approve for 12 months with a quantity limit of #2000mL (twenty 30mg/100mL single dose bags) per 28 days.**

   If no, do not approve.
   DENIAL TEXT: The guideline named **EDARAVONE (Radicava)** requires a diagnosis of amyotrophic lateral sclerosis (ALS) for renewal and the following criteria to be met:
   - Patient has improved or maintained baseline functional ability or demonstrated a less-than-expected decline in functional ability from baseline as measured by functional assessments (e.g., ALSFRS)
   - Patient does not require invasive ventilation
   - Patient has maintained a score of 2 or greater in all 12 items of the ALSFRS-R

RATIONALE
Promote appropriate utilization of **EDARAVONE** based on FDA approved indication and dosing.

FDA APPROVED INDICATIONS
Radicava is indicated for the treatment of amyotrophic lateral sclerosis (ALS).

DOSAGE AND ADMINISTRATION
The recommended dosage of Radicava is an intravenous infusion of 60 mg administered over a 60-minute period according to the following schedule:
- An initial treatment cycle with daily dosing for 14 days, followed by a 14-day drug-free period.
- Subsequent treatment cycles with daily dosing for 10 days out of 14-day periods, followed by 14-day drug-free periods.

CONTINUED ON NEXT PAGE

EDARAVONE (NSA)

AVAILABLE STRENGTHS
Injection: 30 mg/100 mL in a single-dose polypropylene bag; two bags per carton.

The ALSFRS-R is a validated questionnaire-based scale designed to be a clinical rating tool to monitor the progression of patients in clinical practice as well as an outcome measure in clinical trials. The rate of progression of ALS patient population is typically linear, however it is not homogenous, therefore it is difficult to ascertain the general rate of progression for the patient population. The ALSFRS-R scale consists of 12 questions that evaluate the fine motor, gross motor, bulbar, and respiratory function of patients with ALS (speech, salivation, swallowing, handwriting, cutting food, dressing/hygiene, turning in bed, walking, climbing stairs, dyspnea, orthopnea, and respiratory insufficiency). There are four domains: bulbar, fine motor, gross motor and breathing. Each questionnaire item is scored from 0-4, with higher scores representing greater functional ability; the total possible score is 48 points.

CONTINUED ON NEXT PAGE

EDARAVONE (NSA)

FDA APPROVED INDICATIONS (CONTINUED)

Figure 1: ALSFRS-R Questionnaire

Bulbar	Fine Motor	Gross Motor	Breathing

1. Speech
4. Normal speech processes
3. Detectable speech disturbance
2. Intelligible with repeating
1. Speech combined with nonvocal communication
0. Loss of useful speech

2. Salivation
4. Normal
3. Slight but definite excess of saliva in mouth; may have nighttime drooling
2. Moderately excessive saliva; may have minimal drooling
1. Marked excess of saliva with some drooling
0. Marked drooling; requires constant tissue or handkerchief

3. Swallowing
4. Normal eating habits
3. Early eating problems-occasional choking
2. Dietary consistency changes
1. Needs supplemental tube feeding
0. NPO (exclusively parenteral or enteral feeding)

4. Handwriting
4. Normal
3. Slow or sloppy; all words are legible
2. Not all words are legible
1. Able to grip pen but unable to write
0. Unable to grip pen

5a. Cutting Food / Handling Utensils
4. Normal
3. Somewhat slow and clumsy, but no help needed
2. Can cut most foods, although clumsy and slow; some help needed
1. Food must be cut by someone, but can still feed slowly
0. Needs to be fed

5b. Cutting Food / Handling Utensils (Alt. for patients with Gastrostomy)
4. Normal
3. Clumsy but able to perform all manipulations independently
2. Some help needed with closures and fasteners
1. Provides minimal assistance to caregiver
0. Unable to perform any aspect of task

6. Dressing and hygiene
4. Normal function
3. Independent and complete self-care with effort or decreased efficiency
2. Intermittent assistance or substitute methods
1. Needs attendant for self-care
0. Total dependence

7. Turning in bed
4. Normal
3. Somewhat slow and clumsy, but no help needed
2. Can turn alone or adjust sheets, but with great difficulty
1. Can initiate, but not turn or adjust sheets alone
0. Helpless

8. Walking
4. Normal
3. Early ambulation difficulties
2. Walks with assistance
1. Non-ambulatory functional movement only
0. No purposeful leg movement

9. Climbing stairs
4. Normal
3. Slow
2. Mild unsteadiness or fatigue
1. Needs assistance
0. Cannot do

10. Dyspnea
4. None
3. Occurs when walking
2. Occurs with one or more of the following: eating, bathing, dressing (ADL)
1. Occurs at rest, difficulty breathing when either sitting or lying
0. Significant difficulty, considering using mechanical respiratory support

11. Orthopnea
4. None
3. Some difficulty sleeping at night due to shortness of breath. Does not routinely use more than two pillows
2. Needs extra pillow in order to sleep (more than two)
1. Can only sleep sitting up
0. Unable to sleep

12. Respiratory insufficiency
4. None
3. Intermittent use of BiPAP
2. Continuous use of BiPAP
1. Continuous use of BiPAP during the night and day
0. Invasive mechanical ventilation by intubation or tracheostomy

CONTINUED ON NEXT PAGE

EDARAVONE (NSA)

REFERENCES

- Radicava [prescribing information]. Jersey City, NJ: MT Pharma America, Inc.; May 2017. Cedarbaum J, Stambler N, Malt E et al. The ALSFRS-R: a revised ALS functional rating scale that incorporates assessments of respiratory function. J Neurol Sci. 1999 Oct 31;169(1-2):13-21.
- Cedarbaum J, Mitsumoto H, Pestronk A, et al. The ALSFRS @ 20: Evolution of the ALSFRS-R, history, clinimetric properties and future directions [Poster]. Available at: https://cytokinetics.com/wp-content/uploads/2015/10/2011ALS_MND_ASLFRS20.pdf

Library	Commercial	NSA
Yes	No	Yes

Part D Effective: N/A
Commercial Effective: 10/01/17
Created: 08/17
Client Approval: 08/17
P&T Approval: 07/17

ELOSULFASE ALFA

Generic	Brand	HICL	GCN	Exception/Other
ELOSULFASE ALFA	VIMIZIM	40929		

This drug requires a written request for prior authorization.

GUIDELINES FOR USE

1. Does the patient have a diagnosis of Mucopolysaccharidosis type IVA (MPS IVA; Morquio A syndrome)?

   If yes, **approve for lifetime by HICL.**
   If no, do not approve.
   DENIAL TEXT: Our guideline for **ELOSULFASE ALFA** requires a diagnosis of Mucopolysaccharidosis type IVA (MPS IVA; Morquio A syndrome).

RATIONALE
Promote appropriate utilization of Vimizim based on FDA approved indication.

Vimizim is the first agent approved to treat Morquio A syndrome. Prior to the approval of this medication, complications of Morquio A syndrome, such as, skeletal abnormalities, heart disease, hearing and vision loss, and breathing difficulties, are often treated medically and surgically as needed.

Morquio A syndrome, an autosomal recessive lysosomal storage disease, affects approximately 800 individuals in the United States. Morquio A syndrome is classified within a group of diseases called mucopolysaccharidoses (MPS) as MPS IV. Patients with Morquio A syndrome are deficient in the N-acetylgalactosamine-6-sulfate sulfatase (GALNS) enzyme. The first symptoms usually occur at 2-3 years of age. This enzyme deficiency causes difficulties in skeletal development and growth, and patients will typically exhibit symptoms such as abnormal bone development (including the spine), bell-shaped chest with flared ribs at bottom, coarse facial features, widely spaced teeth, hypermobile joints, knock knees, macrocephaly, and short stature. The patient with Morquio A syndrome may have physical exam abnormalities such as kyphoscoliosis, cloudy cornea, aortic regurgitation, enlarged liver, inguinal hernia, and paralysis below the neck due to underdeveloped upper vertebrae.

CONTINUED ON NEXT PAGE

ELOSULFASE ALFA

RATIONALE (CONTINUED)
The most common adverse events observed in clinical trials (occurring in 10% or greater of Vimizim patients) were nausea, vomiting, abdominal pain, chills, headache, pyrexia, and fatigue. In clinical trials 7.7% of patients had anaphylactic reactions and 18.7% had hypersensitivity reactions during or after Vimizim administration.

Vimizim contains a boxed warning regarding the risk of life-threatening anaphylactic reactions that may occur during infusion. Patients must be observed during and after Vimizim infusion by a health care provider trained to manage medical emergencies. Patients with acute febrile or respiratory conditions may be at increased risk due to potential for respiratory compromise during a hypersensitivity reaction; the healthcare provider must carefully consider the patient's clinical condition prior to infusion and consider delaying treatment with Vimizim when appropriate.

The safety and efficacy of Vimizim have not been established in patients less than 5 years old.

DOSAGE
The recommended dose of Vimizim is 2mg per kilogram of body weight administered once weekly as an intravenous infusion. Administer Vimizim over a minimum of 3.5 to 4.5 hours (based on infusion volume). Patients should receive pretreatment with antihistamines, with or without antipyretics, 30 to 60 minutes before administration of Vimizim. If a hypersensitivity reaction occurs during the infusion, administration may be slowed, temporarily stopped or discontinued based on the severity of the reaction. Vimizim should be infused using a low-protein binding infusion set with a low-protein binding 0.2 micrometer in-line filter.

FDA APPROVED INDICATION
Vimizim is a hydrolytic lysosomal glycosaminoglycan (GAG)-specific enzyme indicated for patients with Mucopolysaccharidosis type IVA (MPS IVA; Morquio A syndrome).

REFERENCES

- Vimizim [Prescribing Information]. Novato, CA: Biomarin Pharmaceutical Inc; February 2014.
- FDA Press Announcement on 2/14/14: FDA approves Vimizim to treat rare congenital disorder. Available online at: http://www.fda.gov/NewsEvents/Newsroom/PressAnnouncements/ucm386008.htm Accessed February 24, 2014.

Library	Commercial	NSA
Yes	No	Yes

Part D Effective: N/A
Commercial Effective: 07/01/14
Created: 03/14
Client Approval: 05/14
P&T Approval: 05/14

STANDARD NON-SELF-ADMINISTERED DRUG FORMULARY
PRIOR AUTHORIZATION GUIDELINES

ELOTUZUMAB (NSA)

Generic	Brand	HICL	GCN	Exception/Other
ELOTUZUMAB	EMPLICITI	42842		

This drug requires a written request for prior authorization.

GUIDELINES FOR USE

1. Is the patient 18 years of age or older?

   If yes, continue to #2.
   If no, do not approve.
   DENIAL TEXT: See the denial text at the end of the guideline.

2. Does the patient have a diagnosis of multiple myeloma and meet **ONE** of the following criteria?
   - Empliciti (elotuzumab) will be used in combination with lenalidomide and dexamethasone in patient who has received one to three prior therapies for the treatment of multiple myeloma such as bortezomib, thalidomide, lenalidomide, melphalan, or stem cell transplantation **OR**
   - Empliciti (elotuzumab) will be used in combination with pomalidomide and dexamethasone in patient who has received at least two prior therapies including lenalidomide and a proteasome inhibitor

   If yes, **approve for 12 months by HICL.**
   If no, do not approve.
   DENIAL TEXT: The guideline named **ELOTUZUMAB (Empliciti)** requires a diagnosis of multiple myeloma in adult patients. In addition, ONE of the following must be met for approval:
   - Empliciti must be used in combination with lenalidomide and dexamethasone in patients who have received one to three prior therapies such as bortezomib, thalidomide, lenalidomide, melphalan, or stem cell transplantation OR
   - Empliciti must be used in combination with pomalidomide and dexamethasone in patients who have received at least two prior therapies including lenalidomide and a proteasome inhibitor

RATIONALE
For further information, please refer to the Prescribing Information and/or Drug Monograph for Empliciti.

REFERENCES

- Empliciti [Prescribing Information]. Princeton, NJ: Bristol-Myers Squibb Company; November 2018.

Library	Commercial	NSA
Yes	No	Yes

Part D Effective: N/A
Commercial Effective: 11/19/18
Created: 12/15
Client Approval: 11/18
P&T Approval: 02/16

ENZYME REPLACEMENT THERAPY: GAUCHER DISEASE

Generic	Brand	HICL	GCN	Exception/Other
IMIGLUCERASE	CEREZYME	09022		
TALIGLUCERASE ALFA	ELELYSO	38937		
VELAGLUCERASE ALFA	VPRIV	36874		

GUIDELINES FOR USE

ELELYSO

1. Is the patient being treated for type 1 (non-neuronopathic) Gaucher disease and meets the following criteria?
   - Patient 4 years of age and above

   If yes, **approve for up to 12 months.**
   If no, do not approve.
   DENIAL TEXT: Our guideline for **ENZYME REPLACEMENT THERAPY: GAUCHER DISEASE** requires a diagnosis of type 1 Gaucher disease. In addition, the following criteria must be met:
   - Patient 4 years of age and above

VPRIV

1. Is the patient being treated for type 1 (non-neuronopathic) Gaucher disease and meets the following criteria?
   - Patient 4 years of age and above
   - Previous trial (unless contraindicated) of Elelyso

   If yes, **approve for up to 12 months.**
   If no, do not approve.
   DENIAL TEXT: Our guideline for **ENZYME REPLACEMENT THERAPY: GAUCHER DISEASE** requires a diagnosis of type 1 Gaucher disease. In addition, the following criteria must be met:
   - Patient 4 years of age and above
   - Previous trial (unless contraindicated) of Elelyso

CONTINUED ON NEXT PAGE

ENZYME REPLACEMENT THERAPY: GAUCHER DISEASE

GUIDELINES FOR USE (CONTINUED)

CEREZYME

1. Is the patient being treated for type 1 (non-neuronopathic) Gaucher disease and meets the following criteria?
   - Patient 18 years of age and above
   - Previous trial (unless contraindicated) of Elelyso

   If yes, **approve for up to 12 months.**
   If no, do not approve.
   DENIAL TEXT: Our guideline for **ENZYME REPLACEMENT THERAPY: GAUCHER DISEASE** requires a diagnosis of type 1 Gaucher disease. In addition, the following criteria must be met:
   - Patient 18 years of age and above
   - Previous trial (unless contraindicated) of Elelyso

RATIONALE
Ensure that Cerezyme, Elelyso, and Vpriv are being used to treat patients with type 1 Gaucher disease.

FDA APPROVED INDICATIONS
CEREZYME is indicated for long term enzyme replacement therapy for pediatric and adult patients with type 1 Gaucher disease resulting in one or more of the following conditions: anemia, thrombocytopenia, bone disease, hepatomegaly, or splenomegaly.

ELELYSO is indicated for long term enzyme replacement therapy for adult patients and pediatric patients with type 1 Gaucher disease. Dosing information is available for 4 years of age and older.

VPRIV is indicated for long term enzyme replacement therapy for pediatric and adult patients with type 1 Gaucher disease. Dosing information is available for 4 years of age and older.

REFERENCES

- Genzyme Corporation, Cerezyme package insert. Cambridge, MA. December 2012.
- Pfizer Labs, Elelyso package insert. New York, NY. August 2014.
- Shire Human Genetic Therapies, Inc., Vpriv package insert. Cambridge, MA. April 2015.

Library	Commercial	NSA
Yes	No	Yes

Part D Effective: N/A
Commercial Effective: 07/01/15
Created: 05/05
Client Approval: 05/15
P&T Approval: 05/15

EPOPROSTENOL IV

Generic	Brand	HICL	GCN	Exception/Other
EPOPROSTENOL SODIUM (GLYCINE)	FLOLAN	07323		
EPOPROSTENOL SODIUM (ARGININE)	VELETRI	37762		

GUIDELINES FOR USE

INITIAL CRITERIA (NOTE: FOR RENEWAL CRITERIA SEE BELOW)

1. Does the patient have a diagnosis of pulmonary arterial hypertension (PAH) (WHO Group 1) and meets **ALL** of the following criteria?
   - The requested medication is prescribed by or given in consultation with a cardiologist or pulmonologist
   - Documented confirmatory pulmonary arterial hypertension (PAH) diagnosis based on right heart catheterization with the following parameters:
     - Mean pulmonary artery pressure (PAP) of ≥ 25 mmHg
     - Pulmonary capillary wedge pressure (PCWP) ≤ 15 mmHg
     - Pulmonary vascular resistance (PVR) > 3 Wood units
   - The patient has NYHA/WHO Functional Class III-IV symptoms

   If yes, **approve up to 12 months by HICL.**
   If no, do not approve.
   DENIAL TEXT: The guideline for **EPOPROSTENOL (Flolan, Veletri)** requires a diagnosis of pulmonary arterial hypertension (PAH) (WHO Group 1). The following criteria must also be met.
   - The requested medication is prescribed by or given in consultation with a cardiologist or pulmonologist
   - Documented confirmatory pulmonary arterial hypertension (PAH) diagnosis based on right heart catheterization with the following parameters:
     - Mean pulmonary artery pressure (PAP) of ≥ 25 mmHg
     - Pulmonary capillary wedge pressure (PCWP) ≤ 15 mmHg
     - Pulmonary vascular resistance (PVR) > 3 Wood units
   - The patient has NYHA/WHO Functional Class III-IV symptoms

CONTINUED ON NEXT PAGE

EPOPROSTENOL IV

RENEWAL CRITERIA

1. Does the patient have a diagnosis of pulmonary arterial hypertension (PAH) (WHO Group 1)?

   If yes, continue to #2.
   If no, do not approve.
   DENIAL TEXT: See the renewal denial text at the end of the guideline.

2. Has the patient shown improvement from baseline in the 6-minute walk distance test?

   If yes**, approve for 12 months by HICL.**
   If no, continue to #3.

3. Has the patient remained stable from baseline in the 6-minute walk distance test?

   If yes, continue to #4.
   If no, do not approve.
   DENIAL TEXT: See the renewal denial text at the end of the guideline.

4. Has the patient's WHO functional class remained stable or has improved?

   If yes**, approve for 12 months by HICL.**
   If no, do not approve.
   DENIAL TEXT: See the renewal denial text at the end of the guideline.

DENIAL TEXT: The guideline for **EPOPROSTENOL (Flolan, Veletri)** renewal requires a diagnosis of pulmonary arterial hypertension (PAH). The following criteria must also be met.

- The patient has shown improvement from baseline in the 6-minute walk distance test **OR**
- The patient has a stable 6-minute walk distance test with a stable or improved WHO functional class.

RATIONALE

Ensure appropriate use of Flolan and Veletri based on FDA approved indication.

CONTINUED ON NEXT PAGE

EPOPROSTENOL IV

RATIONALE (CONTINUED)

Diagnosis of PAH involves a logical sequence of steps utilizing different diagnostic tests to assist in confirmation of PAH (chest x-ray, echocardiogram, electrocardiogram, CT angiogram, pulmonary function tests, VQ scan); however, right heart catheterization (RHC) remains the gold standard and is an essential component in the definitive diagnosis, prognosis, and evaluation of PAH. RHC is critical in distinguishing PH due to other etiologies, for example PH due to left heart disease (e.g. diastolic dysfunction) or severe lung disease, which may appear similar to PAH on an echocardiogram. In addition, RHC can be used to monitor the therapeutic and adverse effects of medical interventions, to assess the severity of hemodynamic impairment, and to test the vasoreactivity of the pulmonary circulation.

FDA APPROVED INDICATION

Epoprostenol is indicated for the long-term intravenous treatment of primary pulmonary hypertension and pulmonary hypertension associated with the scleroderma spectrum of disease in NYHA/WHO Class III and Class IV patients who do not respond adequately to conventional therapy.

Veletri is indicated for the treatment of pulmonary arterial hypertension (PAH) (WHO Group 1) to improve exercise capacity. Studies establishing effectiveness included predominantly patients with NYHA Functional Class III-IV symptoms and etiologies of idiopathic or heritable PAH or PAH associated with connective tissue diseases.

REFERENCES

- GlaxoSmithKline. Flolan package insert. Research Triangle Park, NC. April 2015.
- Actelion. Veletri package insert. South San Francisco, CA. June 2012.

Library	Commercial	NSA
Yes	No	Yes

Part D Effective: N/A
Commercial Effective: 10/01/16
Created: 09/05
Client Approval: 09/16
P&T Approval: 08/16

ERIBULIN

Generic	Brand	HICL	GCN	Exception/Other
ERIBULIN MESYLATE	HALAVEN	37256		

This drug requires a written request for prior authorization.

GUIDELINES FOR USE

1. Does the patient have a diagnosis of metastatic breast cancer and meets the following criteria?
   - The patient has received previous treatment with **TWO** chemotherapeutic regimens for the treatment of metastatic disease which should have included at least **ONE** agent from **EACH** of the following chemotherapeutic drug classes:
     - An anthracycline [e.g., daunorubicin (Cerubidine), daunorubicin liposomal (DaunoXome), doxorubicin (Adriamycin), doxorubicin liposomal (Doxil), idarubicin (Idamycin), epirubicin (Ellence), mitoxantrone (Novantrone)]
     - A taxane [e.g., docetaxel (Taxotere), paclitaxel (Taxol or Abraxane)]

     If yes, **approve for 12 months by HICL with a quantity limit of #6 vials (maximum 3 vials per dose) per 21 days.**
     If no, continue to #2.
     DENIAL TEXT: See the denial text at the end of the guideline.

2. Does the patient have a diagnosis of unresectable or metastatic liposarcoma and meets the following criteria?
   - The patient has received previous treatment for liposarcoma, which included an anthracycline [e.g., daunorubicin (Cerubidine), daunorubicin liposomal (DaunoXome), doxorubicin (Adriamycin), doxorubicin liposomal (Doxil), idarubicin (Idamycin), epirubicin (Ellence), mitoxantrone (Novantrone)]?

     If yes, **approve for 12 months by HICL with a quantity limit of #6 vials (maximum 3 vials per dose) per 21 days.**
     If no, do not approve.
     DENIAL TEXT: See the denial text at the end of the guideline.

DENIAL TEXT: Our guideline for **ERIBULIN (Halaven)** requires a diagnosis of metastatic breast cancer and previous treatment with an anthracycline and a taxane OR a diagnosis of unresectable or metastatic liposarcoma and previous treatment with an anthracycline.

CONTINUED ON NEXT PAGE

ERIBULIN

RATIONALE
To ensure appropriate use of Halaven based on FDA indication.

FDA APPROVED INDICATIONS
Halaven is a microtubule inhibitor indicated for the treatment of patients with:
- Metastatic breast cancer who have previously received at least two chemotherapeutic regimens for the treatment of metastatic disease. Prior therapy should have included an anthracycline and a taxane in either the adjuvant or metastatic setting.
- Unresectable or metastatic liposarcoma who have received a prior anthracycline-containing regimen.

REFERENCES
- Halaven [Prescribing Information]. Eisai Inc.: Woodcliff Lake, NJ. January 2016.
- Micromedex® Healthcare Series [database online]. Greenwood Village, CO: Thomson Healthcare. Available at: http://www.thomsonhc.com/hcs/librarian/. [Accessed: June 28, 2011].

Library	Commercial	NSA
Yes	No	Yes

Part D Effective: NA
Commercial Effective: 05/01/16
Created: 11/10
Client Approval: 11/13
P&T Approval: 05/16

ETELCALCETIDE (NSA)

Generic	Brand	HICL	GCN	Exception/Other
ETELCALCETIDE	PARSABIV	44093		

GUIDELINES FOR USE

1. Does the patient have a diagnosis of secondary hyperparathyroidism (HPT) and meet **ALL** of the following criteria?
   - The patient is 18 years of age or older
   - The patient has chronic kidney disease
   - The patient is on hemodialysis
   - The patient is NOT taking another calcimimetic agent (e.g., cinacalcet)

   If yes, **approve for 12 months by HICL with a quantity limit of #36mL per 28 days.**
   If no, do not approve.
   DENIAL TEXT: The guideline named **ETELCALCETIDE (Parsabiv)** requires a diagnosis of secondary hyperparathyroidism (HPT). The following criteria must also be met:
   - The patient is 18 years of age or older
   - The patient has chronic kidney disease
   - The patient is on hemodialysis
   - The patient is NOT taking another calcimimetic agent (e.g., cinacalcet)

RATIONALE
Promote appropriate utilization of **ETELCALCETIDE** based on FDA approved indication and dosage.

FDA APPROVED INDICATIONS
Parsabiv is a calcium-sensing receptor agonist indicated for secondary hyperparathyroidism (HPT) in adult patients with chronic kidney disease (CKD) on hemodialysis.

DOSAGE AND ADMINISTRATION
Parasabiv is available as single-dose vials. Single-dose vials are available in 2.5 mg/0.5mL, 5 mg/1mL, and 10 mg/2 mL strengths.

The recommended starting dose of PARSABIV is 5 mg administered by intravenous (IV) bolus injection three times per week at the end of hemodialysis treatment. Administer PARSABIV only at the end of hemodialysis treatment.

The lowest maintenance dose of PARSABIV is 2.5 mg three times per week, and the highest maintenance dose of PARSABIV is 15 mg three times per week. The maintenance dose of PARSABIV is individualized and determined by titration based on parathyroid hormone (PTH) and corrected serum calcium response .The maintenance dose is the dose that maintains PTH levels within the recommended target range and corrected serum calcium within the normal range.

CONTINUED ON NEXT PAGE

ETELCALCETIDE (NSA)

FDA APPROVED INDICATIONS (CONTINUED)

DOSAGE AND ADMINISTRATION
Ensure corrected serum calcium is at or above the lower limit of normal prior to PARSABIV initiation, a PARSABIV dose increase, or re-initiation of PARSABIV therapy after a dosing interruption.

If a regularly scheduled hemodialysis treatment is missed, DO NOT administer any missed doses. Resume PARSABIV at the end of the next hemodialysis treatment at the prescribed dose. If doses of PARSABIV are missed for more than 2 weeks, re-initiate PARSABIV at the recommended starting dose of 5 mg (or 2.5 mg if that was the patient's last dose).

Monitor corrected serum calcium and PTH levels during dose initiation, dose adjustment, and dose maintenance according to the schedule in Table 1.

Table 1: Recommended Schedule for Monitoring Corrected Serum Calcium and Parathyroid Hormone Levels during PARSABIV Treatment *(from Parasabiv prescribing information)*

	Dose Initiation or Dose Adjustment	Maintenance
Corrected Serum Calcium Levels	1 week after	Every 4 weeks
Parathyroid Hormone Levels	4 weeks after	Per clinical practice

Increase the dose of PARSABIV in 2.5 mg or 5 mg increments in individuals with corrected serum calcium within the normal range and PTH levels above the recommended target range based on the patient's PTH levels no more frequently than every 4 weeks up to a maximum dose of 15 mg three times per week.

Decrease or temporarily discontinue PARSABIV dosing in individuals with PTH levels below the target range. In individuals with a corrected serum calcium below the lower limit of normal but at or above 7.5 mg/dL without symptoms of hypocalcemia, consider decreasing or temporarily discontinuing PARSABIV or use concomitant therapies to increase corrected serum calcium. If the dose is stopped, then re-initiate PARSABIV at a lower dose when the PTH is within the target range and hypocalcemia has been corrected.

Stop PARSABIV and treat hypocalcemia if the corrected serum calcium falls below 7.5 mg/dL or patients report symptoms of hypocalcemia. When the corrected serum calcium is within normal limits, symptoms of hypocalcemia have resolved, and predisposing factors for hypocalcemia have been addressed, re-initiate PARSABIV at a dose 5 mg lower than the last administered dose. If the last administered dose of PARSABIV was 2.5 mg or 5 mg, re-initiate at a dose of 2.5 mg.

CONTINUED ON NEXT PAGE

ETELCALCETIDE (NSA)

REFERENCES

- Parsabiv [Prescribing Information]. Thousand Oaks, CA: Kai Pharmaceuticals; February 2017.

Library	Commercial	NSA
Yes	No	Yes

Part D Effective: N/A
Commercial Effective: 04/01/18
Created: 02/18
Client Approval: 02/18
P&T Approval: 01/18

ETEPLIRSEN

Generic	Brand	HICL	GCN	Exception/Other
ETEPLIRSEN	EXONDYS 51	43770		

GUIDELINES FOR USE

INITIAL CRITERIA (NOTE: FOR RENEWAL CRITERIA SEE BELOW)

1. Does the patient have a diagnosis of Duchenne muscular dystrophy (DMD) and meets **ALL** of the following criteria?
   - Documented genetic testing that confirms mutation in DMD gene is amenable to exon 51 skipping
   - Prescribed by or given in consultation with a neurologist specializing in treatment of DMD at a DMD treatment center
   - Patient is ambulatory
   - Patient is currently receiving treatment with or has contraindication to corticosteroids (e.g., prednisone or prednisolone)

   If yes, **approve for 24 weeks by HICL.**
   APPROVAL TEXT: Renewal requires that the patient has maintained or demonstrated a less than expected decline in ambulatory function as measured by muscle function tests **OR** has maintained or demonstrated a less than expected decline in other muscle function (i.e., pulmonary or cardiac function).

   If no, do not approve.
   DENIAL TEXT: The guideline named **ETEPLIRSEN (Exondys 51)** requires a diagnosis of Duchenne muscular dystrophy (DMD) and that **ALL** of the following criteria are met:
   - Documented genetic testing that confirms mutation in DMD gene is amenable to exon 51 skipping
   - Prescribed by or given in consultation with a neurologist specializing in treatment of DMD at a DMD treatment center
   - Patient is ambulatory
   - Patient is currently receiving treatment with or has contraindication to corticosteroids (e.g., prednisone or prednisolone).

CONTINUED ON NEXT PAGE

ETEPLIRSEN

GUIDELINES FOR USE (CONTINUED)

RENEWAL CRITERIA

2. Over the past 24 weeks, has the patient maintained or demonstrated a less than expected decline in ambulatory ability in muscle function assessments (i.e., 6-minute walking, distance (6MWD), ascending 4 stairs, descending 4 stairs, rise from floor time, 10-meter run/walk time, North Star Ambulatory Assessment (NSAA))?

   If yes, **approve for 12 months by HICL.**
   APPROVAL TEXT: Renewal requires that the patient has maintained or demonstrated a less than expected decline in ambulatory function as measured by muscle function tests **OR** has maintained or demonstrated a less than expected decline in other muscle function (i.e., pulmonary or cardiac function).

   If no, continue to #2.

3. During the past 24 weeks, has the patient maintained or demonstrated a less than expected decline in other muscle function (i.e., pulmonary or cardiac function)?

   If yes, **approve for 12 months by HICL.**
   APPROVAL TEXT: Renewal requires that the patient has maintained or demonstrated a less than expected decline in ambulatory function as measured by muscle function tests **OR** has maintained or demonstrated a less than expected decline in other muscle function (i.e., pulmonary or cardiac function).

   If no, do not approve.
   DENIAL TEXT: The guideline named **ETEPLIRSEN (Exondys 51)** renewal requires ONE of the following criteria has been met:
   - Over the past 24 weeks, the patient has maintained or demonstrated a less than expected decline in ambulatory ability in muscle function assessments (i.e., 6-minute walking, distance (6MWD), ascending 4 stairs, descending 4 stairs, rise from floor time, 10-meter run/walk time, North Star Ambulatory Assessment (NSAA))
   - **OR** during the past 24 weeks, the patient has maintained or demonstrated a less than expected decline in other muscle function (i.e. pulmonary or cardiac function).

RATIONALE
Promote appropriate utilization of **ETEPLIRSEN** based on FDA approved indication.

CONTINUED ON NEXT PAGE

ETEPLIRSEN

RATIONALE (CONTINUED)

Exondys 51 (eteplirsen) is a phosphorodiamidate morpholino oligomer (PMO) that selectively binds to exon 51 of the dystrophin pre-mRNA, enabling the splicing mechanisms to skip exon 51 and restore the open reading frame of the dystrophin protein, which produces a truncated but functional dystrophin protein.

Duchenne muscular dystrophy (DMD) is a rare X-linked genetic disorder that results in progressive muscle weakness, loss of independence, and early mortality. DMD affects 1 in 3,000 to 1 in 6,000 live male births. DMD occurs when there is a mutation, mainly internal deletions in the dystrophin gene that results in a near absent production of the protein dystrophin. Dystrophin contributes to functional muscle integrity by connecting muscle fibers to the surrounding extracellular matrix. Dystrophin is present in muscles at birth but repeated muscle movement leads to breakdown of the protein and production of dystrophin is needed to replenish the degraded protein. Patients with DMD are unable to produce new dystrophin and without this protein, there is progressive muscle cell degeneration and muscle fiber loss. Functional muscle units are replaced by adipose and sclerosis. Additional inflammatory and immunological processes occur in conjunction with dystrophin deficiency, contributing to muscle pathology.

DMD is present at the time of birth, but the disorder does not become apparent until around age 3 – 5 years. Children with DMD may have delayed development including starting to walk at a later age than children without DMD. Normal childhood activities such as running, jumping, and stair climbing are abnormal and done with difficulty, and patients may experience frequent falls. As the child continues to age, they experience progressive muscle weakness and dysfunction. Many patients are wheelchair bound in their early teenage years and most patients succumb to cardiac and/or respiratory failure in their 20's.

The diagnosis of DMD is definitively confirmed by genetic testing. Confirmation of DMD by genetic testing is always required even if DMD is first diagnosed by a muscle biopsy. The genetic testing will identify the types of mutations in the DMD gene, and if no deletions or duplications are detected, DNA sequencing is performed to identify point mutations (including nonsense mutations) that alter the translation of the protein. A full characterization of the mutations is necessary to determine how the genetic reading frame is affected, which is the major determinant of the phenotypic variability of DMD. Knowing which exons of the DMD gene are affected or if there is premature termination of protein production can also determine eligibility for mutation specific treatment options.

CONTINUED ON NEXT PAGE

ETEPLIRSEN

RATIONALE (CONTINUED)

The 6-minute walking distance test (6MWD) is a validated measure of integrated function that is dependent on respiratory, cardiovascular, and nutritional status, as well as skeletal muscle function, and has been used in several studies that measure functional capabilities. Baseline 6MWD is an important predictor of subsequent ambulatory status in patients with DMD, and a baseline 6MWD of 330m or less are correlated with an increased likelihood for future loss of ambulation. Changes in values of 6MWD of 30m (or 10%) from baseline are considered clinically significant. Growing boys with DMD maintain a stable or even improving 6MWD up to about 7 years of age. After age 7, these boys experience a significant decline in walking ability compared with healthy boys of the same age. As walking ability deteriorates, the 6MWD loses value as an appropriate endpoint to measure prognosis due to its dependence on muscle tissue. As such, other endpoints are needed to determine appropriate measures of therapeutic effect in these patients. Studies of patients with DMD has resulted in the observation that the percent predicted of forced vital capacity (FVC) declines at a rate of 5% per year in DMD patients who are 5 – 24 years of age.

There is currently no cure for DMD and treatment is mainly supportive and aimed at delaying disease progression. Corticosteroids such as prednisone and prednisolone have been shown to delay muscle dysfunction and loss of ambulation by several years. Even after the loss of ambulation, treatment with corticosteroid may help preserve respiratory and cardiac function. Despite this benefit, there is no consensus on what the optimal corticosteroid regimen should be, and their long-term use is attributed to detrimental side effects.

DOSAGE
The recommended dosing regimen for eteplirsen is 30mg/kg administered once weekly as a 35 – 60 minute intravenous infusion.

FDA APPROVED INDICATION
Exondys 51 (eteplirsen) is indicated for the treatment of Duchenne muscular dystrophy (DMD) in patients who have a confirmed mutation of the *DMD* gene that is amenable to exon 51 skipping.

This indication is approved under accelerated approval based on an increase in dystrophin in skeletal muscle observed in some patients treated with Exondys 51. A clinical benefit of Exondys 51 has not been established. Continued approval for this indication may be contingent upon verification of a clinical benefit in confirmatory trials.

AVAILABLE STRENGTHS
100mg/2mL vials (50mg/mL)
500mg/10mL vials (50mg/mL)

CONTINUED ON NEXT PAGE

ETEPLIRSEN

REFERENCES

- Exondys 51 [Prescribing Information]. Cambridge, MA: Sarepta Therapeutics, Inc. September 2016.
- FDA grants accelerated approval to first drug for Duchenne muscular dystrophy [Press release]. Updated September 19, 2016. Available from: http://www.fda.gov/newsevents/newsroom/pressannouncements/ucm521263.htm.
- Sarepta Therapeutics. Duchenne Muscular Dystrophy. Disease resources. Available from: http://www.sarepta.com/community/disease-resources
- Bushby K, Finkel R, Birnkrant DJ, et al. Diagnosis and management of Duchenne muscular dystrophy, part 1: diagnosis, and pharmacological and psychosocial management. Lancet Neurol. 2010 Jan; 9(1):77-93.
- Kole R, Krieg AM. Exon skipping therapy for Duchenne muscular dystrophy. Adv Drug Deliv Rev. 2015 Jun 29;87:104-7.
- Skipahead.com. Understanding exon skipping: let's skip ahead. 2016. Available from: http://www.skipahead.com/
- Advances in Duchenne Muscular Dystrophy Natural History and Biomarkers. Industry Therapeutic Update from BioMarin Pharmaceutical Inc. and PTC Therapeutics Inc. Presented June 22, 2015. Available from: http://files.shareholder.com/downloads/PTCT/1345262988x0x836302/7DA38D13-28CC-4C56-8905-3AB6258984F4/PTCT_BMRN_June_22_DMD_Day_FINAL_updated.pdf.
- Mendell JR, Rodino-Klapac LR, Sahenk Z, et al. Eteplirsen for the treatment of Duchenne muscular dystrophy. Ann Neurol. 2013 Nov;74(5):637-47.
- Mendell JR, Goesmans N, Lowes LP, et al. Longitudinal effect of eteplirsen vs. historical control on ambulation in DMD. Ann Neurol. 2015 Nov 17. [Epub ahead of print].

Library	Commercial	NSA
Yes	No	Yes

Part D Effective: N/A
Commercial Effective: 11/01/16
Created: 01/16
Client Approval: 09/16
P&T Approval: 02/16

FULVESTRANT (NSA)

Generic	Brand	HICL	GCN	Exception/Other
FULVESTRANT	FASLODEX	23523		

This drug requires a written request for prior authorization.

GUIDELINES FOR USE

1. Does the patient have a diagnosis of hormone receptor (HR)-positive, human epidermal growth factor receptor 2 (HER2)-negative advanced breast cancer and meet **ALL** of the following criteria?
   - The patient is female and postmenopausal
   - The patient has not previously been treated with endocrine therapy
   - The requested medication will be used as monotherapy

   If yes, **approve for 12 months by HICL. Enter two authorizations by HICL as follows:**
   - **Approve for 1 month for #6 (250mg/5mL) syringes (Total 30mL) for the initial month.**
   - **Approve for 11 months for #2 (250mg/5mL) syringes (Total 10mL) per month for every subsequent month.**

   If no, continue to #2.

2. Does the patient have a diagnosis of hormone receptor (HR)-positive advanced breast cancer and meet **ALL** of the following criteria?
   - The patient is female and postmenopausal
   - The patient has experienced disease progression following endocrine therapy
   - The requested medication will be used as monotherapy

   If yes, **approve for 12 months by HICL. Enter two authorizations by HICL as follows:**
   - **Approve for 1 month for #6 (250mg/5mL) syringes (Total 30mL) for the initial month.**
   - **Approve for 11 months for #2 (250mg/5mL) syringes (Total 10mL) per month for every subsequent month.**

   If no, continue to #3.

CONTINUED ON NEXT PAGE

FULVESTRANT (NSA)

GUIDELINES FOR USE (CONTINUED)

3. Does the patient have a diagnosis of hormone receptor (HR)-positive, human epidermal growth factor receptor 2 (HER2)-negative advanced or metastatic breast cancer and meet **ALL** of the following criteria?
   - The patient is female
   - The patient has experienced disease progression following endocrine therapy
   - The requested medication will be used concurently with Ibrance (palbociclib) or Verzenio (abemaciclib)

   If yes, **approve for 12 months by HICL. Enter two authorizations by HICL as follows:**
   - **Approve for 1 month for #6 (250mg/5mL) syringes (Total 30mL) for the initial month.**
   - **Approve for 11 months for #2 (250mg/5mL) syringes (Total 10mL) per month for every subsequent month.**

   If no, continue to #4.

4. Does the patient have a diagnosis of hormone receptor (HR)-positive, human epidermal growth factor receptor 2 (HER2)-negative advanced or metastatic breast cancer and meet **ALL** of the following criteria?
   - The patient is female and postmenopausal
   - The requested medication will be used in combination with Kisqali (ribociclib)
   - The patient has not received prior endocrine based therapy for metastatic breast cancer (e.g., letrozole, anastrozole, tamoxifen, exemestane) **OR** patient has experienced disease progression on endocrine therapy

   If yes, **approve for 12 months by HICL. Enter two authorizations by HICL as follows:**
   - **Approve for 1 month for #6 (250mg/5mL) syringes (Total 30mL) for the initial month.**
   - **Approve for 11 months for #2 (250mg/5mL) syringes (Total 10mL) per month for every subsequent month.**

   If no, do not approve.
   DENIAL TEXT: See the denial text at the end of the guideline.

CONTINUED ON NEXT PAGE

FULVESTRANT (NSA)

GUIDELINES FOR USE (CONTINUED)

DENIAL TEXT: The guideline named **FULVESTRANT (Faslodex)** requires a diagnosis of hormone receptor (HR)-positive, human epidermal growth factor receptor 2 (HER2)-negative advanced breast cancer, HR-positive advanced breast cancer or HR-positive, HER2-negative advanced or metastatic breast cancer. In addition, the following criteria must be met:

For the diagnosis of hormone receptor (HR)-positive, human epidermal growth factor receptor 2 (HER2)-negative advanced breast cancer, approval requires:

- The patient is female and postmenopausal
- The patient has not previously been treated with endocrine therapy
- The requested medication will be used as monotherapy

For the diagnosis of hormone receptor (HR)-positive advanced breast cancer, approval requires:

- The patient is female and postmenopausal
- The patient has experienced disease progression following endocrine therapy
- The requested medication will be used as monotherapy

For the diagnosis of hormone receptor (HR)-positive, human epidermal growth factor receptor 2 (HER2)-negative advanced or metastatic breast cancer, approval requires ONE of the following:

- The requested medication will be used concurrently with Ibrance (palbociclib) or Verzenio (abemaciclib) and meet ALL of the following:
  - The patient is female
  - The patient has experienced disease progression following endocrine therapy
- The requested medication will be used in combination with Kisqali (ribociclib) and meet ALL of the following:
  - The patient is female and postmenopausal
  - The patient has not received prior endocrine based therapy for metastatic breast cancer (e.g., letrozole, anastrozole, tamoxifen, exemestane) **OR** patient has experienced disease progression on endocrine therapy

CONTINUED ON NEXT PAGE

FULVESTRANT (NSA)

RATIONALE
To ensure appropriate usage Faslodex (fulvestrant) based on FDA approved indications.

FDA APPROVED INDICATIONS
Faslodex is an estrogen receptor antagonist indicated for:
- Treatment of hormone receptor (HR)-positive, human epidermal growth receptor 2 (HER2)-negative advanced breast cancer in postmenopausal women not previously treated with endocrine therapy.
- Treatment of HR-positive advanced breast cancer in postmenopausal women with disease progression following endocrine therapy.
- Treatment of HR-positive, human epidermal growth factor receptor 2 (HER2)-negative advanced or metastatic breast cancer in combination with palbociclib or abemaciclib in women with disease progression after endocrine therapy.
- Treatment of HR-positive, human epidermal growth factor receptor 2 (HER2)-negative advanced or metastatic breast cancer in combination with ribociclib in postmenopausal women not previously treated with endocrine therapy or with disease progression after endocrine therapy.

DOSAGE AND ADMINISTRATION
The recommended monotherapy dose of FASLODEX and when used in combination with palbociclib, abemaciclib, or ribociclib is 500 mg to be administered intramuscularly into the buttocks (gluteal area) slowly (1 - 2 minutes per injection) as two 5 mL injections, one in each buttock, on days 1, 15, 29 and once monthly thereafter.

When Faslodex is used in combination with palbociclib, the recommended dose of palbociclib is a 125 mg capsule taken orally once daily for 21 consecutive days followed by 7 days off treatment to comprise a complete cycle of 28 days. Palbociclib should be taken with food. Please refer to the full prescribing information of palbociclib.

When Faslodex is used in combination with abemaciclib, the recommended dose of abemaciclib is 150 mg orally, twice daily. Abemaciclib may be taken with or without food. Please refer to the Full Prescribing Information for abemaciclib.

When Faslodex is used in combination with ribociclib, the recommended dose of ribociclib is 600mg (three 200mg film-coated tablets) taken orally, once daily for 21 consecutive days followed by 7 days off treatment resulting in a complete cycle of 28 days.

Pre/perimenopausal women treated with the combination Faslodex plus palbociclib or abemaciclib should be treated with luteinizing hormone-releasing hormone (LHRH) agonists according to current clinical practice standards.

CONTINUED ON NEXT PAGE

FULVESTRANT (NSA)

FDA APPROVED INDICATIONS (CONTINUED)

DOSAGE AND ADMINISTRATION
A dose of 250 mg is recommended for patients with moderate hepatic impairment (Child-Pugh class B) to be administered intramuscularly into the buttock (gluteal area) slowly (1 - 2 minutes) as one 5 mL injection on days 1, 15, 29 and once monthly thereafter.

For complete administration instructions, please see full prescribing information of Faslodex, Ibrance, Verzenio and Kisqali.

REFERENCES

- Faslodex [Prescribing Information]. Wilmington, DE: AstraZeneca Pharmaceuticals LP; July 2018.

Library	Commercial	NSA
Yes	No	Yes

Part D Effective: N/A
Commercial Effective: 10/01/18
Created: 08/13
Client Approval: 09/18
P&T Approval: 07/18

GEMTUZUMAB OZOGAMICIN (NSA)

Generic	Brand	HICL	GCN	Exception/Other
GEMTUZUMAB OZOGAMICIN	MYLOTARG	21218		

GUIDELINES FOR USE

1. Does the patient have a diagnosis of newly-diagnosed CD33-positive acute myeloid leukemia (AML) and meet the following criterion?
   - The patient is 18 years of age or older

   If yes, **approve for 12 months by HICL.**
   If no, continue to #2.

2. Does the patient have a diagnosis of relapsed or refractory CD33-positive acute myeloid leukemia (AML) and meet the following criterion?
   - The patient is 2 years of age or older

   If yes, **approve for 12 months by HICL.**
   If no, do not approve.
   DENIAL TEXT: The guideline named **GEMTUZUMAB OZOGAMICIN (Mylotarg)** requires that **ONE** of the following criteria be met:
   - The patient has a diagnosis of newly-diagnosed CD33-positive acute myeloid leukemia (AML) and is 18 years of age or older.
   - The patient has a diagnosis of relapsed or refractory CD33-positive acute myeloid leukemia (AML) and is 2 years of age or older.

RATIONALE
Promote appropriate utilization of GEMTUZUMAB OZOGAMICIN based on FDA approved indications.

FDA APPROVED INDICATIONS
MYLOTARG is a CD33-directed antibody-drug conjugate indicated for:
- Treatment of newly-diagnosed CD33-positive acute myeloid leukemia (AML) in adults
- Treatment of relapsed or refractory CD33-positive AML in adults and in pediatric patients 2 years and older.

CONTINUED ON NEXT PAGE

GEMTUZUMAB OZOGAMICIN (NSA)

FDA APPROVED INDICATIONS (CONTINUED)

DOSAGE AND ADMINISTRATION
Newly-diagnosed, de novo AML (combination regimen):
- *Induction*: 3 mg/m^2 (up to one 4.5 mg vial) on Days 1, 4, and 7 in combination with daunorubicin and cytarabine
  - For patients requiring a second induction cycle, do NOT administer MYLOTARG during the second induction cycle
- *Consolidation*: 3 mg/m^2 on Day 1 (up to one 4.5 mg vial) in combination with daunorubicin and cytarabine.

Newly-diagnosed AML (single-agent regimen):
- *Induction: 6 mg/m2 on Day 1 and 3 mg/m2 on Day 8*
- *Continuation*: For patients without evidence of disease progression following induction, up to 8 continuation courses of MYLOTARG 2 mg/m^2 on Day 1 every 4 weeks.

Relapsed or refractory AML (single-agent regimen):
- 3 mg/m^2 (up to one 4.5 mg vial) on Days 1, 4, and 7.

Patients should be pre-medicated with a corticosteroid, antihistamine, and acetaminophen 1 hour prior to MYLOTARG. Patients should be monitored during and for at least 1 hour after the end of the infusion.

AVAILABLE STRENGTHS
MYLOTARG (gemtuzumab ozogamicin) for injection is a white to off-white lyophilized cake or powder supplied in a carton containing one 4.5 mg single-dose vial for reconstitution and further dilution.

REFERENCES
- Mylotarg [Prescribing Information]. Philadelphia, PA: Wyeth Pharmaceuticals, Inc. September 2017.

Library	Commercial	NSA
Yes	No	Yes

Part D Effective: N/A
Commercial Effective: 01/01/18
Created: 09/17
Client Approval: 12/17
P&T Approval: 10/17

GOLIMUMAB - IV (NSA)

Generic	Brand	HICL	GCN	Exception/Other
GOLIMUMAB - IV	SIMPONI ARIA - IV		34983	

GUIDELINES FOR USE

INITIAL CRITERIA (NOTE: FOR RENEWAL CRITERIA SEE BELOW)

1. Does the patient have a diagnosis of moderate to severe rheumatoid arthritis (RA) and meet **ALL** of the following criteria?
   - Therapy is prescribed by or given in consultation with a rheumatologist
   - The patient has had a previous trial of at least one of the following DMARDs (disease-modifying antirheumatic drugs) such as methotrexate, leflunomide, hydroxychloroquine, or sulfasalazine
   - The patient is concurrently using or has a contraindication to methotrexate
   - The patient is 18 years of age or older
   - The patient has had a previous trial of the formulary preferred immunomodulators: Enbrel **AND** Humira (**NOTE:** pharmaceutical samples acquired from the prescriber or manufacturer assistance program do not qualify)

   If yes, **approve for 6 months by GPID for Simponi Aria 50mg/4mL vials (GPID 34983). APPROVAL TEXT:** Renewal for moderate to severe rheumatoid arthritis (RA) requires concurrent use of methotrexate (unless contraindicated) and that the patient has experienced or maintained a 20% or greater improvement in tender joint count or swollen joint count while on therapy.

   If no, continue to #2.

2. Does the patient have a diagnosis of psoriatic arthritis (PsA) and meet **ALL** of the following criteria?
   - Therapy is prescribed by or given in consultation with a rheumatologist or dermatologist
   - The patient has had a previous trial of at least one of the following DMARDs (disease-modifying antirheumatic drugs) such as methotrexate, leflunomide, hydroxychloroquine, or sulfasalazine
   - The patient is 18 years of age or older
   - The patient has had a previous trial of any **TWO** of the following formulary preferred immunomodulators: Enbrel, Humira, Cosentyx, Stelara, **OR** Otezla (**NOTE:** pharmaceutical samples acquired from the prescriber or manufacturer assistance program do not qualify)

   If yes, **approve for 6 months by GPID for Simponi Aria 50mg/4mL vials (GPID 34983). APPROVAL TEXT:** Renewal for psoriatic arthritis (PsA) requires that the patient has experienced or maintained a 20% or greater improvement in tender joint count or swollen joint count while on therapy.

   If no, continue to #3.

CONTINUED ON NEXT PAGE

GOLIMUMAB - IV (NSA)

INITIAL CRITERIA (CONTINUED)

3. Does the patient have a diagnosis of ankylosing spondylitis (AS) and meet **ALL** of the following criteria?
   - Therapy is prescribed by or given in consultation with a rheumatologist
   - The patient is 18 years of age or older
   - The patient has had a previous trial of any **TWO** of the following formulary preferred immunomodulators: Enbrel, Humira, or Cosentyx (**NOTE:** pharmaceutical samples acquired from the prescriber or manufacturer assistance program do not qualify)

   If yes, **approve for 6 months by GPID for Simponi Aria 50mg/4mL vials (GPID 34983). Approval Text:** Renewal for ankylosing spondylitis (AS) requires that the patient has experienced or maintained an improvement of at least 50% or 2 units in the Bath Ankylosing Spondylitis Disease Activity Index (BASDAI) while on therapy.

   If no, do not approve.
   DENIAL TEXT: The guideline named **GOLIMUMAB - IV (Simponi Aria - IV)** requires a diagnosis of moderate to severe rheumatoid arthritis, psoriatic arthritis, or ankylosing spondylitis. In addition, the following criteria must be met:
   For the diagnosis of moderate to severe rheumatoid arthritis (RA), approval requires:
   - Therapy is prescribed by or given in consultation with a rheumatologist
   - The patient has had a previous trial of at least one of the following DMARDs (disease-modifying antirheumatic drugs) such as methotrexate, leflunomide, hydroxychloroquine, or sulfasalazine
   - The patient is concurrently using or has a contraindication to methotrexate
   - The patient is 18 years of age or older
   - The patient has had a previous trial of the formulary preferred immunomodulators: Humira **AND** Enbrel

   For the diagnosis of psoriatic arthritis (PsA), approval requires:
   - Therapy is prescribed by or given in consultation with a rheumatologist or dermatologist
   - The patient has had a previous trial of at least one of the following DMARDs (disease-modifying antirheumatic drugs) such as methotrexate, leflunomide, hydroxychloroquine, or sulfasalazine
   - The patient is 18 years of age or older
   - The patient has had a previous trial of any **TWO** of the following formulary preferred immunomodulators: Enbrel, Humira, Cosentyx, Stelara, **OR** Otezla

   (Initial denial text continued on next page)

CONTINUED ON NEXT PAGE

GOLIMUMAB - IV (NSA)

INITIAL CRITERIA (CONTINUED)

For the diagnosis of ankylosing spondylitis (AS), approval requires:
- Therapy is prescribed by or given in consultation with a rheumatologist
- The patient is 18 years of age or older
- The patient has had a previous trial of any **TWO** of the following formulary preferred immunomodulators: Enbrel, Humira, **OR** Cosentyx

The use of pharmaceutical samples (from the prescriber or manufacturer assistance program) will not be considered when evaluating the medical condition or prior prescription history for drugs that require prior authorization.

RENEWAL CRITERIA

1. Does the patient have a diagnosis of moderate to severe rheumatoid arthritis (RA) and meet **ALL** of the following criteria?
   - The patient has experienced or maintained a 20% or greater improvement in tender joint count or swollen joint count while on therapy
   - The patient is concurrently using or has a contraindication to methotrexate

   If yes, **approve for 12 months by GPID with a duration of 2 months per fill.**
   If no, continue to #2.

2. Does the patient have a diagnosis of psoriatic arthritis (PsA) **AND** meet the following criterion?
   - The patient has experienced or maintained a 20% or greater improvement in tender joint count or swollen joint count while on therapy

   If yes, **approve for 12 months by GPID with a duration of 2 months per fill.**
   If no, continue to #3.

3. Does the patient have a diagnosis of ankylosing spondylitis (AS) **AND** meet the following criterion?
   - The patient has experienced or maintained an improvement of at least 50% or 2 units (scale of 1-10) in the Bath Ankylosing Spondylitis Disease Activity Index (BASDAI) while on therapy

   If yes, **approve for 12 months by GPID with a duration of 2 months per fill.**
   If no, do not approve.
   DENIAL TEXT: See the renewal denial text at the end of the guideline.

CONTINUED ON NEXT PAGE

GOLIMUMAB - IV (NSA)

RENEWAL CRITERIA (CONTINUED)

RENEWAL DENIAL TEXT: The guideline named **GOLIMUMAB - IV (Simponi Aria - IV)** requires a diagnosis of moderate to severe rheumatoid arthritis, psoriatic arthritis, or ankylosing spondylitis for renewal. In addition, the following criteria must be met:

For the diagnosis of moderate to severe rheumatoid arthritis (RA), approval requires:

- The patient has experienced or maintained a 20% or greater improvement in tender joint count or swollen joint count while on therapy
- The patient is concurrently using or has a contraindication to methotrexate

For the diagnosis of psoriatic arthritis (PsA), approval requires:

- The patient has experienced or maintained a 20% or greater improvement in tender joint count or swollen joint count while on therapy

For the diagnosis of ankylosing spondylitis (AS), approval requires:

- The patient has experienced or maintained an improvement of at least 50% or 2 units (scale of 1-10) in the Bath Ankylosing Spondylitis Disease Activity Index (BASDAI) while on therapy

---

RATIONALE

Promote appropriate utilization of Simponi Aria (golimumab IV) based on FDA approved indication and dosing.

FDA APPROVED INDICATIONS

Simponi Aria is a tumor necrosis factor (TNF) blocker indicated for the treatment of adult patients with:

- Moderately to severely active Rheumatoid Arthritis (RA) in combination with methotrexate
- Active Psoriatic Arthritis (PsA)
- Active Ankylosing Spondylitis (AS)

DOSAGE AND ADMINISTRATION

Dosage in Rheumatoid Arthritis, Psoriatic Arthritis, and Ankylosing Spondylitis

The Simponi Aria dosage regimen is 2 mg per kg given as an intravenous infusion over 30 minutes at weeks 0 and 4, then every 8 weeks thereafter.

For patients with rheumatoid arthritis (RA), Simponi Aria should be given in combination with methotrexate. For patients with psoriatic arthritis (PsA) or ankylosing spondylitis (AS), Simponi Aria may be given with or without methotrexate or other non-biologic Disease-modifying Antirheumatic Drugs (DMARDs). Corticosteroids, nonsteroidal anti-inflammatory drugs (NSAIDs), and/or analgesics may be continued during treatment with Simponi Aria.

The efficacy and safety of switching between intravenous and subcutaneous formulations and routes of administration have not been established.

CONTINUED ON NEXT PAGE

GOLIMUMAB - IV (NSA)

FDA APPROVED INDICATIONS (CONTINUED)

DOSAGE AND ADMINISTRATION

Available Strengths

Each single-use vial contains 50 mg of Simponi Aria per 4 mL of solution. Simponi Aria must be refrigerated and protected from light.

REFERENCES

- Simponi Aria [Prescribing Information]. Horsham, PA: Janssen Biotech, Inc. February 2018.

Library	Commercial	NSA
Yes	No	Yes

Part D Effective: N/A
Commercial Effective: 04/01/18

Created: 11/13
Client Approval: 02/18

P&T Approval: 01/18

GONADOTROPIN RELEASING HORMONE (GNRH) AGONIST (NSA)

Generic	Brand	HICL	GCN	Exception/Other
TRIPTORELIN PAMOATE	TRIPTODUR, TRELSTAR		43603 15344 99764 15338 99763 28507 28506	
HISTRELIN ACETATE	SUPPRELIN LA, VANTAS		23768	
LEUPROLIDE ACETATE	LUPRON DEPOT–PED, LUPRON DEPOT, LUPANETA		84352 84350 84353 30357 30356 80254 84602 84598 84593 30083 34009 34034	
GOSERELIN ACETATE	ZOLADEX		84591 84590	

GUIDELINES FOR USE

INITIAL CRITERIA (NOTE: FOR RENEWAL CRITERIA SEE BELOW)

1. Is the requested medication being used for gender dysphoria?

   If yes, **approve for 12 months for the requested agent and strength by GPID and override quantity limits.**
   If no, continue to #2.

CONTINUED ON NEXT PAGE

GONADOTROPIN RELEASING HORMONE (GNRH) AGONIST (NSA)

INITIAL CRITERIA (CONTINUED)

2. Is the request for Lupron Depot, Zoladex, Vantas, or Trelstar for a patient who has a diagnosis of advanced prostate cancer?

   If yes, **approve for 12 months for the requested agent and strength with the following quantity limits:**
   - **Lupron Depot 7.5mg (GPID 84602): #1 syringe/kit per 28 days (every month).**
   - **Lupron Depot 22.5mg (GPID 84593): #1 syringe/kit per 84 days (every 3 months).**
   - **Lupron Depot 30mg (GPID 84598): #1 syringe/kit per 112 days (every 4 months).**
   - **Lupron Depot 45mg (GPID 30083): #1 syringe/kit per 168 days (every 6 months).**
   - **Zoladex 3.6mg (GPID 84591): #1 implant per 28 days (every month).**
   - **Zoladex 10.8mg (GPID 84590): #1 implant per 84 days (every 3 months).**
   - **Vantas 50mg (NDC 67979-0500-01): #1 kit per 12 months.**
   - **Trelstar 3.75mg (GPID 15344; 99764): #1 Injection per 28 days (every month).**
   - **Trelstar 11.25mg (GPID 15338; 99763): #1 Injection per 84 days (every 3 months).**
   - **Trelstar 22.5mg (GPID 28507; 28506): #1 Injection per 168 days (every 6 months).**

   If no, continue to #3.

3. Is the request for Lupron Depot, Lupaneta, or Zoladex for a patient who has a diagnosis of moderate to severe pain associated with endometriosis **AND** meet **ALL** of the following criteria?
   - The patient is 18 years of age or older
   - The requested medication is prescribed by or in consultation with an obstetrician/gynecologist
   - The patient had a previous trial of or contraindication to a nonsteroidal anti-inflammatory drug (NSAID) **AND** a progestin-containing contraceptive preparation (e.g., combination hormonal contraceptive preparation, progestin-only contraceptive preparation)

   If yes, **approve for 6 months for the requested agent and strength with the following quantity limits:**
   - **Lupron Depot 3.75mg (GPID 80254): #1 syringe/kit per 28 days (every month).**
   - **Lupron Depot 11.25mg (GPID 84350): #1 syringe/kit per 84 days (every 3 months).**
   - **Lupaneta 3.75mg (GPID 34034): #1 syringe/kit per 28 days (every month).**
   - **Lupaneta 11.25mg (GPID 34009): #1 syringe/kit per 84 days (every 3 months).**
   - **Zoladex 3.6mg (GPID 84591): #1 implant per 28 days (every month).**

   If no, continue to #4.

CONTINUED ON NEXT PAGE

GONADOTROPIN RELEASING HORMONE (GNRH) AGONIST (NSA)

INITIAL CRITERIA (CONTINUED)

4. Is the request for Triptodur, Supprelin LA, or Lupron Depot-Ped for a female patient who has a diagnosis of central precocious puberty (CPP) **AND** meets **ALL** of the following criteria?
   - The patient is at least 2 years of age
   - The requested medication is prescribed by or given in consultation with a pediatric endocrinologist
   - Patient has elevated levels of follicle-stimulating hormone (FSH) (level >4.0 mIU/ml) and luteinizing hormone (LH) (level > 0.2 to 0.3 mIU/L) at diagnosis
   - Patient is younger than 8 years of age at the onset of CPP
   - Documentation of pubertal staging using the Tanner scale for:
     - Breast development (stage 2 or above) **AND**
     - Pubic hair growth (stage 2 or above)

   If yes, **approve for 12 months for the requested agent and strength with the following quantity limits:**
   - **Triptodur 22.5mg (GPID 43603): #1 vial/kit (22.5mg triptorelin pamoate) per 24 weeks.**
   - **Supprelin LA 50mg (NDC 67979-0002-01): #1 implant/kit (50mg histrelin) per 52 weeks.**
   - **Lupron Depot-Ped 1-months kits:**
     - **Lupron Depot-Ped 7.5mg (GPID 84352): #1 syringe/kit per 30 days.**
     - **Lupron Depot-Ped 11.25mg 1-month (GPID 84350): #1 syringe/kit per 30 days.**
     - **Lupron Depot-Ped 15mg (GPID 84353): #1 syringe/kit per 30 days.**
   - **Lupron Depot-Ped 3-months kits:**
     - **Lupron Depot-Ped 11.25mg 3-month (GPID 30357): #1 syringe/kit per 90 days.**
     - **Lupron Depot-Ped 30mg (GPID 30356): #1 syringe/kit per 90 days.**

   APPROVAL TEXT: Renewal requires physician attestation that Tanner scale staging at initial diagnosis of CPP has become stable or regresses at three separate medical visits in previous year and that patient has not reached actual age which corresponds to current pubertal age.

   If no, continue to #5.

CONTINUED ON NEXT PAGE

GONADOTROPIN RELEASING HORMONE (GNRH) AGONIST (NSA)

INITIAL CRITERIA (CONTINUED)

5. Is the request for Triptodur, Supprelin LA, or Lupron Depot-Ped for a male patient who has a diagnosis of central precocious puberty (CPP) **AND** meets **ALL** of the following criteria?
   - The patient is at least 2 years of age
   - The requested medication is prescribed by or given in consultation with a pediatric endocrinologist
   - Patient has elevated levels of follicle-stimulating hormone (FSH) (level >5.0 mIU/ml) and luteinizing hormone (LH) (level > 0.2 to 0.3 mIU/L) at diagnosis
   - Patient is younger than 9 years of age at the onset of CPP
   - Documentation of pubertal staging using the Tanner scale for:
     - Genital development (stage 2 or above) **AND**
     - Pubic hair growth (stage 2 or above)

   If yes, **approve for 12 months for the requested agent and strength with the following quantity limits:**
   - **Triptodur 22.5mg (GPID 43603): #1 vial/kit (22.5mg triptorelin pamoate) per 24 weeks.**
   - **Supprelin LA 50mg (NDC 67979-0002-01): #1 implant/kit (50mg histrelin) per 52 weeks.**
   - **Lupron Depot-Ped 1-months kits:**
     - **Lupron Depot-Ped 7.5mg (GPID 84352): #1 syringe/kit per 30 days.**
     - **Lupron Depot-Ped 11.25mg 1-month (GPID 84350): #1 syringe/kit per 30 days.**
     - **Lupron Depot-Ped 15mg (GPID 84353): #1 syringe/kit per 30 days.**
   - **Lupron Depot-Ped 3-months kits:**
     - **Lupron Depot-Ped 11.25mg 3-month (GPID 30357): #1 syringe/kit per 90 days.**
     - **Lupron Depot-Ped 30mg (GPID 30356): #1 syringe/kit per 90 days.**

   APPROVAL TEXT: Renewal requires physician attestation that Tanner scale staging at initial diagnosis of CPP has become stable or regresses at three separate medical visits in previous year and that patient has not reached actual age which corresponds to current pubertal age.

   If no, continue to #6.

6. Is the request for Zoladex to be used as an endometrial-thinning agent prior to endometrial ablation for dysfunctional uterine bleeding?

   If yes, **approve for 12 months with the following quantity limit:**
   - **Zoladex 3.6mg (GPID 84591): #1 implant per 28 days (every month).**

   If no, continue to #7.

CONTINUED ON NEXT PAGE

GONADOTROPIN RELEASING HORMONE (GNRH) AGONIST (NSA)

INITIAL CRITERIA (CONTINUED)

7. Is the request for Zoladex to be used in the palliative treatment of advanced breast cancer **AND** does the patient meet the following criterion?
   - The patient is a premenopausal or perimenopausal female

   If yes, **approve for 12 months with the following quantity limits:**
   - **Zoladex 3.6mg (GPID 84591): #1 implant per 28 days (every month).**

   If no, continue to #8.

8. Is the request for Zoladex **AND** the medication will be used in combination with flutamide for the management of locally confined carcinoma of the prostate?

   If yes, **approve for 4 months for the requested agent and strength with the following quantity limits:**
   - **Zoladex 3.6mg (GPID 84591): #1 implant per 28 days (every month).**
   - **Zoladex 10.8mg (GPID 84590): #1 implant (one time fill).**

   If no, continue to #9.

9. Is the request for Lupron Depot to be used concomitantly with iron therapy for the preoperative hematologic improvement of patients with anemia caused by uterine leiomyomata (fibroids)?

   If yes, **approve by GPID for the requested strength with the following quantity limits and approval durations:**
   - **Lupron Depot 3.75mg (GPID 80254): #1 syringe/kit per 28 days (every month) for 3 months.**
   - **Lupron Depot 11.25mg (GPID 84350): one fill of #1 syringe/kit.**

   If no, do not approve.
   INITIAL DENIAL TEXT: The guideline named **GONADOTROPIN RELEASING HORMONE (GNRH) AGONIST** requires that the patient has gender dysphoria or a diagnosis of advanced prostate cancer, moderate to severe pain associated with endometriosis, or central precocious puberty (CPP). Additionally, Zoladex may be used as an endometrial-thinning agent prior to endometrial ablation for dysfunctional uterine bleeding, in the palliative treatment of advanced breast cancer in pre- and perimenopausal women, or in combination with flutamide for the management of locally confined carcinoma of the prostate; Lupron Depot may be used concomitantly with iron therapy for the preoperative hematologic improvement of patients with anemia caused by uterine leiomyomata (fibroids). In addition, the following criteria must also be met for the requested diagnosis:
   (Initial denial text continued on next page)

CONTINUED ON NEXT PAGE

GONADOTROPIN RELEASING HORMONE (GNRH) AGONIST (NSA)

INITIAL CRITERIA (CONTINUED)

Patients diagnosed with moderate to severe pain associated with endometriosis, approval requires:

- The request is for one of the following agents: Lupron Depot, Lupaneta, or Zoladex
- The patient is 18 years of age or older
- The requested medication is prescribed by or in consultation with an obstetrician/gynecologist
- The patient had a previous trial of or contraindication to a nonsteroidal anti-inflammatory drug (NSAID) **AND** a progestin-containing contraceptive preparation (e.g., combination hormonal contraceptive preparation, progestin-only contraceptive preparation)

Female patients diagnosed with CPP, approval requires:

- The request is for one of the following agents: Triptodur, Supprelin LA, or Lupron Depot-Ped
- The patient is at least 2 years of age
- The requested medication is prescribed by or given in consultation with a pediatric endocrinologist
- Patient has elevated levels of follicle-stimulating hormone (FSH) (level >4.0 mIU/ml) and luteinizing hormone (LH) (level > 0.2 to 0.3 mIU/L) at diagnosis
- Patient is younger than 8 years of age at the onset of CPP
- Documentation of pubertal staging using the Tanner scale for:
  - Breast development (stage 2 or above) **AND**
  - Pubic hair growth (stage 2 or above)

Male patients diagnosed with CPP, approval requires:

- The request is for one of the following agents: Triptodur, Supprelin LA, or Lupron Depot-Ped
- The patient is at least 2 years of age
- The requested medication is prescribed by or given in consultation with a pediatric endocrinologist
- Patient has elevated levels of follicle-stimulating hormone (FSH) (level >5.0 mIU/ml) and luteinizing hormone (LH) (level > 0.2 to 0.3 mIU/L) at diagnosis
- Patient is younger than 9 years of age at the onset of CPP
- Documentation of pubertal staging using the Tanner scale for:
  - Genital development (stage 2 or above) **AND**
  - Pubic hair growth (stage 2 or above)

(Initial denial text continued on next page)

CONTINUED ON NEXT PAGE

GONADOTROPIN RELEASING HORMONE (GNRH) AGONIST (NSA)

INITIAL CRITERIA (CONTINUED)

Requests for Zoladex to be used in the palliative treatment of advanced breast cancer, approval requires:

- The patient is a premenopausal or perimenopausal female

Requests for Lupron Depot, Zoladex, Vantas, or Trelstar for patients with advanced prostate cancer will be approved without requiring additional criteria.

Requests for patients with gender dysphoria will be approved without requiring additional criteria.

Requests for Zoladex to be used as an endometrial-thinning agent prior to endometrial ablation for dysfunctional uterine bleeding or in combination with flutamide for the management of locally confined carcinoma of the prostate will be approved without requiring additional criteria.

Requests for Lupron Depot to be used concomitantly with iron therapy for the preoperative hematologic improvement of patients with anemia caused by uterine leiomyomata (fibroids) will be approved without requiring additional criteria.

RENEWAL CRITERIA

1. Is the requested medication being used for gender dysphoria?

   If yes, **approve for 12 months for the requested agent and strength by GPID.**
   If no, continue to #2.

CONTINUED ON NEXT PAGE

GONADOTROPIN RELEASING HORMONE (GNRH) AGONIST (NSA)

RENEWAL CRITERIA (CONTINUED)

2. Is the request for Lupron Depot, Zoladex, Vantas, or Trelstar for a patient who has a diagnosis of advanced prostate cancer?

   If yes, **approve for 12 months for the requested agent and strength with the following quantity limits:**
   - **Lupron Depot 7.5mg (GPID 84602): #1 syringe/kit per 28 days (every month).**
   - **Lupron Depot 22.5mg (GPID 84593): #1 syringe/kit per 84 days (every 3 months).**
   - **Lupron Depot 30mg (GPID 84598): #1 syringe/kit per 112 days (every 4 months).**
   - **Lupron Depot 45mg (GPID 30083): #1 syringe/kit per 168 days (every 6 months).**
   - **Zoladex 3.6mg (GPID 84591): #1 implant per 28 days (every month).**
   - **Zoladex 10.8mg (GPID 84590): #1 implant per 84 days (every 3 months).**
   - **Vantas 50mg (NDC 67979-0500-01): #1 kit per 12 months.**
   - **Trelstar 3.75mg (GPID 15344; 99764): #1 Injection per 28 days (every month).**
   - **Trelstar 11.25mg (GPID 15338; 99763): #1 Injection per 84 days (every 3 months).**
   - **Trelstar 22.5mg (GPID 28507; 28506): #1 Injection per 168 days (every 6 months).**

   If no, continue to #3.

3. Is the request for Lupron Depot, Lupaneta, or Zoladex for a patient who has a diagnosis of moderate to severe pain associated with endometriosis **AND** meet **ALL** of the following criteria?
   - Physician attestation of improvement of pain related to endometriosis while on therapy
   - The patient is receiving concomitant add-back therapy (i.e., combination estrogen-progestin or progestin-only contraceptive preparation)
   - The patient has **NOT** received a total course of therapy exceeding 12 months

   If yes, **approve for 6 months for the requested agent and strength with the following quantity limits:**
   - **Lupron Depot 3.75mg (GPID 80254): #1 syringe/kit per 28 days (every month).**
   - **Lupron Depot 11.25mg (GPID 84350): #1 syringe/kit per 84 days (every 3 months).**
   - **Lupaneta 3.75mg (GPID 34034): #1 syringe/kit per 28 days (every month).**
   - **Lupaneta 11.25mg (GPID 34009): #1 syringe/kit per 84 days (every 3 months).**
   - **Zoladex 3.6mg (GPID 84591): #1 implant per 28 days (every month).**

   If no, continue to #4.

CONTINUED ON NEXT PAGE

GONADOTROPIN RELEASING HORMONE (GNRH) AGONIST (NSA)

RENEWAL CRITERIA (CONTINUED)

4. Is the request for Triptodur, Supprelin LA, or Lupron-Depot Ped for a patient who has a diagnosis of central precocious puberty (CPP) **AND** meet **ALL** of the following criteria?
   - Physician attestation for **ALL** of the following:
     - Tanner scale staging at initial diagnosis of CPP has stabilized or regressed during three separate medical visits in the previous year
     - Patient has not reached actual age which corresponds to current pubertal age

   If yes, **approve for 12 months for the requested agent and strength with the following quantity limits:**
   - **Triptodur 22.5mg (GPID 43603): #1 vial/kit (22.5mg triptorelin pamoate) per 24 weeks.**
   - **Supprelin LA 50mg (NDC 67979-0002-01): #1 implant/kit (50mg histrelin) per 52 weeks.**
   - **Lupron Depot-Ped 1-months kits:**
     - **Lupron Depot-Ped 7.5mg (GPID 84352): #1 syringe/kit per 30 days.**
     - **Lupron Depot-Ped 11.25mg 1-month (GPID 84350): #1 syringe/kit per 30 days.**
     - **Lupron Depot-Ped 15mg (GPID 84353): #1 syringe/kit per 30 days.**
   - **Lupron Depot-Ped 3-months kits:**
     - **Lupron Depot-Ped 11.25mg 3-month (GPID 30357): #1 syringe/kit per 90 days.**
     - **Lupron Depot-Ped 30mg (GPID 30356): #1 syringe/kit per 90 days.**

   If no, do not approve.
   RENEWAL DENIAL TEXT: The guideline named **GONADOTROPIN RELEASING HORMONE (GNRH) AGONIST** requires that the patient has gender dysphoria or a diagnosis of advanced prostate cancer, moderate to severe pain associated with endometriosis, or central precocious puberty (CPP). In addition, the following criteria must also be met for the requested diagnosis:

   Diagnosis of moderate to severe pain associated with endometriosis, approval requires:
   - The request is for one of the following agents: Lupron Depot, Lupaneta, or Zoladex
   - Physician attestation of improvement of pain related to endometriosis while on therapy
   - The patient is receiving concomitant add-back therapy (i.e., combination estrogen-progestin or progestin-only contraceptive preparation)
   - The patient has **NOT** received a total course of therapy exceeding 12 months

   (Renewal denial text continued on next page)

CONTINUED ON NEXT PAGE

GONADOTROPIN RELEASING HORMONE (GNRH) AGONIST (NSA)

RENEWAL CRITERIA (CONTINUED)

Diagnosis of CPP, approval requires:

- The request is for one of the following agents: Triptodur, Supprelin LA, or Lupron Depot-Ped with physician attestation of all of the following:
  - Tanner scale staging at initial diagnosis of CPP has stabilized or regressed during three separate medical visits in the previous year
  - Patient has not reached actual age which corresponds to current pubertal age

Requests for Lupron Depot, Zoladex, Vantas, or Trelstar for patients with advanced prostate cancer will be approved without requiring additional criteria.

Requests for patients with gender dysphoria will be approved without requiring additional criteria.

RATIONALE

Promote appropriate utilization of **GONADOTROPIN RELEASING HORMONE (GNRH) AGONIST** (Triptodur, Trelstar, Lupaneta, Lupron Depot, Supprelin LA, Lupron Depot-Ped, Zoladex, and Vantas) based on FDA approved indications and dosing and NCCN recommendations.

NCCN guidelines recommend premenopausal patients with hormone-positive disease have ovarian ablation/suppression (with goserelin) and be treated as a postmenopausal woman.

FDA APPROVED INDICATIONS

Triptodur is a GnRH agonist indicated for the treatment of pediatric patients 2 years and older with central precocious puberty (CPP).

Trelstar is a GnRH agonist indicated for the palliative treatment of advanced prostate cancer.

Supprelin LA is a GnRH agonist indicated for the treatment of children with central precocious puberty.

Vantas is a GNRH agonist indicated for the palliative treatment of advanced prostate cancer.

Lupron Depot-Ped is a GnRH agonist indicated for the treatment of children with central precocious puberty.

CONTINUED ON NEXT PAGE

GONADOTROPIN RELEASING HORMONE (GNRH) AGONIST (NSA)

FDA APPROVED INDICATIONS (CONTINUED)

Lupron Depot is a GnRH agonist indicated for:
- Palliative treatment of advanced prostatic cancer
- Management of endometriosis, including pain relief and reduction of endometriotic lesions
- Concomitant use with iron therapy for preoperative hematologic improvement of patients with anemia caused by uterine leiomyomata (fibroids)

Lupaneta is indicated in combination with norethindrone acetate for initial management of the painful symptoms of endometriosis and for management of recurrence of symptoms.

Zoladex is a GnRH agonist indicated for:
- Use in combination with flutamide for the management of locally confined carcinoma of the prostate
- Palliative treatment of advanced carcinoma of the prostate
- The management of endometriosis
- Use as an endometrial-thinning agent prior to endometrial ablation for dysfunctional uterine bleeding
- Use in the palliative treatment of advanced breast cancer in pre- and perimenopausal women

DOSAGE AND ADMINISTRATION

Triptodur

Triptodur must be administered under the supervision of a physician.

The dosage of Triptodur is 22.5 mg reconstituted with accompanying diluent (Sterile Water) 2 mL, and administered as a single intramuscular injection once every 24 weeks. Triptodur treatment should be discontinued at the appropriate age of onset of puberty at the discretion of the physician.

Trelstar

Trelstar must be administered under the supervision of a physician.

Trelstar is administered as a single intramuscular injection in either buttock. The recommended dose is 3.75 mg every 4 weeks, 11.25 mg every 12 weeks, and 22.5 mg every 24 weeks.

Supprelin LA

Supprelin LA must be administered under the supervision of a physician.

The recommended dose of Supprelin LA is one implant every 12 months. The implant is inserted subcutaneously in the inner aspect of the upper arm and provides continuous release of histrelin for 12 months of hormonal therapy.

CONTINUED ON NEXT PAGE

GONADOTROPIN RELEASING HORMONE (GNRH) AGONIST (NSA)

FDA APPROVED INDICATIONS (CONTINUED)

DOSAGE AND ADMINISTRATION
At the time an implant is removed, another implant may be inserted to continue therapy. Discontinuation of Supprelin LA should be considered at the discretion of the physician and at the appropriate time point for the onset of puberty (approximately 11 years for females and 12 years for males).

Vantas
Vantas must be administered under the supervision of a physician.

The recommended dose of Vantas is one implant (50 mg) every 12 months. The implant is inserted subcutaneously in the inner aspect of the upper arm.

Lupron Depot- Ped
Lupron Depot- Ped must be administered under the supervision of a physician.

1-month administration (7.5 mg, 11.25 mg, or 15 mg)
- The starting dose 7.5 mg, 11.25 mg, or 15 mg for 1-month administration is based on the child's weight, as below:

Dosing Recommendations Based on Body Weight for Lupron Depot- Ped 1- month Formulations	
Body Weight	**Recommended Dose**
≤ 25 kg	7.5 mg
> 25-37.5 kg	11.25 mg
> 37.5 kg	15 mg

The dose of Lupron Depot-Ped must be individualized for each child. If adequate hormonal and clinical suppression is not achieved with the starting dose, it should be increased to the next available higher dose (e.g. 11.25 mg or 15 mg at the next monthly injection). Similarly, the dose may be adjusted with changes in body weight.

3-month administration (11.25 mg or 30 mg)
Lupron Depot- Ped 11.25 mg or 30 mg for 3-month administration should be administered once every three months (12 weeks) as a single intramuscular injection.

Each Lupron Depot- Ped 11.25 mg or 30 mg for 3-month administration strength and formulation has different release characteristics. Do not use partial syringes or a combination of syringes to achieve a particular dose. Lupron Depot- Ped 11.25 mg or 30 mg for 3-month administration treatment should be discontinued at the appropriate age of onset of puberty at the discretion of the physician.

CONTINUED ON NEXT PAGE

GONADOTROPIN RELEASING HORMONE (GNRH) AGONIST (NSA)

FDA APPROVED INDICATIONS (CONTINUED)

DOSAGE AND ADMINISTRATION

Lupron Depot

Lupron Depot must be administered under the supervision of a physician.

Lupron Depot is administered as a single intramuscular injection in the gluteal area, anterior thigh, or deltoid. For the treatment of advanced prostate cancer, the recommended dose is 7.5 mg every 4 weeks, 22.5 mg every 12 weeks, 30 mg every 16 weeks, and 45 mg every 24 weeks. For the treatment of endometriosis, Lupron Depot 3.75 mg is administered as a single intramuscular injection every month for up to six injections (6 months of therapy) OR 11.25 mg as a single intramuscular injection every 3 months for up to two injections (6 months of therapy). For concomitant use with iron therapy for the preoperative hematologic improvement of patients with anemia caused by uterine leiomyomata (fibroids), Lupron Depot 3.75 mg is administered as a single intramuscular injection every month for up to 3 months OR 11.25 mg as a single intramuscular injection.

Lupaneta

Lupaneta Pack consists of Lupron Depot and norethindrone acetate tablets.

Lupron Depot must be administered under the supervision of a physician.

For the treatment of endometriosis, Lupron Depot 3.75 mg is administered as a single intramuscular injection every month for up to six injections (6 months of therapy) OR 11.25 mg as a single intramuscular injection every 3 months for up to two injections (6 months of therapy). Norethindrone acetate 5 mg tablets taken orally once daily for up to 6 months. Duration of initial treatment or retreatment should be limited to 6 months.

Zoladex

Zoladex must be administered under the supervision of a physician.

Zoladex 3.6mg implant is dosed every 28 days.

Zoladex 10.8mg implant should be administered subcutaneously every 12 weeks.
For patients with Stage T2b-T4 (Stage B2-C) prostatic carcinoma, treatment should be started 8 weeks prior to initiating radiotherapy and should continue during radiation therapy. A treatment regimen using Zoladex 3.6 mg depot 8 weeks before radiotherapy, followed in 28 days by Zoladex 10.8 mg depot, can be administered. Alternatively, four injections of 3.6 mg depot can be administered at 28-day intervals, two depots preceding and two during radiotherapy.

CONTINUED ON NEXT PAGE

GONADOTROPIN RELEASING HORMONE (GNRH) AGONIST (NSA)

REFERENCES

- Triptodur [Prescribing Information]. Arbor Pharmaceuticals, LLC. Atlanta, GA. June 2017.
- Supprelin LA [Prescribing Information]. Endo Pharmaceuticals. Malvern, PA. May 2017.
- Lupron Depot-Ped [Prescribing Information]. AbbVie Inc. North Chicago, IL. May 2017.
- National Comprehensive Cancer Network, Inc. NCCN Clinical Practice Guidelines in Oncology. Breast Cancer. (Version 1.2018).

Library	Commercial	NSA
Yes	No	Yes

Part D Effective: N/A
Commercial Effective: 10/01/18
Created: 03/18
Client Approval: 09/18
P&T Approval: 07/18

HYALURONATE (NSA)

Generic	Brand	HICL	GCN	Exception/Other
HYALURONATE SODIUM	EUFLEXXA, HYALGAN, GEL-ONE, GELSYN-3, ORTHOVISC, SUPARTZ FX, GENVISC 850, VISCO-3, TRIVISC		21448 32121 32122 41795	ROUTE = INTRAARTIC
HYLAN G-F 20	SYNVISC, SYNVISC-ONE	26552		
HYALURONATE SODIUM, STABILIZED	MONOVISC, DUROLANE		36397 33139	
HYALURONATE, MODIFIED, NON-CROSSLINK	HYMOVIS	42225		

GUIDELINES FOR USE

1. Has the patient received previous treatment on the same knee with Synvisc, Synvisc-One, Hyalgan, Euflexxa, Supartz FX, Gel-One, Monovisc, Orthovisc, Hymovis, Gelsyn-3, Genvisc 850, Visco-3, Trivisc, OR Durolane?

   If yes, continue to #3.
   If no, continue to #2.

2. Does the patient have a diagnosis of osteoarthritis of the knee and meets **ALL** of the following criteria?
   - The patient is at least 21 years of age
   - The patient has failed a minimum of a 6-week trial of non-pharmacologic therapy such as education, exercise, use of insoles or braces, weight reduction and physical therapy
   - The patient had a previous trial of intra-articular steroids

   If yes, **approve for 6 months by GPID with the following quantity limits per affected knee:**
   - **Euflexxa - 6mL (3 syringes)**
   - **Gel-One - 3mL (1 syringe)**
   - **Gelsyn-3 - 6mL (3 syringes)**
   - **Hyalgan - 10mL (5 syringes/vials)**

   (Approval directions continued on next page)

CONTINUED ON NEXT PAGE

HYALURONATE (NSA)

GUIDELINES FOR USE (CONTINUED)

- **Hymovis - 6mL (2 syringes)**
- **Monovisc - 4mL (1 syringe)**
- **Orthovisc - 8mL (4 syringes)**
- **Supartz FX - 12.5mL (5 syringes)**
- **Synvisc - 6mL (3 syringes)**
- **Synvisc-One - 6mL (one syringe)**
- **Genvisc 850 - 12.5mL (5 syringes)**
- **Visco-3 - 7.5mL (3 syringes)**
- **Trivisc – 7.5mL (3 syringes)**
- **Durolane - 3mL (one syringe)**

If no, do not approve.
DENIAL TEXT: See the denial text at the end of the guideline.

3. Has it been at least 6 months since the last treatment with this agent?

If yes, **approve for 6 months by GPID with the following quantity limits per affected knee:**

- **Euflexxa - 6mL (3 syringes)**
- **Gel-One - 3mL (1 syringe)**
- **Gelsyn-3 - 6mL (3 syringes)**
- **Hyalgan - 10mL (5 syringes/vials)**
- **Hymovis - 6mL (2 syringes)**
- **Monovisc - 4mL (1 syringe)**
- **Orthovisc - 8mL (4 syringes)**
- **Supartz FX - 12.5mL (5 syringes)**
- **Synvisc - 6mL (3 syringes)**
- **Synvisc-One - 6mL (one syringe)**
- **Genvisc 850 - 12.5mL (5 syringes)**
- **Visco-3 - 7.5mL (3 syringes)**
- **Trivisc – 7.5mL (3 syringes)**
- **Durolane - 3mL (one syringe)**

If no, do not approve:
DENIAL TEXT: See the denial text at the end of the guideline.

CONTINUED ON NEXT PAGE

HYALURONATE (NSA)

GUIDELINES FOR USE (CONTINUED)

DENIAL TEXT: The guideline named **HYALURONATE** requires a diagnosis of osteoarthritis of the knee. In addition, the following criteria must also be met:

- The patient is at least 21 years of age
- The patient failed a minimum of a 6-week trial of non-pharmacologic therapy such as education, exercise, use of insoles or braces, weight reduction and physical therapy
- The patient had a previous trial of intra-articular steroids

For patients who have been previously treated on the same knee with Synvisc, Synvisc-One, Hyalgan, Euflexxa, Supartz FX, Gel-One, Monovisc, Orthovisc, Hymovis, Gelsyn-3, Genvisc 850, Visco-3, Trivisc, or Durolane, approval requires:

- At least 6 months since the last treatment has been received

RATIONALE

Ensure appropriate use of hyaluronic acids in the treatment of osteoarthritis.

FDA APPROVED INDICATIONS

Durolane, Synvisc, Synvisc-One, Hyalgan, Supartz FX, Euflexxa, Gel-One, Gelsyn-3, Orthovisc, Monovisc, Hymovis, Genvisc 850, Visco-3, and Trivisc are indicated for the treatment of pain in osteoarthritis (OA) of the knee in patients who have failed to respond adequately to conservative nonpharmacologic therapy and simple analgesics, e.g., acetaminophen.

REFERENCES

- Genzyme Corporation. Synvisc product Information. Ridgefield, NJ, March 2010.
- Genzyme Corporation. Synvisc-One product information. Ridgefield, NJ, January 2010.
- Fidia Farmaceutici. Hyalgan product Information. Padua, Italy, Jan 2009.
- Seikagaku Corporation. Supartz product Information. Tokyo, Japan. January 2007.
- Anika Therapeutics Inc. Orthovisc Product information. Woburn, MA. June 2006.
- FDA Approves Monovisc, A New Single Injection Treatment for Treatment of Pain Due to Osteoarthritis of the Knee. Accessed on 4/15/2014 at http://www.businesswire.com/news/home/20140225007021/en/FDA-Approves-MONOVISC%C2%AE-Single-Injection-Treatment-Treatment
- Micromedex® Healthcare Series [database online]. Greenwood Village, CO: Thomson Healthcare. Available at: http://www.thomsonhc.com/hcs/librarian/. [Accessed: June 22, 2010].
- Clinical Pharmacology [database online]. Tampa, FL: Gold Standard, Inc.; 2009. Available at: http://www.clinicalpharmacology.com. [Accessed: June 22, 2010].

CONTINUED ON NEXT PAGE

HYALURONATE (NSA)

REFERENCES (CONTINUED)

- Pagnano M, Westrich G. Successful non-operative management of chronic osteoarthritis pain of the knee: safety and efficacy of retreatment with intra-articular hyaluronans. Osteoarthritis Cartilage. 2005; 13(9):751-61.
- Ferring Pharmaceuticals. Euflexxa product information. Parsippany, NJ. (Revision 9, no date available).
- Recommendations for the Medical Management of Osteoarthritis of the Hip and Knee. Arthritis and Rheumatism 2000; 43:905-1915.
- Fidia Pharma. Hymovis product information. Parsippany, NJ. (No date available).
- Zimmer Inc. Gel-one product information. Warsaw, IN. May 20, 2011.Institut Biochimique SA (IBSA). Gelsyn-3 product information. Pambio-Noranco, Switzerland. 2016.
- Institut Biochimique SA (IBSA). Gelsyn-3 product information. Pambio-Noranco, Switzerland. 2016.
- Durolane Instructions for Use: Information for Prescribers: Available at: https://www.accessdata.fda.gov/cdrh_docs/pdf17/P170007D.pdf. Accessed November 13, 2017.
- Clinical Pharmacology [database online]. Tampa, FL: Gold Standard, Inc.; 2009. Available at: http://www.clinicalpharmacology.com. Accessed November 13, 2017.
- Durolane Brochure. Available at: http://durolane.com/wp-content/uploads/2016/02/DUROLANE_MDbrochure_UK.pdf. Accessed November 13, 2017.
- Durolane Patient Information. Available at: https://www.accessdata.fda.gov/cdrh_docs/pdf17/P170007C.pdf. Accessed November 13, 2017.
- Genvisc 850 Prescribing Information Information. Available at: https://www.accessdata.fda.gov/cdrh_docs/pdf14/P140005d.pdf. Accessed March 15, 2018.
- Visco-3 Prescribing Information. Available at https://www.accessdata.fda.gov/cdrh_docs/pdf/P980044S027d.pdf. Accessed March 15, 2018
- Trivisc Prescribing Information. Available at https://www.accessdata.fda.gov/cdrh_docs/pdf16/P160057D.pdf. Accessed October 15, 2018.

Library	Commercial	NSA
Yes	No	Yes

Part D Effective: N/A
Commercial Effective: 11/01/18

Created: 05/14
Client Approval: 10/18

P&T Approval: 01/18

HYDROXYPROGESTERONE CAPROATE (NSA)

Generic	Brand	HICL	GCN	Exception/Other
HYDROXYPROGESTERONE CAPROATE	MAKENA		39946 40784 44459	
HYDROXYPROGESTERONE CAPROATE	HYDROXY-PROGESTERONE CAPROATE (GENERIC FOR DELALUTIN)		11180	

GUIDELINES FOR USE

1. Is the request for Makena?

   If yes, continue to #2.
   If no, continued to #3.

2. Is the request for the reduction of risk of preterm birth in women with a history of singleton spontaneous preterm birth and meets **ALL** of the following criteria?
   - The patient does **NOT** have multiple gestations (twins, triplets, etc.)
   - The patient has a history of delivery at less than 37 weeks of gestation following spontaneous preterm labor or premature rupture of membranes
   - The patient is at least 16 weeks pregnant but less than 37 weeks pregnant

   If yes, **approve Makena for 6 months by GPID with a fill count of 5 and the following quantity limits:**
   - **Makena 1,250mg/5mL (GPID 39946): #5mL per 28 days.**
   - **Makena 250mg/mL (GPID 40784): #4mL per 28 days.**
   - **Makena 275mg/1.1mL autoinjector (GPID 44459): #4.4mL per 28 days.**

   If no, do not approve.
   DENIAL TEXT: The guideline named **HYDROXYPROGESTERONE CAPROATE (Makena)** requires that the agent will be used for the reduction of risk of preterm birth in women with a history of singleton spontaneous preterm birth. The following criteria must also be met.
   - The patient does **NOT** have multiple gestations (twins, triplets, etc.).
   - The patient is at least 16 weeks pregnant but less than 37 weeks pregnant with a single gestation.
   - The patient has a history of delivery at less than 37 weeks of gestation following spontaneous preterm labor or premature rupture of membranes.

CONTINUED ON NEXT PAGE

HYDROXYPROGESTERONE CAPROATE (NSA)

GUIDELINES FOR USE (CONTINUED)

3. Is the request for use in a non-pregnant female who meets **ONE** of the following criteria?
   - For treatment of advanced adenocarcinoma of the uterine corpus (Stage III or IV)
   - For the management of amenorrhea (primary and secondary) and abnormal uterine bleeding due to hormonal imbalance in the absence of organic pathology, such as submucous fibroids or uterine cancer
   - As a test for endogenous estrogen production
   - For the production of secretory endometrium and desquamation

   If yes, **approve for 12 months by GPID.**
   If no, do not approve.
   DENIAL TEXT: The guideline named **HYDROXYPROGESTERONE CAPROATE (Generic Delalutin)** requires use in non-pregnant females for **ONE** of the following:
   - For treatment of advanced adenocarcinoma of the uterine corpus (Stage III or IV)
   - For the management of amenorrhea (primary and secondary) and abnormal uterine bleeding due to hormonal imbalance in the absence of organic pathology, such as submucous fibroids or uterine cancer
   - As a test for endogenous estrogen production
   - For the production of secretory endometrium and desquamation

---

RATIONALE
Ensure appropriate use of Makena consistent with its FDA approved indication. Ensure appropriate use of hydroxyprogesterone caproate with its FDA approved indication.

FDA APPROVED INDICATIONS
Makena is a progestin indicated to reduce the risk of preterm birth in women with a singleton pregnancy that have a history of singleton spontaneous preterm birth. The effectiveness of Makena is based on improvement in the proportion of women who delivered < 37 weeks of gestation. There are no controlled trials demonstrating a direct clinical benefit, such as improvement in neonatal mortality and morbidity.

Limitation of use: While there are many risk factors for preterm birth, safety and efficacy of Makena has been demonstrated only in women with a prior spontaneous singleton preterm birth. It is not intended for use in women with multiple gestations or other risk factors for preterm birth.

CONTINUED ON NEXT PAGE

HYDROXYPROGESTERONE CAPROATE (NSA)

FDA APPROVED INDICATIONS (CONTINUED)

Hydroxyprogesterone caproate (generic for Delalutin) is indicated in non-pregnant women:
- For the treatment of advanced adenocarcinoma of the uterine corpus (Stage III or IV).
- In the management of amenorrhea (primary and secondary) and abnormal uterine bleeding due to hormonal imbalance in the absence of organic pathology, such as submucous fibroids or uterine cancer.
- As a test for endogenous estrogen production
- For the production of secretory endometrium and desquamation.

DOSAGE AND ADMINISTRATION
MAKENA
- Makena auto-injector: Administer subcutaneously using Makena auto-injector at a dose of 275 mg (1.1 mL) once weekly, in the back of either upper arm by a healthcare provider
- Makena (single- and multi-dose vials): Administer intramuscularly at a dose of 250 mg (1 mL) once weekly in the upper outer quadrant of the gluteus maximus by a healthcare provider
- Begin treatment between 16 weeks, 0 days and 20 weeks, 6 days of gestation
- Continue administration once weekly until week 37 (through 36 weeks, 6 days) of gestation or delivery, whichever occurs first

Hydroxyprogesterone caproate (generic for Delalutin)
- Treatment of advanced adenocarcinoma of the uterine corpus (Stage III or IV)
  - Dosage: 1-7 grams IM per week until relapse occurs or after 12 weeks with no objective response
- Amenorrhea (primary or secondary) and abnormal uterine bleeding due to hormonal imbalance in the absence of organic pathology
  - Dosage: 375mg IM x 1. Then begin cyclic therapy schedule after 4 days of desquamation or, if there is no bleeding, 21 days after initial injection. Discontinue after 4 cycles
- Test for endogenous estrogen production
  - Dosage: 250mg IM once and repeated once for confirmation, 4 weeks after first injection
- Production of secretory endometrium and desquamation
  - Patients not on estrogen therapy – utilize cyclic therapy schedule.
  - Patients currently on estrogen therapy
- Dosage: 375mg IM x 1. Then begin cyclic therapy schedule after 4 days of desquamation or, if there is no bleeding, 21 days after initial injection
- Cyclic therapy schedule
  - 28-day cycle; repeated every four weeks
  - Day 1 of each cycle: 20mg of estradiol valerate injection USP
  - Day 14 of each cycle: 250mg IM of hydroxyprogesterone caproate and 5mg estradiol valerate injection USP

CONTINUED ON NEXT PAGE

HYDROXYPROGESTERONE CAPROATE (NSA)

REFERENCES

- Makena [Prescribing Information]. Waltham, MA: AMAG Pharmaceuticals, Inc. February 2018.
- Hydroxyprogesterone caproate [Prescribing Information]. Santa Ana, CA: McGuff Pharmaceuticals, Inc. August 2015.

Library	Commercial	NSA
Yes	No	Yes

Part D Effective: N/A
Commercial Effective: 04/01/18
Created: 05/11
Client Approval: 03/18
P&T Approval: 01/18

IMMUNE GLOBULIN (NSA)

Generic	Brand	HICL	GCN	Exception/Other
IMMUNE GLOBULIN	BIVIGAM CARIMUNE NF NANOFILTERE FLEBOGAMMA DIF GAMASTAN S-D GAMMAGARD S-D GAMMAPLEX PRIVIGEN GAMMAGARD LIQUID HIZENTRA	04202 41798		
IMMUNE GLOB, GAM CAPRYLATE	GAMUNEX-C GAMMAKED	25631		
IMMUNE GLOBULIN / MALTOSE	OCTAGAM	33220		
IGG/HYALURONIDASE, RECOMBINANT	HYQVIA	41391		
IMMUN GLOB G(IGG)/GLY/IGA 0-50	HYQVIA IG COMPONENT	41995		
IMMUN GLOB G(IGG)/GLY/IGA OV50	CUVITRU	41796		

This drug must be reviewed by a pharmacist.

GUIDELINES FOR USE

1. Is the request for use as a subcutaneous injection?

   If yes, continue to #2.
   If no, continue to #5.

2. Is the request for Hizentra and will be used for **ONE** of the following diagnoses?
   - Primary immunodeficiency disease (PID)
   - Chronic Inflammatory Demyelinating Polyneuropathy (CIDP)

   If yes, **approve for 12 months by HICL.**
   If no, continue to #3.

CONTINUED ON NEXT PAGE

IMMUNE GLOBULIN (NSA)

GUIDELINE FOR USE (CONTINUED)

3. Is the request for Gammagard Liquid, Cuvitru, Gamunex-C, Gammaked, or Hyqvia (**NOTE:** Gammagard, Gamunex-C and Gammaked may be given via SC or IV route.)?

   If yes, continue to #4.
   If no, do not approve.
   DENIAL TEXT: See the denial text at the end of the guideline.

4. Does the patient have a primary immunodeficiency disease (PID)?

   If yes, **approve for 12 months by HICL.**
   If no, do not approve.
   DENIAL TEXT: See the denial text at the end of the guideline.

5. Is the request for a non-self-administered agent (i.e., IV route)?

   If yes, continue to #6.
   If no, guideline does not apply.

6. Does the plan cover non-self-administered agents?

   If yes continue to #7.
   If no, do not approve.
   DENIAL TEXT: See the denial text at the end of the guideline.

7. Is the request for Cuvitru, Hizentra, or Hyqvia (**NOTE**: Cuvitru, Hizentra, and Hyqvia are indicated only for SC route)?

   If yes, do not approve.
   DENIAL TEXT: See the denial text at the end of the guideline.
   If no, continue to #8.

8. Is the requested medication Gamastan S/D (**NOTE**: Gamastan S/D is indicated for intramuscular use only)?

   If yes, continue to #9.
   If no, continue to #10.

CONTINUED ON NEXT PAGE

IMMUNE GLOBULIN (NSA)

GUIDELINE FOR USE (CONTINUED)

9. Is Gamastan S/D being used for hepatitis A, measles, varicella, or rubella prophylaxis, or passive immunization?

   If yes, **approve for 12 months by HICL.**
   If no, do not approve.
   DENIAL TEXT: See the denial text at the end of the guideline.

10. Does the patient have **ONE** of the following diagnoses?
    - Primary Immunodeficiency Disease (PID)
    - Idiopathic Thrombocytopenic Purpura (ITP)
    - Chronic Inflammatory Demyelinating Polyneuropathy (CIDP)
    - Multifocal Motor Neuropathy (MMN)
    - Kawasaki Syndrome
    - B-cell Chronic Lymphocytic Leukemia (CLL) with Hypogammaglobulinemia, Autoimmune Hemolytic Anemia (AIHA), Immune Thrombocytopenic Purpura (ITP), or pure Red Blood Cell Aplasia (PRCA)
    - Guillain-Barre Syndrome (GBS)
    - Myasthenia Gravis
    - Autoimmune Graves' Ophthalmopathy
    - Cytomegalovirus-induced Pneumonitis related to a solid organ transplant
    - Prevention of bacterial infection in an HIV-infected child
    - Reduction of secondary infections in pediatric HIV infections
    - Dermatomyositis or polymyositis
    - Autoimmune uveitis (Birdshot retinochoroidopathy)
    - Lambert-Eaton myasthenic syndrome
    - IgM anti-myelin-associated glycoprotein paraprotein-associated peripheral neuropathy
    - Stiff-man syndrome
    - Neonatal sepsis
    - Rotaviral enterocolitis
    - Toxic shock syndrome
    - Enteroviral meningoencephalitis
    - Toxic Epidermal Necrolysis or Stevens-Johnson syndrome
    - Autoimmune Mucocutaneous Blistering Disease (AMBD) (such as pemphigus vulgaris, bullous pemphigoid, mucous membrane pemphigoid, or epidermolysis bullosa acquisita)

    If yes, **approve for 12 months by HICL.**
    If no, do not approve.
    DENIAL TEXT: See the denial text at the end of the guideline.

CONTINUED ON NEXT PAGE

IMMUNE GLOBULIN (NSA)

GUIDELINES FOR USE (CONTINUED)

DENIAL TEXT: The guideline named **IMMUNE GLOBULIN** requires that the patient has **ONE** of the following diagnoses:

- Primary Immunodeficiency Disease (PID)
- Idiopathic Thrombocytopenic Purpura (ITP)
- Chronic Inflammatory Demyelinating Polyneuropathy (CIDP)
- Multifocal Motor Neuropathy (MMN)
- Kawasaki Syndrome
- B-cell Chronic Lymphocytic Leukemia (CLL) with hypogammaglobulinemia, Autoimmune Hemolytic Anemia (AIHA), Immune Thrombocytopenic Purpura (ITP), or pure Red Cell Blood Aplasia (PRCA)
- Guillain-Barre Syndrome (GBS)
- Myasthenia Gravis
- Autoimmune Graves' Ophthalmopathy
- Cytomegalovirus-induced Pneumonitis related to a solid organ transplant
- Prevention of bacterial infection in an HIV-infected child
- Reduction of secondary infections in pediatric HIV infections
- Dermatomyositis or polymyositis
- Autoimmune uveitis (Birdshot retinochoroidopathy)
- Lambert-Eaton myasthenic syndrome
- IgM anti-myelin-associated glycoprotein paraprotein-associated peripheral neuropathy
- Stiff-man syndrome
- Neonatal sepsis
- Rotaviral enterocolitis
- Toxic shock syndrome
- Enteroviral meningoencephalitis
- Toxic Epidermal Necrolysis or Stevens-Johnson syndrome
- Autoimmune Mucocutaneous Blistering Disease (AMBD) (such as pemphigus vulgaris, bullous pemphigoid, mucous membrane pemphigoid, or epidermolysis bullosa acquisita)

For prophylaxis or passive immunization of hepatitis A, measles, varicella, or rubella, only Gamastan S-D will be approved.

RATIONALE

Ensure appropriate therapeutic use based on FDA approved indications for subcutaneous immune globulin. Although Gammagard Liquid, Gammaked, Gamunex-C may be given intravenously, these products can only be used administered subcutaneously for the treatment of primary immunodeficiency disease (PID).

CONTINUED ON NEXT PAGE

IMMUNE GLOBULIN (NSA)

RATIONALE (CONTINUED)

Ensure appropriate therapeutic use based on FDA approved indications and recommendations from the various professional practice guidelines that discuss the use of non-self-administered immune globulin.

American Academy of Neurology (AAN) 2012 Intravenous Immunoglobulin in the treatment of neuromuscular disorders
AAN evaluated existing evidence for the efficacy of IVIG in treating neuromuscular disorder and made practice recommendations based on evidence level. They also noted that IVIG benefit is generally temporary and longer studies are needed to assess long-term efficacy.

IVIG is as effective as plasmapheresis for treating Guillain-Barre syndrome (GBS) in adults. However, a combination of plasmapheresis and IVIG is likely not superior to monotherapy with either treatment.

IVIG benefit is uncertain in children with GBS however many experts consider it reasonable treatment given its effectiveness for the same condition in adults. There is insufficient data to recommend an optimal IVIG dosing regimen.

IVIG is effective and should be offered for the long-term treatment of CIDP. Dosing, frequency, and duration of IVIG for CIDP may vary by patient. There is insufficient data to assess the comparative efficacy of other CIDP treatments such as steroids, plasmapheresis and immunosuppressants.

IVIG is probably effective for the treatment of myasthenia gravis (MG) in moderately or severely affected patients. A risk benefit analysis should be performed prior to treatment of patients with mild disease. There is insufficient evidence to compare the effectiveness of IVIG and plasmapheresis for the treatment of MG.

IVIG is probably effective and should be considered for the treatment of multifocal motor neuropathy (MMN). MMN requires ongoing treatment but optimal treatment dosing, interval, and duration have not been established.

IVIG is possibly effective for the treatment of nonresponsive dermatomyositis in adults and Lambert-Eaton myasthenic syndrome. There is insufficient evidence to assess the role of IVIG in treating the following conditions: neuropathy associated with IgM paraprotein, inclusion body myositis and postpolio syndrome.

CONTINUED ON NEXT PAGE

RATIONALE (CONTINUED)

American Academy of Allergy, Asthma and Immunology (AAAAI) 2017 evidence review of immunoglobulin in human disease
AAAAI reviewed evidence supporting the use of standard human immunoglobulin preparations. Therapeutic uses are categorized by evidence of benefit as follows: definitely beneficial, probably beneficial, might provide benefit, and unlikely to be beneficial. AAAAI also comments that subcutaneous therapy can reduce the occurrence of systemic adverse events in selected patients and can improve quality of life for patients receiving intravenous immune globulin. Adverse events may also be reduced by matching specific products to specific patient characteristics.

Definitely Beneficial Uses of IVIG

Disease	Evidence category	Strength of recommendation
Primary immune defects with absent B cells	IIb	B
Primary immune defects with hypogammaglobulinemia and impaired specific antibody production	IIb	B
Reduction of secondary infections in pediatric HIV infections	Ib	A
CIDP	Ia	A
Graves ophthalmopathy	Ib	A
Immune thrombocytopenic purpura	Ia	A
Guillain-Barre syndrome	Ib	B
Multifocal motor neuropathy	Ib	A
Kawasaki disease	Ia	A
Cytomegalovirus-induced pneumonitis in solid organ transplants	Ib	A

CONTINUED ON NEXT PAGE

RATIONALE (CONTINUED)

Probably Beneficial Uses of IVIG

Disease	Evidence category	Strength of recommendation
Chronic lymphocytic leukemia with reduced IgG and history of infections	Ib	A
Prevention of bacterial infection in HIV-infected children	Ib	A
Primary immune defects with normal IgG and impaired specific antibody production	III	C
Dermatomyositis	IIa	B
Birdshot Retinochoroidopathy	IIa	B
Henoch-Schönlein purpura	IIb	B
Lambert-Eaton myasthenic syndrome	Ib	B
IgM antimyelin-associated glycoprotein paraprotein-associated peripheral neuropathy	Ib	B
Myasthenia gravis	Ib	B
Stiff-person syndrome	Ib	B
Neonatal sepsis	Ia	A
Rotaviral enterocolitis	Ib	A
Bacterial infections in lymphoproliferative diseases	Ib	B
Toxic shock syndrome	III	C
Enteroviral meningoencephalitis	III	C
Toxic epidermal necrolysis and Stevens-Johnson syndrome	IIa	B

CONTINUED ON NEXT PAGE

IMMUNE GLOBULIN (NSA)

RATIONALE (CONTINUED)

Guidelines for the Prevention and Treatment of Opportunistic Infections Among HIV-Exposed and HIV-Infected Children: Recommendations from CDC, the National Institutes of Health, the HIV Medicine Association of the Infectious Diseases Society of America, the Pediatric Infectious Diseases Society, and the American Academy of Pediatrics 2013
IVIG was commonly used prior to the advent of highly active anti-retroviral therapy (HAART) for infection prophylaxis in symptomatic HIV-infected children. However trimethoprim-sulfamethoxazole is now preferred in this setting. IVIG 400mg/kg every 2-4 weeks is only recommended for primary prevention of serious bacterial infections in HIV-infected children if hypogammaglobulinemia (IgG<400mg/dL) is present or functional antibody deficiency is demonstrated by poor specific antibody titers. IVIG can also be considered for secondary prophylaxis when antibiotic prophylaxis fails to prevent recurrent serious bacterial infections. (Mofenson).
HIV-infected children exposed to varicella and have no history of varicella or zoster; are seronegative for VZV by a sensitive, specific antibody assay; or lack evidence of age-appropriate vaccination should receive passive immunization within 96 hours of exposure. The preferred method of immunization is with human varicella immune globulin (VariZIG). If VariZIG is unavailable IVIG 400mg/kg can be administered once as soon as possible, ideally within 96 hours after exposure. If more than 96 hours have passed since exposure, acyclovir 20mg/kg (max 800mg) per dose orally 4 times a day for 7 days can also be considered.

European Federation of Neurological Societies (EFNS) Guidelines for the use of intravenous immunoglobulin in treatment of neurological diseases 2008
The EFNS state that the efficacy of IVIG has been proven for the following immune-mediated neurological diseases: Guillain-Barre syndrome, chronic inflammatory demyelinating polyradiculoneuropathy, multifocal mononeuropathy, and acute exacerbations and short-term treatment of myasthenia gravis.

CONTINUED ON NEXT PAGE

IMMUNE GLOBULIN (NSA)

RATIONALE (CONTINUED)

National Comprehensive Cancer Network (NCCN) Clinical Practice Guidelines in Oncology Non-Hodgkin's Lymphomas Versions 3.2012
Patients with B-cell chronic lymphocytic leukemia (CLL) are susceptible to infections due to both the underlying disease and immunosuppressive properties of the treatment agents. The main options for decreasing the occurrence of secondary infections for patients with recurrent infections and IgG level <500mg/dL are IVIG, anti-infective prophylaxis, and vaccinations. For patients with serum IVIG <500mg/dL) with recurrent sinopulmonary infections requiring intravenous antibiotic or hospitalization it is recommended that IVIG levels be monitored and IVIG be administered monthly at a dose of 0.3-0.5 g/kg to maintain nadir levels around 500mg/dL.
Autoimmune cytopenias including: autoimmune hemolytic anemia (AIHA), immune thrombocytopenic purpura (ITP), and pure red blood aplasia (PRCA) can occur in patients with CLL. AIHA and ITP can be managed with corticosteroids in most cases. IVIG is an option for steroid-refractory cases. Corticosteroids are typically less effective in PRCA than in AIHA or ITP, however they are still considered a first-line treatment along with IVIG and splenectomy.

The American Society of Hematology 2011 evidence-based practice guideline for immune thrombocytopenia
Initial treatment of pediatric ITP consists of IVIG (0.8-1g/kg) or a short course of corticosteroids. IVIG can also be used if a more rapid increase in the platelet count is desired. For the treatment of adult ITP longer courses of corticosteroids are preferred over shorter courses of corticosteroids or IVIG as first-line treatment. IVIG in combination with corticosteroids can be considered when a more rapid increase in platelet count is required. IVIG dosing is usually 1g/kg for a single dose; however additional doses can be administered if necessary. Pregnant patients with ITP can receive either corticosteroids or IVIG. IVIG should be used as initial treatment of ITP in patients with the hepatitis C virus. Initial treatment of ITP patients with HIV coinfection can include corticosteroids, IVIG, or anti-D immunoglobulin.

Consensus Statement on the Use of Intravenous Immunoglobulin Therapy in the Treatment of Autoimmune Therapy in the Treatment of Autoimmune Mucocutaneous Blistering Diseases
A consensus statement on the use of IVIG for the treatment of autoimmune mucocutaneous blistering diseases (AMBDs) from a group of physicians was published in the Archives of Dermatology. The consensus group considered 5 distinct types of AMBDs: pemphigus vulgaris, bullous pemphigoid, mucous membrane pemphigoid, and epidermolysis bullosa acquista. All are typically treated with corticosteroids or immunosuppressive agents. The use of IVIG treatment is recommended when one of the following is present: failure of conventional therapy, significant adverse effects with conventional therapy, contraindications to conventional therapy, disease progression with conventional therapy, uncontrolled rapid debilitating progressive disease, or rapid progressive epidermolysis bullosa acquista with generalized cutaneous disease. The recommended dose is 2g/kg per cycle, consisting of 3 consecutive daily doses every 3 to 4 weeks. Dosing and frequency may vary among patients depending on severity of disease and response to therapy.

CONTINUED ON NEXT PAGE

IMMUNE GLOBULIN (NSA)

FDA APPROVED INDICATIONS

Drug	PID	ITP	CIDP	Other
Bivigam	IV			
Carimune NF	IV	IV		
Cuvitru *(for SC use only)*	SC			
Flebogamma DIF	IV (5%, 10%)	IV (10%)		
Gamastan S-D *(for IM use only)*				Hepatitis A, Measles, Varicella, Rubella (IM)
Gammagard Liquid	IV/SC			Multifocal motor neuropathy (IV)
Gammagard S-D	IV	IV		B-cell CLL, Kawasaki syndrome (IV)
Gammaked	IV/SC	IV	IV	
Gammaplex	IV (5%, 10%)	IV (5%, 10%)		
Gamunex-C	IV/SC	IV	IV	
Hizentra *(for SC use only)*	SC		SC	
Hyqvia *(for SC use only)*	SC			
Octagam	IV (5%)	IV (10%)		
Privigen	IV	IV	IV	

Bivigam
Is an immune globulin intravenous (human), 10% liquid, indicated for the treatment of:
- Primary humoral immunodeficiency (PI)

Carimune NF
Is a nanofiltered, immune globulin intravenous (human) indicated for:
- Maintenance treatment of patients with primary immunodeficiencies
- Immune thrombocytopenic purpura (ITP)

Cuvitru
Is an immune globulin subcutaneous (human), 20% solution indicated as replacement therapy for:
- Primary humoral immunodeficiency (PI) in adult and pediatric patients two years of age and older.

CONTINUED ON NEXT PAGE

IMMUNE GLOBULIN (NSA)

FDA APPROVED INDICATIONS (CONTINUED)

Flebogamma 5% DIF
Is an immune globulin intravenous (human) indicated for treatment of:
- Primary (inherited) immunodeficiency (PI) in adults and pediatric patients 2 years of age and older

Flebogamma 10% DIF
Is an immune globulin intravenous (human) indicated for treatment of:
- Primary (inherited) immunodeficiency (PI)
- Chronic primary immune thrombocytopenia (ITP) in patients 2 years of age and older

Gamastan S/D
Is an immune globulin (human) for intramuscular administration indicated for:
- Hepatitis A
- Measles (rubeola)
- Varicella
- Rubella

Gammagard Liquid
Is an immune globulin infusion (human) indicated as replacement therapy for:
- Primary humoral immunodeficiency (PI) in adult and pediatric patients two years of age or older. This includes, but is not limited to, common variable immunodeficiency (CVID), X-linked agammaglobulinemia, congenital agammaglobulinemia, Wiskott-Aldrich syndrome, and severe combined immunodeficiencies.
- Multifocal motor neuropathy (MMN)

Gammagard S/D
Is an immune globulin intravenous (human) indicated for:
- Treatment of primary immunodeficiency (PI) in adult and pediatric patients two years of age or older
- Prevention of bacterial infections in hypogammaglobulinemia and/or recurrent bacterial infections associated with B-cell chronic lymphocytic leukemia (CLL)
- Prevention and/or control of bleeding in adult chronic idiopathic thrombocytopenic purpura (ITP) patients
- Prevention of coronary artery aneurysms associated with Kawasaki syndrome in pediatric patients

CONTINUED ON NEXT PAGE

IMMUNE GLOBULIN (NSA)

FDA APPROVED INDICATIONS (CONTINUED)

Gammaked
Is an immune globulin injection (human) 10% liquid that is indicated for the treatment of:
- Primary humoral immunodeficiency (PI) in patients 2 years of age and older.
- Idiopathic thrombocytopenic purpura (ITP)
- Chronic inflammatory demyelinating polyneuropathy (CIDP)

Gammaplex 5%
Is an immune globulin intravenous (human) 5% liquid that is indicated for the treatment of:
- Primary humoral immunodeficiency (PI) in adults and pediatric patients 2 years of age and older
- Chronic immune thrombocytopenic purpura (ITP)

Gammaplex 10%
Is an immune globulin intravenous (human) 10% liquid that is indicated for the treatment of:
- Primary humoral immunodeficiency (PI) in adults
- Chronic immune thrombocytopenic purpura (ITP) in adults

Gamunex-C
Is an immune globulin injection (human) 10% liquid that is indicated for the treatment of:
- Primary humoral immunodeficiency (PI) in patients 2 years of age and older
- Idiopathic thrombocytopenic purpura (ITP) in adults and children
- Chronic inflammatory demyelinating polyneuropathy (CIDP) in adults

Hizentra
Is an immune globulin subcutaneous (human) (IGSC), 20% Liquid indicated for the treatment of:
- Primary immunodeficiency (PI) in adults and pediatric patients 2 years of age and older
- Maintenance therapy in adults with chronic inflammatory demyelinating polyneuropathy (CIDP).

Limitations of Use:
Hizentra maintenance therapy in CIDP has been systematically studied for 6 months and for a further 12 months in a follow-up study. Maintenance therapy beyond these periods should be individualized based upon the patient's response and need for continued therapy.

Hyqvia
Is an immune globulin with a recombinant human hyaluronidase indicated for the treatment of:
- Primary Immunodeficiency (PI) in adults

Limitation of Use:
Safety and efficacy of chronic use of recombinant human hyaluronidase in Hyqvia have not been established in conditions other than PI.

CONTINUED ON NEXT PAGE

IMMUNE GLOBULIN (NSA)

FDA APPROVED INDICATIONS (CONTINUED)

Octagam 5%
Is an immune globulin intravenous (human), 5% liquid, indicated for treatment of:
- Primary humoral immunodeficiency (PI)

Octagam 10%
Is an immune globulin intravenous (human), 10% liquid, indicated for treatment of:
- Chronic immune thrombocytopenic purpura (ITP) in adults

Privigen
Is an immune globulin intravenous (human), 10% liquid, indicated for treatment of:
- Primary humoral immunodeficiency (PI)
- Chronic immune thrombocytopenic purpura (ITP) in patients aged 15 years and older
- Chronic inflammatory demyelinating polyneuropathy (CIDP) in adults

DOSAGE AND ADMINISTRATION

Bivigam
Administer intravenously for PI.

Indication	Dose	Initial Infusion Rate	Maintenance Infusion Rate (if tolerated)
PI	300-800 mg/kg every 3-4 weeks	0.5 mg/kg/min for the first 10 minutes.	Increase every 20 minutes (if tolerated) by 0.8 mg/kg/min up to 6 mg/kg/min.

Carimune NF
Administer intravenously.

Primary immunodeficiency (PI):
- The recommended dose is 0.4 to 0.8 g/kg of body weight administered once every three to four weeks by intravenous infusion.
- The first infusion must be given as a 3% immunoglobulin solution. Subsequent infusions may be given at higher concentrations if tolerated by the patient.
- An initial infusion rate of 0.5 mg/kg/min is recommended. If tolerated, after 30 minutes the rate may be increased to 1 mg/kg/min for the next 30 minutes. Thereafter, the rate may be gradually increased in a stepwise manner up to a maximum of 3 mg/kg/min as tolerated.

CONTINUED ON NEXT PAGE

IMMUNE GLOBULIN (NSA)

FDA APPROVED INDICATIONS (CONTINUED)

DOSAGE AND ADMINISTRATION

Idiopathic thrombocytopenic purpura (ITP):

- The recommended dose is 0.4 g/kg of body weight administered on 2-5 consecutive days.
- A concentration of immunoglobulin solution of 6% is recommended.
- An initial infusion rate of 0.5 mg/kg/min is recommended. If tolerated, after 30 minutes the rate may be increased to 1 mg/kg/min for the next 30 minutes. Thereafter, the rate may be gradually increased in a stepwise manner up to a maximum of 3 mg/kg/min as tolerated.

Cuvitru

Administer subcutaneously at regular intervals from daily up to every two weeks. Cuvitru may be administered subcutaneously utilizing an infusion pump.

- Weekly: Start Hizentra 1 week after last IGIV or Hyqvia infusion

$$\text{Initial Weekly dose} = \frac{\text{Previous IGIV or HYQVIA dose (in grams)}}{\text{No. of weeks between IGIV or HYQVIA doses.}} \times 1.30$$

- Biweekly: Administer twice the calculated weekly dose.
- Frequent dosing (2 to 7 times per week): Divide the calculated weekly dose by the desired number of administrations per week.
- Adjust the dose based on clinical response and serum IgG trough levels.

Flebogamma 5% DIF

Administer intravenously.

Indication	Dose	Initial Infusion Rate	Maintenance Infusion Rate (if tolerated)
PI	300-600 mg/kg given every 3 to 4 weeks	0.5 mg/kg/min	5 mg/kg/min

Flebogamma 10% DIF

Administer intravenously.

Indication	Dose	Initial Infusion Rate	Maintenance Infusion Rate (if tolerated)
PI	300-600 mg/kg given every 3 to 4 weeks	1 mg/kg/min	8 mg/kg/min
ITP	1 g/kg daily for 2 consecutive days	1 mg/kg/min	8 mg/kg/min

CONTINUED ON NEXT PAGE

IMMUNE GLOBULIN (NSA)

FDA APPROVED INDICATIONS (CONTINUED)

DOSAGE AND ADMINISTRATION
Gamastan S/D
Administer only by the intramuscular route. Do not given subcutaneously or intravenously.

Indication	Dose
Hepatitis A (household and institutional contacts)	0.1 mL/kg
Measles	• 0.25 mL/kg to prevent in a susceptible person exposed fewer than 6 days previously • 0.5 mL/kg should be given immediately to a susceptible child who is immunocompromised
Varicella	0.6-1.2 mL/kg
Rubella	0.55 mL/kg

CONTINUED ON NEXT PAGE

IMMUNE GLOBULIN (NSA)

FDA APPROVED INDICATIONS (CONTINUED)

DOSAGE AND ADMINISTRATION

Gammagard Liquid

Prior to switching from intravenous to subcutaneous treatment, obtain the patient's serum IgG trough level to guide subsequent dose adjustments. Start the initial subcutaneous dose approximately one week after the last intravenous infusion.

Indication	Dose	Initial Infusion Rate	Maintenance Infusion Rate (if tolerated)
Intravenous administration			
PI	300-600 mg/kg given every 3 to 4 weeks	0.5 mL/kg/hr	Increase every 30 minutes (if tolerated) up to 5 mL/kg/hr
Multifocal motor neuropathy	0.5-2.4 g/kg/month based on clinical response	0.5 mL/kg/hr	Infusion rate may be increased if tolerated up to 5.4 mL/kg/hr
Subcutaneous administration			
PI	Initial Dose is 1.37 × previous intravenous dose divided by # of weeks between intravenous doses. Maintenance dose is based on clinical response and target IgG trough level.	40 kg BW and greater: 30 mL/site at 20 mL/hr/site. Under 40 kg BW: 20 mL/site at 15 mL/hr/site.	40 kg BW and greater: 30 mL/site at 20 to 30 mL/hr/site. Under 40 kg BW: 20 mL/site at 15 to 20 mL/hr/site.

CONTINUED ON NEXT PAGE

IMMUNE GLOBULIN (NSA)

FDA APPROVED INDICATIONS (CONTINUED)

DOSAGE AND ADMINISTRATION
Gammagard S/D
Administer intravenously.

Indication	Recommended Dosage	Duration	Administration (5% concentration)
PI	300-600 mg/kg	Every 3-4 weeks	Recommended initial rate: 0.5 mL/kg/hr Maximum rate: 4 mL/kg/hr
CLL	400 mg/kg	Every 3-4 weeks	
ITP	1 g/kg	Maximal 3 doses on alternate days	
Kawasaki syndrome	Single 1 g/kg or 400 mg/kg for 4 consecutive days	Begin within 7 days of onset of fever	

Gammaked
Administer intravenously for PI, ITP and CIDP. Gammaked may also be administered subcutaneously for the treatment of PI.

Indication	Dose	Initial Infusion Rate	Maintenance Infusion Rate (if tolerated)
Intravenous administration			
ITP	2 g/kg	1 mg/kg/min	8 mg/kg/min
CIDP	Loading dose: 2 g/kg Maintenance dose: 1 g/kg	2 mg/kg/min	8 mg/kg/min every 3 weeks
PI	300-600 mg/kg	1 mg/kg/min	8 mg/kg/min every 3 weeks
Subcutaneous administration			
PI	1.37 x current IV dose in grams/IV dose interval in weeks	Adult: 20 mL/hr/site Pediatric: 10 mL/hr/site (< 25 kg) 15 mL/hr/site (≥ 25 kg)	Adult: 20 mL/hr/site Pediatric: 10 mL/hr/site (< 25 kg) 20 mL/hr/site (≥ 25 kg) Weekly

CONTINUED ON NEXT PAGE

IMMUNE GLOBULIN (NSA)

FDA APPROVED INDICATIONS (CONTINUED)

DOSAGE AND ADMINISTRATION

Gammaplex 5%

Administer intravenously.

Indication	Dose	Initial Infusion Rate	Maintenance Infusion Rate (if tolerated)
PI	300-800 mg/kg given every 3 to 4 weeks	0.5 mg/kg/min for 15 minutes	Increase gradually every 15 minutes to 4 mg/kg/min
ITP	1 g/kg for 2 consecutive days	0.5 mg/kg/min for 15 minutes	Increase gradually every 15 minutes to 4 mg/kg/min

Gammaplex 10%

Administer intravenously.

Indication	Dose	Initial Infusion Rate	Maintenance Infusion Rate (if tolerated)
PI	300-800 mg/kg given every 3 to 4 weeks	0.5 mg/kg/min for 15 minutes	Increase gradually every 15 minutes to 8 mg/kg/min
ITP	1 g/kg for 2 consecutive days	0.5 mg/kg/min for 15 minutes	Increase gradually every 15 minutes to 8 mg/kg/min

CONTINUED ON NEXT PAGE

IMMUNE GLOBULIN (NSA)

FDA APPROVED INDICATIONS (CONTINUED)

DOSAGE AND ADMINISTRATION

Gamunex-C

Administer intravenously for PI, ITP and CIDP. Gamunex-C may also be administered subcutaneously for the treatment of PI.

Indication	Dose	Initial Infusion Rate	Maintenance Infusion Rate (if tolerated)
Intravenous administration			
ITP	2 g/kg	1 mg/kg/min	8 mg/kg/min
CIDP	Loading dose: 2 g/kg Maintenance dose: 1 g/kg	2 mg/kg/min	8 mg/kg/min every 3 weeks
PI	300-600 mg/kg	1 mg/kg/min	8 mg/kg/min every 3 weeks
Subcutaneous administration			
PI	1.37 x current IV dose in grams/IV dose interval in weeks	Adult: 20 mL/hr/site Pediatric: 10 mL/hr/site (< 25 kg) 15 mL/hr/site (≥ 25 kg)	Adult: 20 mL/hr/site Pediatric: 10 mL/hr/site (< 25 kg) 20 mL/hr/site (≥ 25 kg) weekly

Hizentra

For subcutaneous infusion only. Do not inject into a blood vessel. Administer at regular intervals from daily up to biweekly (every two weeks).

CONTINUED ON NEXT PAGE

IMMUNE GLOBULIN (NSA)

FDA APPROVED INDICATIONS (CONTINUED)

DOSAGE AND ADMINISTRATION

Primary immunodeficiency (PI):

- Before switching to Hizentra, obtain the patient's serum IgG trough level to guide subsequent dose adjustments.
- Weekly: Start Hizentra 1 week after last IGIV or IGSC infusion

$$\text{Initial HIZENTRA dose} = \frac{\text{Previous IGIV dose (in grams)}}{\text{Number of weeks between IGIV doses}} \times 1.37$$

- Biweekly: Start Hizentra 1 or 2 weeks after the last IGIV infusion or 1 week after the last weekly IGSC infusion. Administer twice the calculated weekly dose.
- Frequent dosing (2 to 7 times per week): Start Hizentra 1 week after last IGIV/IGSC infusion. Divide the calculated weekly dose by the desired number of administrations per week.
- Adjust the dose based on clinical response and serum IgG trough levels.

Chronic Inflammatory Demyelinating Polyneuropathy (CIDP):

- Initiate therapy with Hizentra 1 week after the last IGIV infusion.
- The recommended subcutaneous dose is 0.2 g/kg (1 mL/kg) body weight per week, administered in 1 or 2 sessions over 1 or 2 consecutive days.
- If symptoms worsen, consider re-initiating treatment with an IGIV approved for the treatment of CIDP, while discontinuing Hizentra.
- Monitor the patient's clinical response and adjust the duration of therapy based on patient need.

CONTINUED ON NEXT PAGE

IMMUNE GLOBULIN (NSA)

FDA APPROVED INDICATIONS (CONTINUED)

DOSAGE AND ADMINISTRATION

Hyqvia

For subcutaneous infusion only.

- For patients previously on another IgG treatment, give the first dose approximately one week after the last infusion of their previous treatment.
- Increase the dose and frequency from a 1-week dose to a 3- or 4-week dose:

Initial Treatment Interval/Dosage Ramp-Up Schedule

Week	Infusion Number	Dose Interval	Example for 30 grams per 4 weeks
1	1st infusion	1-week-dose	7.5 grams
2	2nd infusion	2-week-dose	15 grams
3	No infusion		
4	3rd infusion	3-week-dose	22.5 grams
5	No infusion		
6	No infusion		
7	4th infusion (if required)	4-week-dose	30 grams

- For patients switching from IGIV, given Hyqvia at the same dose and frequency as the previous intravenous treatment, after the initial dose ramp-up.
- For patients naïve to IGSC treatment or switching from IGSC, give Hyqvia at a dose of 300-600 mg/kg at 3- to 4-week intervals, after initial ramp-up.

Octagam 5%

For intravenous use only.

Indication	Dose	Initial Infusion Rate	Maintenance Infusion Rate (if tolerated)
PI	300-600 mg/kg every 3-4 weeks	0.5 mg/kg/min	3.33 mg/kg/min

Octagam 10%

For intravenous use only.

Indication	Dose	Initial Infusion Rate	Maintenance Infusion Rate (if tolerated)
Chronic ITP	1 g/kg daily for 2 consecutive days	1 mg/kg/min	Up to 12 mg/kg/min

CONTINUED ON NEXT PAGE

IMMUNE GLOBULIN (NSA)

FDA APPROVED INDICATIONS (CONTINUED)

DOSAGE AND ADMINISTRATION

Privigen

For intravenous use only.

Indication	Dose	Initial Infusion Rate	Maintenance Infusion Rate (if tolerated)
PI	200-800 mg/kg every 3-4 weeks	0.5 mg/kg/min	Increase to 8 mg/kg/min
Chronic ITP	1 g/kg daily for 2 consecutive days	0.5 mg/kg/min	Increase to 4 mg/kg/min
CIDP	Loading dose: 2 g/kg in divided doses over 2 to 5 consecutive days Maintenance dose: 1 g/kg administered in 1 to 2 infusions on consecutive days, every 3 weeks	0.5 mg/kg/min	Increase to 4 mg/kg/min

REFERENCES

- Bivigam [Prescribing Information]. Biotest Pharmaceuticals Co.: Boca Raton, FL. January 2017.
- Carimune NF [Prescribing Information]. CSL Behring LLC: Kankakee, IL. September 2013.
- Cuvitru [Prescribing Information]. Baxalta US Inc.: Westlake Village, CA. September 2016.
- Flebogamma 5% DIF [Prescribing Information]. Grifols: Barcelona, Spain. July 2017.
- Flebogamma 10% DIF [Prescribing Information]. Grifols: Barcelona, Spain. July 2017.
- Gamastan S/D [Prescribing Information]. Grifols: Research Triangle Park, NC. June 2017.
- Gammagard Liquid [Prescribing Information]. Baxalta US Inc.: Westlake Village, CA. March 2017.
- Gammagard S/D [Prescribing Information]. Baxalta US Inc.: Westlake Village, CA. March 2017.
- Gammaked [Prescribing Information]. Grifols: Research Triangle Park, NC. September 2016.
- Gammaplex 5% [Prescribing Information]. BPL Inc.: Durham, NC. December 2016.
- Gammaplex 10% [Prescribing Information]. BPL Inc.: Durham, NC. December 2016.
- Gamunex-C [Prescribing Information]. Grifols: Research Triangle Park, NC. March 2017.
- Hizentra [Prescribing Information]. CSL Behring LLC: Kankakee, IL. March 2018.
- Hyqvia [Prescribing Information]. Baxalta US Inc.: Westlake Village, CA. September 2016.
- Octagam 5% [Prescribing Information]. Octapharma USA Inc.: Hoboken, NJ. April 2015.

CONTINUED ON NEXT PAGE

IMMUNE GLOBULIN (NSA)

REFERENCES (CONTINUED)

- Octagam 10% [Prescribing Information]. Octapharma USA Inc.: Hoboken, NJ. August 2015.
- Privigen [Prescribing Information]. CSL Behring LLC: Kankakee, IL. September 2017.
- The American Society of Hematology 2011 evidence-based practice guideline for immune thrombocytopenia. Neunert C, W Lim, M Crowther, et al. 16, s.l. : Blood, April 21, 2011, Vol. 117.
- Centers for Disease Control and Prevention. FDA Approval of an Extended Period for Administering VariZIG for Postexposure Prophylaxis of Varicella. [Online] March 30, 2012. [Cited: July 18, 2012.] http://www.cdc.gov/mmwr/preview/mmwrhtml/mm6112a4.htm .
- Clinical Pharmacology. [Online] Elsevier / Gold Standard, 2012. [Cited: July 18, 2012.] http://clinicalpharmacology-ip.com.
- Consensus Statement on the Use of Intravenous Immunoglobulin Therapy in the Treatment of Autoimmune Mucocutaneous Blistering Diseases. Ahmed AR, MV Dahl. s.l.: Archives of Dermatology, August 2003, Vol. 139.
- EFNS guidelines for the use of intravenous immunoglobulin in treatment of neurological diseases. Elovaara I, S Apostolski, P van Doorn, et al. s.l. : European Journal of Neurology, 2008, Vol. 15Evidence-based guideline: Intravenous immunoglobulin in the treatment of neuromuscular disorders : Report of the Therapeutics and Technology Assessment Subcommittee of the American Academy of Neurology. Patwa HS, V Chaudhry, H Katzberg, et al. s.l. : Neurology, March 27, 2012, Vol. 78.
- Siberry GK, Abzug MJ, Nachman S, et al. Guidelines for the Prevention and Treatment of Opportunistic Infections Among HIV-Exposed and HIV-Infected Children: Recommendations from CDC, NIH, HIVMAIDSA, PIDS, and AAP. Pediatr Infect Dis J. 2013;32 Suppl 2:i-KK4.
- National Comprehensive Cancer Network. NCCN Clinical Practice Guidelines in Oncology Non-Hodgkin's Lymphomas Version 3.2012. NCCN Guidelines. [Online] July 9, 2012. [Cited: July 18, 2012.] http://www.nccn.org/professionals/physician_gls/f_guidelines.asp?button=I+Agree#site.
- Micromedex. Drugdex. [Online] [Cited: July 18, 2012.]
- Perez EE, Orange JS, Bonilla F, et al. Update on the use of immunoglobulin in human disease: A review of evidence.J Allergy Clin Immunol. 2017;139:S1-46.
- Clinical Pharmacology. [Online] Elsevier / Gold Standard, 2016. [Cited: October 5, 2016.] http://clinicalpharmacology-ip.com.

Library	Commercial	NSA
Yes	Yes	Yes

Part D Effective: N/A
Commercial Effective: 07/01/18
Created: 08/12
Client Approval: 05/18
P&T Approval: 04/18

INFLIXIMAB (NSA)

Generic	Brand	HICL	GCN	Exception/Other
INFLIXIMAB	REMICADE	18747		

GUIDELINES FOR USE

INITIAL CRITERIA (NOTE: FOR RENEWAL CRITERIA, SEE BELOW)

1. Does the patient have a diagnosis of moderate to severe rheumatoid arthritis (RA) and meet **ALL** of the following criteria?
   - Therapy is prescribed by or given in consultation with a rheumatologist
   - The patient is currently using or has a contraindication to methotrexate
   - The patient has had a previous trial of at least one of the following DMARDs (disease-modifying antirheumatic drugs) such as methotrexate, leflunomide, hydroxychloroquine, or sulfasalazine
   - The patient has had a previous trial of the formulary preferred immunomodulators: Enbrel and Humira (**NOTE:** pharmaceutical samples acquired from the prescriber or manufacturer assistance program do not qualify)

   If yes, **approve for 6 months by HICL.**
   APPROVAL TEXT: Renewal of **INFLIXIMAB (Remicade)** for moderate to severe rheumatoid arthritis requires that the patient has experienced or maintained a 20% or greater improvement in tender joint count or swollen joint count while on therapy.
   If no, continue to #2.

2. Does the patient have a diagnosis of psoriatic arthritis (PsA) and meet **ALL** of the following criteria?
   - Therapy is prescribed by or given in consultation with a rheumatologist or dermatologist
   - The patient has had a previous trial of at least one of the following DMARDs (disease-modifying antirheumatic drugs) such as methotrexate, leflunomide, hydroxychloroquine, or sulfasalazine
   - The patient is 18 years of age or older
   - The patient has had a previous trial of any **TWO** of the following formulary preferred immunomodulators: Enbrel, Humira, Cosentyx, Stelara, **or** Otezla (**NOTE:** pharmaceutical samples acquired from the prescriber or manufacturer assistance program do not qualify)

   If yes, **approve for 6 months by HICL.**
   APPROVAL TEXT: Renewal of **INFLIXIMAB (Remicade)** for psoriatic arthritis requires that the patient has experienced or maintained a 20% or greater improvement in tender joint count or swollen joint count while on therapy.
   If no, continue to #3.

CONTINUED ON NEXT PAGE

INFLIXIMAB (NSA)

INITIAL CRITERIA (CONTINUED)

3. Does the patient have a diagnosis of ankylosing spondylitis (AS) and meet **ALL** of the following criteria?
   - Therapy is prescribed by or given in consultation with a rheumatologist
   - The patient is 18 years of age or older
   - The patient has had a previous trial of any **TWO** of the following formulary preferred immunomodulators: Enbrel, Humira, or Cosentyx (**NOTE:** pharmaceutical samples acquired from the prescriber or manufacturer assistance program do not qualify)

   If yes, **approve for 6 months by HICL.**
   APPROVAL TEXT: Renewal of **INFLIXIMAB (Remicade)** for ankylosing spondylitis requires that the patient has experienced or maintained an improvement of at least 50% or 2 units (scale of 1-10) in the Bath Ankylosing Spondylitis Disease Activity Index (BASDAI) score while on therapy.
   If no, continue to #4.

4. Does the patient have a diagnosis of severe plaque psoriasis (PsO) and meet **ALL** of the following criteria?
   - Therapy is prescribed by or given in consultation with a dermatologist
   - The patient is 18 years of age or older
   - The patient has plaque psoriasis involving at least 10% body surface area (BSA) **OR** psoriatic lesions affecting the hands, feet, genital area, or face
   - The patient has had a previous trial of at least one or more forms of conventional therapies, such as PUVA (Phototherapy Ultraviolet Light A), UVB (Ultraviolet Light B), topical corticosteroids, calcipotriene, acitretin, methotrexate, or cyclosporine
   - The patient has had a previous trial of any **TWO** of the following formulary preferred immunomodulators: Enbrel, Humira, Cosentyx, Stelara, or Otezla (**NOTE:** pharmaceutical samples acquired from the prescriber or manufacturer assistance program do not qualify)

   If yes, **approve for 6 months by HICL.**
   APPROVAL TEXT: Renewal of **INFLIXIMAB (Remicade)** for plaque psoriasis requires that the patient has achieved or maintained clear or minimal disease or a decrease in PASI (Psoriasis Area and Severity Index) of at least 50% or more while on therapy.
   If no, continue to #5.

CONTINUED ON NEXT PAGE

INFLIXIMAB (NSA)

INITIAL CRITERIA (CONTINUED)

5. Does the patient have a diagnosis of moderate to severe Crohn's disease (CD) and meet **ALL** of the following criteria?
   - Therapy is prescribed by or given in consultation with a gastroenterologist
   - The patient has had a previous trial of at least one of the following conventional therapies, such as corticosteroids (i.e., budesonide, methylprednisolone), azathioprine, mercaptopurine, methotrexate, or mesalamine
   - The patient is 6 years of age or older
   - The patient has had a previous trial of the formulary preferred immunomodulators: Humira **AND** Stelara (**NOTE:** pharmaceutical samples acquired from the prescriber or manufacturer assistance program do not qualify)

   If yes, **approve for 6 months by HICL.**
   If no, continue to #6.

6. Does the patient have a diagnosis of moderate to severe ulcerative colitis (UC) and meet **ALL** of the following criteria?
   - Therapy is prescribed by or given in consultation with a gastroenterologist
   - The patient has had a previous trial of at least one of the following conventional therapies, such as corticosteroids (i.e., budesonide, methylprednisolone), azathioprine, mercaptopurine, methotrexate, or mesalamine
   - The patient is 6 years of age or older
   - The patient has had a previous trial of the formulary preferred immunomodulator: Humira (**NOTE:** pharmaceutical samples acquired from the prescriber or manufacturer assistance program do not qualify)

   If yes, **approve for 6 months by HICL.**
   If no, do not approve.
   DENIAL TEXT: See the initial denial text at the end of the guideline.

CONTINUED ON NEXT PAGE

INFLIXIMAB (NSA)

INITIAL CRITERIA (CONTINUED)

INITIAL DENIAL TEXT: The guideline named **INFLIXIMAB (Remicade)** requires a diagnosis of moderate to severe rheumatoid arthritis, psoriatic arthritis, ankylosing spondylitis, severe plaque psoriasis, moderate to severe Crohn's disease, or moderate to severe ulcerative colitis. In addition, the following criteria must also be met:

For patients with moderate to severe rheumatoid arthritis (RA), approval requires that:

- Therapy is prescribed by or given in consultation with a rheumatologist
- The patient is currently using or has a contraindication to methotrexate
- The patient has had a previous trial of at least one of the following DMARDs (disease-modifying antirheumatic drugs) such as methotrexate, leflunomide, hydroxychloroquine, or sulfasalazine
- The patient has had a previous trial of the formulary preferred immunomodulators: Enbrel **AND** Humira

For patients with psoriatic arthritis (PsA), approval requires that:

- Therapy is prescribed by or given in consultation with a rheumatologist or dermatologist
- The patient has had a previous trial of at least one of the following DMARDs (disease-modifying antirheumatic drugs) such as methotrexate, leflunomide, hydroxychloroquine, or sulfasalazine
- The patient is 18 years of age or older
- The patient has had a previous trial of any **TWO** of the following formulary preferred immunomodulators: Enbrel, Humira, Cosentyx, Stelara, or Otezla

For patients with ankylosing spondylitis (AS), approval requires that:

- Therapy is prescribed by or given in consultation with a rheumatologist
- The patient is 18 years of age or older
- The patient has had a previous trial of any **TWO** of the following formulary preferred immunomodulators: Enbrel, Humira, **OR** Cosentyx

For patients with severe plaque psoriasis (PsO), approval requires that:

- Therapy is prescribed by or given in consultation with a dermatologist
- The patient is 18 years of age or older
- The patient has plaque psoriasis involving at least 10% body surface area (BSA) **OR** psoriatic lesions affecting the hands, feet, genital area, or face
- The patient has had a previous trial of at least one or more forms of conventional therapies, such as PUVA (Phototherapy Ultraviolet Light A), UVB (Ultraviolet Light B), topical corticosteroids, calcipotriene, acitretin, methotrexate, or cyclosporine
- The patient has had a previous trial of any **TWO** of the following formulary preferred immunomodulators: Enbrel, Humira, Cosentyx, Stelara, or Otezla

(Initial denial text continued on next page)

CONTINUED ON NEXT PAGE

INFLIXIMAB (NSA)

INITIAL CRITERIA (CONTINUED)

For patients with moderate to severe Crohn's disease (CD), approval requires that:
- Therapy is prescribed by or given in consultation with a gastroenterologist
- The patient has had a previous trial of at least one of the following conventional therapies, such as corticosteroids (i.e., budesonide, methylprednisolone), azathioprine, mercaptopurine, methotrexate, or mesalamine
- The patient is 6 years of age or older
- The patient has had a previous trial of the formulary preferred immunomodulators: Humira **AND** Stelara

For patients with moderate to severe ulcerative colitis (UC), approval requires that:
- Therapy is prescribed by or given in consultation with a gastroenterologist
- The patient has had a previous trial of at least one of the following conventional therapies, such as corticosteroids (i.e., budesonide, methylprednisolone), azathioprine, mercaptopurine, methotrexate, or mesalamine
- The patient is 6 years of age or older
- The patient has had a previous trial of the formulary preferred immunomodulator: Humira

The use of pharmaceutical samples (from the prescriber or manufacturer assistance program) will not be considered when evaluating the medical condition or prior prescription history for drugs that require prior authorization.

RENEWAL CRITERIA

1. Does the patient have a diagnosis of moderate to severe rheumatoid arthritis (RA) and meet **ALL** of the following criteria?
   - The patient has experienced or maintained a 20% or greater improvement in tender joint count or swollen joint count while on therapy
   - The patient is currently using or has a contraindication to methotrexate

   If yes, **approve for 12 months by HICL.**
   If no, continue to #2.

2. Does the patient have a diagnosis of psoriatic arthritis (PsA) and meet the following criteria?
   - The patient has experienced or maintained a 20% or greater improvement in tender joint count or swollen joint count while on therapy

   If yes, **approve for 12 months by HICL.**
   If no, continue to #3.

CONTINUED ON NEXT PAGE

INFLIXIMAB (NSA)

RENEWAL CRITERIA (CONTINUED)

3. Does the patient have a diagnosis of ankylosing spondylitis (AS) and meet the following criteria?
   - The patient has experienced or maintained an improvement of at least 50% or 2 units (scale of 1-10) in the Bath Ankylosing Spondylitis Disease Activity Index (BASDAI) score while on therapy

   If yes, **approve 12 months by HICL.**
   If no, continue to #4.

4. Does the patient have a diagnosis of severe plaque psoriasis (PsO) and meet the following criteria?
   - The patient has achieved or maintained clear or minimal disease **OR** a decrease in PASI (Psoriasis Area and Severity Index) of at least 50% or more while on therapy

   If yes, **approve for 12 months by HICL.**
   If no, continue to #5.

5. Does the patient have a diagnosis of moderate to severe Crohn's disease (CD)?

   If yes, **approve for 12 months by HICL.**
   If no, continue to #6.

6. Does the patient have a diagnosis of moderate to severe ulcerative colitis (UC)?

   If yes, **approve for 12 months by HICL.**
   If no, do not approve.
   DENIAL TEXT: The guideline named **INFLIXIMAB (Remicade)** requires a diagnosis of moderate to severe rheumatoid arthritis, psoriatic arthritis, ankylosing spondylitis, severe plaque psoriasis, moderate to severe Crohn's disease, or moderate to severe ulcerative colitis for renewal. In addition, the following criteria must also be met:
   Renewal for the diagnosis of moderate to severe rheumatoid arthritis, approval requires that:
   - The patient has experienced or maintained a 20% or greater improvement in tender joint count or swollen joint count while on therapy
   - The patient is currently using or has a contraindication to methotrexate

   Renewal for the diagnosis of psoriatic arthritis, approval requires that:
   - The patient has experienced or maintained a 20% or greater improvement in tender joint count or swollen joint count while on therapy

   (Renewal denial text continued on next page)

CONTINUED ON NEXT PAGE

INFLIXIMAB (NSA)

RENEWAL CRITERIA (CONTINUED)

Renewal for the diagnosis of ankylosing spondylitis, approval requires that:
- The patient has experienced or maintained an improvement of at least 50% or 2 units (scale of 1-10) in the Bath Ankylosing Spondylitis Disease Activity Index (BASDAI) score while on therapy

Renewal for the diagnosis of severe plaque psoriasis, approval requires that:
- The patient has achieved or maintained clear or minimal disease **OR** that the patient has experienced a decrease in PASI (Psoriasis Area and Severity Index) of at least 50% or more while on therapy

---

RATIONALE
To ensure appropriate use of Remicade consistent with its FDA approved indications.

DOSING AND ADMINISTRATION
Remicade is administered by intravenous infusion.

- **Crohn's Disease**: 5 mg/kg at 0, 2, and 6 weeks, then every 8 weeks. Some adult patients who initially respond to treatment may benefit from increasing the dose to 10 mg/kg if they later lose their response.
- **Ulcerative Colitis**: 5 mg/kg at 0, 2, and 6 weeks, then every 8 weeks.
- **Rheumatoid Arthritis**: In conjunction with methotrexate, 3 mg/kg at 0, 2, and 6 weeks, then every 8 weeks. Some patients may benefit from increasing the dose up to 10 mg/kg or treating as often as every 4 weeks.
- **Ankylosing Spondylitis**: 5 mg/kg at 0, 2, and 6 weeks, then every 6 weeks.
- **Psoriatic Arthritis**: 5 mg/kg at 0, 2, and 6 weeks, then every 8 weeks.
- **Plaque Psoriasis**: 5 mg/kg at 0, 2, and 6 weeks, then every 8 weeks.

FDA APPROVED INDICATIONS
Remicade is a tumor necrosis factor (TNF) blocker indicated for:
- **Crohn's Disease:**
  - reducing signs and symptoms and inducing and maintaining clinical remission in adult patients with moderately to severely active disease who have had an inadequate response to conventional therapy.
  - reducing the number of draining enterocutaneous and rectovaginal fistulas and maintaining fistula closure in adult patients with fistulizing disease.
- **Pediatric Crohn's Disease**: reducing signs and symptoms and inducing and maintaining clinical remission in pediatric patients with moderately to severely active disease who have had an inadequate response to conventional therapy.

CONTINUED ON NEXT PAGE

INFLIXIMAB (NSA)

FDA APPROVED INDICATIONS (CONTINUED)

- **Ulcerative Colitis:** reducing signs and symptoms, inducing and maintaining clinical remission and mucosal healing, and eliminating corticosteroid use in adult patients with moderately to severely active disease who have had an inadequate response to conventional therapy.
- **Pediatric Ulcerative Colitis**: reducing signs and symptoms and inducing and maintaining clinical remission in pediatric patients with moderately to severely active disease who have had an inadequate response to conventional therapy.
- **Rheumatoid Arthritis in combination with methotrexate**: reducing signs and symptoms, inhibiting the progression of structural damage, and improving physical function in patients with moderately to severely active disease.
- **Ankylosing Spondylitis:** reducing signs and symptoms in patients with active disease.
- **Psoriatic Arthritis**: reducing signs and symptoms of active arthritis, inhibiting the progression of structural damage, and improving physical function.
- **Plaque Psoriasis:** treatment of adult patients with chronic severe (i.e., extensive and/or disabling) plaque psoriasis who are candidates for systemic therapy and when other systemic therapies are medically less appropriate.

REFERENCES

- Remicade [Prescribing Information]. Janssen Biotech, Inc: Horsham, PA. October 2017.

Library	Commercial	NSA
Yes	No	Yes

Part D Effective: N/A
Commercial Effective: 04/01/18

Created: 02/03
Client Approval: 03/18

P&T Approval: 01/18

INFLIXIMAB-ABDA (NSA)

Generic	Brand	HICL	GCN	Exception/Other
INFLIXIMAB-ABDA	RENFLEXIS	44432		

GUIDELINES FOR USE

INITIAL CRITERIA (NOTE: FOR RENEWAL CRITERIA, SEE BELOW)

1. Does the patient have a diagnosis of moderate to severe rheumatoid arthritis (RA) and meet **ALL** of the following criteria?
   - Therapy is prescribed by or given in consultation with a rheumatologist
   - The patient is currently using or has a contraindication to methotrexate
   - The patient has had a previous trial of at least one of the following DMARDs (disease-modifying antirheumatic drugs) such as methotrexate, leflunomide, hydroxychloroquine, or sulfasalazine
   - The patient has had a previous trial of the formulary preferred immunomodulators: Enbrel **AND** Humira (**NOTE:** pharmaceutical samples acquired from the prescriber or manufacturer assistance program do not qualify)

   If yes, **approve for 6 months by HICL.**
   APPROVAL TEXT: Renewal of **INFLIXIMAB-ABDA (Renflexis)** for moderate to severe rheumatoid arthritis requires that the patient has experienced or maintained a 20% or greater improvement in tender joint count or swollen joint count while on therapy.

   If no, continue to #2.

2. Does the patient have a diagnosis of psoriatic arthritis (PsA) and meet **ALL** of the following criteria?
   - Therapy is prescribed by or given in consultation with a rheumatologist or dermatologist
   - The patient has had a previous trial of at least one of the following DMARDs (disease-modifying antirheumatic drugs) such as methotrexate, leflunomide, hydroxychloroquine, or sulfasalazine
   - The patient is 18 years of age or older
   - The patient has had a previous trial of any **TWO** of the following formulary preferred immunomodulators: Enbrel, Humira, Cosentyx, Stelara, or Otezla (**NOTE:** pharmaceutical samples acquired from the prescriber or manufacturer assistance program do not qualify)

   If yes, **approve for 6 months by HICL.**
   APPROVAL TEXT: Renewal of **INFLIXIMAB-ABDA (Renflexis)** for psoriatic arthritis requires that the patient has experienced or maintained a 20% or greater improvement in tender joint count or swollen joint count while on therapy.

   If no, continue to #3.

CONTINUED ON NEXT PAGE

INFLIXIMAB-ABDA (NSA)

INITIAL CRITERIA (CONTINUED)

3. Does the patient have a diagnosis of ankylosing spondylitis (AS) and meet **ALL** of the following criteria?
   - Therapy is prescribed by or given in consultation with a rheumatologist
   - The patient is 18 years of age or older
   - The patient has had a previous trial of any **TWO** of the following formulary preferred immunomodulators: Enbrel, Humira, **OR** Cosentyx (**NOTE:** pharmaceutical samples acquired from the prescriber or manufacturer assistance program do not qualify)

   If yes, **approve for 6 months by HICL.**
   APPROVAL TEXT: Renewal of **INFLIXIMAB-ABDA (Renflexis)** for ankylosing spondylitis requires that the patient has experienced or maintained an improvement of at least 50% or 2 units (scale of 1-10) in the Bath Ankylosing Spondylitis Disease Activity Index (BASDAI) score while on therapy.

   If no, continue to #4.

4. Does the patient have a diagnosis of severe plaque psoriasis (PsO) and meet **ALL** of the following criteria?
   - Therapy is prescribed by or given in consultation with a dermatologist
   - The patient is 18 years of age or older
   - The patient has plaque psoriasis involving at least 10% body surface area (BSA) **OR** psoriatic lesions affecting the hands, feet, genital area, or face
   - The patient has had a previous trial of at least one or more forms of conventional therapies, such as PUVA (Phototherapy Ultraviolet Light A), UVB (Ultraviolet Light B), topical corticosteroids, calcipotriene, acitretin, methotrexate, or cyclosporine
   - The patient has had a previous trial of any **TWO** of the following formulary preferred immunomodulators: Enbrel, Humira, Cosentyx, Stelara, or Otezla (**NOTE:** pharmaceutical samples acquired from the prescriber or manufacturer assistance program do not qualify)

   If yes, **approve for 6 months by HICL.**
   APPROVAL TEXT: Renewal of **INFLIXIMAB-ABDA (Renflexis)** for severe plaque psoriasis requires that the patient has achieved or maintained clear or minimal disease or a decrease in PASI (Psoriasis Area and Severity Index) of at least 50% or more while on therapy.

   If no, continue to #5.

CONTINUED ON NEXT PAGE

INFLIXIMAB-ABDA (NSA)

INITIAL CRITERIA (CONTINUED)

5. Does the patient have a diagnosis of moderate to severe Crohn's disease (CD) and meet **ALL** of the following criteria?
   - Therapy is prescribed by or given in consultation with a gastroenterologist
   - The patient has had a previous trial of one or more of the following conventional therapies, such as corticosteroids (i.e., budesonide, methylprednisolone), azathioprine, mercaptopurine, methotrexate, or mesalamine
   - The patient is 6 years of age or older
   - The patient has had a previous trial of the formulary preferred immunomodulators: Humira **AND** Stelara (**NOTE:** pharmaceutical samples acquired from the prescriber or manufacturer assistance program do not qualify)

   If yes, **approve for 6 months by HICL.**
   If no, continue to #6.

6. Does the patient have a diagnosis of moderate to severe ulcerative colitis (UC) and meets **ALL** of the following criteria?
   - Therapy is prescribed by or given in consultation with a gastroenterologist
   - The patient has had a previous trial of one or more of the following conventional therapies, such as corticosteroids (i.e., budesonide, methylprednisolone), azathioprine, mercaptopurine, methotrexate, or mesalamine
   - The patient is 18 years of age or older
   - The patient has had a previous trial of the formulary preferred immunomodulatory: Humira (**NOTE:** pharmaceutical samples acquired from the prescriber or manufacturer assistance program do not qualify)

   If yes, **approve for 6 months by HICL.**
   If no, do not approve.
   DENIAL TEXT: See the initial denial text at the end of the guideline.

CONTINUED ON NEXT PAGE

INFLIXIMAB-ABDA (NSA)

INITIAL CRITERIA (CONTINUED)

INITIAL DENIAL TEXT: The guideline named **INFLIXIMAB-ABDA (Renflexis)** requires a diagnosis of moderate to severe rheumatoid arthritis, psoriatic arthritis, ankylosing spondylitis, severe plaque psoriasis, moderate to severe Crohn's disease, or moderate to severe ulcerative colitis. In addition, the following criteria must be met:

For patients with moderate to severe rheumatoid arthritis (RA), approval requires all of the following:

- Therapy is prescribed by or given in consultation with a rheumatologist
- The patient is currently using or has a contraindication to methotrexate
- The patient has had a previous trial of at least one of the following DMARDs (disease-modifying antirheumatic drugs) such as methotrexate, leflunomide, hydroxychloroquine, or sulfasalazine
- The patient has had a previous trial of the formulary preferred immunomodulators: Enbrel and Humira

For patients with psoriatic arthritis (PsA), approval requires all of the following:

- Therapy is prescribed by or given in consultation with a rheumatologist or dermatologist
- The patient has had a previous trial of at least one of the following DMARDs (disease-modifying antirheumatic drugs) such as methotrexate, leflunomide, hydroxychloroquine, or sulfasalazine
- The patient is 18 years of age or older
- The patient has had a previous trial of any **TWO** of the following formulary preferred immunomodulators: Enbrel, Humira, Cosentyx, Stelara, **OR** Otezla

For patients with ankylosing spondylitis (AS), approval requires all of the following:

- Therapy is prescribed by or given in consultation with a rheumatologist
- The patient is 18 years of age or older
- The patient has had a previous trial of any **TWO** of the following formulary preferred immunomodulators: Enbrel, Humira, **OR** Cosentyx

For patients with severe plaque psoriasis (PsO), approval requires all of the following:

- Therapy is prescribed by or given in consultation with a dermatologist
- The patient is 18 years of age or older
- The patient has plaque psoriasis involving at least 10% body surface area (BSA) **OR** psoriatic lesions affecting the hands, feet, genital area, or face
- The patient has had a previous trial of at least one or more forms of conventional therapies, such as PUVA (Phototherapy Ultraviolet Light A), UVB (Ultraviolet Light B), topical corticosteroids, calcipotriene, acitretin, methotrexate, or cyclosporine
- The patient has had a previous trial of any **TWO** of the following formulary preferred immunomodulators: Enbrel, Humira, Cosentyx, Stelara, **OR** Otezla

(Initial denial text continued on next page)

CONTINUED ON NEXT PAGE

INFLIXIMAB-ABDA (NSA)

INITIAL CRITERIA (CONTINUED)

For patients with moderate to severe Crohn's disease (CD), approval requires all of the following:

- Therapy is prescribed by or given in consultation with a gastroenterologist
- The patient has had a previous trial of one or more of the following conventional therapies, such as corticosteroids (i.e., budesonide, methylprednisolone), azathioprine, mercaptopurine, methotrexate, or mesalamine
- The patient is 6 years of age or older
- The patient has had a previous trial of the formulary preferred immunomodulators: Humira **AND** Stelara

For patients with moderate to severe ulcerative colitis (UC), approval requires all of the following:

- Therapy is prescribed by or given in consultation with a gastroenterologist
- The patient has had a previous trial of one or more of the following conventional therapies, such as corticosteroids (i.e., budesonide, methylprednisolone), azathioprine, mercaptopurine, methotrexate, or mesalamine
- The patient is 18 years of age or older
- The patient has had a previous trial of the formulary preferred immunomodulatory: Humira

The use of pharmaceutical samples (from the prescriber or manufacturer assistance program) will not be considered when evaluating the medical condition or prior prescription history for drugs that require prior authorization.

RENEWAL CRITERIA

1. Does the patient have a diagnosis of moderate to severe rheumatoid arthritis (RA) and meets **ALL** of the following criteria?
   - The patient has experienced or maintained a 20% or greater improvement in tender joint count or swollen joint count while on therapy
   - The patient is currently using or has a contraindication to methotrexate

   If yes, **approve for 12 months by HICL.**
   If no, continue to #2.

2. Does the patient have a diagnosis of psoriatic arthritis (PsA) and meets the following criteria?
   - The patient has experienced or maintained a 20% or greater improvement in tender joint count or swollen joint count while on therapy

   If yes, **approve for 12 months by HICL.**
   If no, continue to #3.

CONTINUED ON NEXT PAGE

INFLIXIMAB-ABDA (NSA)

RENEWAL CRITERIA (CONTINUED)

3. Does the patient have a diagnosis of ankylosing spondylitis (AS) and meets the following criteria?
   - The patient has experienced or maintained an improvement of at least 50% or 2 units (scale of 1-10) in the Bath Ankylosing Spondylitis Disease Activity Index (BASDAI) score while on therapy

   If yes, **approve for 12 months by HICL.**
   If no, continue to #4.

4. Does the patient have a diagnosis of severe plaque psoriasis (PsO) and meets the following criteria?
   - The patient has achieved or maintained clear or minimal disease or a decrease in PASI (Psoriasis Area and Severity Index) of at least 50% or more while on therapy

   If yes, **approve for 12 months by HICL.**
   If no, continue to #5.

5. Does the patient have a diagnosis of moderate to severe Crohn's disease (CD)?

   If yes, **approve for 12 months by HICL.**
   If no, continue to #6.

6. Does the patient have a diagnosis of moderate to severe ulcerative colitis (UC)?

   If yes, **approve for 12 months by HICL.**
   If no, do not approve.
   DENIAL TEXT: The guideline named **INFLIXIMAB-ABDA (Renflexis)** requires a diagnosis of moderate to severe rheumatoid arthritis, psoriatic arthritis, ankylosing spondylitis, severe plaque psoriasis, moderate to severe Crohn's disease, or moderate to severe ulcerative colitis for renewal. In addition, the following criteria must be met:
   Renewal for the diagnosis of moderate to severe rheumatoid arthritis requires all of the following:
   - That the patient has experienced or maintained a 20% or greater improvement in tender joint count or swollen joint count while on therapy
   - The patient is currently using or has a contraindication to methotrexate

   Renewal for the diagnosis of psoriatic arthritis requires:
   - That the patient has experienced or maintained a 20% or greater improvement in tender joint count or swollen joint count while on therapy

   (Renewal denial text continued on next page)

CONTINUED ON NEXT PAGE

INFLIXIMAB-ABDA (NSA)

RENEWAL CRITERIA (CONTINUED)

Renewal for the diagnosis of ankylosing spondylitis requires:
- That the patient has experienced or maintained an improvement of at least 50% or 2 units (scale of 1-10) in the Bath Ankylosing Spondylitis Disease Activity Index (BASDAI) score while on therapy

Renewal for the diagnosis of severe plaque psoriasis requires:
- That the patient has achieved or maintained clear or minimal disease or a decrease in PASI (Psoriasis Area and Severity Index) of at least 50% or more while on therapy

---

RATIONALE
To ensure the appropriate use of Renflexis according to FDA-approved indications.

FDA APPROVED INDICATIONS
Renflexis is a tumor necrosis factor (TNF) blocker indicated for:
- **Crohn's Disease:**
  - reducing signs and symptoms and inducing and maintaining clinical remission in adult patients with moderately to severely active disease who have had an inadequate response to conventional therapy.
  - reducing the number of draining enterocutaneous and rectovaginal fistulas and maintaining fistula closure in adult patients with fistulizing disease.
- **Pediatric Crohn's Disease:** reducing signs and symptoms and inducing and maintaining clinical remission in pediatric patients with moderately to severely active disease who have had an inadequate response to conventional therapy.
- **Ulcerative Colitis:** reducing signs and symptoms, inducing and maintaining clinical remission and mucosal healing, and eliminating corticosteroid use in adult patients with moderately to severely active disease who have had an inadequate response to conventional therapy.
- **Rheumatoid Arthritis in combination with methotrexate:** reducing signs and symptoms, inhibiting the progression of structural damage, and improving physical function in patients with moderately to severely active disease.
- **Ankylosing Spondylitis:** reducing signs and symptoms in patients with active disease.
- **Psoriatic Arthritis**: reducing signs and symptoms of active arthritis, inhibiting the progression of structural damage, and improving physical function.
- **Plaque Psoriasis**: treatment of adult patients with chronic severe (i.e., extensive and/or disabling) plaque psoriasis who are candidates for systemic therapy and when other systemic therapies are medically less appropriate.

CONTINUED ON NEXT PAGE

INFLIXIMAB-ABDA (NSA)

FDA APPROVED INDICATIONS (CONTINUED)

DOSING AND ADMINISTRATION
Renflexis is administered by intravenous infusion.

- **Crohn's Disease**: 5 mg/kg at 0, 2, and 6 weeks, then every 8 weeks. Some adult patients who initially respond to treatment may benefit from increasing the dose to 10 mg/kg if they later lose their response.
- **Ulcerative Colitis**: 5 mg/kg at 0, 2, and 6 weeks, then every 8 weeks.
- **Rheumatoid Arthritis**: In conjunction with methotrexate, 3 mg/kg at 0, 2, and 6 weeks, then every 8 weeks. Some patients may benefit from increasing the dose up to 10 mg/kg or treating as often as every 4 weeks.
- **Ankylosing Spondylitis**: 5 mg/kg at 0, 2, and 6 weeks, then every 6 weeks.
- **Psoriatic Arthritis**: 5 mg/kg at 0, 2, and 6 weeks, then every 8 weeks.
- **Plaque Psoriasis**: 5 mg/kg at 0, 2, and 6 weeks, then every 8 weeks.

REFERENCES

- Renflexis [Prescribing Information]. Kenilworth, NJ: Merck & Co., Inc. April 2017.

Library	Commercial	NSA
Yes	No	Yes

Part D Effective: N/A
Commercial Effective: 04/01/18
Created: 07/17
Client Approval: 03/18
P&T Approval: 01/18

INFLIXIMAB-DYYB (NSA)

Generic	Brand	HICL	GCN	Exception/Other
INFLIXIMAB-DYYB	INFLECTRA	43249		

GUIDELINES FOR USE

INITIAL CRITERIA (NOTE: FOR RENEWAL CRITERIA, SEE BELOW)

1. Does the patient have a diagnosis of moderate to severe rheumatoid arthritis (RA) and meet **ALL** of the following criteria?
   - Therapy is prescribed by or given in consultation with a rheumatologist
   - The patient is currently using or has a contraindication to methotrexate therapy
   - The patient has had a previous trial of at least one of the following DMARDs (disease-modifying antirheumatic drugs) such as methotrexate, leflunomide, hydroxychloroquine, or sulfasalazine
   - The patient has had a previous trial of the formulary preferred immunomodulators: Enbrel **AND** Humira (**NOTE:** pharmaceutical samples acquired from the prescriber or manufacturer assistance program do not qualify)

   If yes, **approve for 6 months by HICL.**
   APPROVAL TEXT: Renewal for moderate to severe rheumatoid arthritis requires that the patient has experienced or maintained a 20% or greater improvement in tender joint count or swollen joint count while on therapy.
   If no, continue to #2.

2. Does the patient have a diagnosis of psoriatic arthritis (PsA) and meet **ALL** of the following criteria?
   - Therapy is prescribed by or given in consultation with a rheumatologist or dermatologist
   - The patient has had a previous trial of at least one of the following DMARDs (disease-modifying antirheumatic drugs) such as methotrexate, leflunomide, hydroxychloroquine, or sulfasalazine
   - The patient is 18 years of age or older
   - The patient has had a previous trial of any **TWO** of the following formulary preferred immunomodulators: Enbrel, Humira, Cosentyx, Stelara, or Otezla (**NOTE:** pharmaceutical samples acquired from the prescriber or manufacturer assistance program do not qualify)

   If yes, **approve for 6 months by HICL.**
   APPROVAL TEXT: Renewal for psoriatic arthritis requires that the patient has experienced or maintained a 20% or greater improvement in tender joint count or swollen joint count while on therapy.
   If no, continue to #3.

CONTINUED ON NEXT PAGE

INFLIXIMAB-DYYB (NSA)

INITIAL CRITERIA (CONTINUED)

3. Does the patient have a diagnosis of ankylosing spondylitis (AS) and meet **ALL** of the following criteria?
   - Therapy is prescribed by or given in consultation with a rheumatologist
   - The patient is 18 years of age or older
   - The patient has had a previous trial of any **TWO** of the following formulary preferred immunomodulators: Enbrel, Humira, **OR** Cosentyx (**NOTE:** pharmaceutical samples acquired from the prescriber or manufacturer assistance program do not qualify)

   If yes, **approve for 6 months by HICL.**
   APPROVAL TEXT: Renewal for ankylosing spondylitis requires that the patient has experienced or maintained an improvement of at least 50% or 2 units (scale of 1-10) in the Bath Ankylosing Spondylitis Disease Activity Index (BASDAI) score while on therapy.
   If no, continue to #4.

4. Does the patient have a diagnosis of severe plaque psoriasis (PsO) and meet **ALL** of the following criteria?
   - Therapy is prescribed by or given in consultation with a dermatologist
   - The patient has plaque psoriasis involving at least 10% body surface area (BSA) or psoriatic lesions affecting the hands, feet, genital area, or face
   - The patient is 18 years of age or older
   - The patient has had a previous trial of at least one or more forms of systemic therapies, such as PUVA (Phototherapy Ultraviolet Light A), UVB (Ultraviolet Light B), topical corticosteroids, calcipotriene, acitretin, methotrexate, or cyclosporine
   - The patient has had a previous trial of any **TWO** of the following formulary preferred immunomodulators: Enbrel, Humira, Cosentyx, Stelara, or Otezla (**NOTE:** pharmaceutical samples acquired from the prescriber or manufacturer assistance program do not qualify)

   If yes, **approve for 6 months by HICL.**
   APPROVAL TEXT: Renewal for severe plaque psoriasis requires that the patient has achieved or maintained clear or minimal disease or a decrease in PASI (Psoriasis Area and Severity Index) of at least 50% or more while on therapy.
   If no, continue to #5.

CONTINUED ON NEXT PAGE

INFLIXIMAB-DYYB (NSA)

INITIAL CRITERIA (CONTINUED)

5. Does the patient have a diagnosis of moderate to severe Crohn's disease (CD) and meet **ALL** of the following criteria?
   - Therapy is prescribed by or given in consultation with a gastroenterologist
   - The patient has had a previous trial of one or more of the following conventional therapies, such as corticosteroids (i.e., budesonide, methylprednisolone), azathioprine, mercaptopurine, methotrexate, or mesalamine
   - The patient is 6 years of age or older
   - The patient has had a previous trial of the formulary preferred immunomodulators: Humira **AND** Stelara (**NOTE:** pharmaceutical samples acquired from the prescriber or manufacturer assistance program do not qualify)

   If yes, **approve for 6 months by HICL.**
   If no, continue to #6.

6. Does the patient have a diagnosis of moderate to severe ulcerative colitis (UC) and meet **ALL** of the following criteria?
   - Therapy is prescribed by or given in consultation with a gastroenterologist
   - The patient has had a previous trial of one or more of the following conventional therapies, such as corticosteroids (i.e., budesonide, methylprednisolone), azathioprine, mercaptopurine, methotrexate, or mesalamine
   - The patient is 18 years of age or older
   - The patient has had a previous trial of the formulary preferred immunomodulatory: Humira (**NOTE:** pharmaceutical samples acquired from the prescriber or manufacturer assistance program do not qualify)

   If yes, **approve for 6 months by HICL.**
   If no, do not approve.
   DENIAL TEXT: See the initial denial text at the end of the guideline.

CONTINUED ON NEXT PAGE

INFLIXIMAB-DYYB (NSA)

INITIAL CRITERIA (CONTINUED)

INITIAL DENIAL TEXT: The guideline named **INFLIXIMAB-DYYB (Inflectra)** requires a diagnosis of moderate to severe rheumatoid arthritis, psoriatic arthritis, ankylosing spondylitis, severe plaque psoriasis, moderate to severe Crohn's disease, or moderate to severe ulcerative colitis. In addition, the following criteria must be met:

For patients with moderate to severe rheumatoid arthritis (RA), approval requires:

- Therapy is prescribed by or given in consultation with a rheumatologist
- The patient is currently using or has a contraindication to methotrexate therapy
- The patient has had a previous trial of at least one of the following DMARDs (disease-modifying antirheumatic drugs) such as methotrexate, leflunomide, hydroxychloroquine, or sulfasalazine
- The patient has had a previous trial of the formulary preferred immunomodulators: Enbrel **AND** Humira

For patients with psoriatic arthritis (PsA), approval requires:

- Therapy is prescribed by or given in consultation with a rheumatologist or dermatologist
- The patient has had a previous trial of at least one of the following DMARDs (disease-modifying antirheumatic drugs) such as methotrexate, leflunomide, hydroxychloroquine, or sulfasalazine
- The patient is 18 years of age or older
- The patient has had a previous trial of any **TWO** of the following formulary preferred immunomodulators: Enbrel, Humira, Cosentyx, Stelara, or Otezla

For patients with ankylosing spondylitis (AS), approval requires:

- Therapy is prescribed by or given in consultation with a rheumatologist
- The patient is 18 years of age or older
- The patient has had a previous trial of any **TWO** of the following formulary preferred immunomodulators: Enbrel, Humira, or Cosentyx

For patients with severe plaque psoriasis (PsO), approval requires:

- Therapy is prescribed by or given in consultation with a dermatologist
- The patient has plaque psoriasis involving at least 10% body surface area (BSA) or psoriatic lesions affecting the hands, feet, genital area, or face
- The patient is 18 years of age or older
- The patient has had a previous trial of at least one or more forms of systemic therapies, such as PUVA (Phototherapy Ultraviolet Light A), UVB (Ultraviolet Light B), topical corticosteroids, calcipotriene, acitretin, methotrexate, or cyclosporine
- The patient has had a previous trial of any **TWO** of the following formulary preferred immunomodulators: Enbrel, Humira, Cosentyx, Stelara, or Otezla

(Initial denial text continued on next page)

CONTINUED ON NEXT PAGE

INFLIXIMAB-DYYB (NSA)

INITIAL CRITERIA (CONTINUED)

For patients with moderate to severe Crohn's disease (CD), approval requires:
- Therapy is prescribed by or given in consultation with a gastroenterologist
- The patient has had a previous trial of one or more of the following conventional therapies, such as corticosteroids (i.e., budesonide, methylprednisolone), azathioprine, mercaptopurine, methotrexate, or mesalamine
- The patient is 6 years of age or older
- The patient has had a previous trial of the formulary preferred immunomodulators: Humira **AND** Stelara

For patients with moderate to severe ulcerative colitis (UC), approval requires:
- Therapy is prescribed by or given in consultation with a gastroenterologist
- The patient has had a previous trial of one or more of the following conventional therapies, such as corticosteroids (i.e., budesonide, methylprednisolone), azathioprine, mercaptopurine, methotrexate, or mesalamine
- The patient is 18 years of age or older
- The patient has had a previous trial of the formulary preferred immunomodulatory: Humira

The use of pharmaceutical samples (from the prescriber or manufacturer assistance program) will not be considered when evaluating the medical condition or prior prescription history for drugs that require prior authorization.

RENEWAL CRITERIA

1. Does the patient have a diagnosis of moderate to severe rheumatoid arthritis (RA) **AND** meet **ALL** of the following criteria?
    - The patient has experienced or maintained a 20% or greater improvement in tender joint count or swollen joint count while on therapy
    - The patient is currently using or has a contraindication to methotrexate therapy

    If yes, **approve for 12 months by HICL.**
    If no, continue to #2.

2. Does the patient have a diagnosis of psoriatic arthritis (PsA) **AND** meet the following criterion?
    - The patient has experienced or maintained a 20% or greater improvement in tender joint count or swollen joint count while on therapy

    If yes, **approve for 12 months by HICL.**
    If no, continue to #3.

CONTINUED ON NEXT PAGE

INFLIXIMAB-DYYB (NSA)

RENEWAL CRITERIA (CONTINUED)

3. Does the patient have a diagnosis of ankylosing spondylitis (AS) **AND** meet the following criterion?
   - The patient has experienced or maintained an improvement of at least 50% or 2 units (scale of 1-10) in the Bath Ankylosing Spondylitis Disease Activity Index (BASDAI) score while on therapy

   If yes, **approve for 12 months by HICL.**
   If no, continue to #4.

4. Does the patient have a diagnosis of severe plaque psoriasis (PsO) **AND** meet the following criterion?
   - The patient has achieved or maintained clear or minimal disease or a decrease in PASI (Psoriasis Area and Severity Index) of at least 50% or more while on therapy

   If yes, **approve for 12 months by HICL.**
   If no, continue to #5.

5. Does the patient have a diagnosis of moderate to severe Crohn's disease (CD) or moderate to severe ulcerative colitis (UC)?

   If yes, **approve for 12 months by HICL.**
   If no, do not approve.
   DENIAL TEXT: The guideline named **INFLIXIMAB-DYYB (Inflectra)** requires a diagnosis of moderate to severe rheumatoid arthritis, psoriatic arthritis, ankylosing spondylitis, severe plaque psoriasis, moderate to severe Crohn's disease, or moderate to severe ulcerative colitis for renewal. In addition, the following criteria must be met:
   For the diagnosis of moderate to severe rheumatoid arthritis, approval requires:
   - The patient has experienced or maintained a 20% or greater improvement in tender joint count or swollen joint count while on therapy
   - The patient is currently using or has a contraindication to methotrexate therapy

   For the diagnosis of psoriatic arthritis, approval requires:
   - The patient has experienced or maintained a 20% or greater improvement in tender joint count or swollen joint count while on therapy

   For the diagnosis of ankylosing spondylitis, approval requires:
   - The patient has experienced or maintained an improvement of at least 50% or 2 units (scale of 1-10) in the Bath Ankylosing Spondylitis Disease Activity Index (BASDAI) score while on therapy

   For the diagnosis of severe plaque psoriasis, approval requires:
   - The patient has achieved or maintained clear or minimal disease or a decrease in PASI (Psoriasis Area and Severity Index) of at least 50% or more while on therapy

CONTINUED ON NEXT PAGE

INFLIXIMAB-DYYB (NSA)

RATIONALE
To ensure appropriate use of Inflectra consistent with its FDA approved indications.

FDA APPROVED INDICATIONS
Inflectra is a tumor necrosis factor (TNF) blocker indicated for:

- **Crohn's Disease:**
  - Reducing signs and symptoms and inducing and maintaining clinical remission in adult patients with moderately to severely active disease Crohn's disease who have had an inadequate response to conventional therapy
  - Reducing the number of draining enterocutaneous and rectovaginal fistulas and maintaining fistula closure in adult patients with fistulizing Crohn's disease
- **Pediatric Crohn's Disease:** reducing signs and symptoms and inducing and maintaining clinical remission in pediatric patients 6 years of age and older with moderately to severely active Crohn's disease who have had an inadequate response to conventional therapy
- **Ulcerative Colitis:** reducing signs and symptoms, inducing and maintaining clinical remission and mucosal healing, and eliminating corticosteroid use in adult patients with moderately to severely active ulcerative colitis who have had an inadequate response to conventional therapy.
- **Rheumatoid Arthritis in combination with methotrexate:** reducing signs and symptoms, inhibiting the progression of structural damage, and improving physical function in patients with moderately to severely active rheumatoid arthritis
- **Ankylosing Spondylitis:** reducing signs and symptoms in patients with active ankylosing spondylitis
- **Psoriatic Arthritis**: reducing signs and symptoms of active arthritis, inhibiting the progression of structural damage, and improving physical function in patients with psoriatic arthritis
- **Plaque Psoriasis**: treatment of adult patients with chronic severe (i.e., extensive and/or disabling) plaque psoriasis who are candidates for systemic therapy and when other systemic therapies are medically less appropriate. INFLECTRA should only be administered to patients who will be closely monitored and have regular follow-up visits with a physician.

DOSAGE AND ADMINISTRATION
Inflectra is administered by intravenous infusion.

- **Crohn's Disease/Fistulizing Crohn's disease**: 5 mg/kg at 0, 2, and 6 weeks, then every 8 weeks. Some adult patients who initially respond to treatment and later lose their response may benefit from increasing the dose to 10 mg/kg.
- **Ulcerative Colitis**: 5 mg/kg at 0, 2, and 6 weeks, then every 8 weeks.
- **Rheumatoid Arthritis**: In conjunction with methotrexate, 3 mg/kg at 0, 2, and 6 weeks, then every 8 weeks. Some patients who have an incomplete response may benefit from increasing the dose up to 10 mg/kg or treating as often as every 4 weeks.
- **Ankylosing Spondylitis**: 5 mg/kg at 0, 2, and 6 weeks, then every 6 weeks.
- **Psoriatic Arthritis**: 5 mg/kg at 0, 2, and 6 weeks, then every 8 weeks.
- **Plaque Psoriasis**: 5 mg/kg at 0, 2, and 6 weeks, then every 8 weeks.

CONTINUED ON NEXT PAGE

INFLIXIMAB-DYYB (NSA)

REFERENCES

- Inflectra [Prescribing Information]. Yeonsu-gu, Incheon, Republic of Korea: Celltrion, Inc. November 2017.

Library	Commercial	NSA
Yes	No	Yes

Part D Effective: N/A
Commercial Effective: 04/01/18

Created: 05/16
Client Approval: 03/18

P&T Approval: 01/18

INOTUZUMAB OZOGAMICIN (NSA)

Generic	Brand	HICL	GCN	Exception/Other
INOTUZUMAB OZOGAMICIN	BESPONSA	44438		

GUIDELINES FOR USE

1. Does the patient have a diagnosis of relapsed or refractory B-cell precursor acute lymphoblastic leukemia (ALL) and meet following criterion?
   - The patient is 18 years of age or older

   If yes, continue to #2.
   If no, do not approve.
   DENIAL TEXT: See the denial text at the end of the guideline.

2. Has the patient received 6 cycles of Besponsa treatment previously?

   If yes, do not approve.
   DENIAL TEXT: See the denial text at the end of the guideline.
   If no, **approve for 6 months by HICL.**

DENIAL TEXT: The guideline named **INOTUZUMAB OZOGAMICIN (Besponsa)** requires the following criteria be met:
- A diagnosis of relapsed or refractory B-cell pre-cursor acute lymphoblastic leukemia (ALL)
- The patient is 18 years of age or older
- The patient has **NOT** received 6 cycles of Besponsa previously

RATIONALE
Promote appropriate utilization of INOTUZUMAB OZOGAMICIN based on FDA approved indication.

FDA APPROVED INDICATION
BESPONSA is indicated for the treatment of adults with relapsed or refractory B-cell precursor acute lymphoblastic leukemia

DOSAGE AND ADMINISTRATION
Besponsa is infused for 1 hour at a rate of 50 mL/h at room temperature. Dosing is based on body surface area (m^2) and response to preceding therapy:

CONTINUED ON NEXT PAGE

INOTUZUMAB OZOGAMICIN (NSA)

FDA APPROVED INDICATION (CONTINUED)

DOSAGE AND ADMINISTRATION
Dosing regimens for Cycle 1 and subsequent cycles, depending on the response to treatment:

- **For the first cycle**: the recommended total dose of Besponsa for all patients is 1.8 mg/m^2 per cycle, administered as 3 divided doses on Day 1 (0.8 mg/m^2), Day 8 (0.5 mg/m^2), and Day 15 (0.5 mg/m^2). Cycle 1 is 3 weeks in duration, but may be extended to 4 weeks if the patient achieves a complete remission (CR) or complete remission with incomplete hematologic recovery (CRi), and/or to allow recovery from toxicity.

- **For subsequent cycles**: In patients who achieve a CR or CRi, the recommended total dose of Besponsa is 1.5 mg/m^2 per cycle, administered as 3 divided doses on Day 1 (0.5 mg/m^2), Day 8 (0.5 mg/m^2), and Day 15 (0.5 mg/m^2). Subsequent cycles are 4 weeks in duration.

- **In patients who do not achieve a CR* or CRi****:, the recommended total dose of Besponsa is 1.8 mg/m^2 per cycle given as 3 divided doses on Day 1 (0.8 mg/m^2), Day 8 (0.5 mg/m^2), and Day 15 (0.5 mg/m^2). Subsequent cycles are 4 weeks in duration. Patients who do not achieve a CR or CRi within 3 cycles should discontinue treatment.

*** CR** is defined as < 5% blasts in the bone marrow and the absence of peripheral blood leukemic blasts, full recovery of peripheral blood counts (platelets ≥ 100 × 10^9/L and absolute neutrophil counts [ANC] ≥ 1 × 10^9/L) and resolution of any extramedullary disease.

**** CRi** is defined as < 5% blasts in the bone marrow and the absence of peripheral blood leukemic blasts, incomplete recovery of peripheral blood counts (platelets < 100 × 10^9/L and/or ANC < 1 × 10^9/L) and resolution of any extramedullary disease.

For patients proceeding to hematopoietic stem cell transplant (HSCT), the recommended duration of treatment with Besponsa is 2 cycles. A third cycle may be considered for those patients who do not achieve CR or CRi and minimal residual disease (MRD) negativity after 2 cycles.

For patients not proceeding to HSCT, additional cycles of treatment, up to a maximum of 6 cycles, may be administered.

Patients should be pre-medicated before each dose.

AVAILABLE STRENGTHS
Injection: supplied as a white to off-white lyophilized powder in a single-dose vial for reconstitution and further dilution. Each vial delivers 0.9 mg inotuzumab ozogamicin. Each carton contains one single-dose vial.

CONTINUED ON NEXT PAGE

INOTUZUMAB OZOGAMICIN (NSA)

REFERENCES

- Besponsa [Prescribing Information]. Philadelphia, PA: Wyeth Pharmaceuticals, Inc. August 2017.

Library	Commercial	NSA
Yes	No	Yes

Part D Effective: N/A
Commercial Effective: 01/01/18

Created: 08/17
Client Approval: 12/17

P&T Approval: 10/17

IOBENGUANE IODINE 131 (NSA)

Generic	Brand	HICL	GCN	Exception/Other
IOBENGUANE I 131	AZEDRA	25483		

GUIDELINES FOR USE

1. Does the patient have a diagnosis of unresectable, locally advanced or metastatic pheochromocytoma or paraganglioma and meet ALL of the following criteria?
   - The patient is 12 years of age or older
   - The patient requires systemic anticancer therapy
   - The tumors are iobenguane scan positive
   - The patient has **NOT** previously received 1 dosimetric dose and 2 therapeutic doses of Azedra

   If yes, **approve by GPID for 12 months for all dosages with the following quantity limits:**
   - **Azedra Dosimetric (GPID 45058): #1 vial per 12 months.**
   - **Azedra Therapeutic (GPID 45059): #4 vials per 12 months.**

   If no, do not approve.
   DENIAL TEXT: The guideline named **IOBENGUANE IODINE 131 (Azedra)** requires a diagnosis of unresectable, locally advanced or metastatic pheochromocytoma or paraganglioma. In addition, the following criteria must be met:
   - The patient is 12 years of age or older
   - The patient requires systemic anticancer therapy
   - The tumors are iobenguane scan positive
   - The patient has **NOT** previously received 1 dosimetric dose and 2 therapeutic doses of Azedra

RATIONALE
For further information, please refer to the Prescribing Information and/or Drug Monograph for Azedra.

REFERENCES

- Azedra [Prescribing Information]. New York, NY: Progenics Pharmaceuticals, Inc. Pharmaceuticals Corporation. July 2018.

Library	Commercial	NSA
Yes	No	Yes

Part D Effective: N/A
Commercial Effective: 01/01/19
Created: 11/18
Client Approval: 11/18
P&T Approval: 10/18

IPILIMUMAB (NSA)

Generic	Brand	HICL	GCN	Exception/Other
IPILIMUMAB	YERVOY	37503		

This drug requires a written request for prior authorization.

GUIDELINES FOR USE

INITIAL CRITERIA (NOTE: FOR RENEWAL CRITERIA SEE BELOW)

1. Does the patient have a diagnosis of unresectable or metastatic melanoma **AND** meet the following criterion?
   - The patient is 12 years of age or older

   If yes, **approve and enter two authorizations for 4 months by GPID for 4 fills as follows:**
   - **50mg/10mL (GPID 29688).**
   - **200mg/40mL (GPID 29689).**

   APPROVAL TEXT: Renewal criteria does not apply for this approval.

   If no, continue to #2.

2. Does the patient have a diagnosis of cutaneous melanoma and meet **ALL** of the following criteria?
   - The requested medication will be used for adjuvant treatment
   - There is pathologic involvement of regional lymph nodes of more than 1mm
   - The patient has undergone complete resection, including total lymphadenectomy

   If yes, **approve and enter two authorizations (initial and maintenance dose) for 6 months for both GPIDs (GPIDs 29688, 29689) as follows:**
   - **INITIAL: Approve and enter two authorizations for 4 fills in 3 months for all of the following GPIDs:**
     - **50mg/10mL (GPID 29688).**
     - **200mg/40mL (GPID 29689).**
   - **MAINTENANCE (start 12 weeks after the end date of initial authorization): Approve and enter two authorizations for 1 fill in 3 months for all of the following GPIDs:**
     - **50mg/10mL (GPID 29688).**
     - **200mg/40mL (GPID 29689).**

   APPROVAL TEXT: Renewal requires that the patient does not have any disease recurrence (defined as the appearance of one or more new melanoma lesions: local, regional or distant metastasis) and patient has not been treated with Yervoy for more than 3 years.

   If no, continue to #3.

CONTINUED ON NEXT PAGE

IPILIMUMAB (NSA)

INITIAL CRITEIRA (CONTINUED)

3. Does the patient have a diagnosis of advanced renal cell carcinoma (RCC) and meet **ALL** of the following criteria?
   - The requested medication will be used in combination with Opdivo (nivolumab)
   - The patient has intermediate or poor risk disease
   - The patient has not received prior treatment for advanced renal cell carcinoma

   If yes, **approve and enter two authorizations for 3 months by GPID for 4 fills as follows:**
   - **50mg/10mL (GPID 29688).**
   - **200mg/40mL (GPID 29689).**

   APPROVAL TEXT: Renewal criteria does not apply for this approval.

   If no, continue to #4.

4. Does the patient have a diagnosis of microsatellite instability-high (MSI-H) or mismatch repair deficient (dMMR) metastatic colorectal cancer and meet **ALL** the following criteria?
   - The patient is 12 years of age or older
   - The requested medication will be used in combination with Opdivo (nivolumab)
   - The patient has disease progression following treatment with a fluoropyrimidine, oxaliplatin, and irinotecan

   If yes, **approve and enter two authorizations for 3 months by GPID for 4 fills as follows:**
   - **50mg/10mL (GPID 29688).**
   - **200mg/40mL (GPID 29689).**

   APPROVAL TEXT: Renewal criteria does not apply for this approval.

   If no, do not approve.
   INITIAL DENIAL TEXT: The guideline named **IPILIMUMAB (Yervoy)** requires a diagnosis of unresectable or metastatic melanoma, cutaneous melanoma, advanced renal cell carcinoma, or microsatellite instability-high (MSI-H) or mismatch repair deficient (dMMR) metastatic colorectal cancer. In addition, the following criteria must be met:
   For diagnosis of unresectable or metastatic melanoma, approval requires:
   - The patient is 12 years of age or older

   For diagnosis of cutaneous melanoma, approval requires:
   - The requested medication will be used for adjuvant treatment
   - There is pathologic involvement of regional lymph nodes of more than 1mm
   - The patient has undergone complete resection, including total lymphadenectomy

   (Initial denial text continued on next page)

CONTINUED ON NEXT PAGE

IPILIMUMAB (NSA)

INITIAL CRITEIRA (CONTINUED)

For diagnosis of advanced renal cell carcinoma, approval requires:
- The requested medication will be used in combination with Opdivo (nivolumab)
- The patient has intermediate or poor risk disease
- The patient has not received prior treatment for advanced renal cell carcinoma

For diagnosis of microsatellite instability-high (MSI-H) or mismatch repair deficient (dMMR) metastatic colorectal cancer, approval requires:
- The patient is 12 years of age or older
- The requested medication will be used in combination with Opdivo (nivolumab)
- The patient has disease progression following treatment with a fluoropyrimidine, oxaliplatin, and irinotecan

RENEWAL CRITERIA

1. Has the patient been treated with Yervoy for more than 3 years per claims history?

   If yes, do not approve.
   DENIAL TEXT: See the renewal denial text at the end of the guideline.
   If no, continue to #2.

2. Does the patient have a diagnosis of unresectable or metastatic melanoma **OR** advanced renal cell carcinoma (RCC) **OR** microsatellite instability-high (MSI-H) or mismatch repair deficient (dMMR) metastatic colorectal cancer?

   If yes, do not approve.
   DENIAL TEXT: See the renewal denial text at the end of the guideline.
   If no, continue to #3.

3. Is the request for adjuvant treatment of cutaneous melanoma and has the following criterion been met?
   - There is no evidence of disease recurrence (defined as the appearance of one or more new melanoma lesions: local, regional or distant metastasis)

   If yes, **approve and enter two authorizations for 6 months by GPID for 2 fills as follows:**
   - **50mg/10mL (GPID 29688).**
   - **200mg/40mL (GPID 29689).**

   If no, do not approve.
   DENIAL TEXT: See the renewal denial text at the end of the guideline.

CONTINUED ON NEXT PAGE

IPILIMUMAB (NSA)

RENEWAL CRITEIRA (CONTINUED)

RENEWAL DENIAL TEXT: The guideline named **IPILIMUMAB (Yervoy)** requires that all of the following are met for renewal:

- The patient has not been treated with Yervoy for more than 3 years
- The patient does not have a diagnosis of unresectable or metastatic melanoma **OR** advanced renal cell carcinoma (RCC) **OR** microsatellite instability-high (MSI-H) or mismatch repair deficient (dMMR) metastatic colorectal cancer
- The request is for adjuvant treatment of cutaneous melanoma AND the patient does not have any disease recurrence (defined as the appearance of one or more new melanoma lesions: local, regional or distant) following treatment with Yervoy

RATIONALE

To ensure appropriate utilization of ipilimumab based on its FDA approved indications.

FDA APPROVED INDICATIONS

Ipilimumab is a human cytotoxic T-lymphocyte antigen 4 (CTLA-4)-blocking antibody indicated for:

- The treatment of unresectable or metastatic melanoma in adults and pediatric patients (12 years and older).
- Adjuvant treatment of patients with cutaneous melanoma with pathologic involvement of regional lymph nodes of more than 1 mm who have undergone complete resection, including total lymphadenectomy.
- The treatment of patients with intermediate or poor risk, previously untreated advanced renal cell carcinoma, in combination with nivolumab.
- In combination with nivolumab, for the treatment of adult and pediatric patients 12 years of age and older with microsatellite instability-high (MSI-H) or mismatch repair deficient (dMMR) metastatic colorectal cancer that has progressed following treatment with a fluoropyrimidine, oxaliplatin, and irinotecan. This indication is approved under accelerated approval based on overall response rate and duration of response. Continued approval for this indication may be contingent upon verification and description of clinical benefit in confirmatory trials.

CONTINUED ON NEXT PAGE

IPILIMUMAB (NSA)

FDA APPROVED INDICATIONS (CONTINUED)

DOSAGE AND ADMINISTRATION

- **Unresectable or metastatic melanoma:** 3mg/kg IV over 90 minutes every 3 weeks for a total of 4 doses. In the event of toxicity, doses may be delayed, but all treatment must be administered within 16 weeks of the first dose.
- **Adjuvant melanoma:** 10mg/kg IV over 90 minutes every 3 weeks for 4 doses, followed by 10mg/kg every 12 weeks for up to 3 years or until documented disease recurrence or unacceptable toxicity.
- **Advanced renal cell carcinoma:** Nivolumab 3 mg/kg IV over 30 minutes followed by Yervoy 1 mg/kg IV over 30 minutes on the same day, every 3 weeks for a maximum of 4 doses. After completing 4 doses of the combination, administer nivolumab intravenously over 30 minutes as a single agent until disease progression or unacceptable toxicity, either:
  - 240 mg every 2 weeks or
  - 480 mg every 4 weeks
- **Microsatellite instability-high (MSI-H) or mismatch repair deficient (dMMR) metastatic colorectal cancer (CRC):** The recommended dose in combination with Yervoy (ipilimumab) is Opdivo 3 mg/kg, followed by Yervoy 1mg/kg on the same day every 3 weeks for 4 doses. After completing 4 doses of the combination, administer Opdivo 240 mg as a single agent every 2 weeks

REFERENCES

- Bristol-Myers Squibb Company.Yervoy package insert. Princeton, NJ. July 2018.

Library	Commercial	NSA
Yes	No	Yes

Part D Effective: N/A
Commercial Effective: 08/01/18
Created: 04/11
Client Approval: 07/18
P&T Approval: 07/18

IRINOTECAN LIPOSOMAL

Generic	Brand	HICL	GCN	Exception/Other
IRINOTECAN LIPOSOMAL	ONIVYDE	42715		

GUIDELINES FOR USE

1. Does the patient have a diagnosis of metastatic adenocarcinoma of the pancreas and have **ALL** of the following criteria been met?
   - The patient has experienced disease progression despite a trial of gemcitabine-based therapy.
   - Onivyde (irinotecan liposomal) will be used in combination with fluorouracil and leucovorin.

   If yes, **approve for 12 months by HICL for 2 fills per 28 day supply.**
   If no, continue to #2.
   DENIAL TEXT: Our guideline for **IRINOTECAN LIPOSOMAL** requires a diagnosis of metastatic adenocarcinoma of the pancreas. In addition, the following criteria must also be met:
   - The patient has experienced disease progression despite a trial of gemcitabine-based therapy.
   - Onivyde (irinotecan liposomal) will be used in combination with fluorouracil and leucovorin.

RATIONALE

Promote appropriate utilization of irinotecan liposomal based on FDA approved indication and dosing.

Onivyde is a nanoliposomal encapsulated preparation of irinotecan that enables it to remain in circulation for a longer duration compared with standard irinotecan; this allows for higher drug uptake within tumor cells and conversion of irinotecan to its active form, SN38.

Pancreatic cancer can be difficult to diagnose early and treatment options are limited, especially when the disease has spread to other parts of the body and surgery to remove the tumor is not possible. The majority of these tumors (85%) are adenocarcinomas arising from the ductal epithelium. The disease is rare before the age of 45, but the incidence rises sharply thereafter. On the basis of significant improvements in clinical benefit and survival, gemcitabine was approved for first-line therapy of metastatic pancreatic cancer.

DOSAGE
The recommended dose of Onivyde is 70 mg/m2 administered by intravenous infusion over 90 minutes every 2 weeks, unless the patient is known to be homozygous for the UGT1A1*28 allele, in which case, the first dose should be 50 mg/m2. Onivyde requires pre-medication with a corticosteroid and an anti-emetic 30 minutes prior to the Onivyde infusion. Once the Onivyde infusion is complete, it should be followed by leucovorin 400 mg/m2 intravenously over 30 minutes and then by fluorouracil 2400 mg/m2 intravenously over 46 hours, every 2 weeks.

CONTINUED ON NEXT PAGE

IRINOTECAN LIPOSOMAL

FDA APPROVED INDICATION

Onivyde is a topoisomerase inhibitor indicated, in combination with fluorouracil and leucovorin, for the treatment of patients with metastatic adenocarcinoma of the pancreas after disease progression following gemcitabine-based therapy.

Limitation of Use: Onivyde is not indicated as a single agent for the treatment of patients with metastatic adenocarcinoma of the pancreas.

REFERENCES

- Onivyde [Prescribing Information]. Merrimack Pharmaceuticals, Inc.: Cambridge, MA. October 2015.

Library	Commercial	NSA
Yes	No	Yes

Part D Effective: N/A
Commercial Effective: 01/01/16
Created: 11/15
Client Approval: 11/15
P&T Approval: 11/15

IXABEPILONE

Generic	Brand	HICL	GCN	Exception/Other
IXABEPILONE	IXEMPRA	35083		

This drug requires a written request for prior authorization.

GUIDELINES FOR USE

1. Does the patient have a diagnosis of metastatic or locally advanced breast cancer?

   If yes, continue to #2.
   If no, do not approve.
   DENIAL TEXT: Approval requires a diagnosis of metastatic or locally advanced breast cancer and, 1) trial of a chemotherapy regimen containing an anthracycline (doxorubicin or epirubicin), a taxane (paclitaxel or docetaxel), and Xeloda (capecitabine) or, 2) trial of a chemotherapy regimen containing an anthracycline (doxorubicin or epirubicin) and a taxane (paclitaxel or docetaxel), and being used in combination with Xeloda (capecitabine).

2. Has the patient tried a chemotherapy regimen containing an anthracycline (doxorubicin or epirubicin), a taxane (paclitaxel or docetaxel), and Xeloda (capecitabine)?

   If yes, **approve for 12 months by HICL.**
   APPROVAL TEXT: Please note that this drug has an important FDA safety warning. For more information please ask your doctor or pharmacist.
   If no, continue to #3.

3. Is the requested medication being used in combination with Xeloda (capecitabine)?

   If yes, continue to #4.
   If no, do not approve.
   DENIAL TEXT: Approval requires a diagnosis of metastatic or locally advanced breast cancer and, 1) trial of a chemotherapy regimen containing an anthracycline (doxorubicin or epirubicin), a taxane (paclitaxel or docetaxel), and Xeloda (capecitabine) or, 2) trial of a chemotherapy regimen containing an anthracycline (doxorubicin or epirubicin) and a taxane (paclitaxel or docetaxel), and being used in combination with Xeloda (capecitabine).

CONTINUED ON NEXT PAGE

IXABEPILONE

GUIDELINES FOR USE (CONTINUED)

4. Has the patient tried a chemotherapy regimen containing an anthracycline (doxorubicin or epirubicin) and a taxane (paclitaxel or docetaxel)?

   If yes, **approve for 12 months by HICL.**
   APPROVAL TEXT: Please note that this drug has an important FDA safety warning. For more information please ask your doctor or pharmacist.
   If no, do not approve.
   DENIAL TEXT: Approval requires a diagnosis of metastatic or locally advanced breast cancer and, 1) trial of a chemotherapy regimen containing an anthracycline (doxorubicin or epirubicin), a taxane (paclitaxel or docetaxel), and Xeloda (capecitabine) or, 2) trial of a chemotherapy regimen containing an anthracycline (doxorubicin or epirubicin) and a taxane (paclitaxel or docetaxel), and being used in combination with Xeloda (capecitabine).

RATIONALE

Coverage of Ixempra (ixabepilone) is based on FDA approved indications and NCCN recommendations.

The recommended dose of Ixempra is 40 mg/m^2 infused intravenously over 3 hours every 3 weeks. Dose reduction is required in certain patients with elevated AST, ALT, or bilirubin.

NCCN guidelines recognize multiple chemotherapy treatment options for recurrent or metastatic breast cancer. Ixempra is considered a nonpreferred single agent therapy. NCCN no longer recognizes Ixempra with Xeloda as a valid chemotherapy regimen for the treatment of recurrent or metastatic breast cancer.

Preferred Single Agents	Other Single Agents	Combination Regimens
doxorubicin	cyclophosphamide	cyclophosphamide, doxorubicin, fluorouracil (FAC/CAF)
pegylated liposomal doxorubicin	carboplatin	fluorouracil, epirubicin, cyclophosphamide (FEC)
paclitaxel	docetaxel	doxorubicin, cyclophosphamide (AC)
Xeloda	Abraxane	epirubicin, cyclophosphamide (EC)
gemcitabine	cisplatin	cyclophosphamide, methotrexate, fluorouracil (CML)
Halaven	Ixempra	docetaxel, Xeloda
vinorelbine	epirubicin	gemcitabine, paclitaxel
		gemcitabine carboplatin
		paclitaxel, Avastin

CONTINUED ON NEXT PAGE

STANDARD NON-SELF-ADMINISTERED DRUG FORMULARY
PRIOR AUTHORIZATION GUIDELINES

IXABEPILONE

FDA APPROVED INDICATION

- Ixempra, a microtubule inhibitor, in combination with capecitabine is indicated for the treatment of metastatic or locally advanced breast cancer in patients after failure of an anthracycline and a taxane.
- Ixempra as monotherapy is indicated for the treatment of metastatic or locally advanced breast cancer in patients after failure of an anthracycline, a taxane, and capecitabine.

REFERENCES

- Bristol-Myers Squibb Company. Ixempra package insert. Princeton, NJ. October 2011.
- National Comprehensive Cancer Network, Inc. NCCN Clinical Practice Guidelines in Oncology. Breast Cancer (Version 3.2013).

Library	Commercial	NSA
Yes	No	Yes

Part D Effective: N/A
Commercial Effective: 10/01/13
Created: 08/13
Client Approval: 08/13
P&T Approval: 08/13

LETERMOVIR IV (NSA)

Generic	Brand	HICL	GCN	Exception/Other
LETERMOVIR	PREVYMIS		44062 44063	

GUIDELINES FOR USE

1. Is the patient undergoing an allogeneic hematopoietic stem cell transplant (HSCT) and meet **ALL** of the following criteria?
   - The patient is at least 18 years of age or older
   - The patient is CMV-seropositive [R+]
   - Prevymis will be used for prophylaxis of cytomegalovirus (CMV) infection and disease
   - Prevymis will be initiated between Day 0 and Day 28 post-transplantation (before or after engraftment)
   - Patient is not receiving the medication beyond 100 days post-transplantation

   If yes, **approve for 4 months by GPID for all daily dosage strengths with the following quantity limits:**
   - **240mg/12mL daily dose (GPID 44062): #12mL (one single dose vial) per day.**
   - **480mg/24mL (GPID 44063): #24mL (one single dose vial) per day.**

   If no, do not approve.
   DENIAL TEXT: The guideline named **LETERMOVIR IV (Prevymis)** requires the patient to be undergoing an allogeneic hematopoietic stem cell transplant (HSCT). In addition, the following criteria must also be met:
   - The patient is at least 18 years of age or older
   - The patient is CMV-seropositive [R+]
   - Prevymis will be used for prophylaxis of cytomegalovirus (CMV) infection and disease
   - Prevymis will be initiated between Day 0 and Day 28 post-transplantation (before or after engraftment)
   - Patient is not receiving the medication beyond 100 days post-transplantation

RATIONALE
Promote appropriate utilization of **LETERMOVIR** based on FDA approved indication and dosing.

FDA APPROVED INDICATION
Prevymis is indicated for prophylaxis of cytomegalovirus (CMV) infection and disease in adult CMV seropositive recipients [R+] of an allogeneic hematopoietic stem cell transplant (HSCT).

CONTINUED ON NEXT PAGE

LETERMOVIR IV (NSA)

FDA APPROVED INDICATION (CONTINUED)

DOSAGE AND ADMINISTRATION

The recommended dosage of Prevymis is 480 mg administered orally or intravenously once daily. Prevymis is recommended to be initiated between Day 0 and Day 28 post-transplantation (before or after engraftment), and continue through Day 100 post-transplantation. Dosage of Prevymis should be decreased to 240mg once daily when co-administered with cyclosporine.

- If cyclosporine is initiated after starting Prevymis, the next dose of Prevymis should be decreased to 240mg once daily.
- If cyclosporine is discontinued after starting Prevymis, the next dose of Prevymis should be increased to 480mg once daily.
- If cyclosporine dosing is interrupted due to high cyclosporine levels, no dose adjustment of Prevymis is needed.

Prevymis injection, which contains hydroxypropyl betadex, should be used only in patients unable to take oral therapy. Patients should be switched to oral Prevymis as soon as they are able to take oral medications. Prevymis tablet and injection may be used interchangeably at the discretion of the physician, and no dosage adjustment is necessary when switching formulations.

AVAILABLE STRENGTHS

Tablet: 240mg, 480mg tablets; Injection: 240mg/12 mL (20mg/mL), 480mg/24mL (20mg/mL) single dose vials

REFERENCES

- Prevymis [Prescribing Information]. Merck & Co, Inc.; Whitehouse Station, NJ. November 2017.

Library	Commercial	NSA
Yes	No	Yes

Part D Effective: N/A
Commercial Effective: 04/01/18
Created: 02/18
Client Approval: 03/18
P&T Approval: 01/18

LUTETIUM LU 177 DOTATATE (NSA)

Generic	Brand	HICL	GCN	Exception/Other
LUTETIUM LU 177 DOTATATE	LUTATHERA	44750		

This drug requires a written request for prior authorization.

GUIDELINES FOR USE

1. Does the patient have a diagnosis of somatostatin receptor-positive gastroenteropancreatic neuroendocrine tumors (GEP-NETs) and meet **ALL** of the following criteria?
   - The patient is 18 years of age or older
   - The patient will be treated with long-acting octreotide as maintenance therapy in conjunction with the requested drug
   - The patient has been previously treated with a long acting somatostatin analog (i.e., octreotide or lanreotide) prior to the request of this medication

   If yes, continue to #2.
   If no, do not approve.
   DENIAL TEXT: See the denial text at the end of the guideline.

2. Has the patient received 4 doses of Lutathera previously?

   If yes, do not approve.
   DENIAL TEXT: See the denial text at the end of the guideline.
   If no, **approve for 8 months by HICL with a quantity limit of #1 vial per 56 days.**

DENIAL TEXT: The guideline named **LUTETIUM LU 177 DOTATATE (Lutathera)** requires a diagnosis of somatostatin receptor-positive gastroenteropancreatic neuroendocrine tumors (GEP-NETs). In addition, the following criteria must be met:
- The patient is 18 years of age or older
- The patient will be treated with long-acting octreotide as maintenance therapy in conjunction with the requested drug
- The patient has been previously treated with a long acting somatostatin analog (i.e., octreotide or lanreotide) prior to the request of this medication
- The patient has **NOT** previously received 4 doses of Lutathera

CONTINUED ON NEXT PAGE

LUTETIUM LU 177 DOTATATE (NSA)

RATIONALE
To promote appropriate utilization of Lutathera based on FDA approved indication and dosing.

FDA APPROVED INDICATIONS
Lutathera is a radiolabeled somatostatin analog indicated for the treatment of somatostatin receptor-positive gastroenteropancreatic neuroendocrine tumors (GEP-NETs), including foregut, midgut, and hindgut neuroendocrine tumors in adults.

DOSAGE AND ADMINISTRATION
The recommended Lutathera dose is 7.4 GBq (200 mCi) every 8 weeks for a total of 4 doses. Administer pre- and concomitant medications and administer Lutathera as recommended.

Lutathera is a radiopharmaceutical; handle with appropriate safety measures to minimize radiation exposure. Use waterproof gloves and effective radiation shielding when handling Lutathera. Radiopharmaceuticals, including Lutathera, should be used by or under the control of physicians who are qualified by specific training and experience in the safe use and handling of radiopharmaceuticals, and whose experience and training have been approved by the appropriate governmental agency authorized to license the use of radiopharmaceuticals.

Verify pregnancy status of females of reproductive potential prior to initiating Lutathera.

REFERENCES

- Lutathera [Prescribing Information]. New York, NY: Advanced Accelerator Applications USA, Inc. February 2018.

Library	Commercial	NSA
Yes	No	Yes

Part D Effective: N/A
Commercial Effective: 07/01/18
Created: 05/18
Client Approval: 05/18
P&T Approval: 04/18

MEPOLIZUMAB (NSA)

Generic	Brand	HICL	GCN	Exception/Other
MEPOLIZUMAB	NUCALA	42775		

This drug requires a written request for prior authorization.

GUIDELINES FOR USE

INITIAL CRITERIA (NOTE: FOR RENEWAL CRITERIA SEE BELOW)

1. Does the patient have a diagnosis of eosinophilic granulomatosis with polyangiitis (EGPA), also known as Churg-Strauss syndrome, **AND** meet the following criterion?
   - The patient is 18 years of age or older

   If yes, **approve for 12 months by HICL with a quantity limit of #3 vials (300mg) per 28 days**.
   APPROVAL TEXT: Renewal requires a diagnosis of eosinophilic granulomatosis with polyangiitis (EGPA), also known as Churg-Strauss syndrome.

   If no, continue to #2.

2. Does the patient have a diagnosis of severe asthma with an eosinophilic phenotype and meet **ALL** of the following criteria?
   - The patient is 12 years of age or older
   - The patient has a documented blood eosinophil level of at least 300 cells/mcL within the past 6 months
   - The patient is currently adherent to a maximally tolerated dose of an inhaled corticosteroid plus at least one other maintenance medication (e.g., a long-acting inhaled beta2-agonist, a long-acting muscarinic antagonist, a leukotriene receptor antagonist, theophylline, or oral corticosteroid)
   - The patient has experienced at least 2 or more asthma exacerbations within the past 12 months (exacerbation is defined as an asthma-related event requiring hospitalization, emergency room visit, or systemic corticosteroid burst lasting at least 3 days)
   - The patient has **ONE** of the following:
     - o Asthma Control Test (ACT) score of less than 20
     - o Asthma Control Questionnaire (ACQ) score of at least 1.5 or more
     - o Asthma Therapy Assessment Questionnaire (ATAQ) score of at least 1 or more
   - Nucala will be used as add-on maintenance treatment
   - The patient is not concurrently treated with Xolair, Dupixent, or another anti-IL-5 asthma biologic (e.g., Cinqair, Fasenra)
   - Nucala is prescribed by or given in consultation with a physician specializing in pulmonary medicine or allergy medicine

CONTINUED ON NEXT PAGE

MEPOLIZUMAB (NSA)

INITIAL CRITERIA (CONTINUED)

If yes, **approve for 12 months by HICL with a quantity limit of #1 vial (100mg) per 28 days.**
APPROVAL TEXT: Renewal requires the patient to have experienced a reduction in asthma exacerbations (defined as an asthma-related event requiring hospitalization, emergency room visit, or systemic corticosteroid burst lasting at least 3 days) from baseline AND an improvement in the Asthma Control Test (ACT), Asthma Control Questionnaire (ACQ), or Asthma Therapy Assessment Questionnaire (ATAQ) score from baseline. In addition, if the patient was on maintenance therapy with oral corticosteroids prior to the initiation of Nucala, then the patient must demonstrate a reduction in the total daily dose of oral corticosteroid from baseline for Nucala renewal.

If no, do not approve.
INITIAL DENIAL TEXT: The guideline named **MEPOLIZUMAB (Nucala)** requires a diagnosis of severe asthma with an eosinophilic phenotype or eosinophilic granulomatosis with polyangiitis (EGPA), also known as Churg-Strauss syndrome. In addition, the following criteria must also be met:
For the diagnosis of eosinophilic granulomatosis with polyangiitis (EGPA), approval requires:

- The patient is 18 years of age or older

For the diagnosis of severe asthma with an eosinophilic phenotype, approval requires:

- The patient is 12 years of age or older
- The patient has a documented blood eosinophil level of at least 300 cells/mcL within the past 6 months
- The patient is currently adherent to a maximally tolerated dose of an inhaled corticosteroid plus at least one other maintenance medication (e.g., a long-acting inhaled beta2-agonist, a long-acting muscarinic antagonist, a leukotriene receptor antagonist, theophylline, or oral corticosteroid)
- The patient has experienced at least 2 or more asthma exacerbations within the past 12 months (exacerbation is defined as an asthma-related event requiring hospitalization, emergency room visit, or systemic corticosteroid burst lasting at least 3 days)
- The patient has **ONE** of the following:
  - Asthma Control Test (ACT) score of less than 20
  - Asthma Control Questionnaire (ACQ) score of at least 1.5 or more
  - Asthma Therapy Assessment Questionnaire (ATAQ) score of at least 1or more
- Nucala will be used as add-on maintenance treatment
- The patient is not concurrently treated with Xolair, Dupixent, or another anti-IL-5 asthma biologic (e.g., Cinqair, Fasenra)
- Nucala is prescribed by or given in consultation with a physician specializing in pulmonary medicine or allergy medicine

CONTINUED ON NEXT PAGE

MEPOLIZUMAB (NSA)

GUIDELINES FOR USE (CONTINUED)

RENEWAL CRITERIA

1. Does the patient have a diagnosis of eosinophilic granulomatosis with polyangiitis (EGPA), also known as Churg-Strauss syndrome?

   If yes, **approve for 12 months by HICL with a quantity limit of #3 vials (300mg) per 28 days.**
   If no, continue to #2.

2. Does the patient have a diagnosis of severe asthma **AND** meet all of the following criteria?
   - The patient has experienced a reduction in asthma exacerbations (defined as an asthma-related event requiring hospitalization, emergency room visit, or systemic corticosteroid burst lasting at least 3 days) from baseline
   - The patient has experienced an improvement in the Asthma Control Test (ACT), Asthma Control Questionnaire (ACQ), **OR** Asthma Therapy Assessment Questionnaire (ATAQ) score from baseline

   If yes, continue to #3.
   If no, do not approve.
   DENIAL TEXT: See the renewal denial text at the end of the guideline.

3. Was the patient treated with a maintenance therapy regimen of oral corticosteroids prior to initiation of Nucala?

   If yes, continue to #4.
   If no, **approve for 12 months by HICL with a quantity limit of #1 vial (100mg) per 28 days.**

4. Has the patient reduced their total daily dose of oral corticosteroids from baseline?

   If yes, **approve for 12 months by HICL with a quantity limit of #1 vial (100mg) per 28 days.**
   If no, do not approve.
   DENIAL TEXT: See the renewal denial text at the end of the guideline.

CONTINUED ON NEXT PAGE

MEPOLIZUMAB (NSA)

RENEWAL CRITERIA (CONTINUED)

RENEWAL DENIAL TEXT: The guideline named **MEPOLIZUMAB (Nucala)** requires a diagnosis of severe asthma or eosinophilic granulomatosis with polyangiitis (EGPA), also known as Churg-Strauss syndrome for renewal. In addition, the following criteria must also be met:
For the diagnosis of severe asthma, approval requires:

- The patient has experienced a reduction in asthma exacerbations (defined as an asthma-related event requiring hospitalization, emergency room visit, or systemic corticosteroid burst lasting at least 3 days) from baseline
- The patient has experienced an improvement in the Asthma Control Test (ACT), Asthma Control Questionnaire (ACQ), or Asthma Therapy Assessment Questionnaire (ATAQ) score from baseline
- The patient has reduced their total daily oral corticosteroid dose from baseline, if the patient was on a maintenance therapy with oral corticosteroids prior to initiation of Nucala

RATIONALE

For further information, please refer to the Prescribing Information and/or Drug Monograph for Nucala.

REFERENCES

- Nucala [Prescribing Information]. Philadelphia, PA. GlaxoSmithKline, LLC. December 2017.

Library	Commercial	NSA
Yes	No	Yes

Part D Effective: N/A
Commercial Effective: 01/01/19
Created: 11/15
Client Approval: 11/18
P&T Approval: 10/18

MINOCYCLINE HCL MICROSPHERES (NSA)

Generic	Brand	HICL	GCN	Exception/Other
MINOCYCLINE HCL MICROSPHERES	ARESTIN	25203		

GUIDELINES FOR USE

INITIAL CRITERIA (NOTE: SEE RENEWAL CRITERIA BELOW)

1. Is this medication excluded from coverage?

   If yes, guideline does not apply.
   If no, continue to #2.

2. Does the patient have documentation of a confirmed diagnosis of periodontitis and meets **ALL** of the following criteria?
   - The requested drug will be used as an adjunct to scaling and root planing procedures **OR** used as part of a periodontal maintenance program which includes good oral hygiene and scaling and root planing
   - No history of minocycline or tetracycline sensitivity or allergy
   - No history of candidiasis or active oral candidiasis
   - Not being used for acutely abscessed periodontal pocket
   - Not being used in an immunocompromised individual, such as those immunocompromised by any of the following conditions:
     - Uncontrolled diabetes mellitus
     - Chemotherapy
     - Radiation therapy
     - HIV infection
   - Not being used in the regeneration of alveolar bone, either in preparation for or in conjunction with the placement of endosseous (dental) implants or in the treatment of failing implants
   - Age 18 years or older
   - Prescribed and administered by an oral health care professional

   If yes, **approve for 3 months by HICL for the quantity requested up to a maximum of 48 unit-dose cartridges.**
   If no, do not approve.
   DENIAL TEXT: See the denial text at the end of the guideline.

CONTINUED ON NEXT PAGE

MINOCYCLINE HCL MICROSPHERES (NSA)

INITIAL CRITERIA (CONTINUED)

INITIAL DENIAL TEXT: The guideline named **MINOCYCLINE HCL MICROSPHERES (Arestin)** requires documentation of a confirmed diagnosis of periodontitis. The following criteria must also be met.

- The requested drug will be used as an adjunct to scaling and root planing procedures **OR** used as part of a periodontal maintenance program which includes good oral hygiene and scaling and root planing
- No history of minocycline or tetracycline sensitivity or allergy
- No history of candidiasis or active oral candidiasis
- Not being used for acutely abscessed periodontal pocket
- Not being used in an immunocompromised individual, such as those immunocompromised by any of the following conditions:
  - Uncontrolled diabetes mellitus
  - Chemotherapy
  - Radiation therapy
  - HIV infection
- Not being used in the regeneration of alveolar bone, either in preparation for or in conjunction with the placement of endosseous (dental) implants or in the treatment of failing implants
- Age 18 years or older
- Prescribed and administered by an oral health care professional

RENEWAL CRITERIA

1. Is this medication excluded from coverage?

   If yes, guideline does not apply.
   If no, continue to #2.

CONTINUED ON NEXT PAGE

MINOCYCLINE HCL MICROSPHERES (NSA)

RENEWAL CRITERIA (CONTINUED)

2. Does the patient have documentation of a confirmed diagnosis of periodontitis and meets the following criteria?
   - The requested drug will be used as an adjunct to scaling and root planing procedures **OR** used as part of a periodontal maintenance program which includes good oral hygiene and scaling and root planing

     If yes, **approve for 6 months by HICL for the quantity requested up to a maximum of 48 unit-dose cartridges per 3 months.**
     If no, do not approve.
     DENIAL TEXT: The guideline named **MINOCYCLINE HCL MICROSPHERES (Arestin)** renewal requires documentation of a confirmed diagnosis of periodontitis. The following criteria must also be met.
     - The requested drug will be used as an adjunct to scaling and root planing procedures **OR** used as part of a periodontal maintenance program which includes good oral hygiene and scaling and root planing

---

RATIONALE
Ensure appropriate use of ARESTIN consistent with its FDA approved indication, dosing, contraindications, and precautions. In clinical trials, an average of 29.5 (5-114), 31.7 (4-137), and 31 (5-108) sites were treated at baseline in the scaling and root planning (SRP) alone, SRP + vehicle, and SRP + ARESTIN groups, respectively.

FDA APPROVED INDICATIONS
ARESTIN is indicated as an adjunct to scaling and root planing procedures for reduction of pocket depth in patients with adult periodontitis. ARESTIN may be used as part of a periodontal maintenance program which includes good oral hygiene and scaling and root planing.

DOSAGE
ARESTIN is provided as a dry powder, packaged in a unit dose cartridge with a deformable tip, which is inserted into a spring-loaded cartridge handle mechanism to administer the product.

The oral health care professional removes the disposable cartridge from its pouch and connects the cartridge to the handle mechanism. ARESTIN is a variable dose product, dependent on the size, shape, and number of pockets being treated. In US clinical trials, up to 122 unit dose cartridges were used in a single visit and up to 3 treatments, at 3-month intervals, were administered in pockets with pocket depth of 5 mm or greater.

CONTINUED ON NEXT PAGE

MINOCYCLINE HCL MICROSPHERES (NSA)

REFERENCES

- Arestin [Prescribing Information]. Bridgewater, NJ: OraPharma. August 2015.

Library	Commercial	NSA
Yes	Yes	Yes

Part D Effective: N/A
Commercial Effective: 08/01/18
Created: 08/16
Client Approval: 07/18
P&T Approval: 08/16

MITOXANTRONE

Generic	Brand	HICL	GCN	Exception/Other
MITOXANTRONE HCL	NOVANTRONE	03932		

This drug requires a written request for prior authorization.

GUIDELINES FOR USE

1. Is the prescription written by or supervised by an oncologist?

   If yes, continue to #4.
   If no, continue to #2.

2. Is the patient being treated for pain related to advanced hormone refractory prostate cancer or acute nonlymphocytic leukemia?

   If yes, continue to #4.
   If no, continue to #3.

3. Is the patient being treated for secondary progressive, progressive relapsing or worsening relapsing-remitting multiple sclerosis?

   If yes, continue to #5.
   If no, do not approve.
   DENIAL TEXT: Approval requires supervision by an oncologist or a diagnosis of pain related to advanced refractory prostate cancer or acute nonlymphocytic leukemia or secondary progressive, progressive relapsing or worsening relapsing-remitting multiple sclerosis.

4. **Approve open ended.**
   APPROVAL TEXT: Please note that this drug has an important FDA safety warning. For more information please ask your doctor or pharmacist.

5. **Approve for 12 months. (FDA dosing regimen is 12 mg/m^2 IV every 3 months)**
   APPROVAL TEXT: Please note that this drug has an important FDA safety warning. For more information please ask your doctor or pharmacist.

CONTINUED ON NEXT PAGE

MITOXANTRONE

RATIONALE
To assure safe and appropriate use of mitoxantrone.

FDA APPROVED INDICATIONS
Mitoxantrone is indicated for reducing neurologic disability and/or the frequency of clinical relapses in patients with secondary (chronic) progressive, progressive relapsing, or worsening relapsing-remitting multiple sclerosis; in combination with corticosteroids to treat pain related to advanced hormone-refractory prostate cancer; initial therapy or in combination with other approved drugs for acute nonlymphocytic leukemia in adults.

REFERENCES

- EMD Serono, Inc. Novantrone product labeling. Rockland, MA. September 2009.

Library	Commercial	NSA
Yes	No	Yes

Part D Effective: N/A
Commercial Effective: 10/01/13
Created: 08/08
Client Approval: 08/13
P&T Approval: 08/10

STANDARD NON-SELF-ADMINISTERED DRUG FORMULARY
PRIOR AUTHORIZATION GUIDELINES

MOGAMULIZUMAB-KPKC (NSA)

Generic	Brand	HICL	GCN	Exception/Other
MOGAMULIZUMAB-KPKC	POTELIGEO	45153		

GUIDELINES FOR USE

1. Does the patient have a diagnosis of Mycosis Fungoides (MF) or Sézary syndrome and meet **ALL** of the following criteria?
   - The patient has relapsed or refractory disease
   - The patient has tried and failed at least one prior systemic therapy
   - The patient is 18 years or older

   If yes, **approve for 12 months by HICL.**
   If no, do not approve.
   DENIAL TEXT: The guideline named **MOGAMULIZUMAB-KPKC (Poteligeo)** requires a diagnosis of Mycosis Fungoides (MF) or Sézary syndrome. In addition, the following criteria must be met:
   - The patient has relapsed or refractory disease
   - The patient has tried and failed at least one prior systemic therapy
   - The patient is 18 years or older

RATIONALE
For further information, please refer to the Prescribing Information and/or Drug Monograph for Poteligeo.

REFERENCES

- Poteligeo [Prescribing Information]. Bedminster, NJ: Kyowa Kirin; August 2018.

Library	Commercial	NSA
Yes	No	Yes

Part D Effective: N/A
Commercial Effective: 01/01/19
Created: 11/18
Client Approval: 11/18
P&T Approval: 10/18

MOMETASONE SINUS IMPLANT (NSA)

Generic	Brand	HICL	GCN	Exception/Other
MOMETASONE FUROATE	SINUVA		44214	

GUIDELINES FOR USE

1. Does the patient have non-self-administered (NSA) drug benefit coverage?

   If yes, continue to #2.
   If no, guideline does not apply.

2. Does the patient have a diagnosis of nasal polyps and meet **ALL** of the following criteria?
   - The patient is 18 years of age or older
   - The patient has had previous ethmoid sinus surgery (ESS)
   - The medication is prescribed by or given in consultation with an otolaryngologist
   - The patient is a candidate for repeat ethmoid sinus surgery due to refractory moderate to severe symptoms of nasal obstruction, nasal congestion or nasal polyps in both ethmoid sinuses
   - The patient had a previous trial of at least **TWO** intranasal corticosteroids (e.g., fluticasone, beclomethasone, flunisolide, ciclesonide, mometasone)

   If yes, **approve #2 implants (1 per sinus) by GPID per lifetime.**
   If no, do not approve.
   DENIAL TEXT: The guideline named **MOMETASONE IMPLANT (Sinuva)** requires a diagnosis of nasal polyps. In addition, the following criteria must also be met:
   - The patient is 18 years of age or older
   - The patient has had previous ethmoid sinus surgery (ESS)
   - The medication is prescribed by or given in consultation with an otolaryngologist
   - The patient is a candidate for repeat ethmoid sinus surgery due to refractory moderate to severe symptoms of nasal obstruction, nasal congestion or nasal polyps in both ethmoid sinuses
   - The patient had a previous trial of at least **TWO** intranasal corticosteroids (e.g., fluticasone, beclomethasone, flunisolide, ciclesonide, mometasone)

CONTINUED ON NEXT PAGE

MOMETASONE SINUS IMPLANT (NSA)

RATIONALE
To promote appropriate utilization of SINUVA based on FDA approved indication and dosing.

FDA APPROVED INDICATION
Sinuva Sinus Implant is a corticosteroid-eluting (mometasone furoate) implant indicated for the treatment of nasal polyps in patients ≥ 18 years of age who have had ethmoid sinus surgery

DOSAGE & ADMINISTRATION
One Sinuva Sinus Implant containing 1350 mcg of mometasone furoate. There are no studies evaluating repeat implantation of the Sinuva Sinus Implant.

The Sinuva Sinus Implant is loaded into a delivery system and placed in the ethmoid sinus under endoscopic visualization. The Implant may be left in the sinus to gradually release the corticosteroid over 90 days. The Implant can be removed at Day 90 or earlier at the physician's discretion using standard surgical instruments. Sinuva must be inserted by physicians trained in otolaryngology.

REFERENCES

- Sinuva [Prescribing Information]. Menlo Park, CA: Intersect ENT. December 2017.

Library	Commercial	NSA
Yes	Yes	Yes

Part D Effective: N/A
Commercial Effective: 08/01/18
Created: 05/18
Client Approval: 07/18
P&T Approval: 04/18

NATALIZUMAB (NSA)

Generic	Brand	HICL	GCN	Exception/Other
NATALIZUMAB	TYSABRI	26750		

GUIDELINES FOR USE

INITIAL CRITERIA (NOTE: FOR RENEWAL CRITERIA SEE BELOW)

1. Does the patient have a diagnosis of moderate to severe Crohn's disease (CD) and meets **ALL** of the following criteria?
   - Therapy initiated by or given in consultation with a gastroenterologist
   - Previous trial of at least one of the following conventional agents such as corticosteroids (i.e., budesonide, methylprednisolone), azathioprine, mercaptopurine, methotrexate, or mesalamine
   - The patient is18 years of age or older
   - Previous trial of two preferred formulary TNF (tumor necrosis factor) inhibitors

   If yes, **approve for 6 months by HICL with a quantity limit of 15mL (#1 of 300mg/15mL vial) every 28 days.**
   If no, continue to #2.

2. Does the patient have a relapsing form of multiple sclerosis (MS) and meets **ALL** of the following criteria?
   - The patient is 18 years of age or older
   - Previous trial of at least one formulary alternative for multiple sclerosis

   If yes, **approve for 12 months by HICL with a quantity limit of 15mL (#1 of 300mg/15mL vial) every 28 days.**
   If no, do not approve.
   DENIAL TEXT: The guideline named **NATALIZUMAB (Tysabri)** requires a diagnosis of moderate to severe Crohn's disease or relapsing form of multiple sclerosis (MS). The following criteria must also be met:
   For patients with moderate to severe Crohn's disease, approval requires:
   - Therapy is initiated by or given in consultation with a gastroenterologist
   - Previous trial of at least one of the following conventional agents such as corticosteroids (i.e., budesonide, methylprednisolone), azathioprine, mercaptopurine, methotrexate, or mesalamine
   - The patient is 18 years of age or older
   - Previous trial of two preferred formulary TNF (tumor necrosis factor) inhibitors

   For patients with a relapsing form of multiple sclerosis (MS), approval requires:
   - The patient is 18 years of age or older
   - Previous trial of at least one formulary alternative for multiple sclerosis

CONTINUED ON NEXT PAGE

NATALIZUMAB (NSA)

GUIDELINES FOR USE (CONTINUED)

RENEWAL CRITERIA

1. Is this a renewal for a patient with moderate to severe Crohn's disease who has received at least 12 months of therapy and meets the following criteria?
   - The patient has NOT received more than 3 months of corticosteroids for control of Crohn's disease

   If yes, **approve for 12 months by HICL with a quantity limit of 15mL (#1 of 300mg/15mL vial) every 28 days.**
   If no, continue to #2.

2. Is this a renewal for a patient with moderate to severe Crohn's disease that has received only 6 months of therapy and meets the following criteria?
   - The patient is NOT currently on corticosteroids

   If yes, **approve for 12 months by HICL with a quantity limit of 15mL (#1 of 300mg/15mL vial) every 28 days.**
   If no, continue to #3.

3. Does the patient have a relapsing form of multiple sclerosis (MS)?

   If yes, **approve for 12 months by HICL with a quantity limit of 15mL (#1 of 300mg/15mL vial) every 28 days.**
   If no, do not approve.
   DENIAL TEXT: The guideline named **NATALIZUMAB (Tysabri)** renewal requires a diagnosis of moderate to severe Crohn's disease or relapsing form of multiple sclerosis. The following criteria must also be met:
   Renewal for the diagnosis of moderate to severe Crohn's disease requires:
   - Documentation that the patient has not required more than 3 months of corticosteroid use within the past 12 months to control their Crohn's disease while on Tysabri (natalizumab)
     OR
   - Documentation that the patient has taper off corticosteroids during the first 24 weeks of Tysabri (natalizumab) therapy.

CONTINUED ON NEXT PAGE

NATALIZUMAB (NSA)

RATIONALE
To promote formulary alternatives and ensure appropriate utilization of Tysabri per FDA approved dosing and indication.

NOTE: Only prescribers registered in the TOUCH™ Prescribing Program may prescribe TYSABRI. TYSABRI increases the risk of progressive multifocal leukoencephalopathy (PML), an opportunistic viral infection of the brain that usually leads to death or severe disability. Risk factors for the development of PML include duration of therapy, prior use of immunosuppressants, and presence of anti-JCV antibodies. These factors should be considered in the context of expected benefit when initiating and continuing treatment with TYSABRI. Monitor patients, and withhold TYSABRI immediately at the first sign or symptom suggestive of PML.

FDA APPROVED INDICATIONS
Multiple Sclerosis
TYSABRI is indicated as monotherapy for the treatment of patients with relapsing forms of multiple sclerosis. Tysabri increases the risk of PML. When initiating and continuing treatment with Tysabri, physicians should consider whether the expected benefit of Tysabri is sufficient to offset this risk. See important information regarding the risk of PML with TYSABRI.

Crohn's Disease
TYSABRI is indicated for inducing and maintaining clinical response and remission in adult patients with moderately to severely active Crohn's disease (CD) with evidence of inflammation who have had an inadequate response to, or are unable to tolerate, conventional CD therapies and inhibitors of TNF-α. TYSABRI should not be used in combination with immunosuppressants (e.g., 6-mercaptopurine, azathioprine, cyclosporine, or methotrexate) or inhibitors of TNF-α.

Important Limitations:
In CD, TYSABRI should not be used in combination with immunosuppressants or inhibitors of TNF-α.

DOSING
Multiple Sclerosis
The recommended dose of TYSABRI for multiple sclerosis is 300 mg intravenous infusion over one hour every four weeks.

Crohn's Disease
The recommended dose of TYSABRI for Crohn's disease is 300 mg intravenous infusion over one hour every four weeks. TYSABRI should not be used with concomitant immunosuppressants (e.g., 6-mercaptopurine, azathioprine, cyclosporine, or methotrexate) or concomitant inhibitors of TNF-α. Aminosalicylates may be continued during treatment with TYSABRI.

CONTINUED ON NEXT PAGE

NATALIZUMAB (NSA)

FDA APPROVED INDICATIONS (CONTINUED)

If the patient with Crohn's disease has not experienced therapeutic benefit by 12 weeks of induction therapy, discontinue TYSABRI. For patients with Crohn's disease that start TYSABRI while on chronic oral corticosteroids, commence steroid tapering as soon as a therapeutic benefit of TYSABRI has occurred; if the patient with Crohn's disease cannot be tapered off oral corticosteroids within six months of starting TYSABRI, discontinue TYSABRI. Other than the initial six-month taper, prescribers should consider discontinuing TYSABRI for patients who require additional steroid use that exceeds three months in a calendar year to control their Crohn's disease.

REFERENCES

- Biogen Idec Inc. Tysabri Product Information, Cambridge, MA. December 2013.
- Micromedex® Healthcare Series [database online]. Greenwood Village, Colo: Thomson Healthcare. Available at: https://www.thomsonhc.com/hcs/librarian/PFDefaultActionId/pf.LoginAction. [Accessed: July 6, 2011].
- Polman C, et al. A randomized, placebo-controlled trial of natalizumab for relapsing multiple sclerosis. NEJM 2006; 354:899-910.
- Targan SR et al. Natalizumab for the treatment of active Crohn's disease: Results of the ENCORE Trial. Gastro. 2007; 132:1672-1683.
- Yoursry T et al., Evaluation of patients treated with natalizumab for progressive multifocal leukoencephalopathy. NEJM 2006; 354:924-33.

Library	Commercial	NSA
Yes	No	Yes

Part D Effective: N/A
Commercial Effective: 10/01/16
Created: 08/06
Client Approval: 09/16
P&T Approval: 02/15

NECITUMUMAB

Generic	Brand	HICL	GCN	Exception/Other
NECITUMUMAB	PORTRAZZA	42835		

GUIDELINES FOR USE

1. Will necitumumab be used as a first-line treatment for metastatic squamous non-small cell lung cancer (NSCLC) in combination with gemcitabine and cisplatin?

   If yes, **approve for 12 months by HICL with a quantity limit of #2 vials per 21 days.**
   If no, do not approve.
   DENIAL TEXT: Our guideline for **NECITUMUMAB (Portrazza)** requires that it be used as first-line treatment for metastatic squamous non-small cell lung cancer (NSCLC) in combination with gemcitabine and cisplatin.

RATIONALE

Promote appropriate utilization of **NECITUMUMAB** based on its FDA approved indication.

Lung cancer is the second most common cancer in the United States with about 220,000 new diagnoses each year and the leading cause of cancer-related mortality with an estimated 158,000 deaths per year. About 85% of lung cancers are classified as NSCLC, of which squamous cell carcinomas account for about 25-30%, making them the most common histological subtype after adenocarcinoma. Squamous cell carcinomas are often associated with a history of smoking and are more commonly seen in males.

Treatment selection depends upon tumor staging, histology, molecular profiling to identify driver mutations (e.g., EGFR, anaplastic lymphoma kinase [ALK]), and an evaluation of the patient's overall medical condition. Whereas patients without metastatic disease are treated with curative intent using surgery, chemotherapy, and/or radiation therapy, the primary approach for patients with metastatic disease is palliative systemic chemotherapy. The National Comprehensive Cancer Network (NCCN) Panel recommends targeted tyrosine kinase inhibitor (TKI) therapies such as EGFR inhibitors (Tarceva [erlotinib], Gilotrif [afatinib], Iressa [gefitinib]) or ALK inhibitors (Xalkori [crizotinib], Zykadia [ceritinib], Alecensa [alectinib]) as first-line for patients whose tumors contain a driver mutation; however, these mutations are typically observed with adenocarcinomas rather than with squamous cell carcinomas.

For patients whose mutation status is negative or unknown, the NCCN Panel recommends platinum-based two-drug combination regimens as first-line treatment. Platinum-based chemotherapy prolongs survival, improves symptom control, and yields superior quality of life compared to best supportive care. Based upon superior efficacy compared to cisplatin/pemetrexed, the NCCN Panel recommends cisplatin/gemcitabine as first-line therapy in patients with squamous NSCLC. Two-drug regimens are preferred; a third cytotoxic drug may increase response rate but not survival. As many of the platinum two-drug combinations yield similar objective response rates and survival and differ slightly for toxicity, convenience, and cost, clinicians can individualize therapy for their patients.

CONTINUED ON NEXT PAGE

RATIONALE (CONTINUED)
In December 2015, NCCN updated its guideline to include cisplatin/gemcitabine/necitumumab as a first-line systemic therapy option for advanced or metastatic squamous NSCLC; however, this was designated as a category 3 recommendation, which indicates major NCCN disagreement on the appropriateness of the intervention. NCCN stated that the category 3 recommendation for this regimen is due to its toxicity, cost, and limited improvement in efficacy that is seen when necitumumab is added to cisplatin/gemcitabine. NCCN recommendations (category 1) for first-line treatment options are listed in Table 1.

Table 1. First-line systemic therapy options for advanced or metastatic squamous cell NSCLC

Carboplatin-based regimens	Cisplatin-based regimens	Non-platinum-based regimens
• Carboplatin/albumin-bound paclitaxel • Carboplatin/docetaxel • Carboplatin/etoposide • Carboplatin/gemcitabine • Carboplatin/paclitaxel • Carboplatin/vinorelbine	• Cisplatin/docetaxel • Cisplatin/etoposide • Cisplatin/gemcitabine • Cisplatin/paclitaxel • Cisplatin/vinorelbine	• Gemcitabine/docetaxel • Gemcitabine/vinorelbine

Other monoclonal antibodies have been approved for the treatment of NSCLC, but they occupy different places in therapy from Portrazza. For instance, Avastin (bevacizumab) is indicated for the first-line treatment of advanced NSCLC but only in patients with non-squamous histology. Opdivo (nivolumab) and Cyramza (ramucirumab) are indicated only as subsequent-line therapy for patients who have progressed on or after platinum-based chemotherapy. Erbitux (cetuximab) is a monoclonal antibody that also targets EGFR but is not currently indicated for the treatment of NSCLC.

The SQUIRE trial was a phase 3, multicenter, open-label, randomized trial that evaluated the efficacy of Portrazza in 1,093 patients with squamous NSCLC. Previously untreated patients with stage IV squamous NSCLC and an Eastern Cooperative Oncology Group (ECOG) performance status of 0-2 were randomized 1:1 to receive Portrazza plus gemcitabine/cisplatin or to gemcitabine/cisplatin alone. Baseline characteristics included median age of 62 years, 83% male, 84% Caucasian, 91% smokers, 91% with baseline ECOG performance status of 0-1, and 91% with metastatic disease in at least two sites (most commonly lung and lymph nodes). Gemcitabine/cisplatin was given for up to six cycles; in patients demonstrating at least stable disease (51%), Portrazza was continued alone after the completion of chemotherapy as maintenance treatment until disease progression or toxicity. Blinding was not conducted in this trial because the expected occurrence of acne-like rash would have unmasked most patients and investigators to treatment. The primary endpoint was overall survival.

CONTINUED ON NEXT PAGE

RATIONALE (CONTINUED)
Efficacy results are shown in Table 2.

Table 2. Efficacy results of the SQUIRE trial

Outcome	Portrazza + gemcitabine/cisplatin (n = 545)	Gemcitabine/cisplatin (n = 548)	Hazard ratio (95% CI) p-value
Overall survival (OS)			
Median OS – months	11.5	9.9	0.84 (0.74, 0.96) p = 0.01
Deaths – no. (%)	418 (77)	442 (81)	--
Progression-free survival (PFS)			
Median PFS – months	5.7	5.5	0.85 (0.74, 0.98) p = 0.02
Events – no. (%)	431 (79)	417 (76)	--
Response			
Objective response rate (ORR) – no. (%)	170 (31)	158 (29)	p = 0.40

Portrazza should not be used for the treatment of non-squamous NSCLC due to a risk for increased toxicity and mortality observed in the INSPIRE trial. The INSPIRE trial was a multicenter, open-label trial that evaluated Portrazza in 633 patients with metastatic non-squamous NSCLC. Patients were randomized 1:1 to receive Portrazza plus pemetrexed/cisplatin (n = 315) or pemetrexed/cisplatin alone (n = 318). There was no significant difference in OS (HR 1.01; 95% CI 0.84, 1.21), PFS (HR 0.96; 95% CI 0.80, 1.16), or ORR (31% vs. 32%, respectively). The study was terminated early due to increased all-cause mortality and thromboembolic-related mortality in the Portrazza treatment arm.

FDA APPROVED INDICATION
Portrazza is indicated, in combination with gemcitabine and cisplatin, for first-line treatment of patients with metastatic squamous non-small cell lung cancer.

Limitation of Use: Portrazza is not indicated for treatment of non-squamous non-small cell lung cancer.

DOSAGE
The recommended dose of Portrazza is 800 mg administered as an intravenous (IV) infusion over 60 minutes on Days 1 and 8 of each 3-week cycle prior to gemcitabine and cisplatin infusion. Gemcitabine/cisplatin chemotherapy is given for a maximum of six cycles, and Portrazza is continued thereafter as single-agent maintenance therapy until disease progression or unacceptable toxicity.

CONTINUED ON NEXT PAGE

NECITUMUMAB

DOSAGE (CONTINUED)
Infusion rate should be reduced and pre-medication should be administered with all subsequent infusions for patients who have experienced a Grade 1 or 2 infusion-related reaction with previous Portrazza infusion: diphenhydramine (or equivalent) after the first occurrence; diphenhydramine (or equivalent), acetaminophen (or equivalent), and dexamethasone (or equivalent) after the second occurrence. Portrazza should be permanently discontinued for Grade 3 or 4 infusion-related reactions and certain dermatologic toxicities (e.g., rash that does not resolve, worsening or intolerable reactions at a reduced dose, Grade 3 skin induration/fibrosis, Grade 4).

REFERENCES

- FDA Press Release [Online Press Release]: FDA approves Portrazza to treat advanced squamous non-small cell lung cancer. Available at: http://www.fda.gov/newsevents/newsroom/pressannouncements/ucm474131.htm. Updated November 24, 2015.
- National Comprehensive Cancer Network. NCCN Guidelines: Non-Small Cell Lung Cancer. Available at: http://www.nccn.org/professionals/physician_gls/pdf/nsclc.pdf. Updated December 22, 2015.
- Paz-Ares K, Mezger J, Ciuleanu TE, et al. Necitumumab plus pemetrexed and cisplatin as first-line therapy in patients with stage IV non-squamous non-small-cell lung cancer (INSPIRE): an open-label, randomised, controlled phase 3 study. Lancet Oncol. 2015;16:328-37.
- Portrazza [Prescribing Information]. Indianapolis, IN: Eli Lilly and Company. November 2015.
- Thatcher N, Hirsch FR, Luft AV, et al. Necitumumab plus gemcitabine and cisplatin versus gemcitabine and cisplatin alone as first-line therapy in patients with stage IV squamous non-small-cell lung cancer (SQUIRE): an open-label, randomised, controlled phase 3 trial. Lancet Oncol. 2015;16:763-74.

Library	Commercial	NSA
Yes	No	Yes

Part D Effective: N/A
Commercial Effective: 04/01/16
Created: 12/15
Client Approval: 02/16
P&T Approval: 2/16

NIVOLUMAB (NSA)

Generic	Brand	HICL	GCN	Exception/Other
NIVOLUMAB	OPDIVO	41654		

GUIDELINES FOR USE

1. Does the patient have a diagnosis of unresectable or metastatic melanoma and meet **ALL** of the following criteria?
   - The patient will be using Opdivo as a single agent **OR** in combination with ipilimumab (Yervoy)
   - No concurrent therapy with dabrafenib (Tafinlar), trametinib (Mekinist), vemurafenib (Zelboraf), or cobimetinib (Cotellic)

   If yes, **approve for 12 months by HICL.**
   If no, continue to #2.

2. Does the patient have a diagnosis of melanoma with lymph node involvement or metastatic disease and meet **ALL** of the following criteria?
   - The patient has undergone complete resection
   - The requested medication will be used as an adjuvant treatment

   If yes, **approve for 12 months by HICL.**
   If no, continue to #3.

3. Does the patient have a diagnosis of metastatic squamous non-small cell lung cancer (NSCLC) and meet **ALL** of the following criteria?
   - The patient has disease progression while on or after platinum-based chemotherapy (e.g., cisplatin, carboplatin, oxaliplatin)
   - For patients who have an ALK mutation, there must be disease progression despite also trying an ALK-directed therapy (e.g., crizotinib, ceritinib)
   - For patients who have an EGFR mutation, there must also be disease progression despite also trying an EGFR-directed therapy (e.g., erlotinib, gefitinib, afatinib)

   If yes, **approve for 12 months by HICL.**
   If no, continue to #4.

CONTINUED ON NEXT PAGE

NIVOLUMAB (NSA)

GUIDELINES FOR USE (CONTINUED)

4. Does the patient have a diagnosis of metastatic non-squamous non-small cell lung cancer (NSCLC) and meet **ALL** of the following criteria?
   - Non-small cell lung cancer (NSCLC) tumors express PD-L1 as determined by an FDA-approved test
   - The patient has disease progression while on or after platinum-based chemotherapy (e.g., cisplatin, carboplatin, oxaliplatin)
   - For patients who have an ALK mutation, there must be disease progression despite also trying an ALK-directed therapy (e.g., crizotinib, ceritinib)
   - For patients who have an EGFR mutation, there must also be disease progression despite also trying an EGFR-directed therapy (e.g., erlotinib, gefitinib, afatinib)

   If yes, **approve for 12 months by HICL.**
   If no, continue to #5.

5. Does the patient have a diagnosis of metastatic small cell lung cancer (SCLC) and meet the following criterion?
   - The patient has disease progression after platinum-based chemotherapy (e.g., cisplatin, carboplatin) and at least one other line of therapy

   If yes, **approve for 12 months by HICL.**
   If no, continue to #6.

6. Does the patient have a diagnosis of advanced renal cell carcinoma (RCC) and meet **ONE** of the following criteria?
   - Opdivo will be used as a single agent and meet the following:
     - The patient has previously received **ONE** prior anti-angiogenic therapy (e.g., sunitinib (Sutent), pazopanib (Votrient), cabozantinib (Cabometyx), axitinib (Inlyta), sorafenib (Nexavar))
   - Opdivo will be used in combination with ipilimumab (Yervoy) and meet ALL of the following:
     - The patient has intermediate or poor risk disease
     - The patient has not received prior treatment for advanced renal cell carcinoma

   If yes, **approve for 12 months by HICL.**
   If no, continue to #7.

CONTINUED ON NEXT PAGE

NIVOLUMAB (NSA)

GUIDELINES FOR USE (CONTINUED)

7. Does the patient have a diagnosis of classical Hodgkin lymphoma (cHL) and meet **ALL** of the following criteria?
   - The patient is 18 years of age or older
   - The patient's disease has relapsed or progressed after **ONE** of the following:
     - Autologous hematopoietic stem cell transplantation (HSCT) and Adcetris (brentuximab vedotin)
     - 3 or more lines of systemic therapy that includes autologous HSCT

   If yes, **approve for 12 months by HICL**.
   If no, continue to #8.

8. Does the patient have a diagnosis of recurrent or metastatic head and neck squamous cell carcinoma (HNSCC) **AND** meet the following criterion?
   - The patient has disease progression on or after treatment with a platinum-containing chemotherapy (e.g., cisplatin, carboplatin, oxaliplatin)

   If yes, **approve for 12 months by HICL.**
   If no, continue to #9.

9. Does the patient have a diagnosis of locally advanced or metastatic urothelial carcinoma and meet at least **ONE** of the following criteria?
   - The patient has disease progression during or following platinum-containing chemotherapy (e.g., cisplatin, carboplatin, oxaliplatin).
   - The patient has disease progression within 12 months of neoadjuvant or adjuvant treatment with platinum-containing chemotherapy (e.g., cisplatin, carboplatin, oxaliplatin).

   If yes, **approve for 12 months by HICL.**
   If no, continue to #10.

10. Does the patient have a diagnosis of microsatellite instability-high (MSI-H) or mismatch repair deficient (dMMR) metastatic colorectal cancer and meet **ALL** the following criteria?
    - The patient is 12 years of age or older
    - The patient will be using Opdivo as a single agent OR in combination with ipilimumab (Yervoy)
    - The patient has disease progression following treatment with a fluoropyrimidine, oxaliplatin, and irinotecan

    If yes, **approve for 12 months by HICL.**
    If no, continue to #11.

CONTINUED ON NEXT PAGE

NIVOLUMAB (NSA)

GUIDELINES FOR USE (CONTINUED)

11. Does the patient have a diagnosis of hepatocellular carcinoma **AND** meet the following criterion?
    - The patient has been previously treated with sorafenib (Nexavar)

    If yes, **approve for 12 months by HICL.**
    If no, do not approve.
    DENIAL TEXT: The guideline named **NIVOLUMAB (Opdivo)** requires a diagnosis of unresectable or metastatic melanoma, melanoma with lymph node involvement or metastatic disease, metastatic non-small cell lung cancer (NSCLC), metastatic small cell lung cancer (SCLC), advanced renal cell carcinoma (RCC), classical Hodgkin lymphoma (cHL), recurrent or metastatic head and neck squamous cell carcinoma (HNSCC), locally advanced, or metastatic urothelial carcinoma, microsatellite instability-high (MSI-H) or mismatch repair deficient (dMMR) metastatic colorectal cancer, or hepatocellular carcinoma. In addition, the following criteria must be met:
    For patients with unresectable or metastatic melanoma, approval requires:
    - The patient will be using Opdivo as a single agent OR in combination with ipilimumab (Yervoy)
    - No concurrent therapy with dabrafenib (Tafinlar), trametinib (Mekinist), vemurafenib (Zelboraf), or cobimetinib (Cotellic)

    For patients with melanoma with lymph node involvement or metastatic disease, approval requires:
    - The patient has undergone complete resection
    - The requested medication will be used as an adjuvant treatment

    For patients with metastatic squamous non-small cell lung cancer, approval requires:
    - The patient has disease progression while on or after platinum-based chemotherapy (e.g., cisplatin, carboplatin, oxaliplatin)
    - Additional requirements apply if patient has ALK or EGFR mutations. For patients who have ALK or EGFR mutations, there must be disease progression following ALK-directed therapy (e.g., crizotinib, ceritinib) or EGFR-directed therapy (e.g., erlotinib, gefitinib, afatinib)

    For patients with metastatic non-squamous non-small cell lung cancer, approval requires:
    - The patient has disease progression while on or after platinum-based chemotherapy (e.g., cisplatin, carboplatin, oxaliplatin)
    - Non-small cell lung cancer (NSCLC) tumors express PD-L1 as determined by an FDA-approved test
    - Additional requirements apply if patient has ALK or EGFR mutations. For patients who have ALK or EGFR mutations, there must be disease progression following ALK-directed therapy (e.g., crizotinib, ceritinib) or EGFR-directed therapy (e.g., erlotinib, gefitinib, afatinib)

    (Denial text continued on next page)

CONTINUED ON NEXT PAGE

NIVOLUMAB (NSA)

GUIDELINES FOR USE (CONTINUED)

For patients with metastatic small cell lung cancer (SCLC), approval requires:
- The patient has disease progression after platinum-based chemotherapy (e.g., cisplatin, carboplatin) and at least one other line of therapy

For patients with advanced renal cell carcinoma (RCC), approval requires ONE of the following:
- Opdivo will be used as a single agent and meet the following:
  - The patient has previously received one prior anti-angiogenic therapy (e.g., sunitinib (Sutent), pazopanib (Votrient), cabozantinib (Cabometyx), axitinib (Inlyta), sorafenib (Nexavar))
- Opdivo will be used in combination with ipilimumab (Yervoy) and meet all of the following:
  - The patient has intermediate or poor risk disease
  - The patient has not received prior treatment for advanced renal cell carcinoma

For patients with classical Hodgkin lymphoma (cHL), approval requires:
- The patient is 18 years of age or older
- The patient's disease has relapsed or progressed after ONE of the following:
  - Autologous hematopoietic stem cell transplantation (HSCT) and Adcetris (brentuximab vedotin)
  - 3 or more lines of systemic therapy that includes autologous HSCT

For patients with recurrent or metastatic head and neck squamous cell carcinoma (HNSCC), approval requires:
- The patient has disease progression on or after treatment with a platinum-containing chemotherapy (e.g., cisplatin, carboplatin, oxaliplatin)

For patients with locally advanced or metastatic urothelial carcinoma, approval requires ONE of the following:
- The patient has disease progression during or following platinum-containing chemotherapy (e.g., cisplatin, carboplatin, oxaliplatin)
- The patient has disease progression within 12 months of neoadjuvant or adjuvant treatment with platinum-containing chemotherapy (e.g., cisplatin, carboplatin, oxaliplatin)

For patients with microsatellite instability-high (MSI-H) or mismatch repair deficient (dMMR) metastatic colorectal cancer, approval requires:
- The patient is 12 years of age or older
- The patient will be using Opdivo as a single agent OR in combination with ipilimumab (Yervoy)
- The patient has disease progression following treatment with a fluoropyrimidine, oxaliplatin, and irinotecan

For patients with hepatocellular carcinoma, approval requires:
- The patient has been previously treated with sorafenib (Nexavar)

CONTINUED ON NEXT PAGE

NIVOLUMAB (NSA)

RATIONALE
Promote appropriate utilization of Opdivo based on FDA approved indications.

FDA APPROVED INDICATIONS
Opdivo is a programmed death receptor-1 (PD-1) blocking antibody indicated for the treatment of:

- BRAF V600 wild-type unresectable or metastatic melanoma, as a single agent.
- BRAF V600 mutation-positive unresectable or metastatic melanoma, as a single agent [a].
- Unresectable or metastatic melanoma, in combination with ipilimumab [a].
- Melanoma with lymph node involvement or metastatic disease who have undergone complete resection, in the adjuvant setting.
- Metastatic non-small cell lung cancer and progression on or after platinum based chemotherapy. Patients with EGFR or ALK genomic tumor aberrations should have disease progression on FDA-approved therapy for these aberrations prior to receiving OPDIVO.
- Metastatic small cell lung cancer with progression after platinum-based chemotherapy and at least one other line of therapy. [b]
- Advanced renal cell carcinoma as a single agent in patients who have received prior anti-angiogenic therapy.
- Advanced renal cell carcinoma in combination with ipilimumab in patients with intermediate or poor risk, previously untreated advanced renal cell carcinoma (RCC).
- Adult patients with classical Hodgkin lymphoma who have relapsed or progressed after [b]
  - autologous hematopoietic stem cell transplantation (HSCT) and post-transplantation brentuximab vedotin, or
  - 3 or more lines of systemic therapy that includes autologous HSCT
- Recurrent or metastatic squamous cell carcinoma of the head and neck with disease progression on or after a platinum-based therapy
- Locally advanced or metastatic urothelial carcinoma who[b]:
  - Have disease progression during or following platinum-containing chemotherapy.
  - Have disease progression within 12 months of neoadjuvant or adjuvant treatment with platinum-containing chemotherapy.
- Adult and pediatric (12 years and older) patients with microsatellite instability-high (MSI-H) or mismatch repair deficient (dMMR) metastatic colorectal cancer[b]
  - To be used as single agent or in combination with ipilimumab[b], and
  - Patient has progressed following treatment with a fluoropyrimidine, oxaliplatin, and irinotecan[b].
- Hepatocellular carcinoma previously treated with sorafenib[b].

[a] This indication is approved under accelerated approval based on progression-free survival. Continued approval for this indication may be contingent upon verification and description of clinical benefit in the confirmatory trials.

[b] This indication is approved under accelerated approval based on overall response rate and duration of response. Continued approval for this indication may be contingent upon verification and description of clinical benefit in confirmatory trials.

CONTINUED ON NEXT PAGE

NIVOLUMAB (NSA)

FDA APPROVED INDICATIONS (CONTINUED)

DOSAGE AND ADMINISTRATION
Opdivo is administered as an intravenous infusion over 30 minutes until disease recurrence, progression or unacceptable toxicity.

Unresectable or metastatic melanoma:
- The recommended dose as a single agent is either 240mg every 2 weeks or 480mg every 4 weeks
- The recommended dose in combination with ipilimumab is Opdivo 1mg/kg, followed by ipilimumab 3mg/kg intravenous infusion over 90 minutes on the same day, every 3 weeks for a maximum of 4 doses or until unacceptable toxicity, whichever occurs first. After completing 4 doses of the combination, administer Opdivo as a single agent either 240mg every 2 weeks or 480mg every 4 weeks.

Adjuvant treatment of melanoma with lymph node involvement or metastatic disease:
The recommended dose is 240mg every 2 weeks or 480 mg every 4 weeks for up to 1 year.

Microsatellite instability-high (MSI-H) or mismatch repair deficient (dMMR) metastatic colorectal cancer (CRC):
- The recommended dosing of Opdivo as a single agent is 240mg every 2 weeks
- The recommended dose in combination with ipilimumab is Opdivo 3 mg/kg, followed by ipilimumab 1mg/kg on the same day every 3 weeks for 4 doses. After completing 4 doses of the combination, administer Opdivo 240 mg as a single agent every 2 weeks

Metastatic NSCLC, locally advanced or metastatic urothelial carcinoma, classical Hodgkin lymphoma (cHL), squamous cell carcinoma of the head and neck (SCCHN), and hepatocellular carcinoma (HCC):
The recommended dosing of Opdivo is 240 mg every 2 weeks or 480 mg every 4 weeks.

Metastatic small cell lung cancer (SCLC):
- The recommended dose is 240 mg administered as an intravenous infusion over 30 minutes every 2 weeks until disease progression or unacceptable toxicity.

Advanced renal cell carcinoma:
- The recommended dose as a single agent is either 240mg every 2 weeks or 480mg every 4 weeks
- The recommended dose in combination with ipilimumab is Opdivo 3mg/kg, followed by ipilimumab 1mg/kg intravenous infusion over 30 minutes on the same day, every 3 weeks for 4 doses. After completing 4 doses of the combination, administer Opdivo as a single agent either 240mg every 2 weeks or 480mg every 4 weeks.

CONTINUED ON NEXT PAGE

NIVOLUMAB (NSA)

REFERENCES

- Opdivo [Prescribing Information]. Princeton, NJ: Bristol-Myers Squibb Company; August 2018.

Library	Commercial	NSA
Yes	No	Yes

Part D Effective: N/A
Commercial Effective: 09/17/18
Created: 05/15
Client Approval: 08/18
P&T Approval: 10/18

NUSINERSEN (NSA)

Generic	Brand	HICL	GCN	Exception/Other
NUSINERSEN	SPINRAZA	44016		

GUIDELINES FOR USE

INITIAL CRITERIA (NOTE: FOR RENEWAL CRITERIA SEE BELOW)

1. Does the patient meet **ALL** of the following criteria?
   - Spinal muscular atrophy (SMA) diagnosis as confirmed by documentation of a survival motor neuron (SMN) gene deletion test **OR** Spinal muscular atrophy (SMA) diagnosis as confirmed by documentation of a survival motor neuron 1 (SMN1) gene mutation sequencing if patient is SMN1 heterozygous **OR** For patients who have spinal muscular atrophy (SMA) with a negative SMN gene test, documentation of further diagnostic tests to confirm SMA diagnosis required (e.g., electromyography, nerve conduction study, muscle biopsy)
   - Onset of SMA symptoms occurred before 20 years of age (SMA Type I, II, and III)
   - Documentation of baseline motor function assessment by the neurologist or SMA specialist (e.g., HINE, HFMSE, CHOP-INTEND)
   - Prescribed by or in consultation with a neurologist or SMA specialist at a SMA Specialty Center or Neuromuscular Disease Center

     If yes, **please enter TWO approvals by HICL as follows (total approval duration is 6 months):**
     - **FIRST APPROVAL: approve for 1 month for 3 fills with a quantity limit of #5mL (one 12mg/5mL vial) per each fill**
     - **SECOND APPROVAL: approve for 5 months for 2 fills, with a quantity limit of #5mL (one 12mg/5mL vial) per each fill (Please enter a start date after the end date of the first approval)**

     If no, do not approve.
     DENIAL TEXT: The guideline named **NUSINERSEN (Spinraza)** requires the following criteria must be met:
     - Spinal muscular atrophy (SMA) diagnosis as confirmed by documentation of a survival motor neuron (SMN) gene deletion test **OR** Spinal muscular atrophy (SMA) diagnosis as confirmed by documentation of a survival motor neuron 1 (SMN1) gene mutation sequencing if patient is SMN1 heterozygous **OR** For patients who have spinal muscular atrophy (SMA) with a negative SMN gene test, documentation of further diagnostic tests to confirm SMA diagnosis required (e.g., electromyography, nerve conduction study, muscle biopsy)
     - Onset of SMA symptoms occurred before 20 years of age (SMA Type I, II, and III)
     - Documentation of baseline motor function assessment by the neurologist or SMA specialist (e.g., HINE, HFMSE, CHOP-INTEND)
     - Prescribed by or in consultation with a neurologist or SMA specialist at a SMA Specialty Center or Neuromuscular Disease Center

CONTINUED ON NEXT PAGE

NUSINERSEN (NSA)

GUIDELINES FOR USE (CONTINUED)

RENEWAL CRITERIA

1. Does the patient meet **ONE** of the following criteria?
   - Patient has improved, maintained, or demonstrated less than expected decline in ambulatory ability based on motor function assessments compared to baseline (e.g., HINE, HFMSE, CHOP-INTEND)
   - Patient has improved, maintained, or demonstrated less than expected decline in other muscle function (e.g., pulmonary)

   If yes, **approve for 12 months by HICL for 3 fills with a quantity limit of #5mL (one 12mg/5mL vial) per each fill.**

   If no, do not approve.
   DENIAL TEXT: The guideline named **NUSINERSEN (Spinraza)** renewal requires a diagnosis of Spinal Muscular Atrophy (SMA). The following criteria must be met:
   - The patient has improved, maintained, or demonstrated less than expected decline in ambulatory ability based on motor function assessments compared to baseline (e.g., HINE, HFMSE, CHOP-INTEND) OR the patient has improved, maintained, or demonstrated less than expected decline in other muscle function (e.g., pulmonary)

RATIONALE

Promote appropriate utilization of **NUSINERSEN** based on FDA approved indication.

Spinraza is the first drug approved for the treatment of spinal muscular atrophy (SMA), a rare and often fatal genetic disease affecting muscle strength and movement. SMA is the leading genetic cause of infant death, and prior to the approval of Spinraza, supportive measures were the only available treatment. Spinraza is an antisense oligonucleotide (ASO) that must be administered via intrathecal injection by a healthcare professional. ASO therapies are a relatively novel approach to treatment that works by targeting and binding to mRNA and regulating gene expression; other ASOs include Kynamro (mipomersen) for homozygous familial hypercholesterolemia and Exondys 51 (eteplirsen) for Duchenne muscular dystrophy.

SMA is a rare, autosomal recessive, neurodegenerative disease that is characterized by severe and progressive atrophy of skeletal muscles and generalized weakness. Worldwide incidence ranges from 4 to 10 per 100,000 live births, with a carrier frequency of one in 50 to 90. In the US, the incidence is estimated at 8.3 per 100,000 live births. SMA is the leading genetic cause of infant death.

CONTINUED ON NEXT PAGE

NUSINERSEN (NSA)

RATIONALE (CONTINUED)

Patients with SMA have a mutation in the survival motor neuron (SMN) gene and do not produce enough SMN protein. SMN protein is critical for maintenance of motor neurons in the spinal cord and lower brain stem, and without motor neuron innervation, muscles progressively waste and atrophy. Approximately 95% of SMA patients have homozygous exon 7 deletions that result in producing either insufficient or no SMN protein. However, extra SMN2 genes can help replace SMN protein lost due to SMN1 gene mutations, such that symptoms still occur but are generally less severe. The severity of SMA correlates with the amount of deficient SMN protein.

All patients with SMA present with symmetric muscle weakness that affects the lower limbs more than the upper limbs. There are five SMA subtypes that differ based on the age of onset and severity of symptoms (see Table 1). Affecting about 50% of SMA patients, type 1 is the most common and severe type. Type 1 SMA patients present with symptoms in infancy, do not achieve any motor milestones (e.g., sitting independently, rolling, kicking), and typically die in the first year of life from respiratory failure. Some type 2 and type 3 SMA patients may produce greater amounts of SMN protein and have less severe disease.

CONTINUED ON NEXT PAGE

NUSINERSEN (NSA)

RATIONALE (CONTINUED)

Table 1: SMA subtypes and clinical characteristics

SMA subtype	Onset	Clinical characteristics	Life expectancy
0 (prenatal)	Prenatal	• Reduced fetal movement between 30 and 36 weeks of pregnancy • Severe respiratory compromise, weakness and hypotonia at birth	< 6 months
I (severe, Werdnig-Hoffmann disease)	< 6 months	• Proximal, symmetric muscle weakness, lack of motor development, poor muscle tone, unable to sit without support • Suck and swallowing deficits leading to growth failure and recurrent aspiration • Progressive respiratory muscle weakness	≤ 2 years, some may live longer
II (intermediate, Dubowitz disease)	6 – 12 months	• Poor muscle tone at birth or within months of birth • Able to sit independently with support • Scoliosis develops, unable to stand • Progressive respiratory muscle weakness	68% alive at age 25 years
III (juvenile SMA, Kugelberg-Welander disease)	≥ 18 months	• Independent ambulation is achieved with frequent falls and difficulties with stairs; however with progression ability may be lost	Normal
IV (adult)	20-30 years	• Similar to SMA type III, mild to moderate muscle weakness, tremor and twitching	Normal

Complications from motor neuron deficits go beyond physical limitations in movement. Nutritional deficits from abnormal swallowing and gastrointestinal dysmotility lead to problems with constipation, delayed gastric emptying, and gastroesophageal reflux. Pulmonary function decline results in hypoventilation, restrictive lung disease, and issues with airway clearance. Patients also experience orthopedic complications such as hip dislocation and scoliosis. While all subtypes will progressively deteriorate over time, prognosis varies by the subtype of SMA and can range from mild-moderate disability to death. Diagnosis of SMA is established based on patient family history, physical examination (motor deficits), and molecular genetic testing (SMN1).

CONTINUED ON NEXT PAGE

NUSINERSEN (NSA)

RATIONALE (CONTINUED)

Prior to the approval of Spinraza, there were no approved treatments for SMA, nor is there any known cure for this condition. Treatment was primarily centered on the supportive care: gastrostomy tubes are placed for nutrition, tracheotomy or noninvasive respiratory support for respiratory function decline, and surgical repair for scoliosis. Other supportive measures include mobility support devices such as braces or motorized wheelchairs.

Along with being granted fast track designation, priority review, and orphan drug designation, Spinraza became the first drug approved for the treatment of SMA. Spinraza is an ASO designed to alter the splicing of pre-mRNA from the SMN2 gene in order to increase production of fully functional SMN protein. Although the ENDEAR trial evaluated Spinraza primarily in infantile-onset SMA (i.e., SMA type 1), the FDA application for Spinraza also included data on patients with other subtypes of SMA, such that Spinraza is approved for use in all pediatric and adult patients with SMA. Clinical trials have been conducted with Spinraza in patients with SMA type 1, 2 and 3.

FDA APPROVED INDICATION

Spinraza is a survival motor neuron-2 (SMN2)-directed antisense oligonucleotide indicated for the treatment of spinal muscular atrophy (SMA) in pediatric and adult patients.

DOSAGE AND ADMINISTRATION

The recommended dosing regimen for nusinersen is 12 mg per administration intrathecally. Spinraza treatment should be initiated with 4 loading doses; the first three loading doses should be administered at 14-day intervals; the 4th loading dose should be administered 30 days after the 3rd dose; a maintenance dose should be administered once every 4 months thereafter.

AVAILABLE STRENGTHS

12 mg/5 mL (2.4 mg/mL) single-dose vials

CONTINUED ON NEXT PAGE

NUSINERSEN (NSA)

REFERENCES

- Spinraza [Prescribing Information]. Cambridge, MA: Biogen, Inc. December 2016.
- FDA approves first drug for spinal muscular atrophy [Press release]. Updated December 23, 2016. Available at: http://www.fda.gov/NewsEvents/Newsroom/PressAnnouncements/ucm534611.htm. Accessed December 30, 2016.
- U.S. FDA Approves Biogen's SPINRAZA™ (nusinersen), The First Treatment for Spinal Muscular Atrophy [Press Release]. Updated December 23, 2016. Available at: http://media.biogen.com/press-release/neurodegenerative-diseases/us-fda-approves-biogens-spinraza-nusinersen-first-treatment. Accessed December 30, 2016.
- Biogen and Ionis Pharmaceuticals Announce SPINRAZA (nusinersen) Meets Primary Endpoint at Interim Analysis of Phase 3 CHERISH Study in Later-Onset Spinal Muscular Atrophy [Press Release]. Updated November 7, 2016. Available at: http://media.biogen.com/press-release/corporate/biogen-and-ionis-pharmaceuticals-announce-spinraza-nusinersen-meets-primary-. Accessed December 30, 2016.
- Prior TW, Russman BS. Spinal muscular atrophy. GeneReviews. Available at: www.ncbi.nlm.nih.gov/books/NBK1352/. Accessed December 28, 2016.
- UpToDate, Inc. Spinal muscular atrophy. UpToDate [database online]. Waltham, MA. Updated July 7, 2016. Available at: http://www.uptodate.com/home/index.html. Accessed December 30, 2016.
- Ionis Pharmaceuticals, Inc. An Open-Label Study (SHINE) for Patients with Spinal Muscular Atrophy (SMA) Who Participated in Studies with IONIS-SMNRx [online]. Available at: https://clinicaltrials.gov/ct2/show/NCT02594124. Accessed December 29, 2016.
- Lunn MR, Wang CH. Spinal muscular atrophy. *Lancet.* 2008; 371:2120-33.
- Sugarman EA, Nagan N, Zhu H, et al. Pan-ethnic carrier screening and prenatal diagnosis for spinal muscular atrophy: clinical laboratory analysis of >72,400 specimens. *Eur J Hum Genet*. 2012;20:27–32.

Library	Commercial	NSA
Yes	No	Yes

Part D Effective: N/A
Commercial Effective: 04/01/17

Created: 01/17
Client Approval: 02/17

P&T Approval: 01/17

OBINUTUZUMAB (NSA)

Generic	Brand	HICL	GCN	Exception/Other
OBINUTUZUMAB	GAZYVA	40703		

This drug requires a written request for prior authorization.

GUIDELINES FOR USE

1. Does the patient have a diagnosis of chronic lymphocytic leukemia (CLL) and meet **ALL** of the following criteria?
   - The patient has not received previous treatment for chronic lymphocytic leukemia (CLL)
   - The requested medication will be used in combination with chlorambucil

   If yes, **please enter two approvals as follows:**
   - **Approve for 1 month by HICL for #4 (1000mg/40mL) vials per 28 days.**
   - **Approve for 5 months by HICL for #1 (1000mg/40mL) vial per 28 days with a start date one day after the end date of the first approval.**

   If no, continue to #2.

2. Does the patient have a diagnosis of follicular lymphoma (FL) and meet **ALL** of the following criteria?
   - The patient has relapsed after, or is refractory to, a regimen containing Rituxan (rituximab)
   - The requested medication will be used in combination with bendamustine for the initial six cycles **OR** as monotherapy thereafter

   If yes, **please enter three approvals as follows:**
   - **Approve for 1 month by HICL for #3 (1000mg/40mL) vials per 28 days.**
   - **Approve for 5 months by HICL for #1 (1000mg/40mL) vial per 28 days with a start date one day after the end date of the first approval.**
   - **Approve for 6 months by HICL for #1 (1000mg/40mL) vial per 56 days with a start date one day after the end date of the second approval.**

   If no, continue to #3.

CONTINUED ON NEXT PAGE

OBINUTUZUMAB (NSA)

GUIDELINES FOR USE (CONTINUED)

3. Does the patient have a diagnosis of stage II bulky, III or IV follicular lymphoma (FL) and meet **ALL** of the following criteria?
   - The patient is at least 18 years old
   - The patient has not received previous treatment for stage II bulky, III or IV follicular lymphoma
   - The requested medication will be used in combination with chemotherapy for the initial six or eight cycles [i.e., bendamustine; CHOP (cyclophosphamide, daunorubicin, vincristine, prednisone or prednisolone); CVP (cyclophosphamide, vincristine, prednisone or prednisolone)] **OR** as monotherapy thereafter

   If yes, **please enter three approvals as follows:**
   - **Approve for 1 month by HICL for #3 (1000mg/40mL) vials per 28 days.**
   - **Approve for 7 months by HICL for #1 (1000mg/40mL) vial per 28 days with a start date one day after the end date of the first approval.**
   - **Approve for 4 months by HICL for #1 (1000mg/40mL) vial per 56 days with a start date one day after the end date of the second approval.**

   If no, do not approve.
   DENIAL TEXT: The guideline named **OBINUTUZUMAB (Gazyva)** requires a diagnosis of chronic lymphocytic leukemia (CLL), follicular lymphoma (FL), or stage II bulky, III or IV follicular lymphoma. In addition, the following must be met:
   For the diagnosis of chronic lymphocytic leukemia (CLL), approval requires:
   - The patient has not received previous treatment for chronic lymphocytic leukemia (CLL)
   - The requested medication will be used in combination with chlorambucil

   For the diagnosis of follicular lymphoma (FL), approval requires:
   - The patient has relapsed after, or is refractory to, a regimen containing Rituxan (rituximab)
   - The requested medication will be used in combination with bendamustine for the initial six cycles **OR** as monotherapy thereafter

   For the diagnosis of stage II bulky, III or IV follicular lymphoma (FL), approval requires:
   - The patient is at least 18 years old
   - The patient has not received previous treatment for stage II bulky, III or IV follicular lymphoma
   - The requested medication will be used in combination with chemotherapy for the initial six or eight cycles [i.e., bendamustine; CHOP (cyclophosphamide, daunorubicin, vincristine, prednisone or prednisolone); CVP (cyclophosphamide, vincristine, prednisone or prednisolone)] **OR** as monotherapy thereafter

CONTINUED ON NEXT PAGE

OBINUTUZUMAB (NSA)

RATIONALE
To promote appropriate utilization of Gazyva based on FDA approved indication.

FDA APPROVED INDICATIONS
Gazyva (obinutuzumab) is a CD20-directed cytolytic antibody and is indicated:

- In combination with chlorambucil, for the treatment of patients with previously untreated chronic lymphocytic leukemia (CLL).
- In combination with bendamustine followed by Gazyva monotherapy, for the treatment of patients with follicular lymphoma (FL) who relapsed after, or are refractory to, a rituximab-containing regimen.
- In combination with chemotherapy followed by Gazyva monotherapy in patients achieving at least a partial remission, for the treatment of adult patients with previously untreated stage II bulky, III or IV follicular lymphoma.

DOSAGE AND ADMINISTRATION
Each dose of Gazyva is 1000 mg, administered intravenously.

Chronic Lymphocytic Leukemia (CLL)
Recommended dose for 6 cycles (28-day cycles):

Day of Treatment Cycle		Dose of Gazyva
Cycle 1	Day 1	100 mg
	Day 2	900 mg
	Day 8	1000 mg
	Day 15	1000 mg
Cycles 2-6	Day 1	1000 mg

The dose for chronic lymphocytic leukemia is 100 mg on day 1 and 900 mg on day 2 of Cycle 1, 1000 mg on day 8 and 15 of Cycle 1, and 1000 mg on day 1 of Cycles 2-6.

Relapsed or Refractory Follicular Lymphoma
For patients with relapsed or refractory FL, administer Gazyva in combination with bendamustine in six 28-day cycles. Patients who achieve stable disease, complete response, or partial response to the initial 6 cycles should continue on Gazyva 1000 mg as monotherapy for up to two years.

Recommended dose for 6 treatment cycles:

Day of Treatment Cycle		Dose of Gazyva
Cycle 1	Day 1	1000 mg
	Day 8	1000 mg
	Day 15	1000 mg
Cycles 2-6	Day 1	1000 mg
Monotherapy	Every 2 months for up to 2 years	1000 mg

CONTINUED ON NEXT PAGE

OBINUTUZUMAB (NSA)

FDA APPROVED INDICATIONS (CONTINUED)

DOSAGE AND ADMINISTRATION

Recommended dose for 6 treatment cycles:

Day of Treatment Cycle		Dose of Gazyva
Cycle 1	Day 1	1000 mg
	Day 8	1000 mg
	Day 15	1000 mg
Cycles 2-6	Day 1	1000 mg
Monotherapy	Every 2 months for up to 2 years	1000 mg

Previously Untreated Stage II bulky, III, or IV Follicular Lymphoma

For patients with previously untreated FL, administer Gazyva with one of the following chemotherapy regimens:

- Six 28-day cycles in combination with bendamustine
- Six 21-day cycles in combination with CHOP, followed by 2 additional 21-day cycles of Gazyva alone
- Eight 21-day cycles in combination with CVP

Patients with previously untreated FL who achieve a complete response or partial response to the initial 6 or 8 cycles should continue on Gazyva 1000 mg as monotherapy for up to two years.

Recommended dose for 8 treatment cycles:

- The dose for follicular lymphoma is 1000 mg on day 1, 8, and 15 of Cycle 1, and 1000 mg on day 1 of Cycles 2-8, and then 1000 mg every 2 months for 2 years.

Day of Treatment Cycle		Dose of Gazyva
Cycle 1	Day 1	1000 mg
	Day 8	1000 mg
	Day 15	1000 mg
Cycles 2-8	Day 1	1000 mg
Monotherapy	Every 2 months for up to 2 years	1000 mg

Patients should be premedicated with glucocorticoids, acetaminophen, and an antihistamine before infusion. Dilute and administer as intravenous infusion. Do not administer as an intravenous push or bolus. Patients with neutropenia are strongly recommended to receive antimicrobial prophylaxis throughout the treatment period. Antiviral and antifungal prophylaxis should be considered.

REFERENCES

- Genentech, Inc. Gazyva package insert. South San Francisco, CA. November 2017.

CONTINUED ON NEXT PAGE

OBINUTUZUMAB (NSA)

Library	Commercial	NSA
Yes	No	Yes

Part D Effective: N/A
Commercial Effective: 02/05/18
Created: 11/13
Client Approval: 01/18
P&T Approval: 01/18

OCRELIZUMAB (NSA)

Generic	Brand	HICL	GCN	Exception/Other
OCRELIZUMAB	OCREVUS	44178		

GUIDELINES FOR USE

1. Does the patient have a diagnosis of primary progressive multiple sclerosis (PPMS)?

   If yes, continue to #3.
   If no, continue to #2.

2. Does the patient have a relapsing form of multiple sclerosis (MS), and has the patient tried **TWO** preferred MS agents (oral or injectable): Aubagio, Avonex, Gilenya, Plegridy, Rebif, Tecfidera, or glatiramer; (**Please note:** other MS agents may also require prior authorization)?

   If yes, continue to #3.
   If no, do no approve.
   DENIAL TEXT: The guideline named **OCRELIZUMAB (Ocrevus)** requires a diagnosis of primary progressive multiple sclerosis (PPMS), or the patient has a relapsing form of multiple sclerosis (MS) and has tried TWO of the following preferred MS agents: Aubagio, Avonex, Gilenya, Plegridy, Rebif, Tecfidera, or glatiramer. Please note that other MS agents may also require prior authorization.

3. Is the patient requesting a starting dose?

   If yes, **approve for 12 months by HICL with the following quantity limits:**
   - **FIRST AUTHORIZATION: approve one fill for a quantity of #20mL (two 300mg/10mL vials), override quantity limits for new start dose.**
   - **SECOND AUTHORIZATION: approve #20mL (two 300mg/10mL vials) every 6 months.**

   If no, **approve for 12 months by HICL with a quantity limit of #20mL (two 300mg/10mL vials) every 6 months.**

RATIONALE
Promote appropriate utilization of Ocrevus (ocrelizumab) based on FDA approved indication and dosing.

FDA APPROVED INDICATIONS
Ocrevus is a CD20-directed cytolytic antibody indicated for the treatment of patients with relapsing or primary progressive forms of multiple sclerosis.

CONTINUED ON NEXT PAGE

OCRELIZUMAB (NSA)

FDA APPROVED INDICATIONS (CONTINUED)

DOSAGE AND ADMINISTRATION
Administer Ocrevus under the close supervision of an experienced healthcare professional with access to appropriate medical support to manage severe reactions such as serious infusion reactions.
- Initial dose: 300 mg intravenous infusion, followed two weeks later by a second 300 mg intravenous infusion.
- Subsequent doses: single 600 mg intravenous infusion every 6 months.

HOW SUPPLIED
Injection: 300 mg/10 mL (30 mg/mL) in a single-dose vial.

REFERENCES
- Ocrevus [Prescribing Information]. Genentech, Inc.: San Francisco, CA. March 2017.

Library	Commercial	NSA
Yes	No	Yes

Part D Effective: N/A
Commercial Effective: 01/01/18
Created: 01/17
Client Approval: 12/17
P&T Approval: 01/17

OFATUMUMAB (NSA)

Generic	Brand	HICL	GCN	Exception/Other
OFATUMUMAB	ARZERRA	36708		

This drug requires a written request for prior authorization.

GUIDELINES FOR USE

1. Does the patient have a diagnosis of chronic lymphocytic leukemia (CLL)?

   If yes, continue to #2.
   If no, do not approve.
   DENIAL TEXT: See the denial text at the end of the guideline.

2. Is the patient previously untreated for chronic lymphocytic leukemia (CLL) and meets **ALL** of the following criteria?
   - Fludara (fludarabine)-based therapy is considered inappropriate in this patient
   - The requested medication will be used in combination with chlorambucil

   If yes, **approve as follows by GPID and enter two prior authorizations:**
   - **Approval #1: Approve one fill of Arzerra 100mg/5mL with a quantity limit of #3 vials AND**
   - **Approval #2 (Please enter a start date of 1 WEEK AFTER the start date of the initial PA):**
     - **Approve 12 months of Arzerra 100mg/5mL with a quantity limit of #10 vials per 28 days (total fill count of 12) OR**
     - **Approve 12 months of Arzerra 1,000mg/50mL with a quantity limit of #1 vial per 28 days (total fill count of 12)**

   If no, continue to #3.

CONTINUED ON NEXT PAGE

OFATUMUMAB (NSA)

GUIDELINES FOR USE (CONTINUED)

3. Is the request for the treatment of **relapsed** chronic lymphocytic leukemia (CLL) and does the patient meet the following criteria?
   - The requested medication will be used in combination with Fludara (fludarabine) and cyclophosphamide

   If yes, **approve as follows by GPID and enter two prior authorizations:**
   - **Approval #1: approve one fill of Arzerra 100mg/5mL with a quantity limit of #3 vials AND**
   - **Approval #2 (Please enter a start date of 1 WEEK AFTER the start date of the initial PA):**
     - **Approve 6 months of Arzerra 100mg/5mL with a quantity limit of #10 vials per 28 days (total fill count of 6) OR**
     - **Approve 6 months of Arzerra 1,000mg/50mL with a quantity limit of #1 vial per 28 days (total fill count of 6)**

   If no, continue to #4.

4. For extended treatment of chronic lymphocytic leukemia (CLL), does the patient meet **ALL** of the following criteria?
   - The patient is in complete or partial response
   - The patient has received at least two lines of therapy for recurrent or progressive chronic lymphocytic leukemia (CLL)

   If yes, **approve as follows by GPID and enter two prior authorizations:**
   - **Approval #1: approve one fill of Arzerra 100mg/5mL with a quantity limit of #3 vials AND**
   - **Approval #2 (Please enter a start date of 1 WEEK AFTER the start date of the initial PA):**
     - **Approve 24 months of Arzerra 100mg/5mL with a quantity limit of #10 vials per 8 weeks (total fill count of 13) OR**
     - **Approve 24 months of Arzerra 1,000mg/50mL with a quantity limit of #1 vial per 8 weeks (total fill count of 13)**

   If no, continue to #5.

CONTINUED ON NEXT PAGE

OFATUMUMAB (NSA)

GUIDELINES FOR USE (CONTINUED)

5. For refractory chronic lymphocytic leukemia (CLL), does the patient meet **ALL** of the following criteria?
   - The patient is refractory to Fludara (fludarabine) and Campath (alemtuzumab)

   If yes, **approve as follows by GPID and enter three prior authorizations:**
   - **Approval #1: approve one fill of Arzerra 100mg/5mL with a quantity limit of #3 vials AND**
   - **Approval #2 (Please enter a start date of 1 WEEK AFTER the start date of the initial PA):**
     - **Approve 7 weeks of Arzerra 100mg/5mL with a quantity limit of #20 vials per 7 days (total fill count of 7) OR**
     - **Approve 7 weeks of Arzerra 1,000mg/50mL with a quantity limit of #2 vials per 7 days AND**
   - **Approval #3 (Please enter a start date of 4 WEEKS AFTER the end date of the second approval):**
     - **Approve 16 weeks of Arzerra 100mg/5mL with a quantity limit of #20 vials per 28 days (total fill count of 4) OR**
     - **Approve 16 weeks of Arzerra 1,000mg/50mL with a quantity limit of #2 vials per 28 days (total fill count of 4)**

   If no, do not approve.
   DENIAL TEXT: The guideline named **OFATUMUMAB (Arzerra)** requires a diagnosis of chronic lymphocytic leukemia (CLL). In addition, the following criteria must also be met.
   For patients with previously untreated chronic lymphocytic (CLL), approval requires all of the following:
   - The patient has not received previous treatment for chronic lymphocytic (CLL)
   - Fludara (fludarabine)-based therapy is considered inappropriate in this patient
   - The requested medication will be used in combination with chlorambucil

   For patients with relapsed chronic lymphocytic (CLL), approval requires all of the following:
   - The patient has relapsed chronic lymphocytic (CLL)
   - The requested medication will be used in combination with Fludara (fludarabine) and cyclophosphamide

   (Denial text continued on next page)

CONTINUED ON NEXT PAGE

OFATUMUMAB (NSA)

GUIDELINES FOR USE (CONTINUED)

For patients requesting extended treatment of chronic lymphocytic (CLL), approval requires all of the following:
- The patient is in complete or partial response
- The patient has received at least two lines of therapy for recurrent or progressive chronic lymphocytic leukemia (CLL)

For patients with refractory chronic lymphocytic (CLL), approval requires all of the following:
- The patient is refractory to Fludara (fludarabine) and Campath (alemtuzumab)

RATIONALE
Ensure appropriate utilization of Arzerra (ofatumumab) per FDA-approved indications and dosing.

FDA APPROVED INDICATION
Arzerra (ofatumumab) is a CD20-directed cytolytic monoclonal antibody indicated for the treatment of chronic lymphocytic leukemia (CLL):
- in combination with chlorambucil, for the treatment of previously untreated patients with CLL for whom fludarabine-based therapy is considered inappropriate
- in combination with fludarabine and cyclophosphamide for the treatment of patients with relapse CLL
- for extended treatment of patients who are in complete or partial response
- for the treatment of patients with CLL refractory to fludarabine and alemtuzumab

FDA APPROVED DOSING
Previously untreated CLL in combination with chlorambucil recommended dosage and schedule is:
- 300 mg on Day 1, followed by 1,000 mg on Day 8 (Cycle 1)
- 1,000 mg on Day 1 of subsequent 28-day cycles for a minimum of 3 cycles until best response or a maximum of 12 cycles.

Relapsed CLL in combination with fludarabine and cyclophosphamide recommended dosage and schedule is:
- 300 mg on Day 1 followed by 1,000 mg on Day 8 (Cycle 1)
- 1,000 mg on Day 1 of subsequent 28-day cycles for a maximum of 6 cycles

CONTINUED ON NEXT PAGE

OFATUMUMAB (NSA)

FDA APPROVED INDICATION (CONTINUED)

Extended treatment in CLL recommended dosage schedule is:
- 300 mg on Day 1, followed by
- 1,000 mg 1 week later on Day 8, followed by
- 1,000 mg 7 weeks later and every 8 weeks thereafter for up to a maximum of 2 years

Refractory CLL recommended dosage and schedule is:
- 300 mg initial dose, followed 1 week later by
- 2000 mg weekly for 7 doses, followed 4 weeks later by
- 2000 mg every 4 weeks for 4 doses.

REFERENCES

- Arzerra [Prescribing Information]. East Hanover, NJ: Novartis Pharmaceuticals Corporation. August 2016.

Library	Commercial	NSA
Yes	No	Yes

Part D Effective: N/A
Commercial Effective: 01/01/17
Created: 11/09
Client Approval: 12/16
P&T Approval: 11/16

OLARATUMAB (NSA)

Generic	Brand	HICL	GCN	Exception/Other
OLARATUMAB	LARTRUVO	43867		

GUIDELINES FOR USE

1. Is the request for continuation of Lartruvo therapy (i.e., patient is currently on Lartruvo)?

   If yes, continue to #2.
   If no, do not approve.
   DENIAL TEXT: See the denial text at the end of the guideline.

2. Does the patient have a diagnosis of soft tissue sarcoma (STS) and meet **ALL** of the following criteria?
   - The requested medication will be used in combination with doxorubicin for the first 8 cycles
   - The histologic subtype of sarcoma (e.g., undifferentiated pleomorphic sarcoma, liposarcoma, leiomyosarcoma, synovial sarcoma, malignant peripheral nerve sheath tumors) may be appropriately treated with an anthracycline-containing regimen
   - The patient is not amenable to curative treatment with radiotherapy or surgery

   If yes, **approve for 12 months by HICL.**
   If no, do not approve.
   DENIAL TEXT: The guideline named **OLARATUMAB (Lartruvo)** requires a diagnosis of soft tissue sarcoma. In addition, the following criteria must be met:
   For the diagnosis of soft tissue sarcoma, approval requires:
   - The request is for continuation of Lartruvo therapy (i.e., patient is currently on Lartruvo)
   - The requested medication will be used in combination with doxorubicin for the first 8 cycles
   - The histologic subtype of sarcoma (e.g., undifferentiated pleomorphic sarcoma, liposarcoma, leiomyosarcoma, synovial sarcoma, malignant peripheral nerve sheath tumors) may be appropriately treated with an anthracycline-containing regimen
   - The patient is not amenable to curative treatment with radiotherapy or surgery

RATIONALE

For further information, please refer to the Prescribing Informaiton and/or Drug Monograph for Lartruvo.

REFERENCES

- Lartruvo [Prescribing Information]. Indianapolis, IN: Eli Lilly and Company. August 2018.

Library	Commercial	NSA
Yes	No	Yes

Part D Effective: N/A
Commercial Effective: 02/11/19
Created: 11/16
Client Approval: 02/19
P&T Approval: 11/16

OMALIZUMAB (NSA)

Generic	Brand	HICL	GCN	Exception/Other
OMALIZUMAB	XOLAIR	25399		

This drug requires a written request for prior authorization.

GUIDELINES FOR USE

INITIAL CRITERIA (NOTE: FOR RENEWAL CRITERIA SEE BELOW)

1. Does the patient have a diagnosis of chronic idiopathic urticaria (CIU) and still experiences hives on most days of the week for at least 6 weeks **AND** meets all of the following criteria?
   - The patient is 12 years of age or older
   - The patient has tried a high dose H1 antihistamine (such as four-fold dosing of Clarinex or Xyzal) **AND** leukotriene antagonist for at least 2 weeks
   - Xolair is prescribed by or given in consultation with a physician specializing in allergy or pulmonary medicine

   If yes, **approve for 24 weeks by GPID for the requested product as follows:**
   - **Xolair 150mg vial (GPID 19966) with a quantity limit of #2 vials per 28 days.**
   - **Xolair 75mg/0.5mL syringe (GPID 30555) with a quantity limit of #2mL per 28 days.**
   - **Xolair 150mg/mL syringe (GPID 30556) with a quantity limit of #2mL per 28 days.**

   APPROVAL TEXT: Renewal requires a diagnosis of chronic idiopathic urticaria (CIU).

   If no, continue to #2.

2. Does the patient have moderate to severe persistent asthma and meet **ALL** the following criteria?
   - The patient is 6 years of age or older
   - The patient has a positive skin prick or RAST test to a perennial aeroallergen
   - The patient has a documented baseline IgE serum level greater than or equal to 30 IU/mL
   - The patient is currently adherent to a maximally tolerated inhaled corticosteroid plus at least one other maintenance medication (e.g., long-acting inhaled beta2-agonist, long-acting muscarinic antagonist, a leukotriene receptor antagonist, theophylline, or oral corticosteroid)
   - The patient has experienced at least 2 asthma exacerbations within the past 12 months (exacerbation is defined as an asthma-related event requiring hospitalization, emergency room visit, or systemic corticosteroid burst lasting at least 3 days)

   (Initial criteira continued on next page)

CONTINUED ON NEXT PAGE

OMALIZUMAB (NSA)

INITIAL CRITERIA (CONTINUED)

- The patient has **ONE** of the following:
  - Asthma Control Test (ACT) score of less than 20
  - Asthma Control Questionnaire (ACQ) score of at least 1.5
  - Asthma Therapy Assessment Questionnaire (ATAQ) score of at least 1
- Xolair will be used as add-on maintenance treatment
- The patient is not being concurrently treated with Dupixent or anti-IL5 asthma biologic (e.g., Nucala, Cinqair, Fasenra)
- Xolair is prescribed by or given in consultation with a physician specializing in allergy or pulmonary medicine

If yes, **approve for 12 months by GPID for the requested product as follows:**

- **Xolair 150mg vial (GPID 19966) with a quantity limit of #6 vials per 28 days.**
- **Xolair 75mg/0.5mL syringe (GPID 30555) with a quantity limit of #5mL per 28 days.**
- **Xolair 150mg/mL syringe (GPID 30556) with a quantity limit of #5mL per 28 days.**

APPROVAL TEXT: Renewal for the diagnosis of moderate to severe persistent asthma requires all of the following:

- The patient has experienced a reduction in asthma exacerbations (defined as an asthma-related event requiring hospitalization, emergency room visit, or systemic corticosteroid burst lasting at least 3 days) from baseline during the past 12 months of therapy
- The patient has experienced an improvement in the Asthma Control Test (ACT), Asthma Control Questionnaire (ACQ), or Asthma Therapy Assessment Questionnaire (ATAQ) score from baseline
- The patient has decreased their total daily oral corticosteroid dose from baseline if the patient was on a maintenance regimen of oral corticosteroids prior to initiation of Xolair

If no, do not approve.
DENIAL TEXT: See the initial denial text at the end of the guideline.

CONTINUED ON NEXT PAGE

OMALIZUMAB (NSA)

INITIAL CRITERIA (CONTINUED)

INITIAL DENIAL TEXT: The guideline named **OMALIZUMAB (Xolair)** requires a diagnosis of chronic idiopathic urticaria or moderate to severe persistent asthma. In addition, the following criteria must also be met:

For patients with chronic idiopathic urticaria (CIU), approval requires:

- The patient is 12 years of age or older
- The patient still experiences hives on most days of the week for at least 6 weeks
- The patient has tried a high dose H1 antihistamine (such as four-fold dosing of Clarinex or Xyzal) **AND** leukotriene antagonist for at least 2 weeks
- Xolair is prescribed by or given in consultation with a physician specializing in allergy or pulmonary medicine

For patients with moderate to severe persistent asthma, approval requires:

- The patient is 6 years of age or older
- The patient has a positive skin prick or RAST test to a perennial aeroallergen
- The patient has a documented baseline IgE serum level greater than or equal to 30 IU/mL
- The patient is currently adherent to a maximally tolerated inhaled corticosteroid plus at least one other maintenance medication (e.g., long-acting inhaled beta2-agonist, long-acting muscarinic antagonist, a leukotriene receptor antagonist, theophylline, or oral corticosteroid)
- The patient has experienced at least 2 asthma exacerbations within the past 12 months (exacerbation is defined as an asthma-related event requiring hospitalization, emergency room visit, or systemic corticosteroid burst lasting at least 3 days)
- The patient has **ONE** of the following:
  - Asthma Control Test (ACT) score of less than 20
  - Asthma Control Questionnaire (ACQ) score of at least 1.5
  - Asthma Therapy Assessment Questionnaire (ATAQ) score of at least 1
- Xolair will be used as add-on maintenance treatment
- The patient is not being concurrently treated with Dupixent or anti-IL5 asthma biologic (e.g., Nucala, Cinqair, Fasenra)
- Xolair is prescribed by or given in consultation with a physician specializing in allergy or pulmonary medicine

RENEWAL CRITERIA

1. Does the patient have a diagnosis of chronic idiopathic urticaria (CIU)?

   If yes, **approve for 12 months by GPID for the requested product as follows:**
   - **Xolair 150mg vial (GPID 19966) with a quantity limit of #2 vials per 28 days.**
   - **Xolair 75mg/0.5mL syringe (GPID 30555) with a quantity limit of #2mL per 28 days.**
   - **Xolair 150mg/mL syringe (GPID 30556) with a quantity limit of #2mL per 28 days.**

   If no, continue to #2.

CONTINUED ON NEXT PAGE

OMALIZUMAB (NSA)

RENEWAL CRITERIA (CONTINUED)

2. Does the patient have a diagnosis of moderate to severe persistent asthma and meet **ALL** of the following criteria?
   - The patient has experienced a reduction in asthma exacerbations (defined as an asthma-related event requiring hospitalization, emergency room visit, or systemic corticosteroid burst lasting at least 3 days) from baseline during the past 12 months of therapy
   - The patient has experienced an improvement in the Asthma Control Test (ACT), Asthma Control Questionnaire (ACQ), **OR** Asthma Therapy Assessment Questionnaire (ATAQ) score from baseline

   If yes, continue to #3.
   If no, do not approve.
   DENIAL TEXT: See the renewal denial text at the end of the guideline.

4. Was the patient treated with a maintenance therapy regimen of oral corticosteroids prior to initiation of Xolair?

   If yes, continue to #4.
   If no, **approve for 12 months by GPID for the requested product as follows:**
   - **Xolair 150mg vial (GPID 19966) with a quantity limit of #6 vials per 28 days.**
   - **Xolair 75mg/0.5mL syringe (GPID 30555) with a quantity limit of #5mL per 28 days.**
   - **Xolair 150mg/mL syringe (GPID 30556) with a quantity limit of #5mL per 28 days.**

5. Has the patient decreased their total daily dose of oral corticosteroids from baseline?

   If yes, **approve for 12 months by GPID for the requested product as follows:**
   - **Xolair 150mg vial (GPID 19966) with a quantity limit of #6 vials per 28 days.**
   - **Xolair 75mg/0.5mL syringe (GPID 30555) with a quantity limit of #5mL per 28 days.**
   - **Xolair 150mg/mL syringe (GPID 30556) with a quantity limit of #5mL per 28 days.**

   If no, do not approve.
   DENIAL TEXT: See the renewal denial text at the end of the guideline.

CONTINUED ON NEXT PAGE

OMALIZUMAB (NSA)

RENEWAL CRITERIA (CONTINUED)

RENEWAL DENIAL TEXT: The guideline named **OMALIZUMAB (Xolair)** renewal requires a diagnosis of moderate to severe persistent asthma or chronic idiopathic urticaria. In addition, the following criteria must also be met:

For patients with moderate to severe persistent asthma, approval requires:

- The patient has experienced a reduction in asthma exacerbations (defined as an asthma-related event requiring hospitalization, emergency room visit, or systemic corticosteroid burst lasting at least 3 days) from baseline during the past 12 months of therapy
- The patient has experienced an improvement in the Asthma Control Test (ACT), Asthma Control Questionnaire (ACQ), or Asthma Therapy Assessment Questionnaire (ATAQ) score from baseline
- The patient has decreased their total daily oral corticosteroid dose from baseline if the patient was on a maintenance regimen of oral corticosteroids prior to initiation of Xolair

RATIONALE

For further information, please refer to the Prescribing Information and/or Drug Monograph for Xolair.

REFERENCES

- Xolair [Prescribing Information]. South San Francisco, CA: Genentech, Inc. September 2018.

Library	Commercial	NSA
Yes	No	Yes

Part D Effective: N/A
Commercial Effective: 01/01/19
Created: 08/03
Client Approval: 11/18
P&T Approval: 10/18

PACLITAXEL PROTEIN-BOUND

Generic	Brand	HICL	GCN	Exception/Other
PACLITAXEL PROTEIN-BOUND	ABRAXANE	26856		

This drug requires a written request for prior authorization.

GUIDELINES FOR USE

1. Does the patient have a diagnosis of metastatic breast cancer?

   If yes, continue to #2.
   If no, continue to #3.

2. Has the patient previously tried a chemotherapy regimen containing an anthracycline (doxorubicin or epirubicin) or paclitaxel?

   If yes, **approve for 12 months by HICL.**
   APPROVAL TEXT: Please note that this drug has an important FDA safety warning. For more Information, please ask your doctor or pharmacist.
   If no, do not approve.
   DENIAL TEXT: See the denial text at the end of the guideline.

3. Does the patient have a diagnosis of locally advanced or metastatic Non-Small Cell Lung Cancer (NSCLC) or Small Cell Lung Cancer (SCLC)?

   If yes, **approve for 12 months by HICL.**
   APPROVAL TEXT: Please note that this drug has an important FDA safety warning. For more Information, please ask your doctor or pharmacist.
   If no, continue to #4.

4. Does the patient have a diagnosis of metastatic adenocarcinoma of the pancreas?

   If yes, continue to #5.
   If no, do not approve.
   DENIAL TEXT: See the denial text at the end of the guideline.

CONTINUED ON NEXT PAGE

PACLITAXEL PROTEIN-BOUND

GUIDELINES FOR USE (CONTINUED)

5. Is the requested medication being used in combination with gemcitabine?

   If yes, **approve for 12 months by HICL.**
   APPROVAL TEXT: Please note that this drug has an important FDA safety warning. For more Information, please ask your doctor or pharmacist.
   If no, do not approve.
   DENIAL TEXT: See the denial text at the end of the guideline.

DENIAL TEXT: Approval requires a diagnosis of metastatic breast cancer and trial of a chemotherapy regimen containing an anthracycline (doxorubicin or epirubicin) or paclitaxel; or a diagnosis of locally advanced or metastatic Non-Small Cell Lung Cancer (NSCLC) or Small Cell Lung Cancer (SCLC); or a diagnosis of metastatic adenocarcinoma of the pancreas and will be used in combination with gemcitabine.

RATIONALE

Based on FDA approved indications and NCCN recommendations. Abraxane is indicated for treatment of locally advanced or metastatic NSCLC as first-line treatment in combination with carboplatin, in patients who are not candidates for curative surgery or radiation therapy; metastatic breast cancer after failure of combination chemotherapy for metastatic disease or relapse within 6 months of adjuvant chemotherapy; and metastatic adenocarcinoma of the pancreas as first-line treatment, in combination with gemcitabine. NCCN recommends Abraxane as a first line therapy for patients with advanced NSCLC with performance status of 0-1 and as a substitute for paclitaxel or docetaxel among patients who have experienced hypersensitivity reactions or in whom the standard premedications are contraindicated.

The recommended dose of Abraxane for metastatic breast cancer is 260 mg/m^2 intravenously over 30 minutes every 3 weeks. The recommended dosage for Non-Small Cell Lung Cancer is 100 mg/m^2 intravenously over 30 minutes on Days 1, 8, and 15 of each 21-day cycle; carboplatin AUC 6 mg•min/mL is given intravenously on Day 1 of each 21 day cycle immediately after Abraxane administration. The recommended dose for adenocarcinoma of the pancreas is 125 mg/m^2 intravenously over 30-40 minutes on Days 1, 8, and 15 of each 28-day cycle; administer gemcitabine on Days 1, 8, and 15 of each 28-day cycle immediately after Abraxane.

NCCN guidelines recognize multiple chemotherapy treatment options for recurrent or metastatic breast cancer. Abraxane is considered a nonpreferred single agent therapy.

CONTINUED ON NEXT PAGE

PACLITAXEL PROTEIN-BOUND

RATIONALE (CONTINUED)

Preferred Single Agents	Other Single Agents	Combination Regimens
doxorubicin	cyclophosphamide	cyclophosphamide, doxorubicin, fluorouracil (FAC/CAF)
pegylated liposomal doxorubicin	carboplatin	fluorouracil, epirubicin, cyclophosphamide (FEC)
paclitaxel	docetaxel	doxorubicin, cyclophosphamide (AC)
Xeloda	Abraxane	epirubicin, cyclophosphamide (EC)
gemcitabine	cisplatin	cyclophosphamide, methotrexate, fluorouracil (CML)
Halaven	Ixempra	docetaxel, Xeloda
vinorelbine	epirubicin	gemcitabine, paclitaxel
		gemcitabine carboplatin
		paclitaxel, Avastin

Abraxane versus Paclitaxel: Advanced NSCLC
A phase 3 trial compared Abraxane (100mg/m^2 weekly) with carboplatin to traditional solvent bound paclitaxel (200 mg/m^2 weekly) with carboplatin in untreated patients with stage IIIB to IV NSCLC. Abraxane demonstrated a significantly higher ORR than paclitaxel (33 versus 25 percent). There was a non-significant approximately 10 percent improvement in progression-free survival (6.3 v 5.8 months; HR, 0.902) and overall survival (12.1 v 11.2 months; HR, 0.922) in the Abraxane arm versus the paclitaxel arm, respectively.

CONTINUED ON NEXT PAGE

PACLITAXEL PROTEIN-BOUND

RATIONALE (CONTINUED)
Efficacy Results from Randomized Non-Small Cell Lung Cancer Trial (Intent-to-Treat Population) From Abraxane Prescribing Information

	ABRAXANE (100mg/m^2 weekly) + carboplatin (N = 521)	Paclitaxel Injection (200mg/m^2 every 3 weeks) + carboplatin (N = 531)
Overall Response Rate (ORR)		
Confirmed complete or partial overall response, n (%)	107 (33%)	132 (25%)
95% CI	28.6,36.7	21.2,28.5
P-value (Chi-Square test)	0.005	
Median DoR in months (92% CI)	6.9 (5.6,8.0)	6.0 (5.6,7.1)
Overall Response Rate by Histology		
Carcinoma/Adenocarcinoma	66/254 (26%)	71/264 (27%)
Squamous Cell Carcinoma	94/229 (41%)	54/221 (24%)
Large Cell Carcinoma	3/9 (33%)	2/13 (15%)
Other	7/29 (24%)	5/33 (15%)

CI = confidence interval; DoR = Duration of response

FDA APPROVED INDICATION
Abraxane is a microtubule inhibitor indicated for the treatment of:

- Metastatic Breast Cancer, after failure of combination chemotherapy for metastatic disease or relapse within 6 months of adjuvant chemotherapy. Prior therapy should have included an anthracycline unless clinically contraindicated.
- Locally advanced or metastatic Non-Small Cell Lung Cancer (NSCLC), as first-line treatment in combination with carboplatin, in patients who are not candidates for curative surgery or radiation therapy.
- Metastatic adenocarcinoma of the pancreas as first-line treatment, in combination with gemcitabine.

CONTINUED ON NEXT PAGE

PACLITAXEL PROTEIN-BOUND

REFERENCES

- Celgene Corporation. Abraxane package insert. Summit, NJ. September 2013.
- National Comprehensive Cancer Network, Inc. NCCN Clinical Practice Guidelines in Oncology. Breast Cancer. (Version 3.2013).
- Celgene Corporation. Abraxane (paclitaxel protein-bound particles for injectable suspension) (albumin-bound) Prescribing Information. Drugs at FDA. [Online] September 2013. [Cited: October 7, 2013.] http://www.accessdata.fda.gov/scripts/cder/drugsatfda/index.cfm?fuseaction=Search.Search_Drug_Name
- Socinski MA, Bondarenko I, Karaseva NA, et al. Weekly nab-paclitaxel in combination with carboplatin versus solvent-based paclitaxel plus carboplatin as first-line therapy in patients with advanced non-small-cell lung cancer: final results of a phase III trial. J Clin Oncol. [Online] June 10, 2012. [Cited: October 7, 2013.] http://www.ncbi.nlm.nih.gov/pubmed/22547591
- National Comprehensive Cancer Network. NCCN Clinical Practice Guidelines in Oncology: Non-Small Cell Lung Cancer. Version 1.2014. [Online] October 11, 2013. [Cited: October 29, 2013.] http://www.nccn.org/professionals/physician_gls/pdf/nscl.pdf
- National Comprehensive Cancer Network. NCCN Clinical Practice Guidelines in Oncology Small Cell Lung Cancer Version 2.2014. [Online] September 17, 2013. [Cited: September 25, 2013.] http://www.nccn.org/professionals/physician_gls/pdf/sclc.pdf

Library	Commercial	NSA
Yes	No	Yes

Part D Effective: N/A
Commercial Effective: 01/01/14
Created: 08/13
Client Approval: 11/13
P&T Approval: 11/13

PALIVIZUMAB (NSA)

Generic	Brand	HICL	GCN	Exception/Other
PALIVIZUMAB	SYNAGIS	18564		

This drug requires a written request for prior authorization. Please use the drug specific medication request form.

GUIDELINES FOR USE

INITIAL CRITERIA (NOTE: FOR RENEWAL CRITERIA SEE BELOW)

1. Is the patient under 12 months of age?

   If yes, continue to #2.
   If no, continue to #11.

2. Does the patient have chronic lung disease of prematurity (previously called bronchopulmonary dysplasia (BPD) as defined below?
   - Gestational age < 32 weeks and
   - Patient required greater than 21% supplemental oxygen for at least the first 28 days after birth

   (**Note:** This does not include respiratory distress in the newborn, wheezing, reactive airway disease (RAD), asthma, or cystic fibrosis. Current data does not support the routine use of palivizumab prophylaxis in patients with cystic fibrosis.)

   If yes, continue to #13.
   If no, continue to #3.

3. Is the patient profoundly immunocompromised during the RSV season?

   If yes, continue to #13.
   If no, continue to #4.

4. Did the patient undergo solid-organ transplantation during the RSV season?

   If yes, continue to #13.
   If no, continue to #5.

CONTINUED ON NEXT PAGE

PALIVIZUMAB (NSA)

INITIAL CRITERIA (CONTINUED)

5. Does the patient have **ONE** of the following congenital heart disease conditions?
   - acyanotic heart disease requiring medication to control chronic heart failure (for example, furosemide, epinephrine, dopamine, lidocaine, milrinone, atenolol, propranolol, amlodipine, clonidine) and will require cardiac surgical procedures, or
   - patient has moderate or severe pulmonary hypertension, or
   - cyanotic heart defect patient and medication made in consultation with a pediatric cardiologist (**Note:** This does not include patients with hemodynamically insignificant heart disease, infants with lesions adequately corrected by surgery, infants with mild cardiomyopathy who are not receiving medical therapy for the condition.)

   If yes, continue to #13.
   If no, continue to #6.

6. Was the patient born prematurely?

   If yes, continue to #8.
   If no, continue to #7.

7. Does the patient have congenital abnormalities of the airways (anatomic pulmonary abnormalities) or neuromuscular disease that compromises the handling of respiratory secretions?

   If yes, continue to #13.
   If no, continue to #8.

8. Was the patient born at less than 29 weeks gestational age?

   If yes, continue to #13.
   If no, continue to #9.

9. Is the patient an American Navajo or American White Mount Apache infant?

   If yes, continue to #13.
   If no, continue to #10.

10. Is the patient an Alaska native infant?

    If yes, continue to #13.
    If no, do not approve.
    DENIAL TEXT: See the initial denial text at the end of the guideline.

CONTINUED ON NEXT PAGE

PALIVIZUMAB (NSA)

INITIAL CRITERIA (CONTINUED)

11. Is the patient younger than 24 months of age?

    If yes, continue to #12.
    If no, do not approve.
    DENIAL TEXT: See the initial denial text at the end of the guideline.

12. Does the patient meet **ONE** of the following criteria?
    - profoundly immunocompromised during the RSV season
    - chronic lung disease of prematurity **AND** requires medical support (oxygen, bronchodilator, diuretic, or chronic steroid therapy) within 6 months prior to the start of the second RSV season
    - undergo solid-organ transplantation during RSV season

    If yes, continue to #13.
    If no, do not approve.
    DENIAL TEXT: See the initial denial text at the end of the guideline.

13. **Approve for up to 5 months by HICL (do not enter quantity limit on number of vials) as follows: (Note: Enter the start date as requested, no earlier than October 1st of the current year. End date must be within 5 months and no later than April of the following year.)**

    - **Approve with a start date of October of current year and an end date in February of the following year (10 fill counts).**
    - **Approve with a start date of November of current year and an end date in March of the following year (10 fill counts).**
    - **Approve with a start date of December of current year and an end date in April of the following year (10 fill counts).**
    - **Approve with a start date of January of current year and an end date in April of current year (8 fill counts).**
    - **Approve with a start date of February of current year and an end date in April of current year (6 fill counts).**
    - **Approve with a start date of March of current year and an end date in April of current year (4 fill counts).**
    - **Approve with a start date of April of current year and approved for 1 month (2 fill counts).**

    Note: For requests for start date, earlier than October of current year or with an end date after April of following year, please refer to the CDC website to verify the RSV season for the specified region.

CONTINUED ON NEXT PAGE

PALIVIZUMAB (NSA)

INITIAL CRITERIA (CONTINUED)

INITIAL DENIAL TEXT: The guideline named **PALIVIZUMAB (Synagis)** requires that the patient be either less than 12 months old or less than 24 months at the start of respiratory syncytial virus (RSV) season. In addition, the following criteria must be met:

For patients less than 12 months old, ONE of the following criteria must be met:

- gestational age of less than 29 weeks
- chronic lung disease of prematurity, as defined as gestational age of less than 32 weeks and requiring greater than 21% supplemental oxygen for at least the first 28 days after birth
- profoundly immunocompromised during RSV season
- underwent solid-organ transplantation during RSV season
- congenital heart disease conditions such as acyanotic heart disease requiring medication to control chronic heart failure, moderate to severe pulmonary hypertension, or cyanotic heart defect and medication made in consultation with a pediatric cardiologist
- congenital abnormalities of the airways or neuromuscular disorder that compromises the handling of respiratory secretions
- American Navajo or American White Mount Apache infant, Alaska native infant born prematurely

For patients less than 24 months old, ONE of the following criteria must be met:

- chronic lung disease of prematurity and require medical support (oxygen, bronchodilator, diuretic, or chronic steroid therapy) within 6 months prior to start of the second RSV season
- underwent Solid-organ transplantation during RSV season
- profoundly immunocompromised during RSV season

RENEWAL CRITERIA

1. Is the patient younger than 24 months of age?

   If yes, continue to #2.
   If no, do not approve.
   DENIAL TEXT: See the renewal denial text at the end of the guideline.

2. Did the patient undergo cardiopulmonary bypass surgery during their RSV prophylaxis season?

   If yes, **approve for 1 month by HICL with a fill count of 2 (do not enter quantity limit on number of vials).**
   If no, continue to #3.

CONTINUED ON NEXT PAGE

PALIVIZUMAB (NSA)

RENEWAL CRITERIA (CONTINUED)

3. Is this a request for a second year of coverage (e.g., a previous approval in the previous RSV season)?

   If yes, continue to #4.
   If no, do not approve.
   DENIAL TEXT: See the renewal denial text at the end of the guideline.

4. Does the patient have chronic lung disease of prematurity (previously called bronchopulmonary dysplasia (BPD) and requires medical support (oxygen, bronchodilator, diuretic, or chronic steroid therapy) within 6 months prior to start of the second RSV season; (**Note:** This does not include respiratory distress in the newborn period, wheezing, reactive airway disease (RAD), asthma, or cystic fibrosis. Current data does not support the routine use of palivizumab prophylaxis in patients with cystic fibrosis.)?

   If yes, continue to #5.
   If no, do not approve.
   DENIAL TEXT: See the renewal denial text at the end of the guideline.

CONTINUED ON NEXT PAGE

PALIVIZUMAB (NSA)

RENEWAL CRITERIA (CONTINUED)

5. **Approve for up to 5 months by HICL (do not enter a quantity limit on the number of vials) as follows: (Note: Enter the start date as requested, no earlier than October 1st of the current year. End date must be within 5 months and no later than April of the following year.)**

   - **Approve with a start date of October of current year and an end date in February of the following year (10 fill counts).**
   - **Approve with a start date of November of current year and an end date in March of the following year (10 fill counts).**
   - **Approve with a start date of December of current year and an end date in April of the following year (10 fill counts).**
   - **Approve with a start date of January of current year and an end date in April of current year (8 fill counts).**
   - **Approve with a start date of February of current year and an end date in April of current year (6 fill counts).**
   - **Approve with a start date of March of current year and an end date in April of current year (4 fill counts).**
   - **Approve with a start date of April of current year and approved for 1 month (2 fill counts).**

     Note: For requests for start date earlier than October of current year or with an end date after April of following year, please refer to the CDC website to verify the RSV season for the specified region.

   RENEWAL DENIAL TEXT: Renewal of **PALIVIZUMAB (Synagis)** requires that the patient is under 24 months of age and meets **ONE** of the following criteria:
   - Patient underwent cardiopulmonary bypass surgery during RSV prophylaxis season, or
   - Patient has chronic lung disease of prematurity requiring medical support (e.g., chronic corticosteroid therapy, diuretic therapy, or supplemental oxygen) during the 6 month period before the start of the second RSV season

RATIONALE

To ensure the optimal use of palivizumab in high-risk patients for the prophylaxis of RSV by following the most recent American Academy of Pediatrics guidelines for the use of palivizumab for the prevention of serious RSV infections. Variations in the onset and offset of the RSV reason in different regions may affect the timing of palivizumab administration. A maximum of 5 monthly doses of palivizumab should be adequate for qualifying infants for most RSV seasons. RSV seasons within the continental United States may start in October/November and end in March/April.

CONTINUED ON NEXT PAGE

PALIVIZUMAB (NSA)

FDA APPROVED INDICATIONS

For the prevention of serious, lower respiratory tract disease caused by respiratory syncytial virus (RSV) in pediatric patients at high risk of RSV disease.

REFERENCES

- MedImmune, Inc. Synagis package insert. Gaithersburg, MD. March 2009.
- American Academy of Pediatrics, Committee on Infectious Diseases and Committee on Fetus and Newborn. Revised indications for the use of palivizumab and respiratory syncytial virus immune globulin intravenous for the prevention of respiratory syncytial virus infections. Pediatrics 2003; 112(6):1442-1446.
- American Academy of Pediatrics. Policy statement – modified recommendations for use of palivizumab for prevention of respiratory syncytial virus infections. Pediatrics 2009;124:1694-1701.
- American Academy of Pediatrics, Subcommittee on Diagnosis and Management of Bronchiolitis. Pediatrics 2006; 118; 1774-1798.
- American Academy of Pediatrics, Committee on Infectious Diseases and Bronchiolitis Guidelines Committee. Updated Guidance for Palivizumab Prophylaxis Among Infants and Young Children at Increased Risk of Hospitalization for Respiratory Syncytial Virus Infections. Pediatrics 2014:134:415-420
- Reducing RSV hospitalizations. AAP modifies recommendations for use of palivizumab in high-risk infants, young children. AAP News 2009; 30:1.
- Thomas Healthcare. Palivizumab. DRUGDEX® System [database online]. Greenwood Village, CO. [Accessed: August 7 2009].

Library	Commercial	NSA
Yes	No	Yes

Part D Effective: N/A
Commercial Effective: 03/01/18

Created: 08/09
Client Approval: 01/18

P&T Approval: 11/15

PANITUMUMAB (NSA)

Generic	Brand	HICL	GCN	Exception/Other
PANITUMUMAB	VECTIBIX	34054		

This drug requires a written request for prior authorization.

GUIDELINES FOR USE

1. Does the patient have a diagnosis of metastatic colorectal cancer (mCRC) with wild-type RAS (defined as wild-type in both KRAS and NRAS as determined by an FDA-approved test for this use) and meet **ONE** of the following criteria?
   - Vectibix will be used as monotherapy **AND** the patient has been treated in the past with fluoropyrimidine-, oxaliplatin-, and irinotecan-containing chemotherapy
   - Vectibix will be used in combination with FOLFOX (leucovorin calcium [folinic acid], fluorouracil, oxaliplatin)

   If yes, **approve for 12 months by HICL.**
   If no, do not approve.
   DENIAL TEXT: The guideline named **PANITUMUMAB (Vectibix)** requires a diagnosis of metastatic colorectal cancer (mCRC) with wild-type RAS (defined as wild-type in both KRAS and NRAS as determined by an FDA-approved test for this use). In addition, **ONE** of the following criteria must be met:
   - Vectibix will be used as monotherapy **AND** the patient has been treated in the past with fluoropyrimidine-, oxaliplatin-, and irinotecan-containing chemotherapy
   - Vectibix will be used in combination with FOLFOX (leucovorin calcium [folinic acid], fluorouracil, oxaliplatin)

RATIONALE
To ensure appropriate use of Vectibix consistent with FDA approved indication.

The FOLFOX regimen includes leucovorin calcium (folinic acid), fluorouracil, oxaliplatin.

FDA APPROVED INDICATIONS
Vectibix is an epidermal growth factor receptor (EGFR) antagonist indicated for the treatment of wild type RAS (defined as wild-type in both KRAS and NRAS as determined by an FDA-approved test for this use) metastatic colorectal carcinoma (mCRC):
- In combination with FOLFOX for first-line treatment. **OR**
- As monotherapy following disease progression after prior treatment with fluoropyrimidine, oxaliplatin, and irinotecan-containing chemotherapy.

Limitation of Use: Vectibix is not indicated for the treatment of patients with RAS-mutant mCRC or for whom RAS mutation status is unknown.

CONTINUED ON NEXT PAGE

PANITUMUMAB (NSA)

FDA APPROVED INDICATIONS (CONTINUED)

DOSING
The recommended dose of Vectibix is 6 mg/kg every 14 days administered as an intravenous infusion over 60 minutes (≤ 1000 mg) or 90 minutes (> 1000 mg). Reduce infusion rate by 50% for mild reactions.

REFERENCES

- Vectibix [Prescribing Information]. Thousand Oaks, CA: Amgen Inc., June 2017.

Library	Commercial	NSA
Yes	No	Yes

Part D Effective: N/A
Commercial Effective: 03/01/18
Created: 02/13
Client Approval: 02/18
P&T Approval: 10/17

PATISIRAN (NSA)

Generic	Brand	HICL	GCN	Exception/Other
PATISIRAN	ONPATTRO	45155		

GUIDELINES FOR USE

INITIAL CRITERIA (NOTE: FOR RENEWAL CRITERIA SEE BELOW)

1. Does the patient have a diagnosis of hereditary transthyretin-mediated amyloidosis (hATTR) with polyneuropathy and meet **ALL** of the following criteria?
   - The patient is 18 years of age or older
   - The patient has a documented diagnosis of hereditary TTR amyloidosis (hATTR) as confirmed by **ONE** of the following:
     - Biopsy of tissue/organ to confirm amyloid presence **AND** chemical typing to confirm the presence of TTR protein
     - DNA genetic sequencing to confirm hATTR
   - The requested medication is being prescribed by or given in consultation with a neurologist, cardiologist, physician at an amyloidosis treatment center, or medical geneticist
   - Physician attestation that the patient has Stage 1 or 2 polyneuropathy

   If yes, **approve for 6 months by HICL with a quantity limit of 15mL (30mg) per 21 days.**
   APPROVAL TEXT: Renewal requires physician attestation that the patient has not progressed to stage 3 polyneuropathy as evidenced by functional decline (e.g., wheelchair-bound, bedridden).

   If no, do not approve.
   INITIAL DENIAL TEXT: The guideline named **PATISIRAN (Onpattro)** requires a diagnosis of hereditary transthyretin-mediated amyloidosis (hATTR) with polyneuropathy. In addition, the following criteria must be met:
   - The patient is 18 years of age or older
   - The patient has a documented diagnosis of hereditary TTR amyloidosis (hATTR) as confirmed by **ONE** of the following:
     - Biopsy of tissue/organ to confirm amyloid presence **AND** chemical typing to confirm the presence of TTR protein
     - DNA genetic sequencing to confirm hATTR
   - The requested medication is being prescribed by or given in consultation with a neurologist, cardiologist, physician at an amyloidosis treatment center, or medical geneticist
   - Physician attestation that the patient has Stage 1 or 2 polyneuropathy

CONTINUED ON NEXT PAGE

PATISIRAN (NSA)

GUIDELINES FOR USE (CONTINUED)

RENEWAL CRITERIA

1. Does the patient have a diagnosis of hereditary TTR amyloidosis (hATTR) **AND** meet the following criterion?
   - Physician attestation that the patient has not progressed to stage 3 polyneuropathy as evidenced by functional decline (e.g., wheelchair-bound, bedridden)

     If yes, **approve for 12 months by HICL with a quantity limit of 15mL (30mg) per 21 days.**
     If no, do not approve.
     RENEWAL DENIAL TEXT: The guideline named **PATISIRAN** requires a diagnosis of hereditary TTR amyloidosis (hATTR) and physician attestation that the patient has not progressed to stage 3 polyneuropathy as evidenced by functional decline (e.g., wheelchair-bound, bedridden).

RATIONALE
Promote appropriate utilization of PATISIRAN based on FDA approved indication and dosing and clinical trial data. A list of amyloidosis treatment centers can be viewed at the following link: http://amyloidosis.org/resources/#treatment-centers.

FDA APPROVED INDICATIONS
Onpattro is indicated for the treatment of the polyneuropathy of hereditary transthyretin-mediated amyloidosis in adults.

Hereditary transthyretin amyloidosis (hATTR) is a genetic, rare, severe, debilitating, multi-systemic, progressive, and fatal disorder involving the protein tetramer transthyretin (TTR). Instead of folding properly, production in the liver of TTR protein, due to a mutation, folds into amyloid fibrils that deposit throughout the body. These deposits lead to damage to tissue, resulting in a multitude of clinical signs and symptoms, but primarily affect the heart and nerves.

RNA interference (RNAi) utilizes the universal model for gene expression to influence and silence protein production, a target of disease. Onpattro, a small interfering ribonucleic acid (siRNA) utilizes the cell's endogenous ability for gene expression control and silencing by engaging RNA-induced silencing complex (RISC). TTR-specific mRNA is targeted, which leads to the reduced amount of transthyretin produced and the amount of misfolded monomer that is available to aggregate into amyloid fibrils and deposit in tissues. It is also theorized that the established amyloid deposits (located in tissues and organs) would gradually diminish after reduced rate of deposition (TTR knockdown) was achieved.

CONTINUED ON NEXT PAGE

PATISIRAN (NSA)

FDA APPROVED INDICATIONS (CONTINUED)

DOSING & ADMINISTRATION

Onpattro is available as a lipid complex solution for intravenous infusion supplied as a 10 mg/5 mL solution in a single-dose vial, administered only by a healthcare professional. Dosing is based on actual body weight.

- For patients weighing less than 100 kg, the recommended dosage is 0.3 mg/kg once every 3 weeks.
- For patients weighing 100 kg or more, the recommended dosage is 30 mg once every 3 weeks.

All patients should receive pre-medications 60 minutes prior to Onpattro to reduce the risk of infusion-related reactions. The following pre-medications should be given (pre-medications not available or not tolerated intravenously may be administered as equivalents orally):

- Intravenous corticosteroid (e.g., dexamethasone 10 mg, or equivalent)
- Oral acetaminophen (500 mg)
- Intravenous H1 blocker (e.g., diphenhydramine 50 mg, or equivalent)
- Intravenous H2 blocker (e.g., ranitidine 50 mg, or equivalent)

REFERENCES

- Onpattro [prescribing information]. Cambridge, MA: Alnylam; 2018.
- Holmes R. Amyloidosis: Definition of Amyloid and Amyloidosis, Classification Systems, Systemic Amyloidosis. Available at: https://emedicine.medscape.com/article/335414-overview. Accessed May 10, 2018.
- Coelho T, Ericzon B, Falk R, et al. A Guide to Transthyretin Amyloidosis. Available at: http://www.amyloidosis.org/wp-content/uploads/2017/05/2017-ATTR-guide.pdf. Accessed May 18, 2018.
- Rambaran R, Serpell LC. Amyloid Fibrils. Prion. 2008;2(3):112-117.
- A is for Amyloidosis: Facts. Available at: http://amyloidosis.org/facts/. Accessed May 18, 2018.
- Gertz, M. Hereditary ATTR Amyloidosis: Burden of Illness and Diagnostic Challenges. Am J Manag Care. 2017;23:S107-S112.
- Adams D, Gonzalez-Duarte A, O'Riordan WD, et al. Patisiran, an RNAi Therapeutic, for Hereditary Transthyretin Amyloidosis. NEJM. 2018;379(1):11-21. doi:10.1056/NEJMoa1716153.
- Ando Y, Coelho T, Berk JL, et al. Guideline of transthyretin-related hereditary amyloidosis for clinicians. Orphanet J Rare Dis. 2013;8(1):1-18. doi:10.1186/1750-1172-8-31.
- Buxbaum J. Oligonucleotide Drugs for Transthyretin Amyloidosis. NEJM. 2018;379(1):82-85. doi:10.1056/NEJMe1805499.

CONTINUED ON NEXT PAGE

PATISIRAN (NSA)

REFERENCES (CONTINUED)

- What causes hereditary ATTR (hATTR) amyloidosis? Available at: https://hattrbridge.com/about-hattr-amyloidosis/cause-and-symptoms. Accessed May 18, 2018.
- Gonzalez-Duarte A, Adams D, O'Riordan W, et al. Changes in Neuropathy Stage in Patients with Hereditary Transthyretin-Mediated Amyloidosis Following Treatment with Patisiran, an Investigational RNAi Therapeutic: An Analysis from the Phase 3 APOLLO Study. Available at: http://www.alnylam.com/wp-content/uploads/2018/03/5.-APOLLO-PND-FAP_FINAL.pdf. Accessed May 18, 2018.

Library	Commercial	NSA
Yes	No	Yes

Part D Effective: N/A
Commercial Effective: 09/01/18
Created: 08/18
Client Approval: 08/18
P&T Approval: 07/18

PEGAPTANIB

Generic	Brand	HICL	GCN	Exception/Other
PEGAPTANIB SODIUM	MACUGEN	26805		

This drug requires a written request for prior authorization.

GUIDELINES FOR USE

1. Is this medication being prescribed by an ophthalmologist and/or retina specialist?

   If yes, continue to #2.
   If no, do not approve.
   DENIAL TEXT: See the denial text at the end of the guideline.

2. Does the patient have a diagnosis of neovascular (wet) age-related macular degeneration (AMD)?

   If yes, continue to #3.
   If no, do not approve.
   DENIAL TEXT: See the denial text at the end of the guideline.

3. Is the patient receiving treatment in both eyes at this time?

   If yes**, approve for duration of 12 months by HICL for up to 18 syringes (2 syringes per 6 weeks).**
   If no, and a single eye is being treated, **approve for duration of 12 months by HICL for up to 9 syringes (1 syringe per 6 weeks).**

   DENIAL TEXT: Our guideline for **PEGAPTANIB** requires a diagnosis of neovascular (wet) age-related macular degeneration (AMD) and that the medication is being prescribed by an ophthalmologist and/or retina specialist.

RATIONALE
To ensure appropriate use of MACUGEN consistent with FDA approved indication.

FDA-APPROVED INDICATIONS
Macugen is indicated for the treatment of neovascular (wet) age-related macular degeneration.

REFERENCES

- Macugen [Prescribing Information]. San Dimas, CA: Eyetech Inc.; October 2011.

CONTINUED ON NEXT PAGE

PEGAPTANIB

Library	Commercial	NSA
Yes	No	Yes

Part D Effective: N/A
Commercial Effective: 07/01/14

Created: 05/14
Client Approval: 05/14

P&T Approval: 05/14

PEGLOTICASE (NSA)

Generic	Brand	HICL	GCN	Exception/Other
PEGLOTICASE	KRYSTEXXA	37154		

This drug requires a written request for prior authorization.

GUIDELINES FOR USE

INITIAL CRITERIA (NOTE: FOR RENEWAL CRITERIA SEE BELOW)

1. Does the patient have a diagnosis of chronic gout that is refractory to conventional therapy and meet **ALL** of the following critieria?
   - The patient is 18 years of age or older
   - There is physician attestation of symptomatic gout as evidenced by **ONE** of the following:
     - o At least 3 or more gout flares in the previous 18 months
     - o History of at least 1 gout tophus
     - o Gouty arthritis
   - The patient has a baseline serum uric acid levels ≥ 8 mg/dL while on conventional gout medications (e.g., allopurinol, lesinurad)
   - The patient does not have glucose-6-phosphate dehydrogenase (G6PD) deficiency
   - The patient will not be on concurrent urate-lowering therapy (e.g., xanthine oxidase inhibitors, febuxostat, probenecid, lesinurad) while using pegloticase
   - The patient has experienced failure, contraindication, intolerance or inadequate response to previous therapy with a maximum tolerated dose for **TWO** conventional gout medications for at least 3 months (e.g., allopurinol, probenecid, lesinurad)

   If yes, **approve for 6 months by HICL for #2mL per 28 days.**
   APPROVAL TEXT: Renewal requires sustained serum uric acid levels below 6 mg/dL.

   If no, do not approve.
   INITIAL DENIAL TEXT: The guideline named **PEGLOTICASE (Krystexxa)** requires a diagnosis of chronic gout that is refractory to conventional therapy. In addition, the following criteria must be met:
   - The patient is 18 years of age or older
   - There is physician attestation of symptomatic gout as evidenced by **ONE** of the following:
     - o At least 3 or more gout flares in the previous 18 months
     - o History of at least 1 gout tophus
     - o Gouty arthritis

   (Initial denial text continued on next page)

CONTINUED ON NEXT PAGE

PEGLOTICASE (NSA)

INITIAL CRITERIA (CONTINUED)

- The patient has a baseline serum uric acid levels of at least 8 mg/dL while on conventional gout medications (e.g., allopurinol, lesinurad)
- The patient does not have glucose-6-phosphate dehydrogenase (G6PD) deficiency
- The patient will not be on concurrent urate-lowering therapy (e.g., xanthine oxidase inhibitors, febuxostat, probenecid, lesinurad) while using pegloticase
- The patient has experienced failure, contraindication, intolerance or inadequate response to previous therapy with a maximum tolerated dose for **TWO** conventional gout medications for at least 3 months (e.g., allopurinol, probenecid, lesinurad)

RENEWAL CRITERIA

1. Does the patient have sustained serum uric acid levels below 6 mg/dL?

   If yes, **approve for 12 months by HICL for #2mL per 28 days.**
   If no, do not approve.
   RENEWAL DENIAL TEXT: The guideline named **PEGLOTICASE (Krystexxa)** requires a sustained serum uric level below 6 mg/dL for renewal.

RATIONALE
To ensure appropriate utilization of Krystexxa based on the FDA approved indication and dosing.

FDA APPROVED INDICATIONS
Krystexxa is a PEGylated uric acid specific enzyme indicated for the treatment of chronic gout in adult patients refractory to conventional therapy.

Important Limitations of Use:
Krystexxa is not recommended for the treatment of asymptomatic hyperuricemia.

DOSAGE AND ADMINISTRATION
The recommended dose and regimen of Krystexxa for adult patients is 8 mg (uricase protein) given as an intravenous infusion every two weeks. Do not administer as an intravenous push or bolus. The pegloticase admixture should only be administered by intravenous infusion over no less than 120 minutes via gravity feed, syringe-type pump, or infusion pump.

It is recommended that before starting Krystexxa patients discontinue oral urate-lowering medications and not institute therapy with oral urate-lowering agents while patients are on Krystexxa therapy. Monitor serum uric acid levels before each infusion. Patients should be pre-medicated with antihistamines and corticosteroids.

CONTINUED ON NEXT PAGE

PEGLOTICASE (NSA)

REFERENCES

- Krystexxa [Prescribing Information]. Horizon Pharma Rheumatology LLC. Lake Forest, IL. Jul 2018.

Library	Commercial	NSA
Yes	No	Yes

Part D Effective: N/A
Commercial Effective: 10/01/18
Created: 08/18
Client Approval: 09/18
P&T Approval: 07/18

PEMBROLIZUMAB (NSA)

Generic	Brand	HICL	GCN	Exception/Other
PEMBROLIZUMAB	KEYTRUDA	41369		

GUIDELINES FOR USE

1. Does the patient have a diagnosis of unresectable or metastatic melanoma?

   If yes, **approve for 12 months by GPID for all strengths with the following quantity limits:**
   - **50mg powder (GPID 37028): 4 vials per 21 days.**
   - **100mg/4mL (GPID 37754): 8mL per 21 days.**

   If no, continue to #2.

2. Does the patient have a diagnosis of melanoma with involvement of lymph node(s) following complete resection and meet the following criterion?
   - The requested medication will be used as an adjuvant treatment

   If yes, **approve for 12 months by GPID for all strengths with the following quantity limits:**
   - **50mg powder (GPID 37028): 4 vials per 21 days.**
   - **100mg/4mL (GPID 37754): 8mL per 21 days.**

   If no, continue to #3.

3. Does the patient have a diagnosis of metastatic non-small cell lung cancer (NSCLC) **AND** meet **ALL** of the following criteria?
- The patient has not received prior systemic chemotherapy treatment for metastatic NSCLC
- The tumor is classified as nonsquamous (e.g., adenocarcinoma, large cell carcinoma)
- The medication is used in combination with pemetrexed and platinum chemotherapy
- The patient does not have anaplastic lymphoma kinase (ALK) or epidermal growth factor receptor (EGFR) genomic tumor aberrations

   If yes, **approve for 12 months by GPID for all strengths with the following quantity limits:**
   - **50mg powder (GPID 37028): 4 vials per 21 days.**
   - **100mg/4mL (GPID 37754): 8mL per 21 days.**

   If no, continue to #4.

4. Does the patient have a diagnosis of metastatic non-small cell lung cancer (NSCLC) AND meet **ALL** of the following criteria?
- The patient has not received prior systemic chemotherapy treatment for metastatic NSCLC
- The tumor is classified as squamous
- The medication is used in combination with carboplatin and either paclitaxel or nab-paclitaxel

   If yes, **approve for 12 months by GPID for all strengths with the following quantity limits:**
   - **50mg powder (GPID 37028): 4 vials per 21 days.**
   - **100mg/4mL (GPID 37754): 8mL per 21 days.**

   If no, continue to #5.

CONTINUED ON NEXT PAGE

PEMBROLIZUMAB (NSA)

GUIDELINES FOR USE (CONTINUED)

5. Does the patient have a diagnosis of metastatic non-small cell lung cancer (NSCLC) **AND** meet **ALL** of the following criteria?
   - The patient has not received prior systemic chemotherapy treatment for metastatic NSCLC
   - The medication will be given as a single agent (i.e., not in combination with chemotherapy)
   - NSCLC tumors have high programmed death-ligand (PD-L1) expression [Tumor Proportion Score (TPS) ≥50%] as determined by an FDA-approved test
   - The patient does not have anaplastic lymphoma kinase (ALK) or epidermal growth factor receptor (EGFR) genomic tumor aberrations

   If yes, **approve for 12 months by GPID for all strengths with the following quantity limits:**
   - **50mg powder (GPID 37028): 4 vials per 21 days.**
   - **100mg/4mL (GPID 37754): 8mL per 21 days.**

   If no, continue to #6.

6. Does the patient have a diagnosis of metastatic non-small cell lung cancer (NSCLC) **AND** meet ALL of the following criteria?
   - The medication will be given as a single agent (i.e., not in combination with chemotherapy)
   - NSCLC tumors express programmed death-ligand (PD-L1) [Tumor Proportion Score (TPS) ≥1%] as determined by an FDA-approved test
   - The patient does not have anaplastic lymphoma kinase (ALK) or epidermal growth factor receptor (EGFR) genomic tumor aberrations
   - Disease progression on or after treatment with platinum-containing chemotherapy (e.g., cisplatin, carboplatin, oxaliplatin)

   If yes, **approve for 12 months by GPID for all strengths with the following quantity limits:**
   - **50mg powder (GPID 37028): 4 vials per 21 days.**
   - **100mg/4mL (GPID 37754): 8mL per 21 days.**

   If no, continue to #7.

CONTINUED ON NEXT PAGE

PEMBROLIZUMAB (NSA)

GUIDELINES FOR USE (CONTINUED)

7. Does the patient have a diagnosis of metastatic non-small cell lung cancer (NSCLC) **AND** meet **ALL** of the following criteria?
   - The medication will be given as a single agent (i.e., not in combination with chemotherapy)
   - NSCLC tumors express programmed death-ligand (PD-L1) [Tumor Proportion Score (TPS) ≥1%] as determined by an FDA-approved test
   - The patient has an anaplastic lymphoma kinase (ALK) genomic tumor aberration
   - Disease progression on or after treatment with **ALL** of the following:
     - o Platinum-containing chemotherapy (e.g., cisplatin, carboplatin, oxaliplatin)
     - o ALK-directed therapy [e.g., Xalkori (crizotinib), Zykadia (ceritinib)]

   If yes, **approve for 12 months by GPID for all strengths with the following quantity limits:**
   - **50mg powder (GPID 37028): 4 vials per 21 days.**
   - **100mg/4mL (GPID 37754): 8mL per 21 days.**

   If no, continue to #8.

8. Does the patient have a diagnosis of metastatic non-small cell lung cancer (NSCLC) **AND** meet **ALL** of the following criteria?
   - The medication will be given as a single agent (i.e., not in combination with chemotherapy)
   - NSCLC tumors express programmed death-ligand (PD-L1) [Tumor Proportion Score (TPS) ≥1%] as determined by an FDA-approved test
   - The patient has an epidermal growth factor receptor (EGFR) genomic tumor aberration
   - Disease progression on or after treatment with **ALL** of the following:
     - o Platinum-containing chemotherapy (e.g., cisplatin, carboplatin, oxaliplatin)
     - o EGFR-directed therapy [e.g., Tarceva (erlotinib), Iressa (gefitinib), Gilotrif (afatinib)]

   If yes, **approve for 12 months by GPID for all strengths with the following quantity limits:**
   - **50mg powder (GPID 37028): 4 vials per 21 days.**
   - **100mg/4mL (GPID 37754): 8mL per 21 days.**

   If no, continue to #9.

9. Does the patient have a diagnosis of recurrent or metastatic head and neck squamous cell carcinoma (HNSCC) **AND** meets the following criterion?
   - Disease progression on or after treatment a with platinum-containing chemotherapy (e.g., cisplatin, carboplatin, oxaliplatin)

   If yes, **approve for 12 months by GPID for all strengths with the following quantity limits:**
   - **50mg powder (GPID 37028): 4 vials per 21 days.**
   - **100mg/4mL (GPID 37754): 8mL per 21 days.**

   If no, continue to #10.

CONTINUED ON NEXT PAGE

PEMBROLIZUMAB (NSA)

GUIDELINES FOR USE (CONTINUED)

10. Does the patient have a diagnosis of classical Hodgkin Lymphoma (cHL) **AND** meet **ONE** of the following criteria?
    - The patient has refractory classical Hodgkin Lymphoma (cHL)
    - The patient has relapsed after 3 or more prior lines of therapy

    If yes, **approve for 12 months by GPID for all strengths with the following quantity limits:**
    - **50mg powder (GPID 37028): 4 vials per 21 days.**
    - **100mg/4mL (GPID 37754): 8mL per 21 days.**

    If no, continue to #11.

11. Does the patient have a diagnosis of primary mediastinal large B-cell lymphoma (PMBCL) **AND** meet **ONE** of the following criteria?
    - The patient has refractory PMBCL
    - The patient has relapsed after 2 or more prior lines of therapy

    If yes, **approve for 12 months by GPID for all strengths with the following quantity limits:**
    - **50mg powder (GPID 37028): 4 vials per 21 days.**
    - **100mg/4mL (GPID 37754): 8mL per 21 days.**

    If no, continue to #12.

12. Does the patient have a diagnosis of locally advanced or metastatic urothelial carcinoma **AND** meet **ONE** of the following criteria?
    - Have disease progression during or after treatment with platinum-containing chemotherapy (e.g., cisplatin, carboplatin, oxaliplatin)
    - Have disease progression within 12 months of neoadjuvant or adjuvant treatment with platinum-containing chemotherapy (e.g., cisplatin, carboplatin, oxaliplatin)
    - The patient is not eligible to receive cisplatin-containing chemotherapy and patient's tumors express PD-L1 [Combined Positive Score (CPS) ≥ 10] as determined by an FDA approved test
    - The patient is not eligible for any platinum-containing chemotherapy regardless of PD-L1 status

    If yes, **approve for 12 months by GPID for all strengths with the following quantity limits:**
    - **50mg powder (GPID 37028): 4 vials per 21 days.**
    - **100mg/4mL (GPID 37754): 8mL per 21 days.**

    If no, continue to #13.

CONTINUED ON NEXT PAGE

PEMBROLIZUMAB (NSA)

GUIDELINES FOR USE (CONTINUED)

13. Does the patient have a diagnosis of an unresectable or metastatic tumor that is microsatellite instability-high (MSI-H) or mismatch repair deficient **AND** meet **ONE** of the following criteria?
    - The patient has a solid tumor that has progressed following prior treatment and has no satisfactory alternative treatment options
    - The patient has colorectal cancer that has progressed following treatment with a fluoropyrimidine, oxaliplatin, and irinotecan

    If yes, **approve for 12 months by GPID for all strengths with the following quantity limits:**
    - **50mg powder (GPID 37028): 4 vials per 21 days.**
    - **100mg/4mL (GPID 37754): 8mL per 21 days.**

    If no, continue to #14.

14. Does the patient have a diagnosis of recurrent locally advanced or metastatic gastric or gastroesophageal junction adenocarcinoma **AND** meet **ALL** of the following criteria?
    - The patient has tumors that express PD-L1 [Combined Positive Score (CPS) ≥1] as determined by an FDA-approved test
    - Have disease progression on or after two or more prior lines of therapy including fluoropyrimidine- and platinum-containing chemotherapy and if appropriate, HER2/neu-targeted therapy

    If yes, **approve for 12 months by GPID for all strengths with the following quantity limits:**
    - **50mg powder (GPID 37028): 4 vials per 21 days.**
    - **100mg/4mL (GPID 37754): 8mL per 21 days.**

    If no, continue to #15.

15. Does the patient have a diagnosis of recurrent or metastatic cervical cancer **AND** meet **ALL** of the following criteria?
    - The patient has disease progression on or after chemotherapy
    - The patient has tumors that express PD-L1 [Combined Positive Score (CPS) ≥1] as determined by an FDA-approved test

    If yes, **approve for 12 months by GPID for all strengths with the following quantity limits:**
    - **50mg powder (GPID 37028): 4 vials per 21 days.**
    - **100mg/4mL (GPID 37754): 8mL per 21 days.**

    If no, continue to #16.

CONTINUED ON NEXT PAGE

PEMBROLIZUMAB (NSA)

GUIDELINES FOR USE (CONTINUED)

16. Does the patient have a diagnosis of hepatocellular carcinoma (HCC) AND meet the following criterion?
    - The patient has previously been treated with sorafenib

    If yes, **approve for 12 months by GPID for all strengths with the following quantity limits:**
    - **50mg powder (GPID 37028): 4 vials per 21 days.**
    - **100mg/4mL (GPID 37754): 8mL per 21 days.**

    If no, continue to #17.

17. Does the patient have a diagnosis of recurrent locally advanced or metastatic Merkel cell carcinoma?

    If yes, **approve for 12 months by GPID for all strengths with the following quantity limits:**
    - **50mg powder (GPID 37028): 4 vials per 21 days.**
    - **100mg/4mL (GPID 37754): 8mL per 21 days.**

    If no, do not approve.

    DENIAL TEXT: The guideline named **PEMBROLIZUMAB (Keytruda)** requires a diagnosis of unresectable or metastatic melanoma, melanoma with involvement of lymph node(s) following complete resection, metastatic non-small cell lung cancer (NSCLC), recurrent or metastatic head and neck squamous cell carcinoma (HNSCC), classical Hodgkin Lymphoma (cHL), locally advanced or metastatic urothelial carcinoma, unresectable or metastatic tumor that is microsatellite instability-high (MSI-H) or mismatch repair deficient, recurrent locally advanced or metastatic gastric or gastroesophageal junction adenocarcinoma, recurrent or metastatic cervical cancer, primary mediastinal large B-cell lymphoma (PMBCL), hepatocellular carcinoma (HCC), or recurrent locally advanced or metastatic Merkel cell carcinoma. The following criteria must also be met:

    For patients with a diagnosis of melanoma with involvement of lymph node(s) following complete resection, approval requires:
    - The requested medication will be used as adjuvant treatment

    For patients with metastatic non-small cell lung cancer (NSCLC), approval requires:
    - *For patients who have not received prior systemic chemotherapy treatment for metastatic NSCLC:*
        - *For patients receiving pembrolizumab in combination with pemetrexed and platinum chemotherapy, approval also requires:*
            - The tumor is classified as nonsquamous (e.g., adenocarcinoma, large cell carcinoma)
            - The patient does not have anaplastic lymphoma kinase (ALK) or epidermal growth factor receptor (EGFR) genomic tumor aberrations

    (Denial text continued on next page)

CONTINUED ON NEXT PAGE

PEMBROLIZUMAB (NSA)

GUIDELINES FOR USE (CONTINUED)

- *For patients receiving pembrolizumab in combination with carboplatin and either paclitaxel or nab-paclitaxel, approval also requires:*
  - The tumor is classified as squamous
- *For patients receiving pembrolizumab as a single agent (i.e. not with chemotherapy), approval also requires:*
  - NSCLC tumors have high programmed death-ligand (PD-L1) expression [Tumor Proportion Score (TPS) ≥50%] as determined by an FDA-approved test
  - The patient does not have anaplastic lymphoma kinase (ALK) or epidermal growth factor receptor (EGFR) genomic tumor aberrations

- *For patients who have received prior systemic treatment for metastatic NSCLC and are receiving pembrolizumab as a single agent (i.e., not with chemotherapy), approval also requires:*
  - NSCLC tumors express programmed death-ligand (PD-L1) [Tumor Proportion Score (TPS) ≥1%] as determined by an FDA-approved test
  - For *patients who do not have anaplastic lymphoma kinase (ALK) or epidermal growth factor receptor (EGFR) genomic tumor aberrations, approval also requires:*
    - Disease progression on or after treatment with platinum-containing chemotherapy (e.g., cisplatin, carboplatin, oxaliplatin)
  - *For patients who have anaplastic lymphoma kinase (ALK) genomic tumor aberrations, approval also requires:*
    - Disease progression on or after treatment with ALK-directed therapy [e.g., Xalkori (crizotinib), Zykadia (ceritinib)] and with platinum-containing chemotherapy (e.g., cisplatin, carboplatin, oxaliplatin)
  - *For patients who have epidermal growth factor receptor (EGFR) genomic tumor aberrations, approval also requires:*
    - Disease progression on or after treatment with EGFR-directed therapy [e.g., Tarceva (erlotinib), Iressa (gefitinib), Gilotrif (afatinib)] and with platinum-containing chemotherapy (e.g., cisplatin, carboplatin, oxaliplatin)

For patients with recurrent or metastatic head and neck squamous cell carcinoma (HNSCC), approval requires:

- Disease progression on or after treatment with a platinum-containing chemotherapy (e.g., cisplatin, carboplatin, oxaliplatin)

For patients with classical Hodgkin Lymphoma (cHL), approval requires ONE of the following:

- The patient has refractory classical Hodgkin Lymphoma (cHL)
- The patient has relapsed after 3 or more prior lines of therapy

For patients with primary mediastinal large B-cell lymphoma (PMBCL), approval requires ONE of the following:

- The patient has refractory PMBCL
- The patient has relapsed after 2 or more prior lines of therapy

(Denial text continued on next page)

CONTINUED ON NEXT PAGE

PEMBROLIZUMAB (NSA)

GUIDELINES FOR USE (CONTINUED)

For patients with locally advanced or metastatic urothelial carcinoma, approval requires ONE of the following:

- Disease progression during or after treatment with platinum-containing chemotherapy (e.g., cisplatin, carboplatin, oxaliplatin)
- Disease progression within 12 months of neoadjuvant or adjuvant treatment with platinum-containing chemotherapy (e.g. cisplatin, carboplatin, oxaliplatin)
- The patient is not eligible to receive cisplatin-containing chemotherapy and patient's tumors express PD-L1 [Combined Positive Score (CPS) ≥ 10] as determined by an FDA approved test
- The patient is not eligible for any platinum-containing chemotherapy regardless of PD-L1 status

For patients with unresectable or metastatic tumor that is microsatellite instability-high (MSI-H) or mismatch repair deficient, approval requires one of the following:

- The patient has a solid tumor that has progressed following prior treatment and has no satisfactory alternative treatment options
- The patient has colorectal cancer that has progressed following treatment with a fluoropyrimidine, oxaliplatin, and irinotecan

For patients with recurrent locally advanced or metastatic gastric or gastroesophageal junction adenocarcinoma, approval requires ALL of the following:

- The patient has tumors that express PD-L1 [Combined Positive Score (CPS) ≥1] as determined by an FDA-approved test
- Have disease progression on or after two or more prior lines of therapy including fluoropyrimidine- and platinum-containing chemotherapy and if appropriate, HER2/neu-targeted therapy

For patients with recurrent or metastatic cervical cancer, approval requires:

- The patient has disease progression on or after chemotherapy
- The patient has tumors that express PD-L1 [Combined Positive Score (CPS) ≥1] as determined by an FDA-approved test

For patients with hepatocellular carcinoma, approval requires:

- The patient has previously been treated with sorafenib

RATIONALE

For further information, please refer to the Prescribing Information and/or Drug Monograph for Keytruda.

REFERENCES

- Keytruda [Prescribing Information]. Whitehouse Station, NJ: Merck & Co, Inc.; February 2019.

Library	Commercial	NSA
Yes	No	Yes

CONTINUED ON NEXT PAGE

PEMBROLIZUMAB (NSA)

Part D Effective: N/A
Commercial Effective: 03/18/19
Created: 09/14
Client Approval: 03/19
P&T Approval: 01/19

PEMETREXED (NSA)

Generic	Brand	HICL	GCN	Exception/Other
PEMETREXED DISODIUM	ALIMTA	25905		

This drug requires a written request for prior authorization.

GUIDELINES FOR USE

1. Does the patient have a diagnosis of locally advanced or metastatic, non-squamous, non-small cell lung cancer (NSCLC) and meet **ONE** of the following criteria?
   - The requested medication is being used in combination with cisplatin for initial treatment
   - The requested medication is being used as a single agent, maintenance therapy and meet the following:
     - The patient's disease has not progressed after four cycles of platinum-based first-line chemotherapy

   If yes, **approve for 12 months by HICL.**
   If no, continue to #2.

2. Does the patient have a diagnosis of metastatic, non-squamous, non-small cell lung cancer (NSCLC) and meet **ALL** of the following criteria?
   - The requested medication is being used for initial treatment
   - The requested medication is being used in combination with pembrolizumab and platinum chemotherapy
   - The patient does not have EGFR or ALK genomic tumor aberrations

   If yes, **approve for 12 months by HICL.**
   If no, continue to #3.

3. Does the patient have a diagnosis of recurrent, metastatic non-squamous, non-small cell lung cancer (NSCLC) and meet **ALL** of the following criteria?
   - The requested medication is being used as a single agent
   - The patient has received prior chemotherapy

   If yes, **approve for 12 months by HICL.**
   If no, continue to #4.

CONTINUED ON NEXT PAGE

PEMETREXED (NSA)

GUIDELINES FOR USE (CONTINUED)

4. Does the patient have a diagnosis of malignant pleural mesothelioma and meet **ALL** of the following criteria?
   - The requested medication is being used in combination with cisplatin for initial treatment
   - The patient's disease is unresectable **OR** the patient is not a candidate for curative surgery

   If yes, **approve for 12 months by HICL.**
   If no, do not approve.
   DENIAL TEXT: The guideline named **PEMETREXED (Alimta)** requires ONE of the following diagnoses and related criteria to be met:
   For diagnosis of locally advanced or metastatic, non-squamous, non-small cell lung cancer (NSCLC) approval requires ONE of the following:
   - The requested medication is being used in combination with cisplatin for initial treatment
   - The requested medication is being used as a single agent, maintenance therapy and meet the following:
     - The patient's disease has not progressed after four cycles of platinum-based first-line chemotherapy

   For diagnosis of metastatic, non-squamous, non-small cell lung cancer (NSCLC) approval requires:
   - The requested medication is being used for initial treatment
   - The requested medication is being used in combination with pembrolizumab and platinum chemotherapy
   - The patient does not have EGFR or ALK genomic tumor aberrations

   For diagnosis of recurrent, metastatic non-squamous, non-small cell lung cancer (NSCLC), approval requires:
   - The requested medication is being used as a single agent
   - The patient has received prior chemotherapy

   For diagnosis of malignant pleural mesothelioma, approval requires:
   - The requested medication is being used in combination with cisplatin for initial treatment
   - The patient's disease is unresectable OR the patient is not a candidate for curative surgery

RATIONALE
For further information, please refer to the Prescribing Information and/or Drug Monograph for Alimta.

REFERENCES

- Alimta [Prescribing Information]. Indianapolis, IN: Eli Lilly and Company. January 2019.

Library	Commercial	NSA
Yes	No	Yes

Part D Effective: N/A
Commercial Effective: 02/25/19
Created: 11/13
Client Approval: 02/19
P&T Approval: 07/18

PERTUZUMAB (NSA)

Generic	Brand	HICL	GCN	Exception/Other
PERTUZUMAB	PERJETA	39102		

This drug requires a written request for prior authorization.

GUIDELINES FOR USE

1. Does the patient have a diagnosis of metastatic breast cancer and meet **ALL** of the following criteria?
   - The patient's breast cancer is HER2- positive
   - The patient has not received prior therapy with an anti-HER2 agent or chemotherapy for metastatic disease
   - The requested medication will be used in combination with trastuzumab and docetaxel; (**PAC NOTE:** The patient must have an active prior authorization for trastuzumab [Herceptin] before proceeding)

   If yes, **please enter two approvals as follows:**
   - **Approve for 1 month by HICL for #28mL (two 420mg/14mL) vials per 21 days.**
   - **Approve for 11 months by HICL for #14mL (one 420mg/14mL) vial per 21 days with a start date of 22 days post the first approval start date.**

   If no, continue to #2.

2. Does the patient have a diagnosis of locally advanced, inflammatory, or early stage breast cancer (either greater than 2 cm in diameter or node positive) and meet ALL of the following criteria?
   - The patient's breast cancer is HER2- positive
   - The requested medication will be used in the neoadjuvant setting
   - The requested medication will be used in combination with trastuzumab and chemotherapy as part of a complete treatment regimen for early breast cancer; **(PAC NOTE:** The patient must have an active prior authorization for trastuzumab [Herceptin] before proceeding)

   If yes, **please enter two approvals as follows:**
   - **Approve for 1 month by HICL for #28mL (two 420mg/14mL) vials per 21 days.**
   - **Approve for 5 months by HICL for #14mL (one 420mg/14mL) vial per 21 days with a start date of 22 days post the first approval start date.**

   If no, continue to #3.

CONTINUED ON NEXT PAGE

PERTUZUMAB (NSA)

GUIDELINES FOR USE (CONTINUED)

3. Does the patient have a diagnosis of early breast cancer and meet **ALL** of the following criteria?
   - The patient's breast cancer is HER2- positive
   - The patient is at a high risk of recurrence
   - The requested medication will be used in the adjuvant setting
   - The requested medication will be used in combination with trastuzumab and chemotherapy; **(PAC NOTE:** The patient must have an active prior authorization for trastuzumab [Herceptin] before proceeding)

   If yes, **please enter two approvals as follows:**
   - **Approve for 1 month by HICL for #28mL (two 420mg/14mL) vials per 21 days.**
   - **Approve for 11 months by HICL for #14mL (one 420mg/14mL) vial per 21 days with a start date of 22 days post the first approval start date.**

   If no, do not approve.
   DENIAL TEXT: The guideline named **PERTUZUMAB (Perjeta)** requires a diagnosis of HER2-positive metastatic breast cancer, OR HER2- positive locally advanced, inflammatory, or early stage breast cancer (either greater than 2 cm in diameter or node positive), OR HER2- positive early breast cancer. In addition, the following criteria must be met:
   For the diagnosis of metastatic breast cancer, approval requires:
   - The patient has not received prior therapy with an anti-HER2 agent or chemotherapy for metastatic disease
   - The requested medication will be used in combination with trastuzumab and docetaxel

   For the diagnosis of locally advanced, inflammatory, or early stage breast cancer (either greater than 2 cm in diameter or node positive), approval requires:
   - The requested medication will be used in the neoadjuvant setting
   - The requested medication will be used in combination with trastuzumab and chemotherapy as part of a complete treatment regimen for early breast cancer

   For the diagnosis of early breast cancer, approval requires:
   - The patient is at a high risk of recurrence
   - The requested medication will be used in the adjuvant setting
   - The requested medication will be used in combination with trastuzumab and chemotherapy

RATIONALE
To promote appropriate utilization of Perjeta based on FDA approved indication.

CONTINUED ON NEXT PAGE

PERTUZUMAB (NSA)

FDA APPROVED INDICATIONS

Perjeta is a HER2/neu receptor antagonist indicated for:

- Use in combination with trastuzumab and docetaxel for the treatment of patients with HER2-positive metastatic breast cancer (MBC) who have not received prior anti-HER2 therapy or chemotherapy for metastatic disease.
- Use in combination with trastuzumab and chemotherapy as:
  - Neoadjuvant treatment of patients with HER2-positive, locally advanced, inflammatory, or early stage breast cancer (either greater than 2 cm in diameter or node positive) as part of a complete treatment regimen for early breast cancer.
  - Adjuvant treatment of patients with HER2-positive early breast cancer at high risk of recurrence.

DOSAGE AND ADMINISTRATION

The initial dose of Perjeta is 840 mg administered as a 60-minute intravenous infusion, followed every 3 weeks by a dose of 420 mg administered as an intravenous infusion over 30 to 60 minutes.

Metastitic Breast Cancer

When administered with Perjeta, the recommended initial dose of docetaxel is 75 mg/m2 administered as an intravenous infusion. The dose may be escalated to 100 mg/m2 administered every 3 weeks if the initial dose is well tolerated.

Neoadjuvant Treatment of Breast Cancer

Perjeta should be administered every 3 weeks for 3 to 6 cycles as part of one of the following treatment regimens for early breast cancer.

- Four preoperative cycles of Perjeta in combination with trastuzumab and docetaxel followed by 3 postoperative cycles of fluorouracil, epirubicin, and cyclophosphamide (FEC) as given in NeoSphere.
- Three or four preoperative cycles of FEC alone followed by 3 or 4 preoperative cycles of Perjeta in combination with docetaxel and trastuzumab as given in TRYPHAENA and BERENICE, respectively.
- Six preoperative cycles of Perjeta in combination with docetaxel, carboplatin, and trastuzumab (TCH) (escalation of docetaxel above 75 mg/m2 is not recommended) as given in TRYPHAENA.
- Four preoperative cycles of dose-dense doxorubicin and cyclophosphamide (ddAC) alone followed by 4 preoperative cycles of Perjeta in combination with paclitaxel and trastuzumab as given in BERENICE Following surgery, patients should continue to receive Perjeta and trastuzumab to complete 1 year of treatment (up to 18 cycles).

CONTINUED ON NEXT PAGE

PERTUZUMAB (NSA)

FDA APPROVED INDICATIONS (CONTINUED)

DOSAGE AND ADMINISTRATION

Adjuvant Treatment of Breast Cancer

Perjeta should be administered in combination with trastuzumab every 3 weeks for a total of 1 year (up to 18 cycles) or until disease recurrence or unmanageable toxicity, whichever occurs first, as part of a complete regimen for early breast cancer, including standard anthracyclineand/or taxane-based chemotherapy as given in APHINITY. Perjeta and trastuzumab should start on Day 1 of the first taxane-containing cycle.

Patients should be selected based on HER2 protein overexpression or HER2 gene amplification in tumor specimens. Assessment of HER2 protein overexpression and HER2 gene amplification should be performed using FDA-approved tests specific for breast cancer by laboratories with demonstrated proficiency.

For delayed or missed doses, if the time between two sequential infusions is less than 6 weeks, the 420 mg dose of Perjeta should be administered. Do not wait until the next planned dose. If the time between two sequential infusions is 6 weeks or more, the initial dose of 840 mg Perjeta should be re-administered as a 60-minute intravenous infusion followed every 3 weeks thereafter by a dose of 420 mg administered as an intravenous infusion over 30 to 60 minutes. Perjeta should be discontinued if trastuzumab treatment is discontinued. Dose reductions are not recommended for Perjeta.

REFERENCES

- Genentech, Inc. Perjeta package insert. South San Francisco, CA. December 2017.

Library	Commercial	NSA
Yes	No	Yes

Part D Effective: N/A
Commercial Effective: 01/15/18
Created: 08/12
Client Approval: 12/17
P&T Approval: 01/18

PLERIXAFOR

Generic	Brand	HICL	GCN	Exception/Other
PLERIXAFOR	MOZOBIL	36021		

This drug requires a written request for prior authorization.

GUIDELINES FOR USE

1. Is the prescription written or currently being supervised by a hematologist or an oncologist?

   If yes, continue to #2.
   If no, do not approve.
   DENIAL TEXT: Approval requires initiation or supervision by a hematologist or an oncologist and a diagnosis of non-Hodgkin's lymphoma or multiple myeloma.

2. Is the patient diagnosed with non-Hodgkin's lymphoma or multiple myeloma?

   If yes, continue to #3.
   If no, do not approve.
   DENIAL TEXT: Approval requires initiation or supervision by a hematologist or an oncologist and a diagnosis of non-Hodgkin's lymphoma or multiple myeloma.

3. Is the request for more than 4 vials?

   If yes, obtain patient's weight in kg and **approve for one fill with the following quantity limits:**
   - **IF GREATER THAN 100kg: up to #8 vials (24mg/1.2mL) for 1 day supply.**
   - **IF LESS THAN OR EQUAL TO 100kg: up to #4 vials (24mg/1.2mL) for 1 day supply.**

   If no, **approve for one fill up to #4 vials (24mg/1.2mL) for 1 day supply.**

RATIONALE
Ensure appropriate utilization based on FDA approved indication.

FDA APPROVED INDICATIONS
Plerixafor is indicated in combination with granulocyte-colony stimulating factor (G-CSF) to mobilize hematopoietic stem cells to the peripheral blood for collection and subsequent autologous transplantation in patients with non-Hodgkin's lymphoma and multiple myeloma.

CONTINUED ON NEXT PAGE

PLERIXAFOR

REFERENCES

- Genzyme Corporation. Mozobil package insert, Cambridge, Massachusetts, April 2010.
- Stewart DA, Smith C, et al. Pharmacokinetics and pharmacodynamics of plerixafor in patients with non-Hodgkin lymphoma and multiple myeloma. Biol Blood Marrow Transplant. 2009 Jan; 15(1):39-46.
- Stiff P, Micallef I, et al. Treatment with plerixafor in non-Hodgkin's lymphoma and multiple myeloma patients to increase the number of peripheral blood stem cells when given a mobilizing regimen of G-CSF: implications for the heavily pretreated patient. Biol Blood Marrow Transplant. 2009 Feb; 15(2):249-56.
- Thomson Healthcare. Monograph Name. DRUGDEX® System [database online]. Greenwood Village, CO. Available at: https://www.thomsonhc.com/hcs/librarian/PFDefaultActionId/pf.LoginAction. [Accessed: June 27, 2011].

Library	Commercial	NSA
Yes	No	Yes

Part D Effective: N/A
Commercial Effective: 01/01/14
Created: 02/09
Client Approval: 11/13
P&T Approval: 11/13

PORFIMER

Generic	Brand	HICL	GCN	Exception/Other
PORFIMER SODIUM	PHOTOFRIN	11790		

This drug requires a written request for prior authorization.

GUIDELINES FOR USE

1. Is the requested medication being used for the reduction of obstruction and palliation of symptoms in patients with completely or partially obstructing endobronchial non-small cell lung cancer (NSCLC)?

   If yes, **approve once by HICL.**
   If no, continue to #2.

2. Is the requested medication being used for the treatment of microinvasive endobronchial non-small cell lung cancer (NSCLC) in patients for whom surgery and radiotherapy are not indicated?

   If yes, **approve once by HICL.**
   If no, continue to #3.

3. Is the requested medication being used for the palliation of patients with completely obstructing esophageal cancer, or of patients with partially obstructing esophageal cancer who, in the opinion of their physician, cannot be satisfactorily treated with Nd:YAG laser therapy?

   If yes, **approve once by HICL.**
   If no, continue to #4.

4. Is the requested medication being used for the ablation of high-grade dysplasia in Barrett's esophagus patients who do not undergo esophagectomy?

   If yes, **approve once by HICL.**
   If no, do not approve.
   DENIAL TEXT: Approval requires that requested medication is being used for, 1) the reduction of obstruction and palliation of symptoms in patients with completely or partially obstructing endobronchial non-small cell lung cancer (NSCLC) or, 2) treatment of microinvasive endobronchial non small cell lung cancer (NSCLC) in patients for whom surgery and radiotherapy are not indicated or, 3) the palliation of patients with completely obstructing esophageal cancer, or of patients with partially obstructing esophageal cancer who, in the opinion of their physician, cannot be satisfactorily treated with Nd:YAG laser therapy or, 4) the ablation of high-grade dysplasia in Barrett's esophagus patients who do not undergo esophagectomy.

CONTINUED ON NEXT PAGE

PORFIMER

RATIONALE

Based on FDA approved indications. Photofrin is indicated for reduction of obstruction and palliation of symptoms in patients with completely or partially obstructing endobronchial NSCLC; treatment of microinvasive endobronchial NSCLC in patients for whom surgery and radiotherapy are not indicated; palliation of patients with completely obstructing esophageal cancer, or of patients with partially obstructing esophageal cancer who, in the opinion of their physician, cannot be satisfactorily treated with Nd:YAG laser therapy; and ablation of high-grade dysplasia in Barrett's esophagus patients who do not undergo esophagectomy.

Photofrin versus Nd: YAG Laser Therapy: Endobronchial NSCLC

Two randomized studies were conducted to compare Photofrin versus Nd:YAG laser therapy for reduction of obstruction and palliation of symptomatic patients with partially or completely obstructing endobronchial NSCLC. A course of therapy consisted of one injection of Photofrin (2 mg/kg administered as a slow intravenous injection over 3–5 minutes) followed by up to two nonthermal applications of 630 nm laser light. Assessments were made at one week and at monthly intervals after treatment. Objective tumor response rates (CR + PR), which demonstrate reduction of obstruction, were 59 percent for PDT and 58 percent for Nd:YAG at Week 1. The response rate at 1 month or later was 60 percent for PDT and 41 percent for Nd:YAG.

From Photofrin Prescribing Information

TABLE 11. Efficacy Results from Studies in Late-stage Obstructing Endobronchial Cancer – All Randomized Patients[a]

EFFICACY PARAMETER	PDT N=102 % Patients	Nd:YAG N=109 % Patients
OBJECTIVE TUMOR RESPONSE[b]		
Week 1	59%	58%
Month 1 or later	60%	41%[a]
ATELECTASIS IMPROVEMENT[c]	n=60	N=71
Week 1	35%	18%
Month 1 or later	35%	20%

[a] Statistical comparisons were precluded by the amount of missing data at Month 1 or later (e.g., for tumor response, PDT 28% missing, Nd:YAG 38%).

[b] CR+PR where CR = complete response (absence of bronchoscopically visible tumor) and PR = partial response (increase of ≥50% in the smallest luminal diameter; or any appearance of a lumen for completely obstructing tumors).

[c] In patients with atelectasis at baseline.

CONTINUED ON NEXT PAGE

PORFIMER

FDA APPROVED INDICATIONS

Photofrin is a photodynamic therapy drug indicated for:

Esophageal Cancer

- Palliation of patients with completely obstructing esophageal cancer, or of patients with partially obstructing esophageal cancer who, in the opinion of their physician, cannot be satisfactorily treated with Nd:YAG laser therapy

Endobronchial Cancer

- Treatment of microinvasive endobronchial non-small-cell lung cancer (NSCLC) in patients for whom surgery and radiotherapy are not indicated
- Reduction of obstruction and palliation of symptoms in patients with completely or partially obstructing endobronchial NSCLC

High-Grade Dysplasia in Barrett's Esophagus

- Ablation of high-grade dysplasia (HGD) in Barrett's esophagus (BE) patients who do not undergo esophagectomy

REFERENCES

- Axcan Scandipharm Inc. Photofrin (porfimer sodium) for Injection Prescribing Information. Drugs at FDA. [Online] June 2011. [Cited: October 14, 2013.] **HTTP://WWW.ACCESSDATA.FDA.GOV/SCRIPTS/CDER/DRUGSATFDA/**

Library	Commercial	NSA
Yes	No	Yes

Part D Effective: N/A
Commercial Effective: 01/01/14

Created: 11/13
Client Approval: 11/13

P&T Approval: 11/13

PRALATREXATE (NSA)

Generic	Brand	HICL	GCN	Exception/Other
PRALATREXATE	FOLOTYN	36644		

GUIDELINES FOR USE

1. Will the requested medication be used for the treatment of a patient with relapsed or refractory peripheral T-cell lymphoma (PTCL)?

   If yes, **approve for 12 months by HICL.**
   If no, do not approve.
   DENIAL TEXT: The guideline for **PRALATREXATE (Folotyn)** requires a diagnosis of relapsed or refractory peripheral T-cell lymphoma (PTCL).

RATIONALE
Promote appropriate utilization of **PRALATREXATE** based on FDA approved indication.

DOSAGE
The recommended dose of Folotyn is 30 mg/m^2 administered as an intravenous push over 3-5 minutes via the side port of a free-flowing 0.9% Sodium Chloride Injection, intravenous line once weekly for 6 weeks in 7-week cycles until progressive disease or unacceptable toxicity. The calculated dose of Folotyn should be aseptically withdrawn into a syringe for immediate use. Do not dilute Folotyn.

For patients with severe renal impairment (eGFR 15 to < 30 mL/min/1.73 m^2), the recommended dose of Folotyn is 15 mg/m^2.

FDA APPROVED INDICATION
Folotyn is indicated for the treatment of patients with relapsed or refractory peripheral T-cell lymphoma (PTCL). This indication is based on overall response rate. Clinical benefit such as improvement in progression-free survival or overall survival has not been demonstrated.

REFERENCES

- Folotyn [Prescribing Information]. Westminster, CO: Spectrum Pharmaceuticals. May 2016.

Library	Commercial	NSA
Yes	No	Yes

Part D Effective: N/A
Commercial Effective: 10/01/16
Created: 08/16
Client Approval: 08/16
P&T Approval: 08/16

RAMUCIRUMAB

Generic	Brand	HICL	GCN	Exception/Other
RAMUCIRUMAB	CYRAMZA	41109		

GUIDELINES FOR USE

1. Does the patient have a diagnosis of advanced gastric cancer or gastro-esophageal junction adenocarcinoma and meets the following criteria?
   - The patient has tried or has a contraindication to fluoropyrimidine-containing chemotherapy (fluorouracil [5-FU], capecitabine, floxuridine) **OR** platinum-containing chemotherapy (cisplatin, oxaliplatin, carboplatin)

   If yes, **approve for 12 months by HICL.**
   If no, continue to #2.

2. Does the patient have a diagnosis metastatic non-small cell lung cancer and meets the following criteria?
   - The patient has tried platinum-based chemotherapy (cisplatin, oxaliplatin, carboplatin) **OR**
   - The patient has an EGFR or ALK genomic tumor aberration and has failed a prior FDA approved therapy for EGFR or ALK genomic tumor aberration (examples include Tarceva, Gilotrif, Xalkori, or Zykadia)

   If yes, **approve for 12 months by HICL.**
   If no, continue to #3.

3. Does the patient have a diagnosis of metastatic colorectal cancer and meets the following criteria?
   - The patient has tried bevacizumab, oxaliplatin, and a fluoropyrimidine (i.e., 5-fluorouracil, capecitabine) **AND**
   - Cyramza will be used in combination with FOLFIRI (irinotecan, folinic acid, and 5-fluorouracil)

   If yes, **approve for 12 months by HICL.**
   If no, do not approve.
   DENIAL TEXT: See the denial text at the end of the guideline.

CONTINUED ON NEXT PAGE

RAMUCIRUMAB

GUIDELINE FOR USE (CONTINUED)

DENIAL TEXT: Our guideline for **RAMUCIRUMAB** requires that the patient has a diagnosis of gastric cancer or gastro-esophageal junction adenocarcinoma, metastatic non-small cell lung cancer, or metastatic colorectal cancer. Additional guideline requirements apply.

For the diagnosis of advanced gastric cancer or gastro-esophageal junction adenocarcinoma, approval requires:

- The patient has tried or has a contraindication to fluoropyrimidine-containing chemotherapy (fluorouracil [5-FU], capecitabine, floxuridine) **OR** platinum-containing chemotherapy (cisplatin, oxaliplatin, carboplatin)

For the diagnosis of metastatic non-small cell lung cancer, approval requires:

- The patient has tried platinum-based chemotherapy (cisplatin, oxaliplatin, carboplatin) **OR**
- The patient has an EGFR or ALK genomic tumor aberration and has failed a prior FDA approved therapy for EGFR or ALK genomic tumor aberration (examples include Tarceva, Gilotrif, Xalkori, or Zykadia)

For the diagnosis of metastatic colorectal cancer, approval requires:

- The patient has tried bevacizumab, oxaliplatin, and a fluoropyrimidine (i.e., 5-fluorouracil, capecitabine) **AND**
- Cyramza will be used in combination with FOLFIRI (irinotecan, folinic acid, and 5-fluorouracil)

RATIONALE

Promote clinically appropriate utilization of Cyramza (ramucirumab) based on its FDA approved indication.

Gastric Cancer

Cyramza is the first targeted therapy to secure regulatory approval for patients with advanced or metastatic gastric or gastro-esophageal cancer who have progressed on or following fluoropyrimidine- or platinum-containing chemotherapy. Cyramza provides a chemotherapy-free treatment option by instead targeting blood vessel growth. Elevated serum and tumor levels of vascular endothelial growth factor (VEGF) have also been associated with a poor prognosis in patients with resectable gastric cancer.

There is currently no biomarker that suggests which patients are most likely to benefit from Cyramza; however, it is possible that Cyramza may be used in HER2-negative gastric cancer as well as patients unable to tolerate chemotherapy. The drug's ability to improve survival when administered as a single agent and its modest side effect profile distinguishes it from a multitude of other targeted agents that have proven ineffective in this setting.

CONTINUED ON NEXT PAGE

RAMUCIRUMAB

RATIONALE (CONTINUED)
Non-Small Cell Lung Cancer (NSCLC)
Epidermal growth factor receptor (EGFR) is normally found on the surface of epithelial cells and is often overexpressed in a variety of human malignancies. The prevalence of EGFR mutations in adenocarcinomas is 10% of Western and up to 50% of Asian patients. Higher EGFR mutation frequency in non-smokers, women, and non-mucinous cancers. Presence of EGFR-activating mutations represents a critical biological determinant for proper therapy selection in patients with lung cancer. There is a significant association between EGFR mutations-especially exon 19 deletion and exon 21, exon 18 and exon 20 mutations and sensitivity to TKIs. The exon 20 insertion mutation may predict resistance to clinically achievable levels of TKIs. Gilotrif (afatinib) and Tarceva (erlotinib) are first-line treatment options for metastatic non–small cell lung cancer in patients whose tumors have EGFR exon 19 deletions or exon 21 substitution mutations as detected by a Food and Drug Administration–approved test.

Anaplastic lymphoma kinase (ALK) gene rearrangements represent the fusion between ALK and various partner genes, including echinoderm microtubule-associated protein-like 4 (EML4). ALK fusions have been identified in a subset of patients with NSCLC and represent a unique subset of patients for whom ALK inhibitors may represent a very effective therapeutic strategy. Xalkori (crizotinib) is an oral ALK inhibitor that is approved by the FDA for patients with metastatic NSCLC who have the ALK gene rearrangement (i.e. ALK positive). Zykadia (ceritinib) is currently approved as for the treatment of patients with anaplastic lymphoma kinase (ALK)–positive metastatic non-small cell lung cancer (NSCLC) who have progressed on or are intolerant to crizotinib. The current standard method for detecting ALK NSCLC is fluorescence in situ hybridization (FISH), although other methods are currently being evaluated, including polymerase chain reaction (PCR) and IHC.

FDA APPROVED INDICATION
Cyramza is a human vascular endothelial growth factor receptor 2 antagonist indicated:
- As a single agent, or in combination with paclitaxel, Cyramza is indicated for the treatment of patients with advanced or metastatic, gastric or gastro-esophageal junction adenocarcinoma with disease progression on or after prior fluoropyrimidine- or platinum-containing chemotherapy.

- In combination with docetaxel, for treatment of metastatic nonsmall cell lung cancer with disease progression on or after platinum-based chemotherapy. Patients with EGFR or ALK genomic tumor aberrations should have disease progression on FDA-approved therapy for these aberrations prior to receiving Cyramza.

CONTINUED ON NEXT PAGE

RAMUCIRUMAB

DOSAGE

Gastric Cancer:
The recommended dose of Cyramza either as a single agent or in combination with weekly paclitaxel is 8 mg/kg every 2 weeks administered as an intravenous infusion over 60 minutes. Continue Cyramza until disease progression or unacceptable toxicity. When given in combination, administer Cyramza prior to administration of paclitaxel.

Non-Small Cell Lung Cancer:
Administer Cyramza at 10 mg/kg intravenously on day 1 of a 21-day cycle prior to docetaxel infusion. Continue Cyramza until disease progression or unacceptable toxicity.

Colorectal cancer:
Administer Cyramza at 8 mg/kg intravenously every 2 weeks, prior to FOLFIRI administration. Continue Cyramza until disease progression or unacceptable toxicity.

REFERENCES

- Cyramza [Prescribing Information]. Eli Lilly and Company: Indianapolis, IN. April 2015.
- UpToDate, Inc. Chemotherapy for locally advanced unresectable and metastatic esophageal and gastric cancer. UpToDate [database online]. Waltham, MA. Available at: http://www.uptodate.com/home/index.html. Updated December 3, 2013.
- NCCN Clinical Practice Guidelines in Oncology. Gastric cancer. Available at: http://www.nccn.org [Accessed May 7, 2014].
- NCCN Clinical Practice Guidelines in Oncology. Non-Small Cell Lung Cancer. Available at: http://www.nccn.org [Accessed December 18, 2014].

Library	Commercial	NSA
Yes	No	Yes

Part D Effective: N/A
Commercial Effective: 07/01/15
Created: 04/14
Client Approval: 05/15
P&T Approval: 05/15

RANIBIZUMAB (NSA)

Generic	Brand	HICL	GCN	Exception/Other
RANIBIZUMAB	LUCENTIS	33861		

This drug requires a written request for prior authorization.

GUIDELINES FOR USE

1. Is this medication being prescribed by an ophthalmologist or retina specialist?

   If yes, continue to #2.
   If no, do not approve.
   DENIAL TEXT: See the denial text at the end of the guideline.

2. Does the patient have one of the following diagnoses?
   - Diabetic macular edema (DME)
   - Diabetic retinopathy (DR)

   If yes, continue to #5.
   If no, continue to #3.

3. Does the patient have one of the following diagnoses?
   - Neovascular (wet) age-related macular degeneration (AMD)
   - Macular edema following retinal vein occlusion (RVO)

   If yes, continue to #6.
   If no, continue to #4.

4. Does the patient have a diagnosis of myopic choroidal neovascularization (mCNV)?

   If yes, continue to #7.
   If no, do not approve.
   DENIAL TEXT: See the denial text at the end of the guideline.

CONTINUED ON NEXT PAGE

RANIBIZUMAB (NSA)

GUIDELINES FOR USE (CONTINUED)

5. Is the patient receiving treatment in both eyes at this time?

   If yes, **approve for 12 months by GPID with the following quantity limits:**
   - **0.3mg/0.05mL prefilled syringe (GPID 44547): #0.1mL (two 0.3mg prefilled syringes) per 4 weeks.**
   - **0.3mg/0.05mL vial (GPID 32959): #0.1mL (two 0.3mg vials) per 4 weeks.**

   If no, and a single eye is being treated, **approve for 12 months by GPID with the following quantity limits:**
   - **0.3mg/0.05mL prefilled syringe (GPID 44547): #0.05mL (one 0.3mg prefilled syringes) per 4 weeks.**
   - **0.3mg/0.05mL (GPID 32959): #0.05mL (one 0.3mg vial) per 4 weeks.**

6. Is the patient receiving treatment in both eyes at this time?

   If yes, **approve for 12 months by GPID (27289 or 37135) with a quantity limit of #0.1mL (two 0.5mg vials or prefilled syringes) per 4 weeks.**
   If no, and a single eye is being treated, **approve for 12 months by GPID (27289 or 37135) with a quantity limit of #0.05mL (one 0.5mg vial or prefilled syringe) per 4 weeks.**

7. Is the patient receiving treatment in both eyes at this time?

   If yes, **approve for 3 months by GPID (27289 or 37135) with a quantity limit of #0.1mL (two 0.5mg vials or prefilled syringes) per 4 weeks.**
   If no, and a single eye is being treated, **approve for 3 months by GPID (27289 or 37135) with a quantity limit of #0.05mL (one 0.5mg vial or prefilled syringe) per 4 weeks.**

DENIAL TEXT: The guideline named **RANIBIZUMAB (Lucentis)** requires a diagnosis of neovascular (wet) age-related macular degeneration (AMD), diabetic macular edema (DME), diabetic retinopathy (DR), macular edema following retinal vein occlusion (RVO), or myopic choroidal neovascularization (mCNV), and that the medication is prescribed by an ophthalmologist or retina specialist.

CONTINUED ON NEXT PAGE

RANIBIZUMAB (NSA)

RATIONALE
To ensure appropriate use of Lucentis consistent with its FDA approved indications and dosing.

FDA APPROVED INDICATIONS
Lucentis, a vascular endothelial growth factor VEGF inhibitor, is indicated for the treatment of patients with:
- Neovascular (Wet) Age-related macular degeneration (AMD)
- Macular Edema following Retinal Vein Occlusion (RVO)
- Diabetic Macular Edema (DME)
- Diabetic Retinopathy
- Myopic Choroidal Neovascularization (mCNV)

DOSAGE AND ADMINISTRATION
- Neovascular (Wet) Age-Related Macular Degeneration (AMD): Lucentis 0.5 mg (0.05 mL) by intravitreal injection once a month (approximately 28 days).
- Macular Edema following Retinal Vein Occlusion (RVO): Lucentis 0.5 mg (0.05 mL) by intravitreal injection once a month (approximately 28 days).
- Diabetic Macular Edema (DME) and Diabetic Retinopathy: Lucentis 0.3 mg (0.05 mL) by intravitreal injection once a month (approximately 28 days).
- Myopic Choroidal Neovascularization (mCNV): Lucentis 0.5 mg (0.05 mL) by intravitreal injection once a month (approximately 28 days) for up to 3 months. Patients may be retreated if needed.

AVAILABLE STRENGTHS
- Single-use vials
  - 10mg/mL solution (Lucentis 0.5 mg)
  - 6mg/mL solution (Lucentis 0.3 mg)
- Single-use prefilled syringe
  - 10mg/mL solution (Lucentis 0.5 mg)
  - 6mg/mL solution (Lucentis 0.3 mg)

REFERENCES
- Lucentis [Prescribing Information]. South San Francisco, CA: Genentech; March 2018.

Library	Commercial	NSA
Yes	No	Yes

Part D Effective: N/A
Commercial Effective: 04/16/18
Created: 05/14
Client Approval: 04/16
P&T Approval: 07/17

RESLIZUMAB (NSA)

Generic	Brand	HICL	GCN	Exception/Other
RESLIZUMAB	CINQAIR	43211		

This drug requires a written request for prior authorization.

GUIDELINES FOR USE

INITIAL CRITERIA (NOTE: FOR RENEWAL CRITERIA SEE BELOW)

1. Does the patient have a diagnosis of severe asthma with an eosinophilic phenotype and meet **ALL** of the following criteria?
   - The patient is 18 years of age or older
   - The patient has a documented blood eosinophil level of at least 300 cells/mcL within the past 6 months
   - The patient is currently adherent to a maximally tolerated dose of an inhaled corticosteroid plus at least one other maintenance medication (e.g., a long-acting inhaled beta2-agonist, a long-acting muscarinic antagonist, a leukotriene receptor antagonist, theophylline, or oral corticosteroid)
   - The patient has experienced at least 2 or more asthma exacerbations within the past 12 months (exacerbation is defined as an asthma-related event requiring hospitalization, emergency room visit, or systemic corticosteroid burst lasting at least 3 days)
   - The patient has **ONE** of the following:
     - o Asthma Control Test (ACT) score of less than 20
     - o Asthma Control Questionnaire (ACQ) score of at least 1.5 or more
     - o Asthma Therapy Assessment Questionnaire (ATAQ) score of at least 1 or more
   - Cinqair will be used as add-on maintenance treatment
   - The patient is not being concurrently treated with Xolair, Dupixent, or another anti-IL5 asthma biologic (e.g. Nucala, Fasenra)
   - Cinqair is prescribed by or given in consultation with a physician specializing in pulmonary medicine or allergy medicine

   If yes, **approve for 12 months by HICL.**
   APPROVAL TEXT: Renewal requires the patient to have experienced a reduction in asthma exacerbations (defined as an asthma-related event requiring hospitalization, emergency room visit, or systemic corticosteroid burst lasting at least 3 days) from baseline AND an improvement in Asthma Control Test (ACT), Asthma Control Questionnaire (ACQ), or Asthma Therapy Assessment Questionnaire (ATAQ) score from baseline. In addition, if the patient was on maintenance therapy with oral corticosteroids prior to the initiation of Cinqair, then the patient must demonstrate a reduction in the total daily dose of oral corticosteroids for Cinqair renewal.

   If no, do not approve.
   DENIAL TEXT: See the initial denial text at the end of the guideline.

CONTINUED ON NEXT PAGE

RESLIZUMAB (NSA)

INITIAL CRITERIA (CONTINUED)

INITIAL DENIAL TEXT: The guideline named **RESLIZUMAB (Cinqair)** requires a diagnosis of severe asthma with an eosinophilic phenotype. In addition, the following criteria must also be met:

- The patient is 18 years of age or older
- The patient has a documented blood eosinophil level of at least 300 cells/mcL within the past 6 months
- The patient is currently adherent to a maximally tolerated dose of an inhaled corticosteroid plus at least one other maintenance medication (e.g., a long-acting inhaled beta2-agonist, a long-acting muscarinic antagonist, a leukotriene receptor antagonist, theophylline, or oral corticosteroid)
- The patient has experienced at least 2 or more asthma exacerbations within the past 12 months (exacerbation is defined as an asthma-related event requiring hospitalization, emergency room visit, or systemic corticosteroid burst lasting at least 3 days)
- The patient has **ONE** of the following:
  - Asthma Control Test (ACT) score of less than 20
  - Asthma Control Questionnaire (ACQ) score of at least 1.5 or more
  - Asthma Therapy Assessment Questionnaire (ATAQ) score of at least 1 or more
- Cinqair will be used as add-on maintenance treatment
- The patient is not being concurrently treated with Xolair, Dupixent, or another anti-IL5 asthma biologic (e.g. Nucala, Fasenra)
- Cinqair is prescribed by or given in consultation with a physician specializing in pulmonary medicine or allergy medicine

RENEWAL CRITERIA

1. Does the patient have a diagnosis of severe asthma **AND** meet all of the following criteria?
   - The patient has experienced a reduction in asthma exacerbations (defined as an asthma-related event requiring hospitalization, emergency room visit, or systemic corticosteroid burst lasting at least 3 days) from baseline
   - The patient has experienced an improvement in the Asthma Control Test (ACT), Asthma Control Questionnaire (ACQ), **OR** Asthma Therapy Assessment Questionnaire (ATAQ) score from baseline

   If yes, continue to #2.
   If no, do not approve.
   DENIAL TEXT: See the renewal denial text at the end of the guideline.

CONTINUED ON NEXT PAGE

RESLIZUMAB (NSA)

RENEWAL CRITERIA (CONTINUED)

2. Was the patient treated with a maintenance therapy regimen of oral corticosteroids prior to initiation of Cinqair?

   If yes, continue to #3.
   If no, **approve for 12 months by HICL.**

3. Has the patient decreased their total daily dose of oral corticosteroids from baseline?

   If yes, **approve for 12 months by HICL.**
   If no, do not approve.
   RENEWAL DENIAL TEXT: The guideline named **RESLIZUMAB (Cinqair)** requires a diagnosis of severe asthma. In addition, the following must be met:
   - The patient has experienced a reduction in asthma exacerbations (defined as an asthma-related event requiring hospitalization, emergency room visit, or systemic corticosteroid burst lasting at least 3 days) from baseline
   - The patient has experienced an improvement in the Asthma Control Test (ACT), Asthma Control Questionnaire (ACQ), or Asthma Therapy Assessment Questionnaire (ATAQ) score from baseline
   - The patient has decreased their total daily oral corticosteroid dose from baseline, if the patient was on maintenance therapy with oral corticosteroids prior to initiation of Cinqair

RATIONALE

For further information, please refer to the Prescribing Information and/or Drug Monograph for Cinqair.

REFERENCES

- Cinqair [Prescribing Information]. Frazer, PA. Teva Pharmaceutical Industries Ltd.; March 2016.

Library	Commercial	NSA
Yes	No	Yes

Part D Effective: N/A
Commercial Effective: 01/01/19
Created: 04/17
Client Approval: 11/18
P&T Approval: 10/18

RITUXIMAB (NSA)

Generic	Brand	HICL	GCN	Exception/Other
RITUXIMAB	RITUXAN	16848		

GUIDELINES FOR USE

INITIAL CRITERIA (NOTE: FOR RENEWAL CRITERIA, SEE BELOW)

1. Does the patient have a diagnosis of moderate to severe rheumatoid arthritis (RA) and meet **ALL** of the following criteria?
   - Therapy is prescribed by or given in consultation with a rheumatologist
   - The patient is 18 years of age or older
   - The patient is currently using or has a contraindication to methotrexate
   - The patient has had a previous trial of at least one of the following DMARDs (disease-modifying antirheumatic drugs) such as methotrexate, leflunomide, hydroxychloroquine, or sulfasalazine
   - The patient has had a previous trial of the formulary preferred immunomodulators: Enbrel **AND** Humira (**NOTE:** pharmaceutical samples acquired from the prescriber or manufacturer assistance program do not qualify)

   If yes, **approve for #2 fills by HICL with an end date of 6 months from today.**
   APPROVAL TEXT: Renewal for moderate to severe rheumatoid arthritis requires that the patient has experienced or maintained a 20% or greater improvement in tender joint count or swollen joint count while on therapy.
   If no, continue to #2.

2. Does the patient have a diagnosis of Non Hodgkin's Lymphoma (NHL) and meet **ALL** of the following criteria?
   - Therapy is prescribed by or given in consultation with an oncologist
   - The patient is 18 years of age or older

   If yes, **approve for up to #8 fills by HICL with an end date of 6 months from today.**
   If no, continue to #3.

3. Does the patient have a diagnosis of Chronic Lymphocytic Leukemia (CLL) and meet **ALL** of the following criteria?
   - Therapy is prescribed by or given in consultation with an oncologist
   - The patient is on concurrent chemotherapy
   - The patient is 18 years of age or older

   If yes, **approve up to #6 fills by HICL with an end date of 6 months from today.**
   If no, continue to #4.

CONTINUED ON NEXT PAGE

RITUXIMAB (NSA)

INITIAL CRITERIA (CONTINUED)

4. Does the patient have a diagnosis of Wegener's Granulomatosis (WG) or Microscopic Polyangiitis (MPA) and meet **ALL** of the following criteria?
   - The patient is on concurrent glucocorticoids (such as methylprednisolone or prednisone)
   - The patient is 18 years of age or older

   If yes, **approve for #4 fills by HICL with an end date of 1 month from today.**
   If no, continue to #5.

5. Does the patient have a diagnosis of moderate to severe Pemphigus Vulgaris (PV) and meet the following criteria?
   - The patient is 18 years of age or older

   If yes, **approve for #3 fills by HICL for 12 months.**
   If no, do not approve.
   INITIAL DENIAL TEXT: The guideline named **RITUXIMAB (Rituxan)** requires a diagnosis of moderate to severe rheumatoid arthritis, Non Hodgkin's Lymphoma (NHL), Chronic Lymphocytic Leukemia (CLL), Wegener's Granulomatosis (WG), Microscopic Polyangiitis (MPA), or moderate to severe Pemphigus Vulgaris. The following criteria must also be met.
   For patients with moderate to severe rheumatoid arthritis (RA), all of the following criteria are required for approval:
   - Therapy is prescribed by or given in consultation with a rheumatologist
   - The patient is 18 years of age or older
   - The patient is currently using or has a contraindication to methotrexate
   - The patient has had a previous trial of at least one of the following DMARDs (disease-modifying antirheumatic drugs) such as methotrexate, leflunomide, hydroxychloroquine, or sulfasalazine
   - The patient has had a previous trial of the formulary preferred immunomodulators: Enbrel **AND** Humira

   The use of pharmaceutical samples (from the prescriber or manufacturer assistance program) will not be considered when evaluating the medical condition or prior prescription history for drugs that require prior authorization.
   For patients with Non Hodgkin's Lymphoma (NHL), all of the following criteria are required for approval:
   - Therapy is prescribed by or given in consultation with an oncologist
   - The patient is 18 years of age or older

   (Initial denial text continued on next page)

CONTINUED ON NEXT PAGE

RITUXIMAB (NSA)

INITIAL CRITERIA (CONTINUED)

For patients with Chronic Lymphocytic Leukemia (CLL), all of the following criteria are required for approval:
- Therapy is prescribed by or given in consultation with an oncologist
- The patient is on concurrent chemotherapy
- The patient is 18 years of age or older

For patients with Wegener's Granulomatosis (WG) or Microscopic Polyangiitis (MPA), all of the following criteria are required for approval:
- The patient is on concurrent glucocorticoids (such as methylprednisolone or prednisone)
- The patient is 18 years of age or older

For patients with moderate to severe Pemphigus Vulgaris, approval requires:
- The patient is 18 years of age or older

RENEWAL CRITERIA

1. Does the patient have a diagnosis of moderate to severe rheumatoid arthritis (RA) and has the patient experienced or maintained a 20% or greater improvement in tender joint count or swollen joint count while on therapy?

   If yes, **approve for #3 fills by HICL with an end date of 12 months from today.**
   If no, do not approve.
   RENEWAL DENIAL TEXT: The guideline named **RITUXIMAB (Rituxan)** requires a diagnosis of moderate to severe rheumatoid arthritis (RA) and that the patient has experienced or maintained at least a 20% or greater improvement in tender joint count or swollen joint count from baseline while on therapy for renewal.

RATIONALE
Ensure appropriate utilization of Rituxan based on its FDA approved indications.

FDA APPROVED INDICATIONS
Rituximab (Rituxan) is a CD20-directed cytolytic antibody indicated for the treatment of patients with:
- Non-Hodgkin's Lymphoma (NHL)
- Chronic Lymphocytic Leukemia (CLL)
- Rheumatoid Arthritis (RA) in combination with methotrexate in adult patients with moderately-to-severely-active RA who have inadequate response to one or more TNF antagonist therapies
- Wegener's Granulomatosis (WG) and Microscopic Polyangiitis (MPA) in adult patients in combination with glucocorticoids
- Moderate to severe Pemphigus Vulgaris (PV) in adult patients

CONTINUED ON NEXT PAGE

RITUXIMAB (NSA)

FDA APPROVED INDICATIONS (CONTINUED)

Limitations of Use: Rituxan is not recommended for use in patients with severe, active infections.

DOSAGE AND ADMINISTRATION

Rituxan is administered by intravenous infusion.

- Administer only as an intravenous infusion
- Do not administer as an intravenous push or bolus
- Rituxan should only be administered by a healthcare professional with appropriate medical support to manage severe infusion reactions that can be fatal if they occur
- The dose for NHL is 375 mg/m2
- The dose for CLL is 375 mg/m2 in the first cycle and 500 mg/m2 in cycles 2–6, in combination with FC, administered every 28 days
- The dose as a component of Zevalin® (Ibritumomab tiuxetan) Therapeutic Regimen is 250 mg/m2
- The dose for RA in combination with methotrexate is two-1000 mg intravenous infusions separated by 2 weeks (one course) every 24 weeks or based on clinical evaluation, but not sooner than every 16 weeks. Methylprednisolone 100 mg intravenous or equivalent glucocorticoid is recommended 30 minutes prior to each infusion
- The dose for GPA and MPA in combination with glucocorticoids is 375 mg/m2 once weekly for 4 weeks
- The dose for PV is two-1000 mg intravenous infusions separated by 2 weeks in combination with a tapering course of glucocorticoids, then a 500 mg intravenous infusion at Month 12 and every 6 months thereafter or based on clinical evaluation. Dose upon relapse is a 1000 mg intravenous infusion with considerations to resume or increase the glucocorticoid dose based on clinical evaluation. Subsequent infusions may be no sooner than 16 weeks after the previous infusion. Methylprednisolone 100 mg intravenous or equivalent glucocorticoid is recommended 30 minutes prior to each infusion.

REFERENCES

- Rituxan [Prescribing Information]. South San Francisco, CA: Genentech, Inc. June 2018.

Library	Commercial	NSA
Yes	No	Yes

Part D Effective: N/A
Commercial Effective: 10/01/18

Created: 01/09
Client Approval: 09/18

P&T Approval: 07/18

RITUXIMAB AND HYALURONIDASE HUMAN - SQ (NSA)

Generic	Brand	HICL	GCN	Exception/Other
RITUXIMAB/ HYALURONIDASE, HUMAN - SQ	RITUXAN HYCELA	44378		

GUIDELINES FOR USE

1. Is the patient 18 years of age or older?

   If yes, continue to #2.
   If no, do not approve.
   DENIAL TEXT: See the denial text at the end of the guideline.

2. Has the patient received or will receive at least one full dose of a rituximab product by intravenous infusion prior to the initiation of the requested medication?

   If yes, continue to #3.
   If no, do not approve.
   DENIAL TEXT: See the denial text at the end of the guideline.

3. Does the patient have a diagnosis of Follicular Lymphoma (FL) and meet **ONE** of the following criteria?
   - The medication will be used as a single agent for a patient with relapsed or refractory FL
   - The medication will be used in combination with first line chemotherapy for a patient with previously untreated FL
   - The medication will be used as a single-agent for maintenance therapy for a patient who has achieved a complete or partial response to rituximab in combination with chemotherapy
   - The medication will be used as a single agent after first-line cyclophosphamide, vincristine, and prednisone (CVP) chemotherapy in a patient with non-progressing (including stable disease) FL

   If yes, **approve for 12 months by GPID (36469).**
   If no, continue to #4.

CONTINUED ON NEXT PAGE

RITUXIMAB AND HYALURONIDASE HUMAN - SQ (NSA)

GUIDELINES FOR USE (CONTINUED)

4. Does the patient have a diagnosis of Diffuse Large B-cell Lymphoma (DLBCL) and meet the following criterion?
   - The medication will be used in combination with cyclophosphamide, doxorubicin, vincristine, prednisone (CHOP), or other anthracycline-based chemotherapy regimens for previously untreated Diffuse Large B-cell Lymphoma (DLBCL)

   If yes, **approve for 12 months by GPID (36469).**
   If no, continue to #5.

5. Does the patient have a diagnosis of Chronic Lymphocytic Leukemia (CLL) and meet the following criterion?
   - The medication will be used in combination with fludarabine and cyclophosphamide (FC)

   If yes, **approve for 12 months by GPID (43561).**
   If no, do not approve.
   DENIAL TEXT: See the denial text at the end of the guideline.

DENIAL TEXT: The guideline named **RITUXIMAB AND HYALURONIDASE HUMAN - SQ (Rituxan Hycela)** requires a diagnosis of Follicular Lymphoma (FL), Diffuse Large B-cell Lymphoma (DLBCL), or Chronic Lymphocytic Leukemia (CLL) in adult patients who have received or will receive at least one full dose of a rituximab product by intravenous infusion prior to the initiation of the requested medication. In addition, the following criteria must be met:

For patients with Follicular Lymphoma (FL), one of the following criteria must be met:
- The medication will be used as a single agent for a patient with relapsed or refractory FL
- The medication will be used in combination with first line chemotherapy for a patient with previously untreated FL
- The medication will be used as a single-agent for maintenance therapy for a patient who has achieved a complete or partial response to rituximab in combination with chemotherapy
- The medication will be used as a single agent after first-line cyclophosphamide, vincristine, and prednisone (CVP) chemotherapy in a patient with non-progressing (including stable disease) FL

For patients with Diffuse Large B-cell Lymphoma (DLBCL):
- The medication will be used in combination with cyclophosphamide, doxorubicin, vincristine, prednisone (CHOP), or other anthracycline-based chemotherapy regimens for previously untreated Diffuse Large B-cell Lymphoma (DLBCL)

For patients with Chronic Lymphocytic Leukemia (CLL):
- The medication will be used in combination with fludarabine and cyclophosphamide (FC)

CONTINUED ON NEXT PAGE

RITUXIMAB AND HYALURONIDASE HUMAN - SQ (NSA)

RATIONALE
Ensure appropriate utilization of Rituxan Hycela consistent with FDA approved indication.

Rituxan Hycela is for subcutaneous use only and should only be administered by a healthcare professional with appropriate be fatal if they occur.

All patients must first receive at least one full dose of a rituximab product by intravenous infusion without experiencing severe adverse reactions before starting treatment with Rituxan Hycela. If patients are not able to receive one full dose by intravenous infusion, they should continue subsequent cycles with a rituximab product by intravenous infusion and not switch to Rituxan Hycela until a full intravenous dose is successfully administered.

FDA APPROVED INDICATIONS
Indicated for the treatment of adult patients with:

Follicular Lymphoma (FL)
- Relapsed or refractory, follicular lymphoma as a single agent
- Previously untreated follicular lymphoma in combination with first line chemotherapy and, in patients achieving a complete or partial response to rituximab in combination with chemotherapy, as single-agent maintenance therapy
- Non-progressing (including stable disease), follicular lymphoma as a single agent after first-line cyclophosphamide, vincristine, and prednisone (CVP) chemotherapy

Diffuse Large B-cell Lymphoma (DLBCL)
- Previously untreated diffuse large B-cell lymphoma in combination with cyclophosphamide, doxorubicin, vincristine, prednisone (CHOP) or other anthracycline-based chemotherapy regimens

Chronic Lymphocytic Leukemia (CLL)
- Previously untreated and previously treated CLL in combination with fludarabine and cyclophosphamide (FC)

Limitations of Use:
- Initiate treatment with Rituxan Hycela only after patients have received at least one full dose of a rituximab product by intravenous infusion.
- Rituxan Hycela is not indicated for the treatment of non-malignant conditions.

REFERENCES
- Rituxan Hycela [Prescribing Information]. South San Francisco, CA: Genentech, Inc.; June 2017.

CONTINUED ON NEXT PAGE

RITUXIMAB AND HYALURONIDASE HUMAN - SQ (NSA)

Library	Commercial	NSA
Yes	No	Yes

Part D Effective: N/A
Commercial Effective: 10/01/17
Created: 08/17
Client Approval: 08/17
P&T Approval: 07/17

STANDARD NON-SELF-ADMINISTERED DRUG FORMULARY
PRIOR AUTHORIZATION GUIDELINES

ROMIDEPSIN

Generic	Brand	HICL	GCN	Exception/Other
ROMIDEPSIN	ISTODAX	36898		

This drug requires a written request for prior authorization.

GUIDELINES FOR USE

1. Does the patient have a diagnosis of cutaneous T-cell lymphoma (also known as Mycosis Fungoides/Sezary Syndrome) **AND** meet ONE of the following criteria?
   - The patient has a trial of or contraindication to Zolinza (vorinostat) AND is not able to tolerate oral medications
   - The patient has tried at least one form of systemic therapy (e.g., retinoids, interferons, denileukin diftitox, methotrexate, liposomal doxorubicin, gemcitabine, chlorambucil) AND is able to tolerate oral medications.

   If yes, **approve for 12 months by HICL.**
   If no, continue to #2.

2. Is the requested medication being used for the treatment of peripheral T-cell lymphoma in a patient who has received at least one prior therapy?

   If yes, **approve for 12 months by HICL.**
   If no, do not approve.
   DENIAL TEXT: The guideline named **ROMIDEPSIN (Istodax)** requires a diagnosis of cutaneous T-cell lymphoma or peripheral T-cell lymphoma. The following criteria must also be met.
   For patients with cutaneous T-cell lymphoma, approval requires the following criteria:
   - The patient has a trial of or contraindication to Zolinza (vorinostat) AND is not able to tolerate oral medications.
   - The patient has tried at least one form of systemic therapy (e.g., retinoids, interferon, denileukin diftitox, methotrexate, liposomal doxorubicin, gemcitabine, chlorambucil) AND is able to tolerate oral medications.

   For patients with peripheral T-cell lymphoma, approval requires that the patient has received at least one prior treatment.

RATIONALE
Promote appropriate utilization of **ROMIDEPSIN** based on FDA approved indications.

CONTINUED ON NEXT PAGE

ROMIDEPSIN

FDA APPROVED INDICATIONS

Isotodax is indicated for:

- Treatment of cutaneous T-cell lymphoma (CTCL) in patients who have received at least one prior systemic therapy
- Treatment of peripheral T-cell lymphoma (PTCL) in patients who have received at least one prior therapy

These indications are based on response rate. Clinical benefit such as improvement in overall survival has not been demonstrated.

SYSTEMIC TREATMENT OPTIONS	
Retinoids (bexarotene, retinoic acid, isotretinoin, acitretin)	Chlorambucil (Leukeran)
Interferons (Intron A)	Pentostatin
Extracorporeal photopheresis	Etoposide (VePesid)
Denileukin diftitox (Ontak)	Cyclophosphamide (Cytoxan)
Methotrexate	Temozolomide (Temodar)
Liposomal doxorubicin (Doxil)	Bortezomib (Velcade)
Gemcitabine (Gemzar)	

REFERENCES

- Istodax [Prescribing Information]. Celgene Corporation: Summit, NJ. October 2014.
- National Comprehensive Cancer Network, Inc. The NCCN Clinical Practice Guidelines in Oncology. Non-Hodgkin's Lymphomas. Version 3.2016.

Library	Commercial	NSA
Yes	No	Yes

Part D Effective: N/A
Commercial Effective: 10/01/16
Created: 02/10
Client Approval: 09/16
P&T Approval: 08/16

SEBELIPASE ALFA

Generic	Brand	HICL	GCN	Exception/Other
SEBELIPASE ALFA	KANUMA	42747		

GUIDELINES FOR USE

INITIAL CRITERIA (NOTE: FOR RENEWAL CRITERIA SEE BELOW)

1. Was the medication prescribed by or in consultation with an endocrinologist, hepatologist, gastroenterologist, medical geneticist, or lipidologist?

   If yes, continue to #2.
   If no, do not approve.
   DENIAL TEXT: See the initial denial text at the end of the guideline.

2. Does the patient have a diagnosis of rapidly progressive lysosomal acid lipase (LAL) deficiency presenting within the first 6 months of life (also known as Wolman Disease), as confirmed by the presence of clinical features (e.g., hepatomegaly, elevated serum transaminases, dyslipidemia, splenomegaly) plus **ANY** of the following?
   - A blood test indicating low or absent levels of LAL enzyme activity
   - A dried blood spot test indicating low or absent LAL enzyme activity
   - A genetic test indicating the bi-allelic presence of altered LIPA gene(s)

   If yes, **approve for 12 months by HICL.**
   If no, continue to #3.

CONTINUED ON NEXT PAGE

SEBELIPASE ALFA

INITIAL CRITERIA (CONTINUED)

3. Does the patient have a diagnosis of lysosomal acid lipase (LAL) deficiency presenting after the first 6 months of life and not considered rapidly progressive (also known as cholesteryl ester storage disease (CESD)), as confirmed by the presence of clinical features (e.g., hepatomegaly, elevated serum transaminases, dyslipidemia, splenomegaly) plus **ANY** of the following?
   - A blood test indicating low or absent levels of LAL enzyme activity
   - A dried blood spot test indicating low or absent LAL enzyme activity
   - A genetic test indicating the bi-allelic presence of altered LIPA gene(s)

   If yes, **approve for 6 months by HICL.**
   APPROVAL TEXT: Renewal requires that the patient has a documented improvement in any one of the following clinical parameters associated with lysosomal acid lipase (LAL) deficiency while on therapy with Kanuma:
   - A relative reduction from baseline in any one of the following lipid levels (LDL-c, non-HDL-c, or triglycerides).
   - Normalization of aspartate aminotransferase (AST) based on age- and gender-specific normal ranges.
   - A decrease in liver fat content compared to baseline assessed by abdominal imaging (e.g., multi-echo gradient echo [MEGE] MRI).

   Any one of the following baseline measurements will be required to assess renewal criteria: lipids (LDL-c, Non-HDL-c, or triglycerides), aspartate aminotransferase (AST), or MEGE MRI.

   If no, do not approve.
   DENIAL TEXT: See the initial denial text at the end of the guideline.

DENIAL TEXT: Our guideline for **SEBELIPASE ALFA (Kanuma)** requires that the medication be prescribed by or in consultation with an endocrinologist, hepatologist, gastroenterologist, medical geneticist, or lipidologist, **AND** a diagnosis of lysosomal acid lipase (LAL) deficiency, as confirmed by the presence of clinical features (e.g., hepatomegaly, elevated serum transaminases, dyslipidemia, splenomegaly) plus **ANY** of the following:
- A blood test indicating low or absent levels of LAL enzyme activity
- A dried blood spot test indicating low or absent LAL enzyme activity
- A genetic test indicating the bi-allelic presence of altered LIPA gene(s)

CONTINUED ON NEXT PAGE

SEBELIPASE ALFA

GUIDELINES FOR USE (CONTINUED)

RENEWAL CRITERIA

1. Does the patient have a diagnosis of lysosomal acid lipase (LAL) deficiency presenting after the first 6 months of life and not considered rapidly progressive?

   If yes, continue to #2.
   If no, do not approve.
   DENIAL TEXT: See the renewal denial text at the end of the guideline.

2. Does the patient have documented improvement in any one of the following clinical parameters associated with lysosomal acid lipase (LAL) deficiency during the past 6 months:
   - A relative reduction from baseline in any one of the following lipid levels (LDL-c, Non-HDL-c, or triglycerides)
   - Normalization of aspartate aminotransferase (AST) based on age- and gender-specific normal ranges
   - A decrease in liver fat content compared to baseline assessed by abdominal imaging (e.g., multi-echo gradient echo [MEGE] MRI)

   If yes, **approve for 12 months by HICL.**
   If no, do not approve.
   DENIAL TEXT: See the renewal denial text at the end of the guideline.

DENIAL TEXT: Our guideline for **SEBELIPASE ALFA (Kanuma)** renewal requires a diagnosis of lysosomal acid lipase (LAL) deficiency presenting after the first 6 months of life and not considered rapidly progressive, and that the patient have documented improvement in any one of the following clinical parameters associated with lysosomal acid lipase (LAL) deficiency during the past 6 months:
- A relative reduction from baseline in any one of the following lipid levels (LDL-c, Non-HDL-c, or triglycerides)
- Normalization of aspartate aminotransferase (AST) based on age- and gender-specific normal ranges
- A decrease in liver fat content compared to baseline assessed by abdominal imaging (e.g., multi-echo gradient echo [MEGE] MRI)

CONTINUED ON NEXT PAGE

SEBELIPASE ALFA

RATIONALE

To ensure appropriate use of Kanuma (sebelipase alfa) consistent with FDA approved indication.

Kanuma is a human therapeutic biologic and the first FDA-approved treatment for lysosomal acid lipase (LAL) deficiency. Kanuma was granted orphan drug designation, breakthrough therapy designation, FDA priority review, and the manufacturer of Kanuma was granted a rare pediatric disease voucher. Kanuma is a recombinant form of the human LAL enzyme which serves as a replacement for the lacking enzyme in patients with deficiency. Kanuma is to be administered as an intravenous infusion by a healthcare professional.

LAL deficiency is a rare, autosomal recessive, inherited genetic disorder in which patients have little or no LAL enzyme activity due to mutations in the Lipase A, Lysosomal Acid, Cholesterol Esterase (LIPA) gene which encodes the LAL enzyme. LAL deficiency can be divided into two major phenotypes which differ by rate of progression and severity. When LAL deficiency is diagnosed in infancy, it is referred to as Wolman disease and represents the more rapidly progressing phenotype of the disease. These patients historically have a life expectancy of 3-6 months with a disease course characterized by liver failure, malabsorption, and growth failure.

LAL deficiency presenting post-infancy is generally referred to as cholesteryl ester storage disease (CESD) and causes hepatic steatosis, hepatic fibrosis, and cirrhosis. These patients are also at increased risk for accelerated atherosclerosis and cardiovascular disease. It is estimated that Wolman disease affects 1-2 infants per million births and CESD affects 25 individuals per million births.

Diagnostic criteria for LAL includes the presence of clinical features, blood tests and dried blood spot test for LAL enzyme activity, and genetic testing. Testing for LAL without clinical features is not indicated and may result in false positives, whereas genetic testing shows that both alleles are affected by mutations.

The efficacy of Kanuma in pediatric and adult patients with LAL was assessed in the clinical trial, LAL-CL02. The primary endpoint was normalization of the alanine aminotransferase level (ALT) and secondary endpoints included LDL-c relative reduction, non-HDL-C relative reduction, normalization of aspartate aminotransferase (AST), and triglyceride (TG) relative reduction. Results are provided in Table 1 below. Baseline assessments conducted in participants revealed substantially elevated aminotransferase levels and high LDL-c levels (≥190 mg/dL) in 38 of 66 patients (58%). As the most frequently reported complications of LAL deficiency are hepatic manifestations, the trial addressed common markers of liver injury. Patients treated with Kanuma had a significant reduction in hepatic fat content as assessed by MRI (mean reduction: -32% in the Kanuma group vs. -4.2% in the placebo group). The significance of reductions in ALT values and liver fat content to disease progression has not been established.

CONTINUED ON NEXT PAGE

SEBELIPASE ALFA

RATIONALE (CONTINUED)

Table 1. Pediatric and Adult Patients with LAL Deficiency, Trial Results *[NEJM. Burton et al 2015]*

Endpoint	Population	Sebelipase Alfa (n = 36)	Placebo (n = 30)	Treatment Difference (p-value)
PRIMARY ENDPOINT:				
Normalization of ALT, % (n/N)	All, N = 66	31% (11/36)	7% (2/30)	24% (0.0271)
SECONDARY ENDPOINTS:				
Relative reduction in LDL-c, Mean (SD)	All, N = 66	-28% (22.3)	-6% (13.0)	-22% (<0.0001)
Relative reduction in triglyceride, Mean (SD)	All, N = 66	-25% (29.4)	-11% (28.8)	-14% (0.0375)
Relative increase in HDL-c, Mean (SD)	All, N = 66	20% (16.8)	-0.3% (12.3)	20% (<0.0001)

The efficacy of Kanuma in patients with rapidly progressive LAL deficiency presenting within the first 6 months of life was assessed in the clinical trial, LAL-CL03, a multinational, single-arm, open label, Phase II/III study of nine infants (aged 1 – 6 months at trial entry). Efficacy was assessed by comparing the survival of Kanuma-treated patients at 12 months of age with a historical cohort of 21 untreated patients with similar clinical characteristics and age at onset. In LAL-CL03, improvement in survival was accompanied by substantial and rapid improvements in markers of hepatic injury (i.e., AST/ALT), growth, and hematological abnormalities.

FDA APPROVED INDICATION
Kanuma (sebelipase) is indicated for the treatment of patients with a diagnosis of lysosomal acid lipase (LAL) deficiency.

DOSAGE
Patients with rapidly progressive LAL deficiency presenting within the first 6 months of life:
The recommended starting dosage is 1mg/kg as an intravenous infusion once weekly. For patients who do not achieve an optimal clinical response, increase to 3mg/kg once weekly.

Pediatric and adult patients with LAL deficiency:
The recommended dosage is 1mg/kg as an intravenous infusion once every other week.

CONTINUED ON NEXT PAGE

SEBELIPASE ALFA

AVAILABLE STRENGTH:
- 20mg/10ml solution in a single-use vial

REFERENCES

- Kanuma [Prescribing Information]. Cheshire, CT: Alexion Pharmaceuticals, Inc. December 2015.
- Kanuma [AMCP Dossier]. Cheshire, CT: Alexion Pharmaceuticals, Inc. December 2015.
- Burton, B.K., Balwani, M., Feillet, I., et.al. A Phase 3 Trial of Sebelipase Alfa in Lysosomal Acid Lipase Deficiency. *The New England Journal of Medicine.* Abstract (2015) 373:1010-20.
- Jones, S.A., Rojas-Caro, S., Quinn, A.G., et.al. Impact of sebelipase alfa on survival and liver function in infants with rapidly progressive lysosomal acid lipase deficiency. *Journal of Inherited Metabolic Disease. (2015) 38 (Suppl 1):S35–S378.*
- Lysosomal acid lipase deficiency testing. LabCorp. 2013. http://m3.wyanokecdn.com/8bf88c2ed28280df9ef39e5614da7177.pdf

Library	Commercial	NSA
Yes	No	Yes

Part D Effective: N/A
Commercial Effective: 04/01/16
Created: 12/15
Client Approval: 02/16
P&T Approval: 02/16

SILTUXIMAB

Generic	Brand	HICL	GCN	Exception/Other
SILTUXIMAB	SYLVANT	41101		

This drug requires a written request for prior authorization.

GUIDELINES FOR USE

1. Does the patient have a diagnosis of multi-centric Castleman's disease (MCD)?

   If yes, continue to #2.
   If no, do not approve.
   DENIAL TEXT: See the denial text at the end of the guideline.

2. Is the patient positive for either human immunodeficiency virus (HIV) or human herpesvirus-8 (HHV-8)?

   If yes, do not approve**.**
   DENIAL TEXT: See the denial text at the end of the guideline.
   If no, **approve for 12 months by HICL.**

DENIAL TEXT: Our guideline for **SILTUXIMAB** requires a diagnosis of multi-centric Castleman's disease (MCD) and that the patient is negative for both human immunodeficiency virus (HIV) and human herpesvirus-8 (HHV-8).

RATIONALE
Promote appropriate utilization of Sylvant based on FDA approved indication.

Castleman's disease (CD), also known as angiofollicular lymph node hyperplasia, is comprised of two distinct diseases: unicentric and multicentric. Unicentric CD usually affects a single group of lymph nodes and removal of the mass cures 90-95% of cases. Multicentric CD (MCD) involves more than a single group of lymph nodes and can affect other organs containing lymphoid tissue. Patients with MCD often have serious infections, severe fatigue, night sweats, recurrent fever, and weight loss. Patients may also experience peripheral edema, anemia, hypoalbuminemia, peripheral neuropathy and hepatosplenomegaly. CD is not officially a cancer, but the multicentric disease form is more aggressive than unicentric CD and roughly 20% of patients with MCD develop lymphoma.

Because MCD is a rare disease and most cases are seen in patients who are HIV/HHV-8 positive, the utilization of Sylvant is expected to be relatively minimal given its specific FDA indication for HIV/HHV-8 negative MCD patients.

CONTINUED ON NEXT PAGE

SILTUXIMAB

RATIONALE (CONTINUED)
DOSAGE
Sylvant 11 mg/kg is given over 1 hour as an intravenous infusion administered every 3 weeks until treatment failure (defined as disease progression based on increase in symptoms, radiologic progression or deterioration in performance status) or unacceptable toxicity.

FDA APPROVED INDICATION
Sylvant is indicated for the treatment of patients with Multicentric Castleman's disease (MCD) who are human immunodeficiency virus (HIV) negative and human herpesvirus-8 (HHV-8) negative.

Limitation of Use: Sylvant was not studied in patients with MCD who are HIV positive or HHV-8 positive because Sylvant did not bind to virally produced IL-6 in a nonclinical study.

REFERENCES

- Sylvant [Prescribing Information]. Horsham, PA: Janssen Biotech, Inc; May 2014.

Library	Commercial	NSA
Yes	No	Yes

Part D Effective: N/A
Commercial Effective: 10/01/14
Created: 6/14
Client Approval: 08/14
P&T Approval: 08/14

TALIMOGENE LAHERPAREPVEC

Generic	Brand	HICL	GCN	Exception/Other
TALIMOGENE LAHERPAREPVEC	IMLYGIC	42741		

GUIDELINES FOR USE

1. Does the patient have a diagnosis of unresectable melanoma and have all of the following criteria been met?
   - Patient has a recurrence of melanoma lesions after initial surgery.
   - Patient does not have a history of primary or acquired immunodeficient states, leukemia, lymphoma, or AIDS.
   - Patient is not currently receiving immunosuppressive therapy.
   - The patient is not receiving concurrent medical therapy for the treatment of melanoma including pembrolizumab (Keytruda), nivolumab (Opdivo), ipilimumab (Yervoy), dabrafenib (Tafinlar), trametinib (Mekinist), vemurafenib (Zelboraf), interleukin-2, interferon, dacarbazine, temozolomide (Temodar), paclitaxel, carboplatin, imatinib (Gleevec), melphalan (Alkeran), imiquimod, or radiation therapy.

   If yes, continue to #2.
   If no, do not approve.
   DENIAL TEXT: See the denial text at the end of the guideline.

2. Will Imlygic be injected into cutaneous, subcutaneous, and/or nodal lesions that are visible, palpable, or detectable by ultrasound guidance?

   If yes, **approve for a total of 12 months and enter three prior authorizations (initial, second, and maintenance doses) by GPID as follows:**
   - **First authorization: approve for 1 fill of Imlygic 10^6 (1 million) PFU/mL vial (GPID= 39983): 4mL (#4 vials)**
   - **Second authorization (starting 3 weeks after initial authorization): approve for 1 fill of Imlygic 10^8 (100 million) PFU/mL vial (GPID= 39984): 4mL (#4 vials)**
   - **Third authorization (starting 5 weeks after initial authorization): approve for 11 months for Imlygic 10^8 (100 million) PFU/mL vial (GPID= 39984): 8mL (#8 vials) every 28 days**

   If no, do not approve.
   DENIAL TEXT: See the denial text at the end of the guideline.

CONTINUED ON NEXT PAGE

TALIMOGENE LAHERPAREPVEC

GUIDELINES FOR USE (CONTINUED)

DENIAL TEXT: Our guideline for **TALIMOGENE LAHERPAREPVEC** requires a diagnosis of unresectable melanoma. Additional guideline requirements apply.

- Patient has a recurrence of melanoma lesions after initial surgery.
- Patient does not have a history of primary or acquired immunodeficient states, leukemia, lymphoma, or AIDS.
- Patient is not currently receiving immunosuppressive therapy.
- The patient is not receiving concurrent medical therapy for the treatment of melanoma including pembrolizumab (Keytruda), nivolumab (Opdivo), ipilimumab (Yervoy), dabrafenib (Tafinlar), trametinib (Mekinist), vemurafenib (Zelboraf), interleukin-2, interferon, dacarbazine, temozolomide (Temodar), paclitaxel, carboplatin, imatinib (Gleevec), melphalan (Alkeran), imiquimod, or radiation therapy.
- The request must be for Imlygic to be injected into cutaneous, subcutaneous, and/or nodal lesions that are visible, palpable, or detectable by ultrasound guidance.

RATIONALE

Promote appropriate utilization of Imlygic (talimogene laherparepvec) based on FDA-approved indications.

Imlygic is indicated for the local treatment of unresectable cutaneous, subcutaneous, and nodal lesions in patients with melanoma recurrent after initial surgery. Imlygic is a live, attenuated herpes simplex virus and may cause life-threatening disseminated herpetic infection in patients who are immunocompromised. Imlygic should not be administered to immunocompromised patients, including those with a history of primary or acquired immunodeficient states, leukemia, lymphoma, AIDS or other clinical manifestations of infection with human immunodeficiency viruses, and those on immunosuppressive therapy. Imlygic should be discontinued if there are no injectable lesions to treat or if other treatment is required for melanoma. Other melanoma treatments include pembrolizumab, nivolumab, ipilimumab, dabrafenib, trametinib, vemurafenib, dabrafenib, interleukin-2, interferon, dacarbazine, temozolomide, paclitaxel, carboplatin, imatinib, melphalan, imiquimod, or radiation therapy.

CONTINUED ON NEXT PAGE

TALIMOGENE LAHERPAREPVEC

DOSAGE

Imlygic is administered by injection into cutaneous, subcutaneous, and/or nodal lesions that are visible, palpable, or detectable by ultrasound guidance.

The total injection volume for each treatment visit should not exceed 4 mL for all injected lesions combined. It may not be possible to inject all lesions at each treatment visit or over the full course of treatment. Previously injected and/or uninjected lesion(s) may be injected at subsequent treatment visits. The initial recommended dose is up to 4 mL of Imlygic at a concentration of 10^6 (1 million) PFU per mL. The recommended dose for subsequent administrations is up to 4 mL of IMLYGIC at a concentration of 10^8 (100 million) PFU per mL. The recommended dosing schedule for Imlygic is shown in Table 1.

Table 1. Recommended Dose and Schedule for IMLYGIC

Treatment	Treatment Interval	Maximum Injection Volume per Treatment Visit (all lesions combined)	Dose Strength	Prioritization of Lesions to be Injected
Initial	–	4 mL	10^6 (1 million) PFU per mL	• Inject largest lesion(s) first. • Prioritize injection of remaining lesion(s) based on lesion size until maximum injection volume is reached or until all injectable lesion(s) have been treated.
Second	3 weeks after initial treatment	4 mL	10^8 (100 million) PFU per mL	• Inject any new lesion(s) (lesions that have developed since initial treatment) first. • Prioritize injection of remaining lesion(s) based on lesion size until maximum injection volume is reached or until all injectable lesion(s) have been treated.
All subsequent treatments (including reinitiation)	2 weeks after previous treatment	4 mL	10^8 (100 million) PFU per mL	• Inject any new lesion(s) (lesions that have developed since previous treatment) first. • Prioritize injection of remaining lesion(s) based on lesion size until maximum injection volume is reached or until all injectable lesion(s) have been treated.

CONTINUED ON NEXT PAGE

TALIMOGENE LAHERPAREPVEC

FDA APPROVED INDICATION

Imlygic (talimogene laherparepvec) is indicated for the local treatment of unresectable cutaneous, subcutaneous, and nodal lesions in patients with melanoma recurrent after initial surgery.

AVAILABLE STRENGTHS:

- 10^6 (1 million) PFU/mL 1ml vial
- 10^8 (100 million) PFU/mL 1ml vial

REFERENCES

- Imlygic [Prescribing Information]. Thousand Oaks, CA: Amgen, Inc. October 2015.

Library	Commercial	NSA
Yes	No	Yes

Part D Effective: N/A
Commercial Effective: 12/09/15
Created: 11/15
Client Approval: 11/15
P&T Approval: 11/15

TEMOZOLOMIDE - IV

Generic	Brand	HICL	GCN	Exception/Other
TEMOZOLOMIDE - IV	TEMODAR - IV		17724	

This drug requires a written request for prior authorization.

GUIDELINES FOR USE

1. Does the patient have one of the following diagnoses: metastatic melanoma, anaplastic astrocytoma, glioblastoma multiforme, or small cell lung cancer (SCLC)?

   If yes, **approve for 12 months by GPID.**
   If no, do not approve.
   DENIAL TEXT: Approval requires a diagnosis of metastatic melanoma, anaplastic astrocytoma, glioblastoma multiforme, or small cell lung cancer (SCLC).

RATIONALE

Based on FDA approved indications and NCCN recommendations. Temodar is approved for the treatment of newly diagnosed glioblastoma multiforme concomitantly with radiotherapy and then as maintenance treatment; and refractory anaplastic astrocytoma patients who have experienced disease progression on a drug regimen containing nitrosourea and procarbazine. NCCN recommends Temodar for SCLC patients with relapse <2-3 months, performance status 0-2 or relapse >2-3 up to 6 months (most useful if brain metastases are present); and for the treatment of metastatic melanoma. NCCN considers temozolomide to be a systemic therapy option for advanced or metastatic melanoma. No quantity limit is included within this guideline since there are multiple dosing regimens available, all of which are based on body surface area.

FDA APPROVED INDICATIONS

Temodar is an alkylating drug indicated for the treatment of adult patients with:

- Newly diagnosed glioblastoma multiforme (GBM) concomitantly with radiotherapy and then as maintenance treatment.
- Refractory anaplastic astrocytoma patients who have experienced disease progression on a drug regimen containing nitrosourea and procarbazine.

CONTINUED ON NEXT PAGE

TEMOZOLOMIDE - IV

REFERENCES

- National Comprehensive Cancer Network, Inc. NCCN Clinical Practice Guidelines in Oncology Melanoma. (Version 3.2012).
- National Comprehensive Cancer Network. NCCN Clinical Practice Guidelines in Oncology Small Cell Lung Cancer Version 2.2014. [Online] September 17, 2013. [Cited: September 25, 2013.] http://www.nccn.org/professionals/physician_gls/pdf/sclc.pdf
- Schering Corporation, a subsidiary of Merck & Co., Inc. Temodar package insert. Whitehouse Station, NJ. February 2011.
- Thomson Healthcare. Monograph Name. DRUGDEX® System [database online]. Greenwood Village, CO. Available at: https://www.thomsonhc.com/hcs/librarian/PFDefaultActionId/pf.LoginAction. [Accessed: January 24, 2012].

Library	Commercial	NSA
Yes	No	Yes

Part D Effective: N/A
Commercial Effective: 01/01/14

Created: 02/12
Client Approval: 11/13

P&T Approval: 11/13

TEMSIROLIMUS

Generic	Brand	HICL	GCN	Exception/Other
TEMSIROLIMUS	TORISEL	34870		

This drug requires a written request for prior authorization.

GUIDELINES FOR USE

1. Does the patient have a diagnosis of advanced renal cell carcinoma (RCC)?

   If yes, **approve for 12 months with a quantity limit of #4 kits (vials) per month.**
   If no, do not approve.
   DENIAL TEXT: Approval requires a diagnosis of advanced renal cell carcinoma (RCC).

RATIONALE
Ensure appropriate utilization of temsirolimus based on FDA approved indication and NCCN guidelines.

FDA APPROVED INDICATION
Temsirolimus is indicated for the treatment of advanced renal cell carcinoma.

REFERENCES

- Wyeth Pharmaceuticals Inc. Torisel package insert. Philadelphia, PA. September 2010.
- National Comprehensive Cancer Network, Inc. The NCCN Clinical Practice Guidelines in Oncology. Kidney Cancer. (Version 2.2011).

Library	Commercial	NSA
Yes	No	Yes

Part D Effective: N/A
Commercial Effective: 10/01/13
Created: 05/11
Client Approval: 08/13
P&T Approval: 05/11

THYROTROPIN ALFA FOR INJECTION

Generic	Brand	HICL	GCN	Exception/Other
THYROTROPIN ALFA FOR INJECTION	THYROGEN	18855		

GUIDELINES FOR USE

1. Is the requested product being used as diagnostic tool for serum thyroglobulin (Tg) testing?

   If yes, do not approve.
   DENIAL TEXT: The requested product is not covered for diagnostic purposes under the pharmacy benefit. This product may be covered under the medical benefit.
   If no, continue to #2.

2. Is the requested product being used as adjunctive treatment for radioiodine ablation of thyroid tissue remnants for thyroid cancer without evidence of metastatic disease?

   If yes, **approve one fill of #2 vials.**
   If no, do not approve.
   DENIAL TEXT: Approval requires that the requested product being used as adjunctive treatment for radioiodine ablation of thyroid tissue remnants for thyroid cancer without evidence of metastatic disease.

RATIONALE

To ensure appropriate use of Thyrogen based on FDA approved indication and dosage. Limit diagnostic use to the medical benefit.

Two-injection regimen of Thyrogen 0.9 mg IM, followed by a second 0.9 mg IM injection 24 hours later.

FDA APPROVED INDICATION

Thyrogen (thyrotropin alfa for injection) is indicated for use as an adjunctive diagnostic tool for serum thyroglobulin (Tg) testing with or without radioiodine imaging in the follow-up of patients with well-differentiated thyroid cancer.

Thyrogen (thyrotropin alfa for injection) is indicated for use as an adjunctive treatment for radioiodine ablation of thyroid tissue remnants in patients who have undergone a near-total or total thyroidectomy for well-differentiated thyroid cancer and who do not have evidence of metastatic thyroid cancer.

REFERENCES

- Thyrogen (thyrotropin alfa for injection) [Prescribing Information]. Cambridge, MA: Genzyme Corporation.; July 2012.

CONTINUED ON NEXT PAGE

THYROTROPIN ALFA FOR INJECTION

Library	Commercial	NSA
Yes	No	Yes

Part D Effective: N/A
Commercial Effective: 10/01/13
Created: 08/13
Client Approval: 08/13
P&T Approval: 08/13

TILDRAKIZUMAB-ASMN (NSA)

Generic	Brand	HICL	GCN	Exception/Other
TILDRAKIZUMAB-ASMN	ILUMYA	44823		

GUIDELINES FOR USE

INITIAL CRITERIA (NOTE: FOR RENEWAL CRITERIA SEE BELOW)

1. Does the patient have a diagnosis of moderate to severe plaque psoriasis (PsO) and meet **ALL** of the following criteria?
   - Therapy is prescribed by or given in consultation with a dermatologist
   - The patient has psoriatic lesions involving at least 10% of body surface area (BSA) **OR** psoriatic lesions affecting the hands, feet, genital area, or face
   - The patient has had a previous trial of at least one or more forms of preferred conventional therapies such as PUVA (Phototherapy Ultraviolet Light A), UVB (Ultraviolet Light B), topical corticosteroids, calcipotriene, acitretin, methotrexate, or cyclosporine
   - The patient is 18 years of age or older
   - The patient has had a previous trial of any **TWO** of the following formulary preferred immunomodulators: Cosentyx, Enbrel, Humira, Stelara, or Otezla (**NOTE:** pharmaceutical samples acquired from the prescriber or manufacturer assistance program do not qualify)

   If yes, **approve for 6 months by entering TWO approvals by HICL as follows:**
   - **FIRST APPROVAL: approve for 1 month with a quantity limit of #2mL (#2 100mg/mL syringes) per 28 days.**
   - **SECOND APPROVAL: approve for 5 months with a quantity limit of #1mL (#1 100mg/mL syringe) per 84 days (Please enter a start date of 1 WEEK AFTER the END date of the first approval).**

   APPROVAL TEXT: Renewal for moderate to severe plaque psoriasis requires that the patient has achieved or maintained clear or minimal disease or a decrease in PASI (Psoriasis Area and Severity Index) of at least 50% or more.

   If no, do not approve.
   DENIAL TEXT: See the initial denial text at the end of the guideline.

CONTINUED ON NEXT PAGE

TILDRAKIZUMAB-ASMN (NSA)

INITIAL CRITERIA (CONTINUED)

INITIAL DENIAL TEXT: The guideline named **TILDRAKIZUMAB-ASMN (Ilumya)** requires a diagnosis of moderate to severe plaque psoriasis (PsO). In addition, the following criteria must be met:

- Therapy is prescribed by or given in consultation with a dermatologist
- The patient has psoriatic lesions involving at least 10% of body surface area (BSA) **OR** psoriatic lesions affecting the hands, feet, genital area, or face
- The patient has had a previous trial of at least one or more forms of preferred conventional therapies such as PUVA (Phototherapy Ultraviolet Light A), UVB (Ultraviolet Light B), topical corticosteroids, calcipotriene, acitretin, methotrexate, or cyclosporine
- The patient is 18 years of age or older
- The patient has had a previous trial of any **TWO** of the following formulary preferred immunomodulators: Cosentyx, Enbrel, Humira, Stelara, or Otezla.

The use of pharmaceutical samples (from the prescriber or manufacturer assistance program) will not be considered when evaluating the medical condition or prior prescription history for drugs that require prior authorization.

RENEWAL CRITERIA

1. Does the patient have a diagnosis of moderate to severe plaque psoriasis (PsO) **AND** meet the following criterion?
   - The patient has achieved or maintained clear or minimal disease or a decrease in PASI (Psoriasis Area and Severity Index) of at least 50% or more

     If yes, **approve for 12 months by HICL with a quantity limit of #1mL (#1 100mg/mL syringe) per 84 days.**
     If no, do not approve.
     RENEWAL DENIAL TEXT: The guideline named **TILDRAKIZUMAB-ASMN (Ilumya)** requires a diagnosis of moderate to severe plaque psoriasis (PsO) for renewal. The following criterion must also be met:
     - The patient has achieved or maintained clear or minimal disease or a decrease in PASI (Psoriasis Area and Severity Index) of at least 50% or more

CONTINUED ON NEXT PAGE

TILDRAKIZUMAB-ASMN (NSA)

RATIONALE
Ensure appropriate diagnostic, utilization and safety criteria are used for the management of requests for Ilumya.

FDA APPROVED INDICATIONS
Ilumya is an interleukin-23 antagonist indicated for the treatment of adults with moderate-to-severe plaque psoriasis who are candidates for systemic therapy or phototherapy.

DOSING & ADMINISTRATION
Ilumya is administered by subcutaneous injection. Ilumya should only be administered by a healthcare provider. The recommended dose is 100 mg at Week 0, Week 4, and every 12 weeks thereafter.

DOSAGE FORMS AND STRENGTHS
Single-dose prefilled syringes are available for subcutaneous administration: 100 mg per mL.

REFERENCES

- Ilumya [Prescribing Information]. Whitehouse Station, NJ: Merck & Co.,Inc. March 2018.

Library	Commercial	NSA
Yes	Yes	Yes

Part D Effective: N/A
Commercial Effective: 11/01/18
Created: 08/18
Client Approval: 10/18
P&T Approval: 01/18

TISAGENLECLEUCEL (NSA)

Generic	Brand	HICL	GCN	Exception/Other
TISAGENLECLEUCEL	KYMRIAH	44483		

***********Customer Service/PAC Alert************
(For Internal Use Only)

THIS IS A HIGH-IMPACT MEDICATION. DO NOT OVERRIDE OR APPROVE WITHOUT SUBMITTING FOR PHARMACIST REVIEW.

GUIDELINES FOR USE

1. Does the patient meet **ALL** of the following criteria?
   - Treatment is prescribed by a Kymriah-certified hematologist or oncologist
   - Kymriah will be administered at a treatment center that is certified to administer Kymriah
   - The patient has not received a previous trial of Kymriah

   If yes, continue to #2.
   If no, do not approve.
   DENIAL TEXT: See the denial text at the end of the guideline.

2. Is the patient 25 years of age or younger **AND** have a diagnosis of B-cell precursor acute lymphoblastic leukemia (ALL)?

   If yes, continue to #3.
   If no, continue to #4.

CONTINUED ON NEXT PAGE

TISAGENLECLEUCEL (NSA)

GUIDELINES FOR USE (CONTINUED)

3. Does the physician attest that the patient meets **ONE** of the following criteria?
    - The patient is in second or greater bone marrow relapse
    - The patient is currently in bone marrow relapse after having undergone allogeneic stem cell transplantation (SCT)
    - The patient has not achieved minimal residual disease (MRD) negative complete remission after two cycles of a standard chemotherapy regimen (i.e., primary refractory disease)
    - The patient has not achieved complete remission after one cycle of standard chemotherapy for relapsed leukemia (i.e., chemorefractory relapsed leukemia)
    - The patient has Philadelphia chromosome positive (Ph+) ALL and meets at least **ONE** of the following:
        - The patient has had a previous trial of 2 or more tyrosine kinase inhibitors (TKIs)
        - The patient is unable to tolerate TKI therapy
        - The patient has a contraindication to TKI therapy
    - The patient is not eligible for allogeneic stem cell transplantation (SCT)

    If yes, **approve GPID 43799 for 1 fill.**
    APPROVAL TEXT: Because of the risk of cytokine release syndrome (CRS) and neurological toxicities, the Risk Evaluation and Mitigation Strategy (REMS) program requires that certified healthcare facilities must have on-site, immediate access to tocilizumab (Actemra). The patient must also meet all criteria in the Actemra guideline to be approvable for both agents.

    If no, do not approve.
    DENIAL TEXT: See the denial text at the end of the guideline.

4. Is the patient 18 years of age or older **AND** have **ONE** of the following diagnoses?
    - relapsed or refractory Diffuse large B-cell lymphoma (DLBCL) not otherwise specified
    - High grade B-cell lymphoma
    - DLBCL arising from follicular lymphoma (FL) [i.e. transformed follicular lymphoma (TFL)]

    If yes, continue to #5.
    If no, do not approve.
    DENIAL TEXT: See the denial text at the end of the guideline.

CONTINUED ON NEXT PAGE

TISAGENLECLEUCEL (NSA)

GUIDELINES FOR USE (CONTINUED)

5. Does the physician attest that the patient meets **ALL** of the following criteria?
   - The patient is refractory or has had disease progression (relapsed) after two or more lines of systemic therapy including rituximab and an anthracycline **AND**
   - The patient has had disease progression or relapsed after autologous hematopoietic stem cell transplantation (ASCT) **OR** the patient is not eligible for ASCT

   If yes, **approve GPID 44689 for 1 fill.**
   APPROVAL TEXT: Because of the risk of cytokine release syndrome (CRS) and neurological toxicities, the Risk Evaluation and Mitigation Strategy (REMS) program requires that certified healthcare facilities must have on-site, immediate access to tocilizumab (Actemra). The patient must also meet all criteria in the Actemra guideline to be approvable for both agents

   If no, do not approve.
   DENIAL TEXT: The guideline named **TISAGENLECLEUCEL (Kymriah)** requires a diagnosis of B-cell precursor acute lymphoblastic leukemia (ALL) OR relapsed or refractory diffuse large B-cell lymphoma (DLBCL) not otherwise specified, high grade B-cell lymphoma, or DLBCL arising from follicular lymphoma (FL) [i.e. transformed follicular lymphoma (TFL)]. In addition, the following criteria must be met:
   - Treatment is prescribed by a Kymriah-certified hematologist or oncologist
   - Kymriah will be administered at a treatment center that is certified to administer Kymriah
   - The patient has not had a previous trial of Kymriah

   For diagnosis of B-cell precursor acute lymphoblastic leukemia (ALL), approval requires:
   - The patient is 25 years of age or younger
   - Physician attestation of **ONE** of the following criteria:
     - The patient is in second or greater bone marrow relapse
     - The patient is currently in bone marrow relapse after having undergone allogeneic stem cell transplantation (SCT)
     - The patient has not achieved minimal residual disease (MRD) negative complete remission after two cycles of a standard chemotherapy regimen (i.e., primary refractory disease)
     - The patient has not achieved complete remission after one cycle of standard chemotherapy for relapsed leukemia (i.e., chemorefractory relapsed leukemia)
     - The patient has Philadelphia chromosome positive (Ph+) ALL and meets at least **ONE** of the following:
       - The patient has had a previous trial of 2 or more tyrosine kinase inhibitors (TKIs)
       - The patient is unable to tolerate TKI therapy
       - The patient has a contraindication to TKI therapy
     - The patient is not eligible for allogeneic stem cell transplantation (SCT)

   (Denial text continued on next page)

CONTINUED ON NEXT PAGE

TISAGENLECLEUCEL (NSA)

GUIDELINES FOR USE (CONTINUED)

For diagnosis of relapsed or refractory diffuse large B-cell lymphoma (DLBCL) not otherwise specified, high grade B-cell lymphoma, or DLBCL arising from follicular lymphoma (FL) [i.e. transformed follicular lymphoma (TFL)], approval requires:

- The patient is 18 years of age or older
- Physician attestation of **ALL** of the following criteria:
  - The patient is refractory or has had disease progression (relapsed) after two or more lines of systemic therapy including rituximab and an anthracycline **AND**
  - The patient has had disease progression or relapsed after autologous hematopoietic stem cell transplantation (ASCT) **OR** the patient is not eligible for ASCT

RATIONALE

Promote appropriate utilization of **KYMRIAH** based on FDA approved indication, dosing, and clinical trial design.

NOTE: Kymriah is available only through a restricted program under a Risk Evaluation and Mitigation Strategy (REMS) because of the risk of cytokine release syndrome (CRS) and neurological events. The FDA is requiring that hospitals and their associated clinics that dispense Kymriah be specially certified. As part of that certification, staff involved in the prescribing, dispensing, or administering of Kymriah are required to be trained to recognize and manage CRS and neurological events. Additionally, the certified health care settings are required to have protocols in place to ensure that Kymriah is only given to patients after verifying that tocilizumab is available for immediate administration.

BACKGROUND

Kymriah is the first gene therapy to be approved by the FDA and was granted Priority Review and Breakthrough Therapy designations. Kymriah is an engineered chimeric antigen receptor (CAR) product that targets CD19, a protein expressed on the surface of B cell leukemia and lymphoma cells. The CAR product is utilized in the process of autologous cell therapy in which a patient's own white blood cells are collected, T cells are isolated, the CAR gene is inserted into the T cells, the T cell colony is expanded, and then the engineered T cells are infused back into the patient. This process results in an expanded number of tumor-specific T cells that circulate throughout the body to target and kill cancer cells.

CONTINUED ON NEXT PAGE

TISAGENLECLEUCEL (NSA)

FDA APPROVED INDICATIONS

Kymriah is a CD19-directed genetically modified autologous T cell immunotherapy indicated for the treatment of:

- Patients up to 25 years of age with B-cell precursor acute lymphoblastic leukemia (ALL) that is refractory or in second or later relapse.
- Adult patients with relapsed or refractory (r/r) large B-cell lymphoma after two or more lines of systemic therapy including diffuse large B-cell lymphoma (DLBCL) not otherwise specified, high grade B-cell lymphoma and DLBCL arising from follicular lymphoma.

Limitation of Use: KYMRIAH is not indicated for treatment of patients with primary central nervous system lymphoma (PCNSL).

DOSAGE AND ADMINISTRATION

- Kymriah is supplied as a frozen suspension of genetically modified autologous T cells in one infusion bag labeled for the specific recipient. Kymriah is shipped directly to the cell lab associated with the infusion center. Kymriah is given as a one-time treatment.
- Kymriah is for autologous use and is administered by intravenous infusion only.
- Prior to infusion:
  - Verify the patient's identity
  - Pre-medicate with acetaminophen and an H1-antihistamine
  - Confirm availability of tocilizumab
  - Kymriah dosing is based on the number of chimeric antigen receptor (CAR) positive viable T cells.

- **Pediatric and Young Adult Relapsed or Refractory B-Cell ALL (up to 25 years of age):**
  - For patients 50 kg or less, administer 0.2 to 5.0 x 10^6 CAR-positive viable T cells per kg body weight intravenously.
  - For patients above 50 kg, administer 0.1 to 2.5 x 10^8 CAR-positive viable T cells (non-weight based) intravenously.

- **Adults with Relapsed or Refractory Diffuse Large B-Cell Lymphoma:**
  - Administer 0.6 to 6.0 x 10^8 CAR-positive viable T cells intravenously.

AVAILABLE STRENGTHS

- **Pediatric and Young Adult B-Cell ALL (up to 25 years of age):**
  - A single-dose unit of Kymriah contains 0.2 to 5.0 x 10^6 CAR-positive viable T cells per kg of body weight for patients 50 kg or less, or 0.1 to 2.5 x 10^8 CAR-positive viable T cells for patients more than 50 kg, suspended in a patient-specific infusion bag.
- **Adult Relapsed or Refractory Diffuse Large B-Cell Lymphoma:**
  - A single-dose unit of Kymriah contains 0.6 to 6.0 x 10^8 CAR-positive viable T cells suspended in one or more patient-specific infusion bag.

CONTINUED ON NEXT PAGE

TISAGENLECLEUCEL (NSA)

FDA APPROVED INDICATIONS (CONTINUED)

AVAILABLE STRENGTHS
The actual number of CAR-positive T cells in the product is reported on the Certificate of Analysis that is shipped with Kymriah. The volume in the infusion bag ranges from 10 mL to 50 mL.

REFERENCES

- Kymriah [Prescribing Information]. East Hanover, NJ: Novartis Pharmaceuticals Corporation. May 2018.
- FDA approval brings first gene therapy to the United States. [Press release]. August 30, 2017. Available at: https://www.fda.gov/NewsEvents/Newsroom/PressAnnouncements/ucm574058.htm. Accessed August 31, 2017.
- ClinicalTrials.gov [Internet]. Bethesda (MD): National Library of Medicine (US). Identifier NCT 02435849. Determine Efficacy and Safety of CTL019 in Pediatric Patients With Relapsed and Refractory B-cell ALL (ELIANA). Available at: https://clinicaltrials.gov/ct2/show/NCT02435849?term=eliana&draw=1&rank=1. Accessed October 18, 2017.
- ClinicalTrials.gov [Internet]. Bethesda (MD): National Library of Medicine (US). Identifier NCT 02445248. Study of Efficacy and Safety of CTL019 in Adult DLBCL Patients. Available at: https://clinicaltrials.gov/ct2/show/NCT02445248?term=02445248&rank=1. Accessed May 17, 2018.

Library	Commercial	NSA
Yes	No	Yes

Part D Effective: N/A
Commercial Effective: 10/01/18
Created: 10/17
Client Approval: 09/18
P&T Approval: 07/18

TOCILIZUMAB – IV (NSA)

Generic	Brand	HICL	GCN	Exception/Other
TOCILIZUMAB - IV	ACTEMRA - IV		27366 27367 27368	

GUIDELINES FOR USE

INITIAL CRITERIA (NOTE: FOR RENEWAL CRITERIA, SEE BELOW)

1. Does the patient have a diagnosis of moderate to severe rheumatoid arthritis (RA) and meet **ALL** of the following criteria?
   - Therapy is prescribed by or given in consultation with a rheumatologist
   - The patient has had a previous trial of at least one of the following DMARDs (disease-modifying antirheumatic drugs) such as methotrexate, leflunomide, hydroxychloroquine, or sulfasalazine
   - The patient is 18 years of age or older
   - The patient has had a previous trial of the formulary preferred immunomodulators: Enbrel **AND** Humira (**NOTE:** pharmaceutical samples acquired from the prescriber or manufacturer assistance program do not qualify)

   If yes, **approve for 6 months by GPID for a maximum quantity limit of 40mL per 28 days.**
   APPROVAL TEXT: Renewal for moderate to severe rheumatoid arthritis requires that the patient has experienced or maintained a 20% or greater improvement in tender joint count or swollen joint count while on therapy.

   If no, continue to #2.

2. Does the patient have a diagnosis of polyarticular juvenile idiopathic arthritis (PJIA) and meet **ALL** of the following criteria?
   - Therapy is prescribed by or given in consultation with a rheumatologist
   - The patient has had a previous trial of at least one of the following DMARDs (disease-modifying antirheumatic drugs) such as methotrexate, leflunomide, hydroxychloroquine, or sulfasalazine
   - The patient is 2 years of age or older
   - The patient has had a previous trial of the formulary preferred immunomodulators: Enbrel **AND** Humira (**NOTE:** pharmaceutical samples acquired from the prescriber or manufacturer assistance program do not qualify)

   If yes, **approve for 6 months by GPID.**
   APPROVAL TEXT: Renewal for polyarticular juvenile idiopathic arthritis requires that the patient has experienced or maintained a 20% or greater improvement in tender joint count or swollen joint count while on therapy.

   If no, continue to #3.

CONTINUED ON NEXT PAGE

INITIAL CRITERIA (CONTINUED)

3. Does the patient have a diagnosis of systemic juvenile idiopathic arthritis (SJIA) and meet **ALL** of the following criteria?
   - Therapy is prescribed by or given in consultation with a rheumatologist
   - The patient has had a previous trial of at least one of the following DMARDs (disease-modifying antirheumatic drugs) such as methotrexate, leflunomide, hydroxychloroquine, or sulfasalazine
   - The patient is 2 years of age or older

   If yes, **approve for 6 months by GPID.**
   APPROVAL TEXT: Renewal for systemic juvenile idiopathic arthritis requires that the patient has experienced or maintained a 20% or greater improvement in tender joint count or swollen joint count while on therapy.
   If no, continue to #4.

4. Does the patient meet **ALL** of the following criteria?
   - Request is for the treatment of chimeric antigen receptor (CAR) T cell-induced severe or life-threatening cytokine release syndrome (CRS)
   - The patient is 2 years of age or older

   If yes, **approve for 1 fill by GPID with a quantity limit of 160mL.**
   CLINICAL PHARMACISTS: Patient must also meet all criteria in Kymriah guideline to be approvable for both agents.

   If no, do not approve.
   DENIAL TEXT: The guideline named **TOCILIZUMAB - IV (Actemra - IV)** requires a diagnosis of moderate to severe rheumatoid arthritis (RA), polyarticular juvenile idiopathic arthritis (PJIA), systemic juvenile idiopathic arthritis (SJIA), or chimeric antigen receptor (CAR) T cell-induced severe or life-threatening Cytokine Release Syndrome (CRS). In addition, the following criteria must be met:
   For patients with moderate to severe rheumatoid arthritis, approval requires:
   - Therapy is prescribed by or given in consultation with a rheumatologist
   - The patient has had a previous trial of at least one of the following DMARDs (disease-modifying antirheumatic drugs) such as methotrexate, leflunomide, hydroxychloroquine, or sulfasalazine
   - The patient is 18 years of age or older
   - The patient has had a previous trial of the formulary preferred immunomodulators: Enbrel **AND** Humira

   (Initial denial text continued on next page)

CONTINUED ON NEXT PAGE

TOCILIZUMAB – IV (NSA)

INITIAL CRITERIA (CONTINUED)

For patients with polyarticular juvenile idiopathic arthritis, approval requires:
- Therapy is prescribed by or given in consultation with a rheumatologist
- The patient has had a previous trial of at least one of the following DMARDs (disease-modifying antirheumatic drugs) such as methotrexate, leflunomide, hydroxychloroquine, or sulfasalazine
- The patient is 2 years of age or older
- The patient has had a previous trial of the formulary preferred immunomodulators: Enbrel **AND** Humira

For patients with systemic juvenile idiopathic arthritis, approval requires:
- Therapy is prescribed by or given in consultation with a rheumatologist
- The patient has had a previous trial of at least one of the following DMARDs (disease-modifying antirheumatic drugs) such as methotrexate, leflunomide, hydroxychloroquine, or sulfasalazine
- The patient is 2 years of age or older

For the treatment of chimeric antigen receptor (CAR) T cell-induced severe or life-threatening cytokine release syndrome (CRS), approval requires all:
- The patient is 2 years of age or older

The use of pharmaceutical samples (from the prescriber or manufacturer assistance program) will not be considered when evaluating the medical condition or prior prescription history for drugs that require prior authorization.

RENEWAL CRITERIA

1. Does the patient have a diagnosis of moderate to severe rheumatoid arthritis (RA) **AND** meet the following criterion?
   - The patient has experienced or maintained a 20% or greater improvement in tender joint count or swollen joint count while on therapy

   If yes, **approve for 12 months by GPID for a maximum quantity limit of 40mL per 28 days.**
   If no, continue to #2.

2. Does the patient have a diagnosis of polyarticular juvenile idiopathic arthritis (PJIA) **OR** systemic juvenile idiopathic arthritis (SJIA) **AND** meet the following criterion?
   - The patient has experienced or maintained a 20% or greater improvement in tender joint count or swollen joint count while on therapy

   If yes, **approve for 12 months by GPID.**
   DENIAL TEXT: See the renewal denial text at the end of the guideline.

CONTINUED ON NEXT PAGE

RENEWAL CRITERIA (CONTINUED)

RENEWAL DENIAL TEXT: The guideline named **TOCILIZUMAB - IV (Actemra - IV)** requires a diagnosis of moderate to severe rheumatoid arthritis, polyarticular juvenile idiopathic arthritis, or systemic juvenile idiopathic arthritis and that the patient has experienced or maintained a 20% or greater improvement in tender joint count or swollen joint count while on therapy for renewal.

RATIONALE

Ensure appropriate use of Actemra IV consistent with its FDA approved indications.

FDA APPROVED INDICATIONS

Actemra - IV (tocilizumab - IV) is an interleukin-6 (IL-6) receptor antagonist indicated for the treatment of:

- Adult patients with moderately to severely active rheumatoid arthritis (RA) who have had an inadequate response to one or more Disease-Modifying Anti-Rheumatic Drugs (DMARDs).
- Patients 2 years of age and older with active polyarticular juvenile idiopathic arthritis.
- Patients 2 years of age and older with active systemic juvenile idiopathic arthritis.
- Adults and pediatric patients 2 years of age and older with chimeric antigen receptor (CAR) T cell-induced severe or life-threatening cytokine release syndrome.

DOSAGE AND ADMINISTRATION

Rheumatoid Arthritis	
Recommended Adult Intravenous (IV) Dosage	
When used in combination with DMARDs or as monotherapy the recommended starting dose is 4 mg per kg every 4 weeks followed by an increase to 8 mg per kg every 4 weeks based on clinical response. Doses exceeding 800 mg per infusion are not recommended in RA patients.	
Polyarticular Juvenile Idiopathic Arthritis (PJIA)	
Recommended Intravenous PJIA Dosage Every 4 Weeks	
Patients less than 30 kg weight	10 mg per kg
Patients at or above 30 kg weight	8 mg per kg
Systemic Juvenile Idiopathic Arthritis (SJIA)	
Recommended Intravenous SJIA Dosage Every 2 Weeks	
Patients less than 30 kg weight	12 mg per kg
Patients at or above 30 kg weight	8 mg per kg
Cytokine Release Syndrome (CRS)	
Recommended Intravenous CRS Dosage	
Patients less than 30 kg weight	12 mg per kg
Patients at or above 30 kg weight	8 mg per kg
Alone or in combination with corticosteroids.	
If no clinical improvement in the signs and symptoms of CRS occurs after the first dose, up to 3 additional doses of ACTEMRA may be administered. The interval between consecutive doses should be at least 8 hours. Doses exceeding 800 mg per infusion are not recommended in CRS patients.	

FDA APPROVED INDICATIONS (CONTINUED)

DOSAGE FORMS AND STRENGTHS

Single-use vials of ACTEMRA (20 mg per mL) are available for intravenous administration:

- 80 mg per 4 mL
- 200 mg per 10 mL
- 400 mg per 20 mL

REFERENCE

- Actemra [Prescribing Information]. South San Francisco, CA: Genentech. August 2017.

Library	Commercial	NSA
Yes	No	Yes

Part D Effective: N/A
Commercial Effective: 04/01/18

Created: 02/10
Client Approval: 03/18

P&T Approval: 01/18

TRABECTEDIN

Generic	Brand	HICL	GCN	Exception/Other
TRABECTEDIN	YONDELIS	35367		

GUIDELINES FOR USE

1. Does the patient have a diagnosis of unresectable or metastatic liposarcoma or leiomyosarcoma and meets the following criterion?
   - The patient has received prior therapy with an anthracycline-containing regimen such as doxorubicin

   If yes, **approve for 12 months by HICL.**
   If no, do not approve.
   DENIAL TEXT: Our guideline for **TRABECTEDIN (Yondelis)** requires a diagnosis of unresectable or metastatic liposarcoma or leiomyosarcoma. Additional guideline requirements apply.
   - The patient must have received prior therapy with an anthracycline-containing regimen such as doxorubicin.

RATIONALE
Promote appropriate utilization of Yondelis based on FDA-approved indications.

DOSAGE
Administer at 1.5 mg/m2 body surface area as a 24-hour intravenous infusion, every 3 weeks through a central venous line.

Yondelis requires premedication with dexamethasone 20 mg IV, 30 minutes before each infusion.

FDA APPROVED INDICATION
Yondelis is an alkylating drug indicated for the treatment of patients with unresectable or metastatic liposarcoma or leiomyosarcoma who received a prior anthracycline-containing regimen.

AVAILABLE STRENGTHS
- 1 mg vial

REFERENCES
- Yondelis [Package Insert]. Janssen Products. Horsham, PA. November 2015.

Library	Commercial	NSA
Yes	No	Yes

Part D Effective: N/A
Commercial Effective: 05/01/16
Created: 11/15
Client Approval: 03/16
P&T Approval: 11/15

TRASTUZUMAB (NSA)

Generic	Brand	HICL	GCN	Exception/Other
TRASTUZUMAB	HERCEPTIN	18801		

GUIDELINES FOR USE

1. Does the patient have a diagnosis of breast cancer?

   If yes, continue to #2.
   If no, continue to #4.

2. Is the request for metastatic breast cancer **AND** the patient meets the following criteria?
   - The patient has HER2-overexpressing (HER2-positive) metastatic breast cancer as detected by an FDA-approved test **AND ONE** of the following:
     - Requested medication is being used in combination with paclitaxel for first-line treatment
     - Requested medication is being used as a single agent in patients who have previously tried chemotherapy for metastatic disease

   If yes, **approve for 12 months by HICL.**
   If no, continue to #3.

3. Is the request for adjuvant therapy for breast cancer **AND** the patient meets the following criteria?
   - The patient has HER2-overexpressing (HER2-positive) tumor as detected by an FDA-approved test **AND ONE** of the following:
     - Requested medication is being used as part of a treatment regimen consisting of doxorubicin, cyclophosphamide, and either paclitaxel or docetaxel
     - Requested medication is being used as part of a treatment regimen with docetaxel and carboplatin
     - Requested medication is being used as a single agent following multi-modality anthracycline based therapy (e.g., daunorubicin, doxorubicin, idarubicin, epirubicin, or valrubicin)

   If yes, **approve for 12 months by HICL.**
   If no, do not approve.
   DENIAL TEXT: See the denial text at the end of the guideline.

CONTINUED ON NEXT PAGE

GUIDELINES FOR USE (CONTINUED)

4. Does the patient have a diagnosis of metastatic gastric or gastroesophageal junction adenocarcinoma **AND** meet **ALL** of the following criteria?
   - The patient has HER2-overexpressing (HER2-positive) metastatic cancer as detected by an FDA-approved test
   - Requested medication is being used in combination with cisplatin and capecitabine or 5-fluorouracil
   - The patient has not received prior treatment for metastatic disease

   If yes, **approve for 12 months by HICL.**
   If no, do not approve.
   DENIAL TEXT: The guideline named **TRASTUZUMAB (Herceptin)** requires a diagnosis of breast cancer, metastatic gastric or gastroesophageal junction adenocarcinoma. In addition, the following criteria must be met:
   For the diagnosis of metastatic breast cancer, approval requires:
   - The patient has HER2-overexpressing (HER2-positive) metastatic breast cancer as detected by an FDA-approved test **AND ONE** of the following:
     - Requested medication is being used in combination with paclitaxel for first-line treatment
     - Requested medication is being used as a single agent in patients who have previously tried chemotherapy for metastatic disease

   For use as adjuvant therapy for breast cancer, approval requires:
   - The patient has HER2-overexpressing (HER2-positive) tumor as detected by an FDA-approved test **AND ONE** of the following:
     - Requested medication is being used as part of a treatment regimen consisting of doxorubicin, cyclophosphamide, and either paclitaxel or docetaxel
     - Requested medication is being used as part of a treatment regimen with docetaxel and carboplatin
     - Requested medication is being used as a single agent following multi-modality anthracycline based therapy (e.g., daunorubicin, doxorubicin, idarubicin, epirubicin, or valrubicin)

   For the diagnosis of metastatic gastric or gastroesophageal junction adenocarcinoma, approval requires:
   - The patient has HER2-overexpressing (HER2-positive) metastatic cancer as detected by an FDA-approved test
   - Requested medication is being used in combination with cisplatin and capecitabine or 5-fluorouracil
   - The patient has not received prior treatment for metastatic disease

CONTINUED ON NEXT PAGE

TRASTUZUMAB (NSA)

RATIONALE

For further information, please refer to the Prescribing Information and/or Drug Monograph for Herceptin.

REFERENCES

- Genentech, Inc. Herceptin package insert. South San Francisco, CA. November 2018.

Library	Commercial	NSA
Yes	No	Yes

Part D Effective: N/A
Commercial Effective: 02/25/19
Created: 08/12
Client Approval: 02/19
P&T Approval: 05/15

USTEKINUMAB

Generic	Brand	HICL	GCN	Exception/Other
USTEKINUMAB	STELARA	36187		

GUIDELINES FOR USE

INITIAL CRITERIA (NOTE: FOR RENEWAL CRITERIA SEE BELOW)

1. Does the patient have a diagnosis of moderate to severe plaque psoriasis (PsO) **OR** moderate to severe plaque psoriasis (PsO) with co-existent psoriatic arthritis (PsA) and meet **ALL** of the following criteria?
   - Therapy is prescribed by or given in consultation with a dermatologist
   - The patient has plaque psoriasis involving at least 10% body surface area (BSA) or psoriatic lesions affecting the hands, feet, genital area, or face
   - The patient has had a previous trial of at least one or more forms of preferred conventional therapies such as PUVA (Phototherapy Ultraviolet Light A), UVB (Ultraviolet Light B), topical corticosteroids, calcipotriene, acitretin, methotrexate, or cyclosporine
   - The patient is 12 years of age or older
   - Documentation of the patient's current weight

   If yes, **approve for a total of 6 months by GPID as follows:**
   Patients weighing 100kg (220 lbs) or less:
   Enter both of the following approvals:
   - **Loading dose: Approve for 1 month with a quantity limit of 0.5mL (one 45mg/0.5mL prefilled syringe or one 45mg/0.5mL vial) per 28 days for 1 fill.**
   - **Maintenance dose: Approve for 5 months with a quantity limit of 0.5mL (one 45mg/0.5mL prefilled syringe or one 45mg/0.5mL vial) per 84 days for 2 fills with a start date after the end date of the previous fill.**

   Patients weighing over 100kg (220 lbs):
   Enter both of the following approvals:
   - **Loading dose: Approve for 1 month with a quantity limit of 1mL (two 45mg/0.5mL prefilled syringes, two 45mg/0.5mL vials, or one 90mg/mL prefilled syringe) per 28 days for 1 fill.**
   - **Maintenance dose: Approve for 5 months with a quantity limit of 1mL (two 45mg/0.5mL prefilled syringes, two 45mg/0.5mL vials, or one 90mg/mL prefilled syringe) per 84 days for 2 fills with a start date after the end date of the previous fill.**

   APPROVAL TEXT: Renewal for moderate to severe plaque psoriasis **OR** moderate to severe PsO with co-existent psoriatic arthritis requires that the patient has achieved or maintained clear or minimal disease **OR** a decrease in PASI (Psoriasis Area and Severity Index) of at least 50% or more **AND** documentation of the patient's current weight.

   If no, continue to #2.

CONTINUED ON NEXT PAGE

USTEKINUMAB

INITIAL CRITERIA (CONTINUED)

2. Does the patient have a diagnosis of psoriatic arthritis (PsA) without co-existent plaque psoriasis (PsO) and meet **ALL** of the following criteria?
   - Therapy is prescribed by or given in consultation with a rheumatologist or dermatologist
   - The patient has had a previous trial of at least one of the following DMARDs (disease-modifying antirheumatic drugs) such as methotrexate, leflunomide, hydroxychloroquine, or sulfasalazine
   - The patient is 18 years of age or older

   If yes, **approve for a total of 6 months by GPID as follows:**
   - **Loading dose: Approve for 1 month with a quantity limit of 0.5mL (one 45mg/0.5mL prefilled syringe or one 45mg/0.5mL vial) per 28 days for 1 fill.**
   - **Maintenance dose: Approve for 5 months with a quantity limit of 0.5mL (one 45mg/0.5mL prefilled syringe or one 45mg/0.5mL vial) per 84 days for 2 fills with a start date after the end date of the previous fill.**

   APPROVAL TEXT: Renewal for psoriatic arthritis requires that the patient has experienced or maintained a 20% or greater improvement in tender joint count or swollen joint count while on therapy.

   If no, continue to #3.

3. Does the patient have a diagnosis of moderately to severely active Crohn's disease (CD) and meet **ALL** of the following criteria?
   - Therapy is prescribed by or given in consultation with a gastroenterologist
   - The patient has had a previous trial of at least one of the following conventional agents such as corticosteroids (i.e., budesonide, methylprednisolone), azathioprine, mercaptopurine, methotrexate, or mesalamine
   - The patient is 18 years of age or older
   - Documentation of the patient's current weight

   If yes, continue to #4.
   If no, do not approve.
   DENIAL TEXT: See the initial denial text at the end of the guideline.

CONTINUED ON NEXT PAGE

USTEKINUMAB

INITIAL CRITERIA (CONTINUED)

4. Does the patient have non-self-administered (NSA) drug benefit coverage?

   If yes, continue to #5.
   If no, **approve maintenance dose for 6 months by GPID with a quantity limit of 1mL (two 45mg/0.5mL prefilled syringes, two 45mg/0.5mL vials, or one 90mg/mL prefilled syringe) per 56 days for 3 fills.**
   APPROVAL TEXT: Stelara subcutaneous has been approved for 6 months for maintenance treatment. Stelara intravenous loading dose is excluded from your pharmacy benefit coverage.

5. Has the patient **already received** the intravenous loading dose of Stelara for the treatment of moderately to severely active Crohn's disease (CD)?

   If yes, **approve for 6 months by GPID with a quantity limit of 1mL (two 45mg/0.5mL prefilled syringes, two 45mg/0.5mL vials, or one 90mg/mL prefilled syringe) per 56 days for 3 fills.**

   If no, **enter two approvals for a total of 6 months by GPID as follows:**
   First approval - Please enter one of the following loading doses based on the patient's weight (NOTE: Do not enter a loading dose if the member does not have coverage for non-self-administered drug benefit. Please deny for benefit exclusion.):
   Patients weighing 55kg (121 lbs.) or less:
   - **Loading dose: Approve for 2 months by GPID with a quantity limit of 52mL (two 130mg/26mL vials) per 56 days for 1 fill.**

   Patients weighing over 55kg up to 85kg (122 lbs. up to 187 lbs.):
   - **Loading dose: Approve for 2 months by GPID with a quantity limit of 78mL (three 130mg/26mL vials) per 56 days for 1 fill.**

   Patients weighing over 85kg (187 lbs.):
   - **Loading dose: Approve for 2 months by GPID with a quantity limit of 104mL (four 130mg/26mL vials) per 56 days for 1 fill.**

   Second approval:
   - **Maintenance dose: Approve for 4 months by GPID with a quantity limit of 1mL (two 45mg/0.5mL prefilled syringes, two 45mg/0.5mL vials, or one 90mg/mL prefilled syringe) per 56 days for 2 fills with a start date after the end date of the previous fill.**

CONTINUED ON NEXT PAGE

USTEKINUMAB

INITIAL CRITERIA (CONTINUED)

INITIAL DENIAL TEXT: The guideline named **USTEKINUMAB (Stelara)** requires a diagnosis of moderate to severe plaque psoriasis, **OR** moderate to severe plaque psoriasis with co-existent psoriatic arthritis, psoriatic arthritis without co-existent plaque psoriasis, or moderately to severely active Crohn's disease. In addition, the following criteria must be met:

For patients with moderate to severe plaque psoriasis (PsO) OR moderate to severe plaque psoriasis (PsO) with co-existent psoriatic arthritis (PsA), approval requires all of the following criteria:

- Therapy is prescribed by or given in consultation with a dermatologist
- The patient has plaque psoriasis involving at least 10% body surface area (BSA) or psoriatic lesions affecting the hands, feet, genital area, or face
- The patient has had a previous trial of at least one or more forms of preferred conventional therapies such as PUVA (Phototherapy Ultraviolet Light A), UVB (Ultraviolet Light B), topical corticosteroids, calcipotriene, acitretin, methotrexate, or cyclosporine
- The patient is 12 years of age or older
- Documentation of the patient's current weight

For patients with psoriatic arthritis (PsA) without co-existent plaque psoriasis (PsO), approval requires all of the following criteria:

- Therapy is prescribed by or given in consultation with a rheumatologist or dermatologist
- The patient has had a previous trial of at least one of the following DMARDs (disease-modifying antirheumatic drugs) such as methotrexate, leflunomide, hydroxychloroquine, or sulfasalazine
- The patient is 18 years of age or older

For patients with moderately to severely active Crohn's disease (CD), approval requires all of the following criteria:

- Therapy is prescribed by or given in consultation with a gastroenterologist
- The patient has had a previous trial of at least one of the following conventional agents such as corticosteroids (i.e., budesonide, methylprednisolone), azathioprine, mercaptopurine, methotrexate, or mesalamine
- The patient is 18 years of age or older
- Documentation of the patient's current weight

RENEWAL CRITERIA

- Does the patient have a diagnosis of psoriatic arthritis (PsA) without co-existent plaque psoriasis (PsO) and experienced or maintained a 20% or greater improvement in tender joint count or swollen joint count while on therapy?

  If yes, **approve for 12 months by GPID with a quantity limit of 0.5mL (one 45mg/0.5mL prefilled syringe or one 45mg/0.5mL vial) per 84 days.**
  If no, continue to #2.

CONTINUED ON NEXT PAGE

USTEKINUMAB

RENEWAL CRITERIA (CONTINUED)

2. Does the patient have a diagnosis of moderate to severe plaque psoriasis (PsO) **OR** moderate to severe plaque psoriasis (PsO) with co-existent psoriatic arthritis (PsA) and meet **ALL** of the following criteria?
   - The patient has achieved or maintained clear or minimal disease **OR** a decrease in PASI (Psoriasis Area and Severity Index) of at least 50% or more
   - Documentation of the patient's current weight

   If yes, **approve for 12 months by GPID as follows:**
   Patients weighing 100kg (220 lbs.) or less:
   - **Approve for 12 months with a quantity limit of 0.5mL (one 45mg/0.5mL prefilled syringe or one 45mg/0.5mL vial) per 84 days.**

   Patients weighing over 100kg (220 lbs.):
   - **Approve for 12 months with a quantity limit of 1mL (two 45mg/0.5mL prefilled syringes, two 45mg/0.5mL vials, or one 90mg/mL prefilled syringe) per 84 days.**

   If no, continue to #3.

3. Does the patient have a diagnosis of moderately to severely active Crohn's disease (CD)?

   If yes, **approve for 12 months by GPID with a quantity limit of 1mL (two 45mg/0.5mL prefilled syringes, two 45mg/0.5mL vials, or one 90mg/mL prefilled syringe) per 56 days.**

   If no, do not approve.
   DENIAL TEXT: The guideline named **USTEKINUMAB (Stelara)** requires a diagnosis of psoriatic arthritis without co-existent plaque psoriasis, moderate to severe plaque psoriasis **OR** moderate to severe plaque psoriasis with co-existent psoriatic arthritis, or moderately to severely active Crohn's disease. The following criteria must also be met:
   - **Renewal for the diagnosis of psoriatic arthritis without co-existent plaque psoriasis** requires that the patient has experienced or maintained a 20% or greater improvement in tender joint count or swollen joint count while on therapy.
   - **Renewal for the diagnosis of moderate to severe plaque psoriasis OR moderate to severe plaque psoriasis with co-existent psoriatic arthritis** requires that the patient has achieved or maintained clear or minimal disease **OR** a decrease in PASI (Psoriasis Area and Severity Index) of at least 50% or more **AND** documentation of the patient's current weight.

CONTINUED ON NEXT PAGE

USTEKINUMAB

RATIONALE
Ensure that appropriate diagnostic, utilization, and safety criteria are utilized for the management of Stelara.

FDA APPROVED INDICATIONS
Stelara is a human interleukin-12 and -23 antagonist indicated for the treatment of:
- Adult patients with:
  - Moderate to severe plaque psoriasis (PsO) who are candidates for phototherapy or systemic therapy
  - Psoriatic arthritis (PsA), alone or in combination with methotrexate
  - Moderately to severely active Crohn's disease (CD) who have
    - Failed or were intolerant to treatment with immunomodulators or corticosteroids, but never failed a tumor necrosis factor (TNF) blocker or
    - Failed or were intolerant to treatment with one or more TNF blockers
- Adolescent patients (12 years or older) with moderate to severe plaque psoriasis, who are candidates for phototherapy or systemic therapy.

DOSAGE AND ADMINISTRATION
Psoriasis Adult Subcutaneous Recommended Dosage:
- For patients weighing ≤100 kg (220 lbs), the recommended dose is 45 mg initially and 4 weeks later, followed by 45 mg every 12 weeks.
- For patients weighing >100 kg (220 lbs), the recommended dose is 90 mg initially and 4 weeks later, followed by 90 mg every 12 weeks.

For adolescent patients (12 years and older) Subcutaneous Recommended Dosage:
Weight based dosing is recommended at the initial dose, 4 weeks later, then every 12 weeks thereafter.
- Less than 60 kg: 0.75 mg/kg
- 60 kg to 100 kg: 45 mg
- Greater than 100 kg: 90 mg

Psoriatic Arthritis
- The recommended dose is 45 mg initially and 4 weeks later, followed by 45 mg every 12 weeks.
- For patients with co-existent moderate-to-severe plaque psoriasis weighing >100kg (220 lbs), the recommended dose is 90mg initially and 4 weeks later, followed by 90mg every 12 weeks.

Crohn's Disease
- Intravenous Induction Adult Dosage Regimen: A single intravenous infusion dose using the weight-based dosage regimen specified in Table 1.

CONTINUED ON NEXT PAGE

USTEKINUMAB

FDA APPROVED INDICATIONS (CONTINUED)

DOSAGE AND ADMINISTRATION

Table 1. Initial Intravenous Dosage of Stelara

Body weight of patient at the time of dosing	Dose	Number of 130 mg/26 mL (5 mg/mL) vials
≤55 kg	260 mg	2
>55 – 85 kg	390 mg	3
> 85 kg	520 mg	4

- Subcutaneous Maintenance Adult Dosage Regimen: The recommended maintenance dosage is a subcutaneous 90 mg dose administered 8 weeks after the initial intravenous dose, then every 8 weeks thereafter.

REFERENCES

- Stelara [Prescribing Information]. Horsham, PA: Janssen Biotech, Inc. February 2018.

Library	Commercial	NSA
Yes	Yes	Yes

Part D Effective: N/A
Commercial Effective: 04/30/18

Created: 10/09
Client Approval: 03/18

P&T Approval: 01/18

VEDOLIZUMAB (NSA)

Generic	Brand	HICL	GCN	Exception/Other
VEDOLIZUMAB	ENTYVIO	41146		

GUIDELINES FOR USE

INITIAL CRITERIA (NOTE: FOR RENEWAL CRITERIA SEE BELOW)

1. Does the patient have a diagnosis of moderate to severe Crohn's (CD) disease and meet **ALL** of the following criteria?
   - Therapy is prescribed by or given in consultation with a gastroenterologist
   - The patient has had a previous trial of at least one of the following conventional therapies, such as corticosteroids (i.e., budesonide, methylprednisolone), azathioprine, mercaptopurine, methotrexate, or mesalamine
   - The patient is 18 years of age or older
   - The patient has had a previous trial of the formulary preferred immunomodulators: Humira **AND** Stelara (**NOTE:** pharmaceutical samples acquired from the prescriber or manufacturer assistance program do not qualify)

   If yes, **approve for 4 months as follows:**
   Please enter two authorizations by HICL as follows:
   - **FIRST APPROVAL: Approve for 1 month (total fill count of 1) with a quantity limit of #600mg (#2 vials) for the first 4 weeks, then**
   - **SECOND APPROVAL: Approve for 3 months (total fill count of 2) with a quantity limit of #300mg (#1 vial) per 56 days.**

   If no, continue to #2.

CONTINUED ON NEXT PAGE

VEDOLIZUMAB (NSA)

INITIAL CRITERIA (CONTINUED)

2. Does the patient have a diagnosis of moderate to severe ulcerative colitis (UC) and meet **ALL** of the following criteria?
   - Therapy is prescribed by or given in consultation with a gastroenterologist
   - The patient has had a previous trial of at least one of the following conventional therapies, such as corticosteroids (i.e., budesonide, methylprednisolone), azathioprine, mercaptopurine, methotrexate, or mesalamine
   - The patient is 18 years of age or older
   - The patient has had a previous trial of the formulary preferred immunomodulator: Humira (**NOTE:** pharmaceutical samples acquired from the prescriber or manufacturer assistance program do not qualify)

   If yes, **approve for 4 months as follows:**
   Please enter two authorizations by HICL as follows:
   - **FIRST APPROVAL: Approve for 1 month (total fill count of 1) with a quantity limit of #600mg (#2 vials) for the first 4 weeks, then**
   - **SECOND APPROVAL: Approve for 3 months (total fill count of 2) with a quantity limit of #300mg (#1 vial) per 56 days.**

   If no, do not approve.
   INITIAL DENIAL TEXT: The guideline named **VEDOLIZUMAB (Entyvio)** requires a diagnosis of moderate to severe Crohn's disease or moderate to severe ulcerative colitis. In addition, the following criteria must also be met:
   For patients with moderate to severe Crohn's disease, approval requires all of the following:
   - Therapy is prescribed by or given in consultation with a gastroenterologist
   - The patient has had a previous trial of at least one of the following conventional therapies, such as corticosteroids (i.e., budesonide, methylprednisolone), azathioprine, mercaptopurine, methotrexate, or mesalamine
   - The patient is 18 years of age or older
   - The patient has had a previous trial of the formulary preferred immunomodulators: Humira **AND** Stelara

   (Initial denial text continued on next page)

CONTINUED ON NEXT PAGE

VEDOLIZUMAB (NSA)

INITIAL CRITERIA (CONTINUED)

For patients with moderate to severe ulcerative colitis, approval requires all of the following:

- Therapy is prescribed by or given in consultation with a gastroenterologist
- The patient has had a previous trial of at least one of the following conventional therapies, such as corticosteroids (i.e., budesonide, methylprednisolone), azathioprine, mercaptopurine, methotrexate, or mesalamine
- The patient is 18 years of age or older
- The patient has had a previous trial of the formulary preferred immunomodulator: Humira

The use of pharmaceutical samples (from the prescriber or manufacturer assistance program) will not be considered when evaluating the medical condition or prior prescription history for drugs that require prior authorization.

RENEWAL CRITERIA

1. Does the patient have a diagnosis of moderate to severe Crohn's disease (CD) or moderate to severe ulcerative colitis (UC)?

   If yes, **approve for 12 months by HICL with a quantity limit of #1 vial (300mg) per 8 weeks (total 6 fills in 12 months).**
   If no, do not approve.
   RENEWAL DENIAL TEXT: The guideline named **VEDOLIZUMAB (Entyvio)** requires a diagnosis of moderate to severe Crohn's disease or moderate to severe ulcerative colitis for renewal.

RATIONALE
Ensure appropriate use of Entyvio consistent with its FDA approved indications.

FDA APPROVED INDICATIONS
Entyvio is an integrin receptor antagonist indicated for:

Adult Ulcerative Colitis (UC)
Adult patients with moderately to severely active UC who have had an inadequate response with, lost response to, or were intolerant to a tumor necrosis factor (TNF) blocker or immunomodulator; or had an inadequate response with, were intolerant to, or demonstrated dependence on corticosteroids:

- inducing and maintaining clinical response
- inducing and maintaining clinical remission
- improving endoscopic appearance of the mucosa
- achieving corticosteroid-free remission

CONTINUED ON NEXT PAGE

VEDOLIZUMAB (NSA)

FDA APPROVED INDICATIONS (CONTINUED)

Adult Crohn's Disease (CD)
Adult patients with moderately to severely active CD who have had an inadequate response with, lost response to, or were intolerant to a TNF blocker or immunomodulator; or had an inadequate response with, were intolerant to, or demonstrated dependence on corticosteroids:

- achieving clinical response
- achieving clinical remission
- achieving corticosteroid-free remission

DOSAGE AND ADMINISTRATION

The recommended dosage in Ulcerative colitis (UC) and Crohn's disease (CD) is 300 mg infused intravenously over approximately 30 minutes at zero, two and six weeks, then every eight weeks thereafter.

REFERENCES

- Entyvio [Prescribing Information]. Deerfield, IL: Takeda Pharmaceuticals America, Inc. February 2018.

Library	Commercial	NSA
Yes	No	Yes

Part D Effective: N/A
Commercial Effective: 06/22/18
Created: 05/14
Client Approval: 06/18
P&T Approval: 01/18

VESTRONIDASE ALFA-VJBK (NSA)

Generic	Brand	HICL	GCN	Exception/Other
VESTRONIDASE ALFA-VJBK	MEPSEVII	44653		

GUIDELINES FOR USE

INITIAL CRITERIA (NOTE: FOR RENEWAL CRITERIA SEE BELOW)

1. Does the patient have a diagnosis of Mucopolysaccharidosis VII (MPS VII, Sly syndrome) and meet **ALL** of the following criteria?
   - The patient is 5 years of age or older
   - The patient has a documented urinary GAG (glycosaminoglycan) level of greater than three times the upper level of normal based on the laboratory assay
   - MPS VII diagnosis confirmed by documentation of beta-glucuronidase enzyme activity deficiency or genetic testing
   - The patient has at least one of the following clinical signs of MPS VII: enlarged liver and spleen, joint limitations, airway obstructions or pulmonary dysfunction
   - The patient has NOT undergone successful bone marrow or stem cell treatment for MPS VII
   - The patient has limitation in mobility, but remains sufficiently ambulatory for the six-minute walk test (6MWT) to be measured and evaluated
   - The requested medication is prescribed by or given in consultation with a physician specializing in genetic or metabolic disorders

   If yes, **approve for 6 months by HICL.**
   APPROVAL TEXT: Renewal requires the patient has improved, maintained, or demonstrated less than expected decline in ambulatory ability based on 6MWT compared to baseline.
   If no, do not approve.
   DENIAL TEXT: The guideline named **VESTRONIDASE ALFA-VJBK (Mepsevii)** requires a diagnosis of Mucopolysaccharidosis VII (MPS VII, Sly syndrome). In addition, the following criteria must be met:
   - The patient is 5 years of age or older
   - The patient has a documented urinary GAG (glycosaminoglycan) level of greater than three times the upper level of normal based on the laboratory assay
   - MPS VII diagnosis confirmed by documentation of beta-glucuronidase enzyme activity deficiency or genetic testing
   - The patient has at least one of the following clinical signs of MPS VII: enlarged liver and spleen, joint limitations, airway obstructions or pulmonary dysfunction
   - The patient has not undergone successful bone marrow or stem cell treatment for MPS VII
   - The patient has limitation in mobility, but remains retains ambulatory capacity for the six-minute walk test (6MWT) to be measured and evaluated
   - The requested medication is prescribed by or given in consultation with a physician specializing in genetic or metabolic disorders

CONTINUE ON NEXT PAGE

VESTRONIDASE ALFA-VJBK (NSA)

GUIDELINES FOR USE (CONTINUED)

RENEWAL CRITERIA

1. Does the patient have a diagnosis of Mucopolysaccharidosis VII (MPS VII, Sly syndrome) **AND** meet the following criterion?
   - Patient has improved, maintained, or demonstrated less than expected decline in ambulatory ability based on 6MWT compared to baseline

   If yes, **approve for 12 months by HICL.**
   If no, do not approve.
   DENIAL TEXT: The guideline named **VESTRONIDASE ALFA-VJBK (Mepsevii)** requires a diagnosis of Mucopolysaccharidosis VII (MPS VII, Sly syndrome) for renewal. The following criteria must also be met:
   - Patient has improved, maintained, or demonstrated less than expected decline in ambulatory ability based on 6MWT compared to baseline

---

RATIONALE
Promote appropriate utilization of **VESTRONIDASE ALFA-VJBK** based on FDA approved indication and dosing.

FDA APPROVED INDICATION
Mepsevii is a recombinant human lysosomal beta glucuronidase indicated in pediatric and adult patients for the treatment of Mucopolysaccharidosis VII (MPS VII, Sly syndrome).

Limitations of Use: The effect of Mepsevii on the central nervous system manifestations of MPS VII has not been determined.

DOSAGE AND ADMINISTRATION
The recommended dosage of Mepsevii is 4 mg/kg administered every two weeks as an intravenous infusion under the supervision of a healthcare professional. Premedication with a non-sedating antihistamine with or without an anti-pyretic is recommended 30 to 60 minutes prior to the start of the infusion. Administer the infusion over approximately 4 hours. In the first hour of infusion, infuse 2.5% of the total volume. After the first hour, the rate can be increased to infuse the remainder of the volume over 3 hours as tolerated.

AVAILABLE STRENGTHS
Injection: Mepsevii 10 mg/5 mL (2 mg/mL) solution, single-dose vial

CONTINUED ON NEXT PAGE

VESTRONIDASE ALFA-VJBK (NSA)

REFERENCES

- Mepsevii [Prescribing Information]. Novato, CA: Ultragenyx Pharmaceutical Inc. November 2017.

Library	Commercial	NSA
Yes	No	Yes

Part D Effective: N/A
Commercial Effective: 04/01/18
Created: 03/18
Client Approval: 03/18
P&T Approval: 01/18

VINCRISTINE LIPOSOMAL

Generic	Brand	HICL	GCN	Exception/Other
VINCRISTINE SULFATE LIPOSOMAL	MARQIBO	39542		

This drug requires a written request for prior authorization.

GUIDELINES FOR USE

1. Does the patient have a diagnosis of Philadelphia chromosome-negative (Ph-) acute lymphoblastic leukemia (ALL) and meets **ALL** of the following criteria?
   - The patient has experienced a Ph- ALL relapse two or more times
   - The patient has tried at least two anti-leukemia therapies (refer to Table 1)

   If yes, **approve for 12 months by HICL with a quantity limit of #4 kits per 28 days.**
   If no, do not approve.
   DENIAL TEXT: Our guideline for **VINCRISTINE LIPOSOMAL (Marqibo)** requires a diagnosis of Philadelphia chromosome-negative (Ph-) acute lymphoblastic leukemia (ALL); patient has experienced a Ph- ALL relapse two or more times; and the patient has tried at least two anti-leukemia therapies.

RATIONALE
To promote appropriate utilization of Marqibo based on FDA approved indication and NCCN guidelines.

In the US, approximately 6,000 patients are diagnosed with ALL on an annual basis of which approximately 1,600 patients can be categorized as Ph- ALL in second or greater relapse. The median age of diagnosis for ALL is 14 years. ALL represents 75 to 80 percent of childhood acute leukemias. Vincristine is indicated for the treatment of a number of malignancies including ALL, Hodgkin's disease, malignant glioma, neuroblastoma, non-Hodgkin's lymphoma, rhabdomyosarcoma, and Wilms' tumor. It is also used off-label for head and neck cancer, idiopathic thrombocytopenic purpura, Kaposi's sarcoma, multiple myeloma, small cell lung cancer, thymoma, and trophoblastic disease. The National Comprehensive Cancer Network (NCCN) guidelines recommend vincristine, corticosteroids, and anthracyclines as the basis of an induction regimen for Ph- ALL.

Marqibo can be accessed through Spectrum Therapy Access Resources (STAR) which is a reimbursement support, co-pay assistance, and patient assistance program designed to help patients and healthcare professionals gain appropriate access to drugs.

CONTINUED ON NEXT PAGE

VINCRISTINE LIPOSOMAL

RATIONALE (CONTINUED)

Table 1: Examples of Anti-Leukemia Therapies

CALGB 8811 Larson regimen: daunorubicin, vincristine, prednisone, Oncaspar (pegaspargase), and cyclophosphamide
Linker 4-drug regimen: daunorubicin, vincristine, prednisone, and Oncaspar
Hyper-CVAD +/- Rituxan (rituximab): hyper-fractioned cyclophosphamide, vincristine, doxorubicin, and dexamethasone, alternating with high-dose methotrexate and cytarabine; with or without rituximab for CD20-positive disease
MRC UKALLXII/ECOG2993 regimen: daunorubicin, vincristine, prednisone, and Oncaspar (induction phase I); and cyclophosphamide, cytarabine, and 6-merceaptopurine (induction phase II)
GRAALL-2003 regimen: daunorubicin, vincristine, prednisone, Oncaspar, and cyclophosphamide (patients aged <60 years)
COG AALL-0434 regimen with nelarabine (for T-ALL): daunorubicin, vincristine, prednisone, and Oncaspar; Arranon (nelarabine) added to consolidation regimen
CCG-1961 regimen: daunorubicin, vincristine, prednisone, Oncaspar (patients age ≤21 years)
PETHEMA ALL-96 regimen: daunorubicin, vincristine, prednisone, Oncaspar, and cyclophosphamide (patients aged <30 years)
CALGB 10403 regimen: daunorubicin, vincristine, prednisone, and Oncaspar (patients aged <40 years)
DFCI ALL regimen based on DFCI Protocol 00-01: doxorubicin, vincristine, prednisone, high-dose methotrexate, and Oncaspar (patients ages <50 years)
Clolar (clofarabine)-containing regimens
cytarabine-containing regimens
alkylator combination regimens
Arranon (for T cell based-ALL)
augmented hyper-CVAD (hyper-fractionated cyclophosphamide, intensified vincristine, doxorubicin, intensified dexamethasone, and Oncaspar; alternating with high-dose methotrexate and cytarabine)

Induction Regimens for Ph- ALL (Adult patients aged ≥40 years)

- CALGB 8811 Larson regimen: daunorubicin, vincristine, prednisone, Oncaspar (pegaspargase), and cyclophosphamide
- Linker 4-drug regimen: daunorubicin, vincristine, prednisone, and Oncaspar
- Hyper-CVAD +/- Rituxan (rituximab): hyper-fractioned cyclophosphamide, vincristine, doxorubicin, and dexamethasone, alternating with high-dose methotrexate and cytarabine; with or without rituximab for CD20-positive disease
- MRC UKALLXII/ECOG2993 regimen: daunorubicin, vincristine, prednisone, and Oncaspar (induction phase I); and cyclophosphamide, cytarabine, and 6-merceaptopurine (induction phase II)

CONTINUED ON NEXT PAGE

VINCRISTINE LIPOSOMAL

RATIONALE (CONTINUED)

Induction Regimens for patients aged 15-39 years

- GRAALL-2003 regimen: daunorubicin, vincristine, prednisone, Oncaspar, and cyclophosphamide (patients aged <60 years)
- COG AALL-0434 regimen with nelarabine (for T-ALL): daunorubicin, vincristine, prednisone, and Oncaspar; Arranon (nelarabine) added to consolidation regimen
- CCG-1961 regimen: daunorubicin, vincristine, prednisone, Oncaspar (patients age ≤21 years)
- PETHEMA ALL-96 regimen: daunorubicin, vincristine, prednisone, Oncaspar, and cyclophosphamide (patients aged <30 years)
- CALGB 10403 regimen: daunorubicin, vincristine, prednisone, and Oncaspar (patients aged <40 years)
- DFCI ALL regimen based on DFCI Protocol 00-01: doxorubicin, vincristine, prednisone, high-dose methotrexate, and Oncaspar (patients ages <50 years)

NCCN recommends monthly vincristine prednisone pulses for 2 to 3 years with weekly methotrexate and daily 6-mercaptpurine as tolerated for the maintenance treatment of Ph- ALL.

Recommended salvage regimens for relapsed or refractory ALL include:

- Clolar (clofarabine)-containing regimens
- cytarabine-containing regimens
- alkylator combination regimens
- Arranon (for T cell based-ALL)
- augmented hyper-CVAD (hyper-fractionated cyclophosphamide, intensified vincristine, doxorubicin, intensified dexamethasone, and Oncaspar; alternating with high-dose methotrexate and cytarabine)
- Marqibo

FDA APPROVED INDICATIONS

Marqibo is a vinca alkaloid indicated for the treatment of adult patients with Philadelphia chromosome-negative (Ph-) acute lymphoblastic leukemia (ALL) in second or greater relapse or whose disease has progressed following two or more anti-leukemia therapies. This indication is based on overall response rate. Clinical benefit such as improvement in overall survival has not been verified.

DOSAGE

Administer Marqibo at a dose of 2.25 mg/m^2 intravenously over 1 hour once every 7 days.
Each single-dose vial of Marqibo contains 5 mg/31 mL (0.16 mg/mL) vincristine sulfate.

CONTINUED ON NEXT PAGE

VINCRISTINE LIPOSOMAL

REFERENCES

- Marqibo [Prescribing Information]. South San Francisco, CA: Talon Therapeutics, Inc.; October 2012. Available at: http://www.spectrumpharm.com/downloads/Marqibo_prescribing_infomation_1210.pdf. [Accessed September 3, 2013]
- Spectrum Pharmaceuticals Launches Marqibo® (vinCRIStine sulfate LIPOSOME injection) and Ships First Commercial Orders. Available at: http://investor.spectrumpharm.com/releasedetail.cfm?ReleaseID=788214. [Accessed September 3, 2013]
- Silverman JA, Deitcher SR. Marqibo (vincristine sulfate liposome injection) improves the pharmacokinetics and pharmacodynamics of vincristine. *Cancer Chemother Pharmacol* (2013) 71:555–564. Available at: http://www.ncbi.nlm.nih.gov/pmc/articles/PMC3579462/pdf/280_2012_Article_2042.pdf. [Accessed September 3, 2013]
- A Phase 3 Study to Evaluate Marqibo® in the Treatment of Subjects ≥ 60 Years Old With Newly Diagnosed ALL. Available at: http://clinicaltrials.gov/ct2/show/NCT01439347?term=vsli&rank=6. [Accessed September 3, 2013]
- NCCN Clinical Practice Guidelines in Oncology. Acute Lymphoblastic Leukemia Version 1.2013. Available at: http://www.nccn.org/professionals/physician_gls/pdf/all.pdf. [Accessed September 3, 2013]
- O'brien S, Schiller G, Lister J, et al. High-dose vincristine sulfate liposome injection for advanced, relapsed, and refractory adult Philadelphia chromosome-negative acute lymphoblastic leukemia. *J Clin Oncol*. 2013 Feb 20; 31(6):676-83. Available at: http://www.ncbi.nlm.nih.gov/pubmed/23169518?dopt=Abstract. [Accessed September 3, 2013]
- OPTIMAL>60, Improvement of Therapy of Elderly Patients With CD20+ DLBCL Using Rituximab Optimized and Liposomal Vincristine. Available at: http://clinicaltrials.gov/ct2/show/NCT01478542?term=nct01478542&rank=1 [Accessed September 5, 2013]

Library	Commercial	NSA
Yes	No	Yes

Part D Effective: N/A
Commercial Effective: 05/01/16
Created: 10/13
Client Approval: 03/16
P&T Approval: 11/13

VORETIGENE NEPARVOVEC-RZYL (NSA)

Generic	Brand	HICL	GCN	Exception/Other
VORETIGENE NEPARVOVEC-RZYL	LUXTURNA	44720		

***********Customer Service/PAC Alert************
(For Internal Use Only)

THIS IS A HIGH-IMPACT MEDICATION. DO NOT OVERRIDE OR APPROVE WITHOUT SUBMITTING FOR PHARMACIST REVIEW.

GUIDELINES FOR USE

1. Does the patient have a diagnosis of biallelic RPE65 mutation-associated retinal dystrophy and meet **ALL** of the following criteria?
   - Biallelic RPE65 mutation-associated retinal dystrophy is confirmed by documentation of genetic testing
   - The patient is 3 years of age or older
   - The requested medication is prescribed by or in consultation with an ophthalmologist or retinal specialist
   - The patient has a visual acuity of 20/60 or worse or a visual field less than 20 degrees in any meridian in both eyes
   - The treating physician attests that the patient has sufficient retinal cells as demonstrated by sufficient retinal thickness
   - The patient does NOT have pre-existing eye conditions that may lead to blindness independently of RPE65-mutation associated retinal dystrophy (e.g., leukemia with CNS/optic nerve involvement, macular edema or CMV retinitis)
   - Patient has NOT previously received gene therapy (including Luxturna) for the treatment of vision loss
   - The procedure and administration of Luxturna will be completed at a designated specialty Luxturna treatment center

   If yes, **approve for 1 fill per lifetime by HICL with a quantity limit of 0.5mL (one single dose vial) per affected eye.**
   If no, do not approve.
   DENIAL TEXT: See the denial text at the end of the guideline

CONTINUED ON NEXT PAGE

VORETIGENE NEPARVOVEC-RZYL (NSA)

GUIDELINES FOR USE (CONTINUED)

DENIAL TEXT: The guideline named **VORETIGENE NEPARVOVEC-RZYL (Luxturna)** requires that the patient has a diagnosis of confirmed biallelic RPE65 mutation-associated retinal dystrophy. In addition, the following criteria must be met:

- Biallelic RPE65 mutation-associated retinal dystrophy is confirmed by documentation of genetic testing
- The patient is 3 years of age or older
- The requested medication is prescribed by or in consultation with an ophthalmologist or retinal specialist
- The patient has a visual acuity of 20/60 or worse or a visual field less than 20 degrees in any meridian in both eyes
- The treating physician attests that the patient has sufficient retinal cells as demonstrated by sufficient retinal thickness
- The patient does NOT have pre-existing eye conditions that may lead to blindness independently of RPE65-mutation associated retinal dystrophy (e.g., leukemia with CNS/optic nerve involvement, macular edema or CMV retinitis)
- Patient has NOT previously received gene therapy (including Luxturna) for the treatment of vision loss
- The procedure and administration of Luxturna will be completed at a designated specialty Luxturna treatment center

---

RATIONALE

Promote appropriate utilization of **LUXTURNA** based on FDA approved indication.

FDA APPROVED INDICATIONS

Luxturna is an adeno-associated virus vector-based gene therapy indicated for the treatment of patients with confirmed biallelic RPE65 mutation-associated retinal dystrophy. Patients must have viable retinal cells as determined by the treating physician(s).

DOSAGE AND ADMINISTRATION

- The recommended dose of Luxturna for each eye is 1.5×10^{11} vector genomes (vg), administered by subretinal injection in a total volume of 0.3 mL.
- Luxturna is administered by a surgeon via subretinal injection.
  - Perform subretinal administration of Luxturna to each eye on separate days within a close interval, but no fewer than 6 days apart.
  - Recommend systemic oral corticosteroids equivalent to prednisone at 1 mg/kg/day (maximum of 40 mg/day) for a total of 7 days (starting 3 days before administration of Luxturna to each eye), and followed by a tapering dose during the next 10 days.

CONTINUED ON NEXT PAGE

VORETIGENE NEPARVOVEC-RZYL (NSA)

FDA APPROVED INDICATIONS (CONTINUED)

AVAILABLE STRENGTH(S)

Luxturna is a suspension for subretinal injection, supplied in a 0.5 mL extractable volume in a single-dose 2 mL vial for a single administration in one eye. The supplied concentration ($5x10^{12}$vg/mL) requires a 1:10 dilution prior to administration.

REFERENCES

- Luxturna [Prescribing Information]. Spark Therapeutics, Inc: Philadelphia, PA. December 2017.

Library	Commercial	NSA
Yes	No	Yes

Part D Effective: N/A
Commercial Effective: 04/01/18
Created: 03/18
Client Approval: 03/18
P&T Approval: 01/18

ZIV-AFLIBERCEPT

Generic	Brand	HICL	GCN	Exception/Other
ZIV-AFLIBERCEPT	ZALTRAP		32988 32989	

This drug requires a written request for prior authorization.

GUIDELINES FOR USE

1. Does the patient have a diagnosis of metastatic colorectal cancer (mCRC)?

   If yes, continue to #2.
   If no, do not approve.
   DENIAL TEXT: See the denial text at the end of the guideline.

2. Has the patient tried an oxaliplatin-containing regimen (such as FOLFOX)?

   If yes, continue to #3.
   If no, do not approve.
   DENIAL TEXT: See the denial text at the end of the guideline.

3. Is Zaltrap being used in combination with FOLFIRI or irinotecan?

   If yes, **approve for 12 months by GPID.**
   If no, do not approve.
   DENIAL TEXT: See the denial text at the end of the guideline.

DENIAL TEXT: Approval requires a diagnosis of metastatic colorectal cancer, a trial of an oxaliplatin-containing regimen (such as FOLFOX), and concurrent use with FOLFIRI or irinotecan.

RATIONALE

To ensure appropriate use of Zaltrap consistent with FDA approved indication and National Comprehensive Cancer Network (NCCN) recommendations.

CONTINUED ON NEXT PAGE

ZIV-AFLIBERCEPT

RATIONALE (CONTINUED)
Zaltrap is a fully humanized recombinant fusion protein that inhibits angiogenesis by binding to the vascular endothelial growth factor (VEGF)-A receptor. In addition to blocking all human VEGF-A isoforms, Zaltrap also inhibits VEGF-B, and placental growth factor (PlGF) with a higher affinity than native receptors. Zaltrap is given as a 4mgg intravenous infusion over 1 hour every 2 weeks. It should not be given as an intravenous push or bolus. It is given in combination with the FOLFIRI chemotherapy regimen. Zaltrap therapy must be suspended for both 4 weeks prior to and 4 weeks following major surgery. Aflibercept, marketed as Eylea, is approved for the treatment of macular degeneration.

NCCN Guidelines Version 2.2013: Colon Cancer / NCCN Guidelines Version 3.2013 Rectal Cancer

Surgical removal is the preferred treatment for early stage disease. Surgery is accompanied by adjuvant chemotherapy for patients with high-risk features or more extensive cancer involvement.

Primary treatment options for resectable synchronous metastases are:
- Chemotherapy (FOLFIRI, FOLFOX, or CapeOX) with or without AvastinChemotherapy (FOLFIRI or FOLFOX) with or without Vectibix (*KRAS* wild-type patients only)
- Chemotherapy (FOLFIRI) with or without Erbitux (*KRAS* wild-type patients only)
- Staged resection
- Infusional IV 5-FU with radiation

Primary treatment options for unresectable metachronous metastases previously treated with adjuvant FOLFOX are:
- FOLFIRI with or without Avastin
- FOLFIRI with or without Zaltrap
- Irinotecan with or without Avastin
- Irinotecan with or without Zaltrap
- FOLFIRI or irinotecan with Erbitux or Vectibix (*KRAS* wild-type patients only)

Initial therapy options for treatment of mCRC in patients appropriate for intensive therapy are:
- FOLFOX, with or without Avastin
- FOLFOX, with or without Vectibix (KRAS wild-type patients only)
- CapeOX with or without Avastin
- FOLFIRI with or without Avastin
- FOLFIRI with our without Erbitux or Vectibix (KRAS wild-type patients only)
- 5-FU/leucovorin or Xeloda with or without Avastin
- FOLFOXIRI

CONTINUED ON NEXT PAGE

ZIV-AFLIBERCEPT

RATIONALE (CONTINUED)
Initial therapy options for treatment of mCRC in patients not appropriate for intensive therapy are:
- Infusional 5-FU with leucovorin or Xeloda with or without Avastin
- Erbitux (KRAS wild-type patients only)
- Vectibix (*KRAS* wild-type patients only)

Zaltrap in combination with FOLFIRI is a recommended therapeutic regimen following progression of mCRC after an oxaliplatin containing chemotherapy regimen. Stivarga is considered a treatment option in therapy after first, second, or third progression, depending on previous lines of therapy.
Other treatment options after first or second progression include:
- Erbitux or Vectibix with irinotecan (KRAS wild-type patients only)
- FOLFOX, FOLFIRI, CapeOX, or irinotecan with or without Avastin
- Irinotecan and oxaliplatin with or without Avastin

FDA APPROVED INDICATIONS
Zaltrap, in combination with 5-fluorouracil, leucovorin, irinotecan-(FOLFIRI), is indicated for patients with metastatic colorectal cancer (mCRC) that is resistant to or has progressed following an oxaliplatin-containing regimen.

REFERENCES
- Zaltrap [Prescribing Information]. Bridgewater, NJ: Sanofi-Aventis U.S. LLC.
- National Comprehensive Cancer Network. Colon Cancer Guideline Version 2.2013. Available at: http://www.nccn.org/professionals/physician_gls/pdf/colon.pdf [Accessed January 16, 2013].
- National Comprehensive Cancer Network. Rectal Cancer Guideline Version 3.2013. Available at: http://www.nccn.org/professionals/physician_gls/pdf/rectal.pdf [Accessed January 16, 2013].

Library	Commercial	NSA
Yes	No	Yes

Part D Effective: N/A
Commercial Effective: 01/01/14
Created: 02/13
Client Approval: 11/13
P&T Approval: 11/13

INDEX

H

I

K

L

M

N

O

P

R

S

T

U

V

X

Y

Z