Priority Health Medicare Part B

References & Summary of Evidence

For Part B Prior Authorization and Step Therapy

November 2025

This document is updated frequently. Last revised: October 30, 2025

References & Summary of Evidence

For Medicare Part B Prior Authorization and Step Therapy

Priority Health Medicare complies with National Coverage Determinations (NCDs), Local Coverage Determinations (LCDs), Local Coverage Article (LCA), and other coverage and benefit conditions included in Traditional Medicare law for Part B drugs. These resources contain coverage criteria set by the Centers of Medicare & Medicaid Services (CMS) or a Medicare Administrative Contractor (MAC) to determine if a drug is reasonable and necessary for the treatment of a condition.

When coverage criteria do not exist or are not fully established in an NCD, LCD/LCA, or other Medicare statute or regulation, Priority Health Medicare may create internal coverage criteria based on CMS-approved compendium and current evidence in widely used treatment guidelines or clinical literature.

In accordance with Medicare law, when internal coverage criteria are created, Priority Health provides a publicly accessible summary of evidence considered during the development of the internal coverage criteria, a list of the sources of such evidence, and an explanation of the rationale supporting the adoption of the internal coverage criteria. This document presents this information.

A Medicare Administrative Contractor (MAC) establishes LCDs for Medicare Part A and Part B (A/B) medical drugs and services and Medicare Durable Medical Equipment (DME) for defined geographic areas or jurisdictions. Michigan falls under A/B MAC Jurisdiction 8 and DME MAC Jurisdiction B. For more information on NCDs, MACs, and LCDs/LCAs, refer to the Medicare Benefit Policy Manual, Chapter 15, CMS.GOV, and the Medicare Coverage Database.

Actemra IV *(tocilizumab)*
Priority Health Part B Step Therapy Drug: Yes
Additional Priority Health Part B Criteria: Yes
Actemra (tocilizumab) is an interleukin-6 inhibitor (IL-6i) indicated for multiple inflammatory conditions including rheumatoid arthritis (RA), giant cell arteritis, and juvenile idiopathic arthritis (JIA). It is available in both an intravenous (IV) and subcutaneous (SC) formulation, and indications may vary based on formulation. Currently, only the SC formulation is approved for the systemic sclerosis-associated interstitial lung disease (SSc-ILD) indication. For RA and JIA, guidelines favor the use of biologic DMARDs (bDMARD) in those with moderate or high disease activity despite previous conventional synthetic (csDMARD) trials. Guidelines do not currently favor one bDMARD class over another, however tumor necrosis factor inhibitors (TNFis) have the most documented safety and efficacy profiles. Infliximab agents (including Inflectra and Renflexis) are TNFis that work to block the activity of TNF, a cytokine that causes inflammation. It is this inflammation that is the primary target in the treatment of conditions like RA and JIA. Actemra has not been studied in combination with other bDMARDs (e.g., TNFis, interleukin receptor antagonists, etc) OR targeted synthetic DMARDs (Janus Kinase or JAK inhibitors) due to an increased risk of infection and increased immunosuppression. As such, use of Actemra in combination with other biologic agents or targeted synthetic DMARDs is not recommended. Actemra has not been studied with Otezla and has no studies to support co-administration. The Food and Drug Administration (FDA) has determined the biosimilars to be highly similar to their reference product (Actemra) and supports the use of approved biosimilars. Step therapy is applied to certain Part B drugs, biologics, or biosimilars in a way that lowers costs and improves the quality of care for Medicare beneficiaries per the Centers for Medicare & Medicaid Services (CMS) guidance.
References 1. Actemra [Package Insert]. South San Francisco, CA: Genentech USA, Inc.; 2013. 2. Fraenkel L, et al. 2021 American College of Rheumatology Guideline for the Treatment of Rheumatoid Arthritis. Arthritis Care & Research. 2021 Jul; 73 (7):924-939. 3. Ringold et al. 2019 American College of Rheumatology/Arthritis Foundation Guideline for the Treatment of JIA. Arthritis Care and Research. Vol 71 No 6 Jun 2019

Adakveo *(crizanlizumab)*
Priority Health Part B Step Therapy Drug: Yes
Additional Priority Health Part B Criteria: Yes
Adakveo (crizanlizumab-tmca) injection is a selectin blocker indicated to reduce the frequency of vaso-occlusive crises in adults and pediatric patients aged 16 years and older with sickle cell disease (SCD). Vaso-occlusive crises or VOCs (also referred to as recurrent acute pain crises) are the most common manifestations of SCD. A VOC is defined as pain resulting from tissue ischemia caused by vaso-occlusion commonly occurring in the bone(s) and bone marrow, which typically are associated with pain of sudden onset typically in the extremities, chest, and back. The Evidence-Based Management of Sickle Cell Disease: Expert Panel Report (EPR), 2014 states that hydroxyurea can reduce the frequency of sickle cell-related pain and the incidence of acute chest syndrome (ACS). Hydroxyurea has multiple mechanisms of action and benefits for people who have SCD including increasing high fetal hemoglobin (HbF) levels, raising red blood cell (RBC) volume, and improving cellular deformability and rheology (which increases blood flow and reduces vaso-occlusion). Hydroxyurea also lowers the number of circulating leukocytes and reticulocytes and alters the expression of adhesion molecules, which lead to vaso-occlusion. Hydroxyurea metabolism releases nitric oxide, which may also contribute to local vasodilation. The Expert Panel recommendations also advise that a clinical response to treatment with hydroxyurea may take 3 to 6 months. Therefore, a 6-month trial is recommended prior to considering hydroxyurea as a treatment failure. The report does not include recommendations for Adakveo yet.
References 1. Adakveo [Package Insert]. East Hanover, NJ: Novartis Pharmaceuticals Corporation; 2019. 2. National Heart, Lung, and Blood Institute. Evidence-based management of sickle cell disease: expert panel report, 2014.
Aduhelm *(aducanumab-avwa)*
Priority Health Part B Step Therapy Drug: No
Additional Priority Health Part B Criteria: No
Adulhelm is indicated for the treatment of Alzheimer's disease in patients with mild cognitive impairment or mild dementia stage of disease, the population in which treatment was initiated in clinical trials. The Centers for Medicare & Medicaid Services (CMS) released a national policy for coverage of monoclonal anti-amyloid antibodies approved by the Food and Drug Administration

(FDA) for the treatment of Alzheimer's disease. Under this national policy, Medicare covers FDA approved anti-amyloid antibodies under Coverage with Evidence Development (CED) when they are furnished in accordance with the prespecified coverage criteria for patients who have a clinical diagnosis of MCI due to Alzheimer's disease or mild Alzheimer's disease dementia, both with confirmed presence of amyloid beta pathology consistent with Alzheimer's disease. Monoclonal antibodies directed against amyloid that are approved based on evidence from a surrogate endpoint considered reasonably likely to predict clinical benefit may be covered in a randomized controlled trial conducted under an investigational new drug (IND) application. Monoclonal antibodies directed against amyloid that are approved based on evidence from a direct measure of clinical benefit may be covered in CMS-approved prospective comparative studies (study data may be collected in a registry). Refer to CMS's NCD: Monoclonal Antibodies Directed Against Amyloid for the Treatment of Alzheimer's Disease for a full description of criteria and evidence.

In 2 randomized studies terminated prior to the planned completion in patients with Alzheimer's disease (AD), high dose aducanumab-avwa significantly reduced clinical decline at week 78 compared with placebo in 1 trial, but not in the other. In a small, exploratory third study, rate of clinical decline was also significantly reduced at 1 year with high dose aducanumab-avwa. The estimated brain levels of amyloid beta plaque were significantly reduced in a subgroup analysis in all 3 studies

Priority Health follows Medicare's National Coverage Determination (NCD) 200.3 for Monoclonal Antibodies Directed Against Amyloid for the Treatment of Alzheimer's Disease (AD).

References

1. Aduhelm [Package Insert]. Cambridge, MA; Biogen Inc.: 2021

2. Centers for Medicare & Medicaid Services. National Coverage Determination (NCD) 200.3 Monoclonal Antibodies Directed Against Amyloid for the Treatment of ALZHEIMER's Disease (AD).

Adzynma *(ADAMTS13, recombinant-krhn)*

Priority Health Part B Step Therapy Drug: No

Additional Priority Health Part B Criteria: Yes

Adzynma is a human recombinant form of the A disintegrin and metalloproteinase with thrombospondin motifs 13 enzyme (rADAMTS13). The ADAMTS13 protein is involved with blood clotting. Adzynma replaces the missing or deficient ADAMTS13 enzyme in patients diagnosed with congenital thrombotic thrombocytopenic purpura (cTTP). TTP is a rare blood disorder that results in blood clots forming in small blood vessels throughout the body which can cause ischemic end organ damage.

A diagnosis may be made based upon a thorough clinical evaluation, a detailed patient history and identification of characteristic findings. The clinical diagnosis is confirmed by the finding of severely deficient (<10%) ADAMTS13 activity and the presence of an anti-ADAMTS13 antibody in patients with iTTP. People with cTTP will present similarly with very low ADAMTS13 activity, but without evidence of an ADAMTS13 antibody inhibitor. The diagnosis of cTTP is confirmed by genetic testing for variants in the ADAMTS13 gene.

References

1. Adzynma [prescribing information]. Lexington, MA: Takeda Pharmaceuticals U.S.A., Inc.; 2023

2. Clinicaltrials.gov. A Study of BAX 930 in Children, Teenagers, and Adults Born With Thrombotic Thrombocytopenic Purpura (TTP). (NCT 03393975) Available at: https://clinicaltrials.gov/study/NCT03393975

3. National Organization of Rare Diseases. Thrombotic thrombocytopenic purpura. 2023. https://rarediseases.org/rarediseases/thrombotic-thrombocytopenic-purpura/

Alhemo *(concizumab-mtci)*

Priority Health Part B Step Therapy Drug: Yes

Additional Priority Health Part B Criteria: Yes

Alhemo is an anti-tissue factor pathway inhibitor (anti-TFPI) product indicated for the routine prophylaxis to prevent or reduce frequency of bleeding episodes in adults and pediatric patients ≥ 12 years of age with hemophilia A (congenital Factor VIII deficiency) with or without Factor VIII inhibitors or hemophilia B (congenital Factor IX deficiency) with or without Factor IX inhibitors. Hemophilia A is a genetic bleeding disorder caused by insufficient levels of factor VIII. Hemophilia B is a genetic bleeding disorder caused by insufficient levels of factor IX. Symptoms for both vary from mild to severe based on the level of factor activity with severe disease noted to have factor levels less than 1% and often have bleeding for no known reason, particularly in joints and muscles.

Other treatment options for hemophilia A include factor VIII replacement products, Hemlibra (a bi-specific Factor IXa- and Factor X-directed antibody), and gene therapy with Roctavian. Other treatment options for hemophilia B include factor IX replacement products and gene therapy with Beqvez and Hemgenix.

For treatment of hemophilia A or hemophilia B with inhibitors, bypassing agents, such as FEIBA or NovoSeven may be used for treatment of acute bleeding episodes or prophylaxis. Immune tolerance induction (ITI) is also a treatment strategy utilizing factor VIII or factor IX to eradicate inhibitor antibodies. For treatment of hemophilia A with inhibitors, Hemlibra may also be used for treatment.

World Federation of Hemophilia guidelines recommends use of prophylaxis therapy in patients with moderate to severe hemophilia A or B. Both the WFH and the CDC define moderate to severe as listed below.

- ·Mild hemophilia A: factor activity is 5-40 IU/dL (5 to <40% of normal)
- ·Moderate hemophilia A: factor activity is 1-5 IU/dL (1-5% of normal)
- ·Severe hemophilia A: factor activity is <1 IU/dL (<1% of normal)

Alhemo is not yet addressed in current guidelines. The National Bleeding Disorders Foundation Medical and Scientific Advisory Council (MASAC) recommends factor VIII and factor IX products as treatment of choice for patients with hemophilia A and B in whom such agents are necessary. MASAC also provides recommendations for the use of Hemlibra for patients with hemophilia A with and without inhibitors. The International Society on Thrombosis and Hemostasis practice guidelines state that in patients with severe hemophilia A with inhibitors, prophylaxis with Hemlibra is recommended over bypassing agents (conditional recommendation based on very low-certainty evidence). The World Federation of Hemophilia (WFH) 2020 guideline recommends ITI be considered for patients with hemophilia A that develop persistent low-responding inhibitors and recommends Hemlibra prophylaxis over bypassing agent prophylaxis in those that fail or never underwent ITI.

Alhemo was approved based on results from phase III Explorer7 and Explore8 trials. The Explore7 trial included patients ages 12 and up with hemophilia A or B with factor VIII or IX inhibitors. This trial demonstrated superiority to on-demand based treatment with bypassing agents for a reduction in annualized bleeding rates. The Explore8 trial included patients ages 12 and up with hemophilia A or B without factor VIII or IX inhibitors. This trial demonstrated superiority to on-demand based treatment with bypassing agents for a reduction in annualized bleeding rates.

Step therapy is applied to certain Part B drugs, biologics, and biosimilars in a way that lowers costs and improves the quality of care for Medicare beneficiaries per the Centers for Medicare & Medicaid Services (CMS) guidance

References

1. Alhemo® subcutaneous injection [prescribing information]. Plainsboro, NJ: Novo Nordisk; December 2024.

2. Clinicaltrials.gov. Research Study to Look at How Well the Drug Concizumab Works in Your Body if You Have Haemophilia With Inhibitors (explorer7). (NCT 04083781) Available at: https://clinicaltrials.gov/study/NCT04083781

3. Clinicaltrials.gov. Research Study to Look at How Well the Drug Concizumab Works in Your Body if You Have Haemophilia Without Inhibitors (explorer8). (NCT04082429) Available at: https://clinicaltrials.gov/study/NCT04082429

4. National Bleeding Disorders Foundation (NBDF). MASAC (Medical and Scientific Advisory Council) recommendations concerning products licensed for the treatment of hemophilia

and selected disorders of the coagulation system. MASAC Document #284. Endorsed by the NBDF Board of Directors on April 11, 2024. Available at: https://www.bleeding.org/sites/default/files/document/files/MASAC-Products-Licensed.pdf.

5. Matsushita T, Shapiro A, Abraham A, et al. Phase 3 Trial of Concizumab in Hemophilia with Inhibitors. N Engl J Med. 2023;389(9):783-794. doi:10.1056/NEJMoa2216455

6. Srivastava A, Santagostino E, Dougall A, et al. WFH Guidelines for the Management of Hemophilia, 3rd edition [published correction appears in Haemophilia. 2021 Jul;27(4):699. doi: 10.1111/hae.14308]. Haemophilia. 2020;26 Suppl 6:1-158. doi:10.1111/hae.14046.

7. Rezende SM, Neumann I, Angchaisuksiri P, et al. International Society on Thrombosis and Haemostasis clinical practice guideline for the treatment of congenital hemophilia A and B based on the Grading of Recommendations Assessment, Development, and Evaluation methodology. J Thromb Haemost. 2024;22:2629-2652

8. The Centers for Disease Control (CDC). Diagnosing Hemophilia. May 2024. Available at: https://www.cdc.gov/hemophilia/testing/index.html

9. Centers for Medicare & Medicaid Services. Medicare Advantage Prior Authorization and Step Therapy for Part B Drugs. August 7, 2018. Retrieved from https://www.cms.gov/newsroom/fact-sheets/medicare-advantage-prior-authorization-and-step-therapy-part-b-drugs.

10. Centers for Medicare & Medicaid Services. (2018, August 7). Prior Authorization and Step Therapy for Part B Drugs in Medicare Advantage [Memorandum]. Retrieved from https://www.cms.gov/Medicare/Health-Plans/HealthPlansGenInfo/Downloads/MA_Step_Therapy_HPMS_Memo_8_7_2018.pdf

Alyglo *(immune globulin intravenous, human-stwk)*

Priority Health Part B Step Therapy Drug: Yes

Additional Priority Health Part B Criteria: No

Alyglo (immune globulin intravenous, human-stwk) is approved for the treatment of primary humoral immunodeficiency (PI) in adults. This includes, but is not limited to, congenital agammaglobulinemia, common variable immunodeficiency (CVID), Wiskott-Aldrich syndrome, and severe combined immunodeficiencies.

Alyglo is an immunoglobulin therapy that incorporates an extra step in the manufacturing process to reduce clotting factor XIa to undetectable levels. Clotting factor XIa has been identified as one of the causes of IVIG-related blood clots. Different IVIG products use different purification processes to remove clotting factor XIa. There is no data to support that this product offers additional clinical benefit over other IVIG products.

Step therapy is applied to certain Part B drugs, biologics, and biosimilars in a way that lowers costs and improves the quality of care for Medicare beneficiaries per the Centers for Medicare & Medicaid Services (CMS) guidance.

Priority Health also follows LCD L34771 for Immune Globulins.

References

1. Alyglo. [Package insert]. Teaneck, NJ; GC Biopharma: 2023.

2. Gammagard Liquid [package insert]. Westlake Village, CA: Baxter Healthcare Corporation; 2016

3. Gammagard S/D [package insert]. Westlake Village, CA: Baxter Healthcare Corporation; 2016

4. Centers for Medicare & Medicaid Services. Local Coverage Determination (LCD) L34771: Immune Globulins

5. Centers for Medicare & Medicaid Services. Medicare Advantage Prior Authorization and Step Therapy for Part B Drugs. August 7, 2018. Retrieved from https://www.cms.gov/newsroom/fact-sheets/medicare-advantage-prior-authorization-and-step-therapy-part-b-drugs.

6. Centers for Medicare & Medicaid Services. (2018, August 7). Prior Authorization and Step Therapy for Part B Drugs in Medicare Advantage [Memorandum]. Retrieved from https://www.cms.gov/Medicare/Health-Plans/HealthPlansGenInfo/Downloads/MA_Step_Therapy_HPMS_Memo_8_7_2018.pdf

7. Centers for Medicare & Medicaid Services. Local Coverage Determination (LCD) L34771 Immune Globulins.

Alymsys *(bevacizumab-maly)*

Priority Health Part B Step Therapy Drug: Yes

Additional Priority Health Part B Criteria: No

Alymsys (bevacizumab-maly) is biosimilar to Avastin® (bevacizumab). Bevacizumab is a vascular endothelial growth factor inhibitor indicated for the treatment of multiple cancers including a) metastatic colorectal cancer, in combination with intravenous fluorouracil-based chemotherapy for first- or second-line treatment; b) metastatic colorectal cancer, in combination with fluoropyrimidine-irinotecan- or fluoropyrimidine oxaliplatin-based chemotherapy for second-line treatment in patients who have progressed on a first-line bevacizumab product-containing regimen; c) unresectable, locally advanced, recurrent or metastatic non-squamous non-small cell lung cancer, in combination with carboplatin and paclitaxel for first-line treatment; d) recurrent glioblastoma in adult; e) metastatic renal cell carcinoma in combination with interferon alfa, and more.

Myvasi (bevacizumab-awwb) is biosimilar to Avastin® (bevacizumab). Zirabev (bevacizumab-bvzr) is biosimilar to Avastin® (bevacizumab). Per NCCN guidelines, an FDA-approved biosimilar is an appropriate substitute for bevacizumab.

References

1. Alymsys [Package Insert]. Bridgewater, NJ; Amneal Pharmaceuticals LLC.: 2022

2. Centers for Medicare & Medicaid Services Medicare Coverage Database. Local Coverage Determination (LCD) L37205: Chemotherapy Drugs and their Adjuncts.

3. Mvasi [Package Insert]. Thousand Oaks, CA; Amgen Inc.: 2023

4. Zirabev [Package Insert]. New York, NY; Pfizer Inc.: 2023

5. National Comprehensive Cancer Network. Central Nervous System Cancers (Version 1.2024)

6. National Comprehensive Cancer Network. Colon Cancer (Version 2.2024)

7. National Comprehensive Cancer Network. Kidney Cancer (Version 3.2024)

8. National Comprehensive Cancer Network. Non-Small Cell Lung Cancer (Version 5.2024)

Amvuttra *(vutrisiran)*

Priority Health Part B Step Therapy Drug: No

Additional Priority Health Part B Criteria: Yes

Amvuttra (vutrisiran) injection is a transthyretin-directed small interfering RNA indicated for the treatment of the polyneuropathy of hereditary transthyretin-mediated amyloidosis (hATTR amyloidosis) in adults. It is also indicated for the treatment of the cardiomyopathy of wild-type or hereditary transthyretin-mediated amyloidosis (ATTR-CM) in adults to reduce cardiovascular mortality, cardiovascular hospitalizations, and urgent heart failure visits

Transthyretin (TTR) amyloidosis is caused by the extracellular deposition of amyloid fibrils composed of TTR. TTR is predominantly produced by the liver and is a plasma transport protein for thyroxine and vitamin A. TTR amyloidosis is caused by mutations that destabilize the TTR protein. The disease can present as an infiltrative cardiomyopathy (familial amyloid cardiomyopathy) or as a progressive, axonal sensory autonomic and motor neuropathy (familial amyloidotic polyneuropathy; TTR-FAP, also referred to as FAP or ATTR-PN). The disease induces peripheral neuropathy, initially affecting the lower limbs generally including toes, extending above the ankle, and moving toward the proximal lower limbs with motor deficits. Cardiomyopathy is caused by the buildup of misfolded transthyretin proteins, which form amyloid fibrils. These fibrils accumulate in the heart muscle, leading to stiffening of the heart walls, which impairs the ability of the heart to pump effectively. This can lead to symptoms such as shortness of breath, heart failure, and irregular heart rhythms.

Scoring systems for evaluating TTR-FAP include systems based on the stages of peripheral and autonomic neuropathies proposed by Coutinho, disease staging based on polyneuropathy disability (PND) score, the Portuguese classification to evaluate the severity of TTR-FAP, sensory impairment scoring, autonomic dysfunction scoring, and scoring of motor function for muscle weakness. Coutinho et al. divides clinical staging of TTR-FAP into stage 0 (no symptoms), stage I (unimpaired ambulation; mostly mild sensory, motor, and autonomic neuropathy in the lower limbs), stage II (assistance with ambulation required; mostly moderate impairment progression to the lower limbs, upper limbs, and trunk) and stage III (wheelchair-bound or bedridden; severe sensory, motor, and autonomic involvement of all limbs). The PND score divides neuropathic symptoms into stage 0 (no impairment), stage I (sensory disturbances but preserved walking capability), stage II (impaired walking capability but ability to walk without a stick or crutches), stage IIIA (walking only with the help of one stick or crutch), stage IIIB (walking with the help of two sticks or crutches), and stage IV (confined to a wheelchair or bedridden).

Myocardial infiltration by transthyretin amyloid leads to concentric bi-ventricular hypertrophy with increased myocardial echogenicity. Echocardiographic features often include a small left ventricular (LV) cavity, biatrial enlargement, thickened valves and interatrial septum, and diastolic dysfunction with a restrictive filling pattern. Cardiac MRI (CMR) with late gadolinium enhancement (LGE) is useful for detecting extracellular amyloid deposits, showing diffuse subendocardial or transmural enhancement with 85–90% sensitivity and specificity. Nuclear imaging with technetium-99m pyrophosphate (Tc-PYP) is the only non-biopsy method that can definitively diagnose ATTR-CM. A grade 2 or 3 uptake on Tc-PYP scan confirms diagnosis with 100% specificity in the absence of monoclonal protein. Genetic testing is recommended post-diagnosis to distinguish between hereditary and wild-type ATTR-CM.

There is no data to support the efficacy and safety in use of disease-modifying therapies in liver transplant recipients or for use of pharmacotherapy in patients with stage 0 disease or with later-stage disease or cardiomyopathy. As such the 'Guideline of transthyretin-related hereditary amyloidosis for clinicians' recommends these populations should be treated only within the confines of a clinical trial.

Tafamidis and tafamidis meglumine are indicated for the treatment of cardiomyopathy of wild type or hereditary transthyretin-mediated amyloidosis (ATTR-CM) to reduce cardiovascular mortality and cardiovascular-related hospitalization. They are TTR stabilizers that work by reducing further ATTR deposition and can slow disease progression. Tafamidis has demonstrated a reduction in all-cause mortality and cardiovascular hospitalization in hATTR-CM patients with heart failure of NYHA functional Classes I and II. In contract, Amvuttra works by reducing the production of both wild-type and mutant TTR proteins. There is insufficient data to directly compare the net health benefit of vutrisiran monotherapy for ATTR-CM versus tafamidis.

Amvuttra was studied in patients with polyneuropathy caused by hereditary transthyretin-mediated amyloidosis that were in Stage 1 or Stage 2 of the disease and had Val30Met mutation in the transthyretin gene or one of 21 other mutations. Amvuttra significantly

improved clinical manifestations of neuropathy over 9 months compared with placebo. Currently, there is no literature supporting the use of one product over another, or the use the use of any product in combination with other therapies for ATTR (e.g., tafamidis). Amvuttra has not been studied in patients with prior liver transplant.

Amvuttra was studied in patients with ATTR-CM who had New York Heart Association (NYHA) class II heart failure. The majority of patients (88%) had wild-type ATTR. Among those with variant ATTR, 13 distinct pathogenic TTR mutations were identified, with the V122I variant being the most prevalent. Amvuttra was associated with a significantly lower risk of the composite endpoint of all-cause mortality and recurrent cardiovascular events compared with placebo.

To date, there is insufficient evidence to support the use of Amvuttra with other therapies for hATTR amyloidosis, including TTR stabilizers or TTR-lowering agents. As such, use of Amvuttra in combination with other TTR stabilizers or TTR-lowering agents is not recommended.

Step therapy is applied to certain Part B drugs, biologics, and biosimilars in a way that lowers costs and improves the quality of care for Medicare beneficiaries per the Centers for Medicare & Medicaid Services (CMS) guidance.

References

1. Amvuttra (prescribing information). Cambridge, MA: Alnylam Pharmaceuticals, Inc.; 2022.

2. Ando Y, Coelho T, Berk JL, et al. Guideline of transthyretin-related hereditary amyloidosis for clinicians. Orphanet Journal of Rare Diseases. 2013;8:31. Doi: 10.1186/1750-1172-8-31.

3. Karam C, et al. Diagnosis and treatment of hereditary transthyretin amyloidosis with polyneuropathy in the United States: Recommendations from a panel of experts. Muscle Nerve. 2024 Mar;69(3):273-287. doi: 10.1002/mus.28026. Epub 2024 Jan 4. PMID: 38174864

4. Institute for Clinical and Economic Review. Final Evidence Report: Disease-Modifying Therapies for Transthyretin Amyloid Cardiomyopathy. ICER; September 5, 2024. Available at: https://icer.org/wp-content/uploads/2024/03/ICER_ATTR-CM_Final-Report_For-Publication_10212024.pdf

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https://www.cms.gov/Medicare/HealthPlans/HealthPlansGenInfo/Downloads/MA_Step_Therapy_HPMS_Memo_8_7_2018.pdf

Anzemet *(dolasetron)*

Priority Health Part B Step Therapy Drug: Yes

Additional Priority Health Part B Criteria: No

Anzemet is a 5-HT(3) receptor antagonist. It is thought that by inhibiting 5-HT(3) signaling through receptor blockade in the chemoreceptor trigger zone, nausea and emetic triggers are disrupted.

Other agents within this class include ondansetron, granisetron, and palonosetron. Palonosetron has a much longer half-life than the other three, but otherwise the class is thought to be interchangeable. One study compared the safety and efficacy of Anzemet versus ondansetron in the prevention of cisplatin-induced nausea/vomiting and found no statistically significant differences in either response rates or tolerability. Another study compared granisetron versus ondansetron in the prevention of cisplatin-induced nausea/vomiting and also concluded no significant differences in safety or efficacy.

References

1. Anzemet [Package Insert]. Bridgewater, NJ; sanofi-aventis U.S. LLC: 2013

2. Hesketh P, et al. Double-blind, randomized comparison of the antiemetic efficacy of intravenous dolasetron mesylate and intravenous ondansetron in the prevention of acute cisplatin-induced emesis in patients with cancer. J Clin Oncol.1996;14(8):2242

3. Navari R, et al. Comparative clinical trial of granisetron and ondansetron in the prophylaxis of cisplatin-induced emesis. J Clin Oncol. 1995;13(5):1242

Asceniv *(immune globulin)*

Priority Health Part B Step Therapy Drug: Yes

Additional Priority Health Part B Criteria: No

Intravenous immunoglobulin (IVIG) are human derived antibodies used to treat various autoimmune, infectious, and idiopathic diseases including, but not limited to: Chronic Inflammatory Demyelinating Polyneuropathy (CIDP), Chronic Lymphocytic Leukemia (CLL), multiple myeloma, myasthenia gravis, and Immune Thrombocytopenia (ITP).

Primary immunodeficiency affects the body's natural immune system's ability to combat infection. These are genetic disorders that can be treated by undergoing hemopoietic stem cell transplantation, by receiving preventative medicine (like antibiotics to reduce infection

risk) or managing with supportive care. IVIG plays a role in these patients' treatment by reducing infection risk and limiting the potential for disease complications.

Myasthenia gravis is a rare autoimmune disease that can lead to fatigue and generalized muscle weakness. Treatment options include corticosteroids and immunosuppressive therapies (azathioprine, mycophenolate, e.g.), but some patients will continue to show symptoms despite these treatments and are categorized as 'refractory' (per the 2016 International Consensus Guidance for Management of Myasthenia Gravis). These patients have functional impairment requiring further medical intervention. In severe cases, referred to as 'myasthenic crisis', patients experience a loss in respiratory muscle function requiring intubation or mechanical ventilation. The 2016 International Consensus recommends IVIG be used in these cases to allow the patient to recover from the crisis. IVIG acts to bridge myasthenia gravis patients from exacerbation to recovery while further immunosuppressive care is allowed time to take effect.

There are multiple IVIG products available. No clinical trials have been conducted comparing the efficacy of one therapy to another. For treatment of primary immune deficiency disorder, the following are some, but not all, FDA-approved IVIG products to treat these conditions: Asceniv, Bivigam, Carimune, Privigen, Gammagard Liquid, and Octagam. Certain patient specific factors may affect which IVIG product is selected. Diabetic patients may want to avoid products containing maltose or glucose (Gammagard S/D, Octagam, e.g.). Patients with low tolerance for increased intravascular volume may want to avoid products high in sodium or albumin content (Bivigam, e.g.).

Priority Health also follows LCD L34771 for Immune Globulins.

References

1. Asceniv [Package Insert]. Boca Raton, FL; ADMA Biologics

2. Bonilla FA, et al. Practice parameter for the diagnosis and management of primary immunodeficiency. J Allergy Clin Immunol. 2015; 136 (5): 1186 – 205

3. Sanders DB, et al. International consensus guidance for management of myasthenia gravis: executive summary. Neurology. 2016 Jul 26; 87 (4): 419 - 25

4. Centers for Medicare & Medicaid Services. Local Coverage Determination (LCD) L34771: Immune Globulins

Avastin *(bevacizumab)* Chemotherapy (J9035) only

Priority Health Part B Step Therapy Drug: Yes

Additional Priority Health Part B Criteria: No

Avastin is bevacizumab injection. Bevacizumab is a vascular endothelial growth factor inhibitor indicated for the treatment of multiple cancers including a) metastatic colorectal cancer, in combination with intravenous fluorouracil-based chemotherapy for first- or

second-line treatment; b) metastatic colorectal cancer, in combination with fluoropyrimidine-irinotecan- or fluoropyrimidine oxaliplatin-based chemotherapy for second-line treatment in patients who have progressed on a first-line bevacizumab product-containing regimen; c) Unresectable, locally advanced, recurrent or metastatic non-squamous non-small cell lung cancer, in combination with carboplatin and paclitaxel for first-line treatment; d) recurrent glioblastoma in adult; e) metastatic renal cell carcinoma in combination with interferon alfa, and more.

Myvasi (bevacizumab-awwb) is biosimilar to Avastin® (bevacizumab). Zirabev (bevacizumab-bvzr) is biosimilar to Avastin® (bevacizumab). Per NCCN guidelines, an FDA-approved biosimilar is an appropriate substitute for bevacizumab.

References

1. Avastin [Package Insert]. South San Francisco, CA; Genentech, Inc.: 2019

2. Centers for Medicare & Medicaid Services. Local Coverage Determination (LCD) L37205: Chemotherapy Drugs and their Adjuncts.

3. Mvasi [Package Insert]. Thousand Oaks, CA; Amgen Inc.: 2023

4. Zirabev [Package Insert]. New York, NY; Pfizer Inc.: 2023

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6. National Comprehensive Cancer Network. Colon Cancer (Version 2.2024)

7. National Comprehensive Cancer Network. Kidney Cancer (Version 3.2024)

8. National Comprehensive Cancer Network. Non-Small Cell Lung Cancer (Version 5.2024)

Aveed *(testosterone undecanoate)*

Priority Health Part B Step Therapy Drug: Yes

Additional Priority Health Part B Criteria: Yes

Per the 2018 Endocrine Society Clinical Practice guideline, testosterone therapy is recommended in hypogonadal men to induce and maintain secondary sex characteristics and correct symptoms of testosterone deficiency. After treatment initiation, patients should be evaluated for compliance and response to testosterone treatment, as well as adverse effects.

Testosterone levels vary diurnally and can also vary based on several factors. In accordance with FDA label and clinical practice guidelines, hypogonadism should be confirmed by ensuring serum testosterone concentrations are below the normal range on 2 or more separate mornings. Per the American Urological Association (AUA) Guideline on Evaluation and Management of Testosterone Deficiency, a total testosterone level below 300 nanograms per deciliter (ng/dL) is a reasonable cut-off to support the diagnosis of low

testosterone. However, references ranges may vary per lab. In addition, the clinical diagnosis of testosterone deficiency should only be made when a patient has low total testosterone levels combined with symptoms and/or signs of low testosterone.

Per the Clinical Guideline from the American College of Physicians Testosterone Treatment in Adult Men With Age-Related Low Testosterone, clinicians should consider intramuscular rather than transdermal formulations when initiating testosterone treatment as costs are considerably lower and clinical effectiveness and harms are similar. Evidence from 20 observational studies with a mean follow-up ranging from 0.73 to 10.3 years showed no increased risk for mortality, cardiovascular events, prostate cancer, or pulmonary embolism or deep venous thrombosis. No consistent differences were observed in harms according to transdermal versus intramuscular formulations in the included observational studies that addressed the comparison. Evidence from indirect comparisons suggests no substantial differences in clinical effectiveness, benefits, or harms between intramuscular and transdermal testosterone applications, although very little evidence exists from direct comparisons of the 2 formulations.

Per the Endocrine Treatment of Gender-Dysphoric/Gender-Incongruent Persons: An Endocrine Society Clinical Practice Guideline transgender and gender diverse (TGD) persons may require medically necessary gender-affirming hormone therapy (GAHT) to achieve changes consistent with their embodiment goals, gender identity, or both. Masculinizing GAHT typically consists of testosterone. Clinical studies have demonstrated the efficacy of several different androgen preparations to induce masculinization in transgender males. Regimens to change secondary sex characteristics follow the general principle of hormone replacement treatment of male hypogonadism. Clinicians can use either parenteral or transdermal preparations to achieve testosterone values in the normal male range. The guidelines do not recommend one testosterone product over another. In general, the goal is to target serum levels of the sex steroids to match the levels associated with the individual's gender identity, although optimal target ranges have not been established

Step therapy is applied to certain Part B drugs, biologics, or biosimilars in a way that lowers costs and improves the quality of care for Medicare beneficiaries per the Centers for Medicare & Medicaid Services (CMS) guidance.

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3. Qaseem, A et al. Testosterone Treatment in Adult Men with Age-Related Low Testosterone: A Clinical Guideline from the American College of Physicians. Ann Intern Med 2020; 172(2): 126-133.

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Avsola *(infliximab-axxq)*

Priority Health Part B Step Therapy Drug: Yes

Additional Priority Health Part B Criteria: Yes

Avsola (infliximab) is a tumor necrosis factor inhibitor (TNFi) indicated for several conditions including Crohn's Disease (CD), Ulcerative Colitis (UC), fistulizing CD, Rheumatoid Arthritis (RA), active ankylosing spondylitis (AS), psoriatic arthritis (PsA), and plaque psoriasis (PsO).

Ankylosing spondylitis 'AS' and non-radiographic axial spondyloarthritis 'NRAS' are related conditions. The 2019 American College of Rheumatology recommendations for AS and NRAS are similar. Recommended first-line agents include nonsteroidal anti-inflammatory drugs (NSAIDs) due to their well-known safety and efficacy profiles. For patients who have active disease despite treatment with NSAIDs, treatment with a TNFi is recommended. Guidelines do not favor one TNFi over another.

Hidradenitis suppurativa (HS) is a chronic, painful skin condition that varies in presentation. There are no established treatment guidelines for this condition, but the foundation for HS has put forth evidence-based recommendations. Initial treatment includes topical and systemic antibiotics with progression to biologics if refractory or unresponsive to initial treatment. Antibiotics have been used to treat HS for decades; there is robust evidence to show symptom improvement and patient tolerability. Biologic agents (e.g., TNFi, interleukin inhibitors) have shown some benefit in small studies but lack the robust support to make strong recommendations for dosing, appropriate goals of therapy, and duration of treatment.

The 2018 American College of Gastroenterology (ACG) guidelines recommend mercaptopurine, azathioprine, and methotrexate in symptomatic CD despite prior corticosteroid use. TNFi agents are effective in those with inadequate response to these initial therapies.

Per the 2020 American Gastroenterology Association guidelines, multiple agents effectively induce and maintain remission of UC, including corticosteroids, 5-aminosalicylates '5-ASA', and biologics. Treatment of mild-to-moderate UC is typically started with 5-ASA therapy. In those who do not respond to 5-ASA therapy, induction can be achieved through short-term corticosteroids. Once induction is achieved, maintenance can be managed with thiopurines. Methotrexate is not recommended for induction or maintenance of remission in UC, whereas biologic agents do have support for use in these treatment areas. Guidelines

do not favor one biologic over another, nor do they favor biologics over thiopurine monotherapy for those in remission.

For Rheumatoid Arthritis (RA), guidelines favor the use of biologic DMARDs (bDMARD) for moderate or high disease activity despite prior conventional synthetic DMARDs (csDMARD). Guidelines do not favor one bDMARD over another, however TNFi agents have the most documented safety and efficacy profiles.

Per the 2020 Joint AAD-NPF guidelines (non-biologic), recommended treatments include methotrexate, cyclosporine, and acitretin. Methotrexate and cyclosporine are category A recommendations, whereas acitretin is a category B recommendation. The 2019 Joint AAD-NPF guidelines (biologics) recommend (category A) the use of biologics in treating psoriasis but do not suggest one agent over another. TNFis, interleukin-12/23, IL-23, and IL-17 inhibitors have all shown efficacy in this condition.

Per the 2018 American College of Rheumatology (ACR)/National Psoriasis Foundation (NPF) guidelines, methotrexate, sulfasalazine, cyclosporine, and leflunomide may be used in patients with non-severe Psoriatic Arthritis (PsA) and have robust safety and efficacy evidence to support their use. If initial treatment is not sufficient, switching to a biologic is suggested.

There is limited data on the concurrent use of infliximab products with other biologic agents, targeted synthetic DMARDs (JAK inhibitors), and PDE4 inhibitors (Otezla). Given the absence of strong clinical evidence and the potential for increased infection risk, it is not recommended to use infliximab products in combination with these agents.

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Treatment Network Recommendations for the Treatment of Ankylosing Spondylitis and Nonradiographic Axial Spondyloarthritis. Arthritis Rheumatol. 2019 Oct;71(10):1599-1613

Azmiro *(testosterone cypionate)*

Priority Health Part B Step Therapy Drug: Yes

Additional Priority Health Part B Criteria: Yes

Per the 2018 Endocrine Society Clinical Practice guideline, testosterone therapy is recommended in hypogonadal men to induce and maintain secondary sex characteristics and correct symptoms of testosterone deficiency. After treatment initiation, patients should be evaluated for compliance and response to testosterone treatment, as well as adverse effects.

Testosterone levels vary diurnally and can also vary based on several factors. In accordance with FDA label and clinical practice guidelines, hypogonadism should be confirmed by ensuring serum testosterone concentrations are below the normal range on 2 or more separate mornings. Per the American Urological Association (AUA) Guideline on Evaluation and Management of Testosterone Deficiency, a total testosterone level below 300 nanograms per deciliter (ng/dL) is a reasonable cut-off to support the diagnosis of low testosterone. However, references ranges may vary per lab. In addition, the clinical diagnosis of testosterone deficiency should only be made when a patient has low total testosterone levels combined with symptoms and/or signs of low testosterone.

Per the Endocrine Treatment of Gender-Dysphoric/Gender-Incongruent Persons: An Endocrine Society Clinical Practice Guideline transgender and gender diverse (TGD) persons may require medically necessary gender-affirming hormone therapy (GAHT) to achieve changes consistent with their embodiment goals, gender identity, or both. Masculinizing GAHT typically consists of testosterone. Clinical studies have demonstrated the efficacy of several different androgen preparations to induce masculinization in transgender males. Regimens to change secondary sex characteristics follow the general principle of hormone replacement treatment of male hypogonadism. Clinicians can use either parenteral or transdermal preparations to achieve testosterone values in the normal male range. The guidelines do not recommend one testosterone product over another. In general, the goal is to target serum levels of the sex steroids to match the levels associated with the individual's gender identity, although optimal target ranges have not been established

Step therapy is applied to certain Part B drugs, biologics, or biosimilars in a way that lowers costs and improves the quality of care for Medicare beneficiaries per the Centers for Medicare & Medicaid Services (CMS) guidance.

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Beizray *(docetaxel)*

Priority Health Part B Step Therapy Drug: Yes

Additional Priority Health Part B Criteria: Yes

Beizray (docetaxel) is a microtubule inhibitor indicated for treatment of breast cancer, non-small cell lung cancer (NSCLC), castration-resistant prostate cancer (CRPC), gastric adenocarcinoma (GC), and squamous cell carcinoma of the head and neck (SCCHN).

Beizray is a new formulation of docetaxel that was developed to be polysorbate 80 free. It is solubilized in human-derived Albumin leading to a reduction in adverse events associated with synthetic excipients. The presence of polysorbate 80 in the intravenous formulation of docetaxel has been implicated in hypersensitivity systemic reactions (HSRs) that were observed in the early clinical studies. In those studies, the incidence of HSRs ranged from 5% to 40%, with most events being grade 2 in severity on the four-point scale of the National Cancer Institute common toxicity criteria. Consequently, patients treated with the conventional formulation of docetaxel are premedicated with oral corticosteroids. Aside from the potential to lessen hypersensitivity reactions, there is no data to support a safety or efficacy benefit of Beizray over generic docetaxel. In addition, Beizray carries the same hypersensitivity warnings in its labeling as docetaxel (Taxotere).

Step therapy is applied to certain Part B drugs, biologics, or biosimilars in a way that lowers costs and improves the quality of care for Medicare beneficiaries per the Centers for Medicare & Medicaid Services (CMS) guidance.

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1. Beizray [Package Insert]. Zhuhai, Guangdong, 519090, China; Zhuhai Beihai Biotech Co., Ltd.: 2024

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4. Centers for Medicare & Medicaid Services. Medicare Advantage Prior Authorization and Step Therapy for Part B Drugs. August 7, 2018. Retrieved from https://www.cms.gov/newsroom/fact-sheets/medicare-advantage-prior-authorization-and-step-therapy-part-b-drugs.

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Benlysta IV *(belimumab)* vial

Priority Health Part B Step Therapy Drug: Yes

Additional Priority Health Part B Criteria: No

Benlysta is a B-lymphocyte stimulator (BLyS)-specific inhibitor indicated for the treatment of patients aged 5 years and older with active systemic lupus erythematosus (SLE) who are receiving standard therapy and patients aged 5 years and older with active lupus nephritis (LN) who are receiving standard therapy. Benlysta has not been studied and there is no data to support use in combination with other biologic drug or Lupkynis.

In the absence of contraindications, the 2019 European League Against Rheumatism–European Renal Association–European Dialysis and Transplant Association (EULAR/ERA–EDTA) recommends hydroxychloroquine (HCQ) for all patients with SLE or LN. Glucocorticoids (GC) can provide rapid symptom relief, but various detrimental effects limit use. Initiation of immunosuppressive (IS) drugs facilitates GC tapering and may prevent disease flares. Immunosuppressive options include methotrexate, azathioprine, mycophenolate mofetil, and cyclophosphamide.

The 2019 EULAR/ERA–EDTA guidelines state that the diagnostic and prognostic value of kidney biopsy for LN remains indispensable and recommends it not be substituted by other clinical or laboratory variables. Class II does not usually require immunosuppressive therapy. Classes III-IV include an induction regimen followed by maintenance treatment with mycophenolate or azathioprine.

Guidelines recommend Benlysta be considered as an add-on treatment to facilitate GC sparing, control extra-renal lupus activity, and decrease the risk for extra-renal flares. Guidelines recommend Benlysta be considered in extrarenal disease with inadequate control (ongoing disease activity or frequent flares) to first-line treatments (typically including combination of HCQ and prednisone with or without IS agents), and inability to taper GC daily dose to acceptable levels. Treatment in SLE should aim at remission or at low disease activity in all organ systems (if remission cannot be achieved). In LN, therapy should aim at least partial remission (≥50% reduction in proteinuria to subnephrotic levels

and serum creatinine within 10% from baseline) to complete renal remission (proteinuria <500 mg/24 hours and SCr within 10% from baseline). Some patients may require longer treatment duration and half of patients not reaching this goal may still have stable long-term kidney function.

Benlysta was studied in patients with active SLE disease and a Safety of Estrogens in Lupus Erythematosus National Assessment-Systemic Lupus Erythematosus Disease Activity Index (SELENA-SLEDAI) score of >4 and showed no significant differences between any of the groups receiving Benlysta and the placebo group in the percent change in SELENA-SLEDAI score at 24 weeks or in time to first flare within 52 weeks. However, Benlysta did appear to be beneficial in the subgroup of patients who were autoantibody positive (antinuclear antibody titer 1:80 or greater and/or anti-double-stranded DNA [anti-dsDNA] 30 IU/ml or greater at day 0). Benlysta was then further studied in patients with active SLE disease with a SELENA-SLEDAI score ≥6 and positive autoantibody test results. Patients receiving Benlysta 10 mg/kg plus standard therapy achieved a significantly higher SRI-4 response than the group receiving placebo plus standard therapy. The SRI uses the SELENA-SLEDAI score as an objective measure of reduction in global disease activity; along with the British Isles Lupus Assessment Group (BILAG) organ domain score(s) and the Physician's Global Assessment (PGA) score.

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Beqvez *(fidanacogene elaparvovec-dzkt)*
Priority Health Part B Step Therapy Drug: No
Additional Priority Health Part B Criteria: Yes
Beqvez is an adeno-associated virus (AAV) vector-based gene therapy that is indicated as a one-time therapy for the prevention of bleeding episodes in adult individuals with moderate-severe to severe hemophilia B. Hemophilia B is a rare genetic bleeding disorder in which affected individuals have insufficient levels of factor IX. It is the second most common type of hemophilia and caused by mutations in the F9 gene. This gene is located on the X chromosome and thus the disease is inherited as an X-linked recessive trait. Symptoms can range from mild, going almost unnoticed to severe where patients have a factor level of less than 1% and often have bleeding for no known reason, especially in joints and muscles. Mild cases typically do not need prophylactic therapy and may only require on-demand factor for injuries or surgery while severe cases require preventative treatment. Standard of care for hemophilia B includes the use of factor IX replacement therapy. To have been enrolled in the BENEGENE-2 trial, patients needed to be stable on factor IX therapy prior to administration. Note that patients in the study population had a FIX activity level of less than or equal to 2% of normal. There is no data to support use of Beqvez following prior use of Beqvez or another AAV-based gene therapy.
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Bivigam *(immune globulin)*

Priority Health Part B Step Therapy Drug: Yes

Additional Priority Health Part B Criteria: No

Intravenous immunoglobulin (IVIG) are human derived antibodies used to treat various autoimmune, infectious, and idiopathic diseases including, but not limited to: Chronic Inflammatory Demyelinating Polyneuropathy (CIDP), Chronic Lymphocytic Leukemia (CLL), multiple myeloma, myasthenia gravis, and Immune Thrombocytopenia (ITP).

Primary immunodeficiency affects the body's natural immune system's ability to combat infection. These are genetic disorders that can be treated by undergoing hemopoietic stem cell transplantation, by receiving preventative medicine (like antibiotics to reduce infection risk) or managing with supportive care. IVIG plays a role in these patients' treatment by reducing infection risk and limiting the potential for disease complications.

Myasthenia gravis is a rare autoimmune disease that can lead to fatigue and generalized muscle weakness. Treatment options include corticosteroids and immunosuppressive therapies (azathioprine, mycophenolate, e.g.), but some patients will continue to show symptoms despite these treatments and are categorized as 'refractory' (per the 2016 International Consensus Guidance for Management of Myasthenia Gravis). These patients have functional impairment requiring further medical intervention. In severe cases, referred to as 'myasthenic crisis', patients experience a loss in respiratory muscle function requiring intubation or mechanical ventilation. The 2016 International Consensus recommends IVIG be used in these cases to allow the patient to recover from the crisis. IVIG acts to bridge myasthenia gravis patients from exacerbation to recovery while further immunosuppressive care is allowed time to take effect.

There are multiple IVIG products available. No clinical trials have been conducted comparing the efficacy of one therapy to another. For treatment of primary immune deficiency disorder, the following are some, but not all, FDA-approved IVIG products to treat these conditions: Asceniv, Bivigam, Carimune, Privigen, Gammagard Liquid, and Octagam. Certain patient specific factors may affect which IVIG product is selected. Diabetic patients may want to avoid products containing maltose or glucose (Gammagard S/D, Octagam, e.g.). Patients with low tolerance for increased intravascular volume may want to avoid products high in sodium or albumin content (Bivigam, e.g.).

Priority Health follows LCD L34771 for Immune Globulins.

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2. Bonilla FA, et al. Practice parameter for the diagnosis and management of primary immunodeficiency. J Allergy Clin Immunol. 2015; 136 (5): 1186 – 205

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4. Centers for Medicare & Medicaid Services. Local Coverage Determination (LCD) L34771: Immune Globulins

Bkemv *(eculizumab-aeeb)*

Priority Health Part B Step Therapy Drug: Yes

Additional Priority Health Part B Criteria: Yes

Bkemv is a biosimilar to Soliris and was granted the FDA's interchangeability designation, which allows it to be used in place of the branded reference product without needing to change the prescription.

Eculizumab is a monoclonal antibody that binds to the complement C5 protein and stops activation of the complement system, a part of the body's immune system. This binding prevents the breakdown of red blood cells in the bloodstream (called intravascular hemolysis). Like Soliris, Bkemv has a Boxed Warning regarding the increased risk of serious and life-threatening meningococcal infections caused by Neisseria meningitidis.

AHUS consists of acute hemolytic anemia with fragmented red blood cells (microangiopathic hemolytic anemia), thrombocytopenia, and acute kidney injury. Mutations in complement genes, or antibodies to their protein products, result in unregulated activity of the alternate complement pathway, endothelial injury, and TMA (lesions in the kidneys and other organs). Signs of TMA include increases in serum LDH and serum creatinine levels and a decrease in platelet count. aHUS is diagnosed with laboratory and clinical aspects along with exclusion of other causes of HUS and thrombotic thrombocytopenic purpura.

PNH is a hematopoietic stem cell disorder caused by a gene mutation that leads to abnormal red blood cells. Flow cytometry is the method of choice for identifying cells deficient in GPI-linked proteins and is the gold standard test to confirm the diagnosis of PNH. In PNH, thrombotic tendencies can occur in the extremities and atypical locations, such as hepatic portal (Budd-Chiari Syndrome), splenic, or mesenteric veins. Treatment options include supportive care (e.g. red blood cell transfusion), allogeneic hematopoietic stem cell transplantation, and complement therapy.

The Food and Drug Administration (FDA) considers biosimilars to be highly similar with no clinically meaningful differences to the biologic reference product. Biosimilars are considered safe and effective and provide an option to increase access to lifesavings drugs at lower costs. The FDA and current treatment guidelines do not favor one product (biologic or biosimilar) over another.

Step therapy is applied to certain Part B drugs, biologics, and biosimilars in a way that lowers costs and improves the quality of care for Medicare beneficiaries per the Centers for Medicare & Medicaid Services (CMS) guidance.

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Bomyntra *(denosumab-bnht)*

Priority Health Part B Step Therapy Drug: Yes

Additional Priority Health Part B Criteria: Yes

Bomyntra is a biosimilar to Xgeva. It has been approved by the FDA for all indications of its reference biologic. The FDA has also provisionally determined Bomyntra to be interchangeable with Xgeva. Denosumab (including the biosimilars and reference product) is a monoclonal antibody that inhibits nuclear factor kappa-B ligand (RANKL), reducing osteoclast activity and bone resorption, which increases bone mass and strength. It also blocks RANKL from activating osteoclast-like giant cells. Denosumab is indicated for the prevention of skeletal-related events in patients with multiple myeloma or bone metastases from solid tumors as well as other cancer-related conditions involving bone loss.

The Food and Drug Administration (FDA) considers biosimilars to be highly similar with no clinically meaningful differences to the biologic reference product. Biosimilars are considered safe and effective and provide an option to increase access to lifesavings drugs at lower costs. The FDA and current treatment guidelines do not favor one product (biologic or biosimilar) over another.

Step therapy is applied to certain Part B drugs, biologics, and biosimilars in a way that lowers costs and improves the quality of care for Medicare beneficiaries per the Centers for Medicare & Medicaid Services (CMS) guidance.

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Boniva IV *(ibandronate sodium)*

Priority Health Part B Step Therapy Drug: Yes

Additional Priority Health Part B Criteria: No

Ibandronate (Boniva) injection is a bisphosphonate indicated for the treatment of osteoporosis in postmenopausal women.

The American Association of Clinical Endocrinologists (AACE) Clinical Practice Guidelines for the Diagnosis and Treatment of Postmenopausal Osteoporosis 2020 Update strongly recommends pharmacologic therapy for the following patients with listed T-scores in the spine, femoral neck, total hip, or 1/3 radius of: a) between −1.0 and −2.5 and a history of fragility fracture of the hip or spine, b) −2.5 or lower, or c) between −1.0 and −2.5 if the FRAX® 10-year probability for major osteoporotic fracture is ≥20% or the 10-year probability of hip fracture is ≥3% in the U.S. or above the country-specific threshold in other countries or regions.

Four bisphosphonates (alendronate, ibandronate, risedronate, and zoledronate) are available in the U.S. which are all available as generic preparations. The AACE Guidelines recommend (in the absence of contraindications) those who have “high fracture risk” can be started on oral agents.

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Botulinum toxins type A and type B
Botox *(onabotulinumtoxin A)*
Daxxify *(daxibotulinumtoxinA-lanm)*
Dysport *(abobotulinumtoxin A)*
Myobloc *(rimabotulinumtoxin B)*
Xeomin *(incobotulinumtoxin A)*

Priority Health Part B Step Therapy Drug: Yes

Additional Priority Health Part B Criteria: Yes

Voluntary muscular contraction depends on the release of the neurotransmitter, acetylcholine. Botulinum toxin, a neurotoxin, is injected into the muscle to block the release of acetylcholine, leading to weakness or paralysis of the muscle.

Multiple commercial botulinum toxin type A and type B products are currently available: Botox (onabotulinumtoxinA), Daxxify (daxibotulinumtoxinA), Dysport (abobotulinumtoxinA), Myobloc (rimabotulinumtoxinB), and Xeomin (incobotulinumtoxinA). However, the various botulinum toxin products are not interchangeable and approved indications for these products differ. Medical expertise is required to convert patients from one product or formulation to another.

At comparable doses, the botulinum toxin A can be considered therapeutically equivalent and one botulinum toxin A product is not considered superior to the others.

The American Academy of Neurology guidelines provide a level A recommendation (established as effective and should be offered for migraine prevention) for multiple beta blockers and antiepileptic drugs and a level B recommendation (probably effective and should be considered for migraine prevention) for some anti-depressants when used for migraine prevention. Updated guidelines also provide a level A recommendation for botulinum in chronic and episodic migraine prevention.

For clinically significant sialorrhea, anticholinergic medications may be helpful. An example includes glycopyrrolate, particularly because of its relatively low central nervous system activity.

The American Urological Association recommends the use of botulinum toxin A as a third-line treatment option in patients who have been refractory to first- and second-line overactive bladder treatments (Grade B). First- line treatments include behavioral therapies (Grade B); Second-line treatments include anti-muscarinic agents and oral B3-adrenoceptors agonists (Grade B).

Traditional options have not been shown to be less efficacious than botulinum toxins. Given their well-known safety profiles, traditional options should be considered first-line in most

indications, including migraine prevention, hyperhidrosis, chronic anal fissures, sialorrhea, overactive bladder and detrusor over activity.

References

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11. Evidence-based guideline update: Pharmacologic treatment for episodic migraine prevention in adults | Neurology

12. Practice guideline update summary: Botulinum neurotoxin for the treatment of blepharospasm, cervical dystonia, adult spasticity, and headache | Neurology

Casgevy *(exagamglogene autotemcel)*

Priority Health Part B Step Therapy Drug: Yes

Additional Priority Health Part B Criteria: Yes

Sickle cell disease (SCD) is a group of inherited disorders caused by a mutation in the beta globin gene, resulting in an abnormal hemoglobin called sickle hemoglobin (HbS). With SCD, these sickled red blood cells cannot bend or move easily through the rest of the body, blocking blood flow and causing severe episodes of pain, referred to as vaso-occlusive

events (VOEs), and other serious health complications including stroke, deep vein thrombosis, and infections.

Several medications are available and effective in reducing the occurrence of VOEs. Hydroxyurea is the mainstay of therapy while other SCD medications like Endari are also recommended for patients either alone or in combination with hydroxyurea.

Safety and efficacy of Casgevy in SCD were evaluated in the CLIMB-121 trial. Participants had severe SCD with documented βS/βS, βS/β0, and βS β+ genotypes, which represent more severe forms of the disease. Severe SCD was defined by having at least 2 VOEs each year during the previous 2 years despite appropriate supportive care (such as hydroxyurea). Key exclusion criteria included advanced liver disease, prior treatment with an allogenic stem cell transplant, and prior or current malignancy or immunodeficiency disorder. There is currently no data supporting administration of Casgevy following administration of another gene therapy or a stem cell transplant.

Individuals are required to undergo hematopoietic stem cell (HSC) mobilization followed by apheresis to obtain CD34+ cells for CASGEVY manufacturing. Therefore, adequate organ function is required to support the myeloablative conditioning regimen associated with Casgevy, and patients should be clinically stable to undergo this HSCT process.

Currently, there are no compendia supported uses for this therapy outside the FDA-indication(s).

References

1. Casgevy [prescribing information]. Boston, MA: Vertex Pharmaceuticals Incorporated; 2024.

2. Centers for Disease Control and Prevention. Sickle cell disease (SCD). Available at: https://www.cdc.gov/ncbddd/sicklecell/index.html.

3. National Heart, Lung, and Blood Institute. Evidence-based management of sickle cell disease: expert panel report, 2014.

4. Clinicaltrials.gov. A safety and efficacy study evaluating CTX001 in subjects with severe sickle cell disease. Available at: https://classic.clinicaltrials.gov/ct2/show/NCT03745287.

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Cimzia *(certolizumab pegol)*
Priority Health Part B Step Therapy Drug: Yes
Additional Priority Health Part B Criteria: Yes

Cimzia is a tumor necrosis factor inhibitor (TNFi) indicated for certain inflammatory conditions including Crohn's Disease (CD), Rheumatoid Arthritis (RA), active ankylosing spondylitis (AS), psoriatic arthritis (PsA), and plaque psoriasis (PsO).

Ankylosing spondylitis (AS) and non-radiographic axial spondyloarthritis (NRAS) are related conditions. The 2019 American College of Rheumatology recommendations for AS and NRAS are similar. Recommended first-line agents include nonsteroidal anti-inflammatory drugs (NSAIDs) due to their well-known safety and efficacy profiles. For patients who have active disease despite treatment with NSAIDs, treatment with a TNFi (adalimumab, Enbrel, Simponi Aria) is recommended. Cosentyx has a role in those who do not respond to initial TNFi agent. Guidelines do not favor one TNFi over another, nor do they address JAK inhibitors (Rinvoq, Xeljanz), however these agents have since been FDA-approved for use in those who had previously had inadequate response to a TNFi.

The 2018 American College of Gastroenterology (ACG) guidelines recommend mercaptopurine, azathioprine, and methotrexate in symptomatic CD despite prior corticosteroid use. TNFi agents (e.g., adalimumab) are effective in those with inadequate response to these initial therapies. Other bDMARDs (e.g., Skyrizi) and tsDMARDs (e.g., Rinvoq) are not addressed by the guidelines, however these agents have since been FDA-approved for use in this condition.

For Rheumatoid Arthritis (RA), guidelines favor the use of biologic DMARDs (bDMARD) for moderate or high disease activity despite prior conventional synthetic DMARDs (csDMARD). Guidelines do not favor one bDMARD (e.g., Skyrizi, tocilizumab, Cosentyx) over another nor do they favor tsDMARD (e.g., Xeljanz, Rinvoq) over bDMARD.

Per the 2020 Joint AAD-NPF guidelines (non-biologic), recommended treatments include methotrexate, cyclosporine, and acitretin. Methotrexate and cyclosporine are category A recommendations, whereas acitretin is a category B recommendation. The 2019 Joint AAD-NPF guidelines (biologics) recommend (category A) the use of biologics in treating psoriasis but do not suggest one agent over another. TNFis, interleukin-12/23 inhibitors (IL-12/IL-23i), IL-23i, and IL-17i have all shown efficacy in this condition. These include adalimumab, Enbrel, Skyrizi, and Cosentyx. Otezla is also a recommended treatment option included in the guidelines.

Per the 2018 American College of Rheumatology (ACR)/National Psoriasis Foundation (NPF) guidelines, methotrexate, sulfasalazine, cyclosporine, and leflunomide may be used in patients with non-severe Psoriatic Arthritis (PsA) and have robust safety and efficacy evidence to support their use. If initial treatment is not sufficient, switching to a biologic (adalimumab, Enbrel, Simponi Aria, Skyrizi) or JAK inhibitor (Rinvoq, Xeljanz) is recommended.

There is limited data on the concurrent use of Cimzia with other biologic agents, targeted synthetic DMARDs (JAK inhibitors), and PDE4 inhibitors (Otezla). Given the absence of strong clinical evidence and the potential for increased infection risk, it is not recommended to use Cimzia in combination with these agents.

The Food and Drug Administration (FDA) considers biosimilars to be highly similar with no clinically meaningful differences to the biologic reference product. Biosimilars are considered safe and effective and provide an option to increase access to lifesavings drugs at lower costs. The FDA and current treatment guidelines do not favor one product (biologic or biosimilar) over another.

Step therapy is applied to certain Part B drugs, biologics, or biosimilars in a way that lowers costs and improves the quality of care for Medicare beneficiaries per the Centers for Medicare & Medicaid Services (CMS) guidance.

References

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Cinqair *(reslizumab)*

Priority Health Part B Step Therapy Drug: Yes

Additional Priority Health Part B Criteria: Yes

Cinqair (reslizumab) is an interleukin-5 (IL-5) antagonist indicated for severe eosinophilic asthma add-on therapy. IL-5 is responsible for the growth and survival of eosinophils which contribute to inflammation in the lungs.

The Global Initiative for Asthma (GINA) Guidelines on difficult-to-treat & severe asthma in adolescent and adult patients recommend using type 2-targeted biologic agents as add-on for patients with exacerbations and/or poor symptom control despite taking at least high-dose inhaled corticosteroids (ICS) and long-acting beta agonist (LABA) combinations, and who have allergic or eosinophilic biomarkers or need maintenance oral corticosteroids. Type 2-inflammation is defined as blood eosinophils ≥150µl and/or FeNO ≥20 ppb and/or sputum eosinophils ≥2% and/or asthma is clinically allergen driven. GINA guidelines also advise treatment should be optimized prior to initiating a biologic agent. For therapy optimization, consider trials of non-biologic medications in addition to medium/high dose ICS, such as LABA, long-acting muscarinic agonists (LAMA), and leukotriene receptor antagonists (LTRA).

Four studies demonstrated safety and efficacy of Cinqair. Patients received either reslizumab 3mg/kg IV every 4 weeks or placebo. Patients were followed to assess impact of drug on asthma exacerbations and lung function (FEV1). An exacerbation was defined as 1) worsening of symptoms requiring systemic corticosteroids; 2) increase in dose of existing inhaled or oral corticosteroids; or 3) need for asthma-related emergency treatment (hospital admission, urgent care or unscheduled office visit with physician). Results showed a decrease in the number of exacerbations, an increase in time to first exacerbation, and an overall improvement in lung function (FEV1).

Cinqair has not been studied in combination with other biologic agents due to an increased risk of infection and increased immunosuppression. As such, use of Cinqair in combination with other biologic agents is not recommended.

References

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Cinryze *(C1 esterase inhibitor [human])*
Priority Health Part B Step Therapy Drug: Yes
Additional Priority Health Part B Criteria: No

Cinryze is indicated for routine prophylaxis against angioedema attacks in patients with Hereditary Angioedema (HAE).

Hereditary angioedema (HAE) is a rare disease caused by low levels of a protein in the blood called C1 inhibitor. C1 inhibitor helps to regulate pathways in the body to prevent inflammation. Without proper levels of C1 inhibitor, a small protein (peptide) known as bradykinin builds up. Bradykinin causes vascular permeability, resulting in excessive leakage of fluid into the body tissues and episodes of swelling.

HAE is divided into 3 types with type 1 being the most common. Type 1 is caused by reduced levels of C1 inhibitor while Type 2 is caused by dysfunctional C1 inhibitor, and Type 3 is a rare form associated with normal C1 inhibitor levels. The US Hereditary Angioedema Association (HAEA) Medical Advisory Board 2020 Guidelines for the Management of HAE divide medications for long-term prophylaxis of HAE into 2 categories, first line and second line. Cinryze (an intravenous formulation of C1 inhibitor), Haegarda (a subcutaneous formulation of C1 inhibitor), and a monoclonal inhibitor of plasma kallikrein (lanadelumab or Takhyzro) are recommended as first-line therapies. Anabolic androgens like Danazol and antifibrinolytics like tranexamic acid or epsilon aminocaproic acid are recommended as second-line therapies. When long-term prophylaxis is indicated for patients with HAE, the US HAEA guidelines recommend the use of any of the first-line agents.

Step therapy is applied to certain Part B drugs, biologics, and biosimilars in a way that lowers costs and improves the quality of care for Medicare beneficiaries per the Centers for Medicare & Medicaid Services (CMS) guidance.

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https://www.cms.gov/Medicare/Health-Plans/HealthPlansGenInfo/Downloads/MA_Step_Therapy_HPMS_Memo_8_7_2018.pdf.

Conexxence *(denosumab-bnht)*

Priority Health Part B Step Therapy Drug: Yes

Additional Priority Health Part B Criteria: Yes

Conexxence is a biosimilar to Prolia. It has been approved by the FDA for all indications of its reference biologic. The FDA has also provisionally determined Conexxence to be interchangeable with Prolia. Denosumab (including the biosimilars and reference product) is a monoclonal antibody that inhibits nuclear factor kappa-B ligand (RANKL), reducing osteoclast activity and bone resorption, which increases bone mass and strength. It also blocks RANKL from activating osteoclast-like giant cells. Denosumab is indicated for the treatment of postmenopausal women with osteoporosis at high risk for fracture as well as other conditions involving excessive bone loss, such as those caused by hormone therapy in cancer patients.

The Food and Drug Administration (FDA) considers biosimilars to be highly similar with no clinically meaningful differences to the biologic reference product. Biosimilars are considered safe and effective and provide an option to increase access to lifesavings drugs at lower costs. The FDA and current treatment guidelines do not favor one product (biologic or biosimilar) over another.

Step therapy is applied to certain Part B drugs, biologics, and biosimilars in a way that lowers costs and improves the quality of care for Medicare beneficiaries per the Centers for Medicare & Medicaid Services (CMS) guidance.

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Cosentyx IV *(secukinumab)*
Priority Health Part B Step Therapy Drug: Yes
Additional Priority Health Part B Criteria: Yes

Cosentyx is an interleukin-17 (IL-17) receptor A antagonist indicated for Plaque Psoriasis (PsO), Psoriatic Arthritis (PsA), Rheumatoid Arthritis (RA), and Ankylosing Spondylitis (AS).

Ankylosing spondylitis 'AS' and non-radiographic axial spondyloarthritis 'NRAS' are related conditions. The 2019 American College of Rheumatology recommendations for AS and NRAS are similar. Recommended first-line agents include nonsteroidal anti-inflammatory drugs (NSAIDs) due to their well-known safety and efficacy profiles. For patients who have active disease despite treatment with NSAIDs, treatment with a TNFi (infliximab, adalimumab, Enbrel, Simponi Aria) is recommended. Cosentyx has a role in those who do not respond to initial TNFi agent. Guidelines do not favor one TNFi over another, nor do they address JAK inhibitors (Rinvoq, Xeljanz), however these agents have since been FDA-approved for use in those who had previously had inadequate response to a TNFi.

For Rheumatoid Arthritis (RA), guidelines favor the use of biologic DMARDs (bDMARD) for moderate or high disease activity despite prior conventional synthetic DMARDs (csDMARD). Guidelines do not favor one bDMARD (e.g., Skyrizi, tocilizumab, Cosentyx, infliximab) over another nor do they favor tsDMARD (Xeljanz, Rinvoq) over bDMARD.

Per the 2018 American College of Rheumatology (ACR)/National Psoriasis Foundation (NPF) guidelines, methotrexate, sulfasalazine, cyclosporine, and leflunomide may be used in patients with non-severe Psoriatic Arthritis (PsA) and have robust safety and efficacy evidence to support their use. If initial treatment is not sufficient, switching to a biologic (infliximab, adalimumab, Enbrel, Simponi Aria, Skyrizi) or JAK inhibitor (Rinvoq, Xeljanz) is recommended.

Per the 2020 Joint AAD-NPF guidelines (non-biologic), recommended treatments include methotrexate, cyclosporine, and acitretin. Methotrexate and cyclosporine are category A recommendations, whereas acitretin is a category B recommendation. The 2019 Joint AAD-NPF guidelines (biologics) recommend (category A) the use of biologics in treating psoriasis but do not suggest one agent over another. TNFis, interleukin-12/23 inhibitors (IL-12/IL-23i), IL-23i, and IL-17i have all shown efficacy in this condition. These include infliximab, adalimumab, Enbrel, Skyrizi, and Cosentyx. Otezla is also a recommended treatment option included in the guidelines.

There is limited data on the concurrent use of Cosentyx with other biologic agents, targeted synthetic DMARDs (JAK inhibitors), and PDE4 inhibitors (Otezla). Given the absence of strong clinical evidence and the potential for increased infection risk, it is not recommended to use Cosentyx in combination with these agents.

References

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2. Fraenkel L, et al. 2021 American College of Rheumatology Guideline for the Treatment of Rheumatoid Arthritis. Arthritis Care & Research. 2021 Jul; 73 (7):924-939.

3. Singh JA, et al. 2018 American College of Rheumatology/National Psoriasis Foundation Guideline for the Treatment of Psoriatic Arthritis. Arthritis Rheumatol. 2019 Jan; 71 (1): 5-32.

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Docivyx *(docetaxel)*

Priority Health Part B Step Therapy Drug: Yes

Additional Priority Health Part B Criteria: No

Docivyx (docetaxel) is a microtubule inhibitor indicated for treatment of breast cancer, non-small cell lung cancer (NSCLC), castration-resistant prostate cancer (CRPC), gastric adenocarcinoma (GC), and squamous cell carcinoma of the head and neck (SCCHN).

Docivyx is a new formulation of docetaxel that was developed to be polysorbate 80 free. The presence of polysorbate 80 in the intravenous formulation of docetaxel has been implicated in hypersensitivity systemic reactions (HSRs) that were observed in the early clinical studies. In those studies, the incidence of HSRs ranged from 5% to 40%, with most events being grade 2 in severity on the four-point scale of the National Cancer Institute common toxicity criteria. Consequently, patients treated with the conventional formulation of docetaxel are premedicated with oral corticosteroids. Aside from the potential to lessen hypersensitivity reactions, there is no data to support a safety or efficacy benefit of Docivyx over generic docetaxel. In addition, Docivyx carries the same hypersensitivity warnings its labeling as docetaxel (Taxotere).

Step therapy is applied to certain Part B drugs, biologics, or biosimilars in a way that lowers costs and improves the quality of care for Medicare beneficiaries per the Centers for Medicare & Medicaid Services (CMS) guidance.

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6. Centers for Medicare & Medicaid Services. Local Coverage Determination (LCD) L37205: Chemotherapy Drugs and their Adjuncts.

Durysta *(bimatoprost intraocular implant)*

Priority Health Part B Step Therapy Drug: Yes

Additional Priority Health Part B Criteria: No

Glaucoma is a leading cause of blindness and is impacted by elevated intraocular pressure (IOP). Durysta (bimatoprost intracameral implant [biodegradable]) is indicated for open-angle glaucoma or ocular hypertension patients, working to lower IOP and slow disease progression. The goal of treatment is to maintain IOP in a target range to preserve visual function and overall quality of life.

Bimatoprost is one of several prostaglandin F receptor agonists, including topical inagents (latanoprost, travoprost, tafluprost). The American Academy of Ophthalmology (AAO) recommends this class as first-line in IOP reduction due to the high efficacy, high tolerability, and convenient once-daily dosing. The AAO does not favor the use of one prostaglandin F receptor agonist over another. There are no studies comparing Durysta with another prostaglandin, but the majority of the other prostaglandins and Durysta were individually studied against timolol ophthalmic solution and found to be non-inferior in their abilities to lower IOP.

Lowering IOP can be achieved with monotherapy or multiple agents. If a drug fails to reduce IOP sufficiently, the AAO recommends switching to an alternative (as monotherapy) or adding a second medication with a different mechanism of action until the desired IOP level is attained.

References

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2. American Academy of Ophthalmology: Primary Open-Angle Glaucome Preferred Practice Pattern, 2020.

Elevidys *(delandistrogene moxeparvovec-rokl)*
Priority Health Part B Step Therapy Drug: No
Additional Priority Health Part B Criteria: Yes
Elevidys is a gene therapy for the treatment of Duchenne muscular dystrophy (DMD). DMD is a rare, progressive X-linked disease resulting from mutation(s) of the DMD gene, also known as the Dystrophin gene. Due to the mutation(s), the dystrophin protein, which is key for maintaining the structural integrity of muscle cells, is not produced or very minimally produced. Elevidys encodes for a micro-dystrophin protein to replace the missing dystrophin protein. Elevidys was granted initial accelerated approval in patients aged 4 to 5 years based on clinical trial results showing increase levels of micro-dystrophin and secondary endpoint favoring improvement in NSAA score in patients aged 4 to 5 years. Full FDA approval for treatment of ambulatory patients with DMD age 4 years and older was granted based on results of confirmatory phase IIII trial EMBARK. This trial included only patients age 4 to less than 8 years old who were ambulatory and also were required to have anti-rAAVrh74 titer of less than 1:400. Accelerated approval for non-ambulatory patients age 4 and older was granted based on trial data showing an increase in micro-dystrophin levels in this population, but data showing a statistically significant improvement in a patient clinical outcome has not been confirmed yet. Thus, clinical study data to date has only confirmed possible clinical benefit to use of this product in patients age 4 to less than 8 years, who are ambulatory, and have a anti-rAAVrh74 titer of less than 1:400. Support for FDA-approved indications can be found in the manufacturer's prescribing information. Per the prescribing information, patients selected for treatment should have anti-AAVrh74 total binding antibody titers <1:400, and Elevidys is contraindicated in patients with any deletion in exon 8 and or exon 9 in the DMD gene.
Emblaveo *(aztreonam and avibactam)*
Priority Health Part B Step Therapy Drug: Yes
Additional Priority Health Part B Criteria: Yes
Emblaveo (aztreonam and avibactam; ATM-AVI), is a monobactam/β-lactamase inhibitor combination antibiotic, for the treatment of adults with complicated intra[1]abdominal infections (cIAIs) with limited or no alternative options, in combination with metronidazole (MTZ). Emblaveo received both FDA Fast Track and Qualified Infectious Disease Product (QIDP) designations. A QIDP designation is granted as part of the FDA's Generating Antibiotic Incentives Now (GAIN) program, which offers incentives for certain antibacterial and antifungal products, most notably a 5-year exclusivity extension, which is added to any exclusivity for which the application qualifies upon approval.

Emblaveo's approval was supported by the Phase 3 REVISIT trial (NCT03329092), which consisted of 412 hospitalized patients with a cIAI in the safety population. Patients were randomly assigned 2:1 to receive either ATM-AVI with MTZ or meropenem (MER) with or without colistin for 5–14 days. Among patients with cIAIs, the adjudicated clinical cure rate was 76.4% (159 of 208) for the ATM-AVI group and 74.0% (77 of 104) for the MER group.

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Encelto *(revakinagene taroretcel-lwey)*

Priority Health Part B Step Therapy Drug: No

Additional Priority Health Part B Criteria: Yes

Encelto is the first FDA-approved treatment for MacTel type 2 and is a surgically implanted, allogeneic encapsulated cell-based gene therapy that continually delivers recombinant human ciliary neurotrophic factor (rhCNTF) to the retina to slow disease progression.

MacTel type 2 is a rare macular degenerative disease typically diagnosed in middle age. The disease does not cause total blindness but significantly impacts quality of life due to progressive central vision loss. MacTel type 2 occurs bilaterally but may not affect each eye in the same way or to the same degree. In the United States, MacTel type 2 has a prevalence of about 0.1% in individuals over 40 years of age.

The approval of Encelto was based on results from two Phase 3, randomized, multicenter studies (Study 1: NTMT-03-A [NCT03316300] and Study 2: NTMT-03-B [NCT03319849]). Treatment with revakinagene taroretcel-lwey implant compared with sham was evaluated in in adults with macular telangiectasia type 2. Patients were required to have a photoreceptor inner segment/outer segment (IS/OS PR) break (loss) in ellipsoid zone (EZ) between 0.16 and 2 mm(2) measured by spectral domain-optical coherence tomography (SD-OCT) and best corrected visual acuity (BCVA) of 54-letter score or better (20/80 or better) as measured by the Early Treatment Diabetic Retinopathy Study (ETDRS) chart at screening. Patients with neovascular MacTel were excluded. The rate of change in the area of ellipsoid zone (EZ) loss was significantly

improved with the revakinagene taroretcel-lwey implant compared with sham over 24 months in 2 randomized studies of adults with MacTel.

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Enjaymo *(sutimlimab-jome)*

Priority Health Part B Step Therapy Drug: Yes

Additional Priority Health Part B Criteria: Yes

Enjaymo (sutimlimab-jome) injection is a classical complement inhibitor indicated for the treatment of hemolysis in adults with cold agglutinin disease (CAD) to be given as 6,500 mg (in patients weighing 39 kg to less than 75 kg) or 7,500 mg by intravenous infusion (in patients weighing 75 kg or more) weekly for two weeks then every two weeks thereafter.

Cold agglutinin disease (CAD) is the “least uncommon” subtype of cold antibody-mediated autoimmune hemolytic anemias (cAIHA). ‘Diagnosis and treatment of autoimmune hemolytic anemia in adults: Recommendations from the First International Consensus Meeting’ defines primary CAD with chronic hemolysis, a significant CA titre (most often defined as > 64) at 4 °C, typical findings by the DAT, and the absence of an underlying clinical disease. The group suggests treatment would usually not be recommended for patients whose Hb is > 10 g/dL, but exceptions could be made for some populations. Symptoms may include acrocyanosis, Raynaud phenomenon, hemoglobinuria, and circulatory symptoms. For most patients without relevant symptoms or problems, consider watchful waiting. For patients with CAD requiring therapy, blood transfusions can be given when indicated and rituximab with or without bendamustine should be considered first line.

Treatment goal is to improve quality of life and increase hemoglobin levels in patients with symptom-producing anemia, which may include achievement of transfusion independency and/or improvement or resolution of disabling cold-induced circulatory symptoms.

Enjaymo was studied in the CARDINAL study, which included patients with cold agglutinin disease and a recent transfusion (within 6 months) with an Hb of 10 g/dL or less and total bilirubin level above the normal range plus one or more symptoms. The single arm study found 54% of patients treated with Enjaymo achieved a normalization of hemoglobin to 12 g/dL or more or an increase of 2 g/dL or more from baseline at weeks 23, 25, and 26 without

red blood cell transfusion or need for non-protocol cold agglutinin disease medications from week 5 to 26.

Enjaymo has not been studied in combination with other biologic drugs. As such, use of Enjaymo in combination with other biologic drugs is not recommended and will not be covered.

References

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Entyvio *(vedolizumab)*

Priority Health Part B Step Therapy Drug: Yes

Additional Priority Health Part B Criteria: Yes

Entyvio is an integrin receptor antagonist indicated for Ulcerative Colitis (UC) and Crohn's Disease (CD).

Per the 2020 American Gastroenterology Association guidelines, multiple agents effectively induce and maintain remission of UC, including corticosteroids, 5-aminosalicylates '5-ASA', and biologics. Treatment of mild-to-moderate UC is typically started with 5-ASA therapy. In those who do not respond to 5-ASA therapy, induction can be achieved through short-term corticosteroids. Once induction is achieved, maintenance can be managed with thiopurines. Methotrexate is not recommended for induction or maintenance of remission in UC, whereas biologic agents do have support for use in these treatment areas. Guidelines do not favor one biologic over another, nor do they favor biologics over thiopurine monotherapy for those in remission. The guidelines do not address tsDMARDs (Rinvoq, Xeljanz), however these agents have since been FDA-approved for use in this condition.

The 2018 American College of Gastroenterology (ACG) guidelines recommend mercaptopurine, azathioprine, and methotrexate in symptomatic CD despite prior corticosteroid use. Tumor necrosis factor (TNF) inhibitors are effective in those with inadequate response to these initial therapies. Other bDMARDs (Skyrizi, Entyvio) and tsDMARDs (Rinvoq) are not addressed by the guidelines, however these agents have since been FDA-approved for use in this condition.

Entyvio has been evaluated alongside other biologics, Otezla, and JAK inhibitors for the treatment of irritable bowel disease. However, the current evidence on the efficacy and safety of these combination therapies primarily comes from uncontrolled observational studies. More well-controlled and adequately powered clinical trials are necessary to support concurrent use in efficacy and safety as combining these drugs poses a risk of

serious infections. Therefore, it is not recommended to use Entyvio in combination with other biologic agents, Otezla, or JAK inhibitors.

References

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2. Feuerstein JD, Isaacs KL, Schneider Y, et al. AGA clinical practice guidelines on the management of moderate to severe ulcerative colitis. Gastroenterology. 2020; 158: 1450–6

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Epogen *(epoetin alpha)*

Priority Health Part B Step Therapy Drug: Yes

Additional Priority Health Part B Criteria: No

Erythropoiesis-stimulating agents (ESAs), including epoetin alfa and darbepoetin alfa, are primarily used to manage cancer- and chemotherapy-induced anemia (CIA). Use of erythropoiesis-stimulating agents (ESAs) to manage anemia raises hemoglobin (HgB) levels and reduces the need for RBC transfusions. Depending on clinical circumstances, ESAs may be3 offered to patients with chemotherapy-associated anemia whose cancer treatment is not curative in intent and whose hemoglobin (HgB) has declined to < 10 g/dL. RBC transfusion is also an option, depending on the severity of the anemia or clinical circumstance. ESAs may be offered to patients with lower risk myelodysplastic syndromes and a serum erythropoietin level ≤ 500 IU/L. In patients with myeloma, non-Hodgkin lymphoma, or chronic lymphocytic leukemia, clinicians should observe the hematologic response to cancer treatment before considering an ESA. In all cases, blood transfusion is a treatment option that should be considered. Per the American Society of Clinical Oncology (ASCO)/American Society of Hematology (ASH) Practice Guideline Update on Management of Cancer-Associated Anemia With Erythropoiesis-Stimulating Agents, the expert panel considers epoetin beta and alfa, darbepoetin, and biosimilar epoetin alfa to be equivalent with respect to effectiveness and safety. It is recommended that starting and modifying doses of ESAs follow FDA guidelines. HgB may be increased to the lowest concentration needed to avoid or reduce the need for RBC transfusions, which may vary by patient and condition. ESAs should be discontinued in patients who do not respond within 6 to 8 weeks. Patients who do not respond to ESA treatment should be reevaluated for underlying tumor progression, iron deficiency, or other etiologies for anemia.

Per the Kidney Disease Improving Global Outcomes (KDIGO) Clinical Practice Guideline for Anemia in CKD, after diagnosing anemia in a patient with CKD all correctable causes should be treated before considering ESA therapy. Above all, this recommendation is based on the observation that iron supplementation given to CKD patients with proven iron deficiency or impaired iron availability ('functional iron deficiency') generally leads to an increase in Hb. However, the correction of other deficiency states also may ameliorate

anemia. In initiating and maintaining ESA therapy, they recommend balancing the potential benefits of reducing blood transfusions and anemia-related symptoms against the risks of harm in individual patients (e.g., stroke, vascular access loss, hypertension). For adult CKD non-dialysis patients with Hb concentration 10.0 g/dl they suggest that the decision whether to initiate ESA therapy be individualized based on the rate of fall of Hb concentration, prior response to iron therapy, the risk of needing a transfusion, the risks related to ESA therapy and the presence of symptoms attributable to anemia. For adult CKD stage 5 patients, they suggest that ESA therapy be used to avoid having the Hb concentration fall below 9.0 g/dl (90 g/l) by starting ESA therapy when the hemoglobin is between 9.0–10.0 g/ dl (90–100 g/l). Individualization of therapy is reasonable as some patients may have improvements in quality of life at higher Hb concentration and ESA therapy may be started above 10.0 g/dl (100 g/l). In all adult patients, they recommend that ESAs not be used to intentionally increase the Hb concentration above 13 g/dl (130 g/l).

Priority Health follows LCD L34633 for Erythropoiesis Stimulating Agents (ESAs)

References

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2. Centers for Medicare & Medicaid Services. Local Coverage Determination (LCD) L34633 Erythropoiesis Stimulating Agents.

3. Eknoyan G, Lameire N, Kasiske BL, et al. KDIGO clinical practice guideline for anemia in chronic kidney disease. 2012 August 2. J Intern Society of Nephrol. 2 (4): 282- 335.

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Epysqil *(eculizumab-aagh)*

Priority Health Part B Step Therapy Drug: Yes

Additional Priority Health Part B Criteria: Yes

Epysqil is a biosimilar to Soliris and was granted the FDA's interchangeability designation, which allows it to be used in place of the branded reference product without needing to change the prescription.

Eculizumab is a monoclonal antibody that binds to the complement C5 protein and stops activation of the complement system, a part of the body's immune system. This binding prevents the breakdown of red blood cells in the bloodstream (called intravascular hemolysis). Like Soliris, Epysqil has a Boxed Warning regarding the increased risk of serious and life-threatening meningococcal infections caused by Neisseria meningitidis.

AHUS consists of acute hemolytic anemia with fragmented red blood cells (microangiopathic hemolytic anemia), thrombocytopenia, and acute kidney injury.

Mutations in complement genes, or antibodies to their protein products, result in unregulated activity of the alternate complement pathway, endothelial injury, and TMA (lesions in the kidneys and other organs). Signs of TMA include increases in serum LDH and serum creatinine levels and a decrease in platelet count. aHUS is diagnosed with laboratory and clinical aspects along with exclusion of other causes of HUS and thrombotic thrombocytopenic purpura.

PNH is a hematopoietic stem cell disorder caused by a gene mutation that leads to abnormal red blood cells. Flow cytometry is the method of choice for identifying cells deficient in GPI-linked proteins and is the gold standard test to confirm the diagnosis of PNH. In PNH, thrombotic tendencies can occur in the extremities and atypical locations, such as hepatic portal (Budd-Chiari Syndrome), splenic, or mesenteric veins. Treatment options include supportive care (e.g. red blood cell transfusion), allogeneic hematopoietic stem cell transplantation, and complement therapy.

The Food and Drug Administration (FDA) considers biosimilars to be highly similar with no clinically meaningful differences to the biologic reference product. Biosimilars are considered safe and effective and provide an option to increase access to lifesavings drugs at lower costs. The FDA and current treatment guidelines do not favor one product (biologic or biosimilar) over another.

Step therapy is applied to certain Part B drugs, biologics, and biosimilars in a way that lowers costs and improves the quality of care for Medicare beneficiaries per the Centers for Medicare & Medicaid Services (CMS) guidance.

References

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Erzofri *(paliperidone palmitate)*

Priority Health Part B Step Therapy Drug: Yes

Additional Priority Health Part B Criteria: No

Erzofri is an atypical antipsychotic prescribed for the treatment of schizophrenia and schizoaffective disorder in adults. It can be used alone or in combination with mood stabilizers or antidepressants.

The American Psychiatric Association's Practice Guideline for the Treatment of Patients With Schizophrenia advises that individuals with schizophrenia should be treated with an antipsychotic medication and monitored for both effectiveness and side effects. The selection of an antipsychotic agent should be tailored to the specific needs of each patient. The guideline does not favor either second-generation or first-generation antipsychotics due to the limited number of direct comparisons between these drugs. It also recommends that patients be offered long-acting injectable antipsychotic medications if they prefer this form of treatment or have a history of poor or uncertain adherence.

No new clinical efficacy trials were required for FDA approval of Erzofri. Approval was based on earlier trials with Invega Sustenna and an open-label study showing that the bioavailability of paliperidone palmitate with Erzofri was similar to that with Invega Sustenna. Erzofri has not been shown to offer any advantage in efficacy or safety over Invega Sustenna or other extended-release formulations of paliperidone palmitate that are administered every three or six months.

Step therapy is applied to certain Part B drugs, biologics, or biosimilars in a way that lowers costs and improves the quality of care for Medicare beneficiaries per the Centers for Medicare & Medicaid Services (CMS) guidance.

References

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Evenity *(romosozumab-aqqg)*
Priority Health Part B Step Therapy Drug: Yes
Additional Priority Health Part B Criteria: Yes

Evenity (romosozumab-aqqg) is a humanized IgG2 monoclonal antibody and sclerostin inhibitor indicated for the treatment of osteoporosis in postmenopausal women at high risk for fracture, defined as a history of osteoporotic fracture, or multiple risk factors for fracture; or patients who have failed or are intolerant to other available osteoporosis therapy.

The American Association of Clinical Endocrinologists (AACE) Clinical Practice Guidelines for the Diagnosis and Treatment of Postmenopausal Osteoporosis 2020 Update strongly recommends pharmacologic therapy for the following patients with listed T-scores in the spine, femoral neck, total hip, or 1/3 radius of: a) between −1.0 and −2.5 and a history of fragility fracture of the hip or spine, b) −2.5 or lower, or c) between −1.0 and −2.5 if the FRAX® 10-year probability for major osteoporotic fracture is ≥20% or the 10-year probability of hip fracture is ≥3% in the U.S. or above the country-specific threshold in other countries or regions.

Four agents (alendronate, risedronate, zoledronate, and denosumab) have evidence for "broad-spectrum" antifracture efficacy (spine, hip, and nonvertebral fracture risk reduction) and, in the absence of contraindications, are recommended as initial options for most patients who are candidates for treatment. A significant decrease in Bone Mineral Density (BMD) or recurrent fractures in a patient who is compliant to therapy may indicate a treatment failure.

Contraindications to oral bisphosphonate administration include the inability to remain upright for 30 to 60 minutes and the presence of anatomic or functional esophageal abnormalities that might delay transit of the tablet (e.g., achalasia, stricture, or dysmotility). Also, bisphosphonates should be used with caution in patients with reduced kidney function.

The guidelines suggest that anabolic and dual-action agents may be preferred as initial therapy for patients at very high risk of fracture. Indicators of very high risk include a history of multiple fractures, a significantly low T-score (e.g., below −3.0), or a history of injurious falls. To maintain bone density gains and fracture protection, treatment with an anabolic agent should be followed by an antiresorptive therapy such as a bisphosphonate or denosumab.

After 12 monthly doses, the anabolic effect of Evenity wanes. As such, Evenity is limited to a 12 month duration of treatment. If osteoporosis therapy is still necessary, continued treatment with an antiresorptive agent should be considered (bisphosphonates, e.g.).

Step therapy is applied to certain Part B drugs, biologics, and biosimilars in a way that lowers costs and improves the quality of care for Medicare beneficiaries per the Centers for Medicare & Medicaid Services (CMS) guidance.

References

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Evkeeza *(evinacumab-dgnb)*

Priority Health Part B Step Therapy Drug: Yes

Additional Priority Health Part B Criteria: No

Evkeeza is an angiopoietin-like 3 (ANGPTL3) inhibitor indicated as an adjunct to other low-density lipoprotein-cholesterol (LDL-C) lowering therapies for the treatment of adult and pediatric patients, aged 5 years and older, with homozygous familial hypercholesterolemia (HoFH). It is a recombinant human monoclonal antibody that binds to and inhibits ANGPTL3, a member of the angiopoietin-like protein family that is expressed primarily in the liver and plays a role in the regulation of lipid metabolism. Evinacumab-dgnb reduces LDL-C independent of the presence of LDL receptor (LDLR) by promoting very low-density lipoprotein (VLDL) processing and clearance upstream of LDL formation. Patients with HoFH often have mutations in the LDLR gene, encoding for the LDL receptor (LDLR). Given the mechanism of action of statins, which exert their lipid-lowering effect partly by increasing the hepatic expression of LDLR, it is expected that homozygous FH subjects carrying null mutations on LDLR gene would not respond. However, these patients are responsive to statins, although to a lesser extent.

The 2018 Guideline on the Management of Blood Cholesterol, by American College of Cardiology/American Heart Association, recommends treatment with high intensity or maximally tolerated statin therapy for adult patients with LDL-C levels > 190 mg/dL due to the increased risk of atherosclerotic cardiovascular disease (ASCVD) and both premature and recurrent coronary events. If maximally tolerated statin therapy fails to reduce LDL-C by at least 50% and/or the LDL-C level remains > 100 mg/dL, the guideline suggests that additional ASCVD risk reduction can be derived from the addition of ezetimibe to statin therapy. Should LDL-C remain > 100 mg/dL despite treatment with a maximally tolerated

statin and ezetimibe, addition of a PCSK9 inhibitor ((i.e. evolocumab, alirocumab) may be considered. In patients at very high risk whose LDL-C level remains ≥70 mg/dL (≥1.8 mmol/L) on maximally tolerated statin and ezetimibe therapy, adding a PCSK9 inhibitor is reasonable. Evolocumab (Repatha) and alirocumab (Praluent) both have approved indications as adjuncts to other LDL-C lowering therapies for the treatment of HoFH.

For children and adolescents 10 years of age and older with an LDL-C > 190 mg/dL or > 160 mg/dL with a clinical presentation consistent with familial hypercholesterolemia who do not respond adequately to 3 to 6 months of lifestyle therapy, the 2018 guidelines suggest initiation of statin therapy. Use of non-statin therapies to further treat HoFH in children is not addressed in the guidelines. However, Repatha is approved by the FDA for use in pediatric patients 10 years of age and older with HoFH in combination with diet and other LDL-C lowering therapies.

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Fasenra *(benralizumab)*

Priority Health Part B Step Therapy Drug: Yes

Additional Priority Health Part B Criteria: Yes

Fasenra (benralizumab) is an interleukin-5 (IL-5) antagonist indicated for severe eosinophilic asthma add-on therapy and for the treatment of adult patients with eosinophilic granulomatosis with polyangiitis (EGPA). IL-5 is responsible for the growth and survival of eosinophils which contribute to inflammation in the body.

The Global Initiative for Asthma (GINA) Guidelines on difficult-to-treat & severe asthma in adolescent and adult patients recommend using type 2-targeted biologic agents as add-on for patients with exacerbations and/or poor symptom control despite taking at least high-dose inhaled corticosteroids (ICS) and long-acting beta agonist (LABA) combinations, and who have allergic or eosinophilic biomarkers or need maintenance oral corticosteroids. Type 2-inflammation is defined as blood eosinophils ≥150µl and/or FeNO ≥20 ppb and/or sputum eosinophils ≥2% and/or asthma is clinically allergen driven. GINA guidelines also advise treatment should be optimized prior to initiating a biologic agent. For therapy optimization, consider trials of non-biologic medications in addition to medium/high dose

ICS, such as LABA, long-acting muscarinic agonists (LAMA), and leukotriene receptor antagonists (LTRA). The European Academy of Allergy and Clinical Immunology (EAACI) Biologicals Guideline for severe asthma recommends Fasenra as add-on therapy in adults and pediatric patients 12 years and older with uncontrolled severe asthma uncontrolled by high-dosage ICS + LABA with baseline blood eosinophil cell counts >300 cells/μL or >150 cells/μL for oral corticosteroid (OCS)-dependent patients.

Fasenra was evaluated for safety and efficacy in three studies (SIROCCO, CALIMA, and ZONDA). In SIROCCO and CALIMA, patients with severe asthma despite previous treatments with medium-to-high dose ICS were randomized to receive Fasenra 30 mg every 4 weeks, every 8 weeks (following induction dosing every 4 weeks x 3 cycles), or placebo. Both studies found Fasenra reduced the number of exacerbations (defined as a need for systemic corticosteroids in response to uncontrolled symptoms OR a temporary increase in steroid maintenance doses) vs placebo. Lung function was also improved on treatment (FEV1). In the ZONDA study, significantly more patients were able to reduce the amount of daily corticosteroid use as a result of Fasenra adjunct treatment.

According to the 2021 American College of Rheumatology/Vasculitis Foundation Guideline for the Management of Antineutrophil Cytoplasmic Antibody–Associated Vasculitis, non-severe (vasculitis without life or organ-threatening manifestations) EGPA should be treated with glucocorticoid monotherapy. Additional first-line options include methotrexate, azathioprine, and mycophenolate. In adults with non-severe EGPA who are not in remission, the guidelines recommend adding mepolizumab to systemic glucocorticoids rather than cyclophosphamide, rituximab, or methotrexate. The guidelines do not mention Fasenra, however it is an (IL-5) antagonist, like mepolizumab, and decreases eosinophil levels and inflammation in the body. For patients with severe EGPA and organ or life-threatening disease manifestations, the guidelines recommend including cyclophosphamide or rituximab in the remission induction regimen rather than glucocorticoids alone. The efficacy of benralizumab in severe EGPA has not been established since patients with severe disease were excluded from the clinical trial, therefore use in severe EGPA is not supported.

Fasenra has not been studied in combination with other biologic agents due to an increased risk of infection and increased immunosuppression. As such, use of Fasenra in combination with other biologic agents is not recommended.

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Fylnetra *(pegfilgrastim-pbbk)*

Priority Health Part B Step Therapy Drug: Yes

Additional Priority Health Part B Criteria: No

Hematopoietic growth factors are defined by their ability to promote proliferation and differentiation of hematopoietic progenitors into mature blood cells. Colony-stimulating factors (CSFs) are hematopoietic growth factors that regulate the growth and differentiation of cells towards the myeloid and erythroid lineages. Myeloid growth factors (MGFs), such as granulocyte colony-stimulating factors (G-CSF), are primarily used to reduce the incidence of febrile neutropenia (FN) in patients with non-myeloid malignancies receiving myelosuppressive chemotherapy.

Chemotherapy-induced neutropenia is a major risk factor for infection-related morbidity and mortality and also a significant dose-limiting toxicity in cancer treatment. Prophylactic treatment with granulocyte-colony stimulating factors (G-CSFs), such as filgrastim (including approved biosimilars) or pegfilgrastim is available to reduce the risk of chemotherapy-induced neutropenia. NCCN guideline recommends prophylactic G-CSF use if a patient's risk of developing FN is >20% (category 1). The American Society of Clinical Oncology (ASCO) and European Organization for Research and Treatment of Cancer (EORTC) guidelines have also adopted the 20% threshold for considering routine prophylactic MGF support. The National Comprehensive Cancer Network (NCCN) Panel defines intermediate risk as a 10% to 20% probability of developing FN or a neutropenic event that would compromise treatment. For patients receiving intermediate-risk chemotherapy regimens, the panel recommends individualized consideration of prophylactic G-CSF use based on the presence of patient-specific risk factors.

Administration of CSFs to mobilize peripheral-blood progenitor cell (PBPC) often in conjunction with chemotherapy and their administration after autologous, but not allogeneic, PBPC transplantation is the current standard of care. Among autologous PBPC patients, post-transplant G-CSF use has been associated with savings in the duration of hospitalization and overall medical costs. The use of CSFs to mobilize peripheral blood progenitor cells (PBPC) and to shorten the period of neutropenia after cytoreduction and PBPC transplantation, is well established. Individuals receiving CSFs for mobilization should have their platelet counts monitored. Filgrastim is indicated for the mobilization of hematopoietic progenitor cells into the peripheral blood for collection by leukapheresis.

Several studies have shown that CSF administration can produce modest decreases in the duration of neutropenia when begun shortly after completion of the initial induction chemotherapy for the treatment of acute myeloid leukemia (AML). CSF use can be recommended after the completion of consolidation chemotherapy because of the potential to decrease the incidence of infection and eliminate the likelihood of hospitalization in some patients receiving intensive post-remission chemotherapy. CSFs can increase the absolute neutrophil count in neutropenic patients with myelodysplastic syndromes (MDS). In the treatment of acute lymphocytic leukemia (ALL), CSFs are recommended after the initial first few days of chemotherapy of the initial induction or first post- remission course.

Current recommendations for the management of patients exposed to lethal doses of total body radiotherapy, but not doses high enough to lead to certain death due to injury to other organs, includes the prompt administration of CSF or pegylated G-CSF. Hematopoietic growth factors can increase the survival, proliferation, amplification, and differentiation of granulocyte progenitors to produce neutrophils.

Per NCCN guidelines on Hemopoietic growth Factors, an FDA-approved biosimilar is an appropriate substitute for filgrastim and pegfilgrastim.

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Gamifant *(emapalumab-lzsg)*
Priority Health Part B Step Therapy Drug: Yes
Additional Priority Health Part B Criteria: Yes
Gamifant is an interferon gamma (IFNγ) neutralizing antibody indicated for the treatment of primary hemophagocytic lymphohistiocytosis (HLH) with refractory, recurrent or progressive disease or intolerance with conventional HLH therapy and HLH/macrophage activation syndrome (MAS) in known or suspected Still's disease, including systemic Juvenile Idiopathic Arthritis (sJIA), with an inadequate response or intolerance to glucocorticoids, or with recurrent MAS. Hemophagocytic Lymphohistiocytosis (HLH) is a life-threatening hyperinflammatory syndrome characterized by excessive activation of macrophages and cytotoxic T lymphocytes. This immune dysregulation leads to widespread tissue damage and organ dysfunction. Primary HLH is a genetic condition resulting from mutations that impair lymphocyte cytotoxic function and immune regulation. It predominantly affects pediatric patients. Secondary HLH is acquired and more commonly observed in adults. It is typically triggered by infections, malignancies, or autoimmune conditions. When secondary HLH occurs in autoimmune diseases—such as systemic juvenile idiopathic arthritis or Still's disease—it is referred to as Macrophage Activation Syndrome (MAS) or MAS-HLH. The Consensus-Based Guidelines for the Recognition, Diagnosis, and Management of Hemophagocytic Lymphohistiocytosis recommends testing for HLH promptly in all patients admitted to intensive care units (ICUs) with an unexplained or disproportionate inflammatory response, especially those with rapid clinical deterioration. Meeting five or more of eight HLH 2004 diagnostic criteria serves as a valuable diagnostic tool for HLH. Early aggressive critical care interventions are often required to manage the multisystem organ failure associated with hemophagocytic lymphohistiocytosis. Early steroid treatment is indicated for patients with familial hemophagocytic lymphohistiocytosis and is often valuable in patients with secondary hemophagocytic lymphohistiocytosis without previous therapy, including macrophage activation syndrome without persistent or relapsing disease. In familial HLH and severe, persistent, or relapsing secondary MAS, the addition of prompt individualized, age-adjusted etoposide treatment is recommended. In patients with macrophage activation syndrome, whose disease does not sufficiently respond, interleukin-1 inhibition and/or cyclosporine is recommended. Gamifant is recommended as salvage therapy for primary HLH and was still under investigation for use in secondary HLH when these guidelines per published. Step therapy is applied to certain Part B drugs, biologics, and biosimilars in a way that lowers costs and improves the quality of care for Medicare beneficiaries per the Centers for Medicare & Medicaid Services (CMS) guidance.

References

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Granix *(tbo-filgrastim)*

Priority Health Part B Step Therapy Drug: Yes

Additional Priority Health Part B Criteria: No

Hematopoietic growth factors are defined by their ability to promote proliferation and differentiation of hematopoietic progenitors into mature blood cells. Colony-stimulating factors (CSFs) are hematopoietic growth factors that regulate the growth and differentiation of cells towards the myeloid and erythroid lineages. Myeloid growth factors (MGFs), such as granulocyte colony-stimulating factors (G-CSF), are primarily used to reduce the incidence of febrile neutropenia (FN) in patients with non-myeloid malignancies receiving myelosuppressive chemotherapy.

Chemotherapy-induced neutropenia is a major risk factor for infection-related morbidity and mortality and also a significant dose-limiting toxicity in cancer treatment. Prophylactic treatment with granulocyte-colony stimulating factors (G-CSFs), such as filgrastim (including approved biosimilars) or pegfilgrastim is available to reduce the risk of chemotherapy-induced neutropenia. NCCN guideline recommends prophylactic G-CSF use if a patient's risk of developing FN is >20% (category 1). The American Society of Clinical Oncology (ASCO) and European Organization for Research and Treatment of Cancer (EORTC) guidelines have also adopted the 20% threshold for considering routine prophylactic MGF support. The National Comprehensive Cancer Network (NCCN) Panel

defines intermediate risk as a 10% to 20% probability of developing FN or a neutropenic event that would compromise treatment. For patients receiving intermediate-risk chemotherapy regimens, the panel recommends individualized consideration of prophylactic G-CSF use based on the presence of patient-specific risk factors.

Administration of CSFs to mobilize peripheral-blood progenitor cell (PBPC) often in conjunction with chemotherapy and their administration after autologous, but not allogeneic, PBPC transplantation is the current standard of care. Among autologous PBPC patients, post-transplant G-CSF use has been associated with savings in the duration of hospitalization and overall medical costs. The use of CSFs to mobilize peripheral blood progenitor cells (PBPC) and to shorten the period of neutropenia after cytoreduction and PBPC transplantation, is well established. Individuals receiving CSFs for mobilization should have their platelet counts monitored. Filgrastim is indicated for the mobilization of hematopoietic progenitor cells into the peripheral blood for collection by leukapheresis.

Several studies have shown that CSF administration can produce modest decreases in the duration of neutropenia when begun shortly after completion of the initial induction chemotherapy for the treatment of acute myeloid leukemia (AML). CSF use can be recommended after the completion of consolidation chemotherapy because of the potential to decrease the incidence of infection and eliminate the likelihood of hospitalization in some patients receiving intensive post-remission chemotherapy. CSFs can increase the absolute neutrophil count in neutropenic patients with myelodysplastic syndromes (MDS). In the treatment of acute lymphocytic leukemia (ALL), CSFs are recommended after the initial first few days of chemotherapy of the initial induction or first post- remission course.

Current recommendations for the management of patients exposed to lethal doses of total body radiotherapy, but not doses high enough to lead to certain death due to injury to other organs, includes the prompt administration of CSF or pegylated G-CSF. Hematopoietic growth factors can increase the survival, proliferation, amplification, and differentiation of granulocyte progenitors to produce neutrophils.

Per NCCN guidelines on Hemopoietic growth Factors, an FDA-approved biosimilar is an appropriate substitute for filgrastim and pegfilgrastim.

References

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2. Aapro MS, Bohlius J, Cameron DA, et al.; European Organization for Research and Treatment of Cancer. 2010 update of EORTC guidelines for the use of granulocyte-colony stimulating factor to reduce the incidence of chemotherapy-induced febrile neutropenia in adult patients with lymphoproliferative disorders and solid tumors. Eur J Cancer. 2011; 47 (1): 8-32. 2.

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5. National Comprehensive Cancer Network. Hematopoietic growth factors (Version 3.2024) 2024 Jan 30. Available at: https://www.nccn.org/professionals/physician_gls/pdf/growthfactors.pdf. Accessed on May 20, 2024

Hemgenix *(etranacogene dezaparvovec-drlb)*

Priority Health Part B Step Therapy Drug: No

Additional Priority Health Part B Criteria: Yes

Hemgenix is an adeno-associated virus (AAV) vector-based gene therapy indicated as a one-time treatment for adults with hemophilia B (congenital Factor IX deficiency) who use Factor IX prophylaxis therapy, have a current or historical life-threatening hemorrhage, or who have repeated, serious spontaneous bleeding episodes.

Hemophilia B is a rare genetic bleeding disorder in which affected individuals have insufficient levels of factor IX. It is the second most common type of hemophilia and caused by mutations in the F9 gene. This gene is located on the X chromosome and is thus inherited as an X-linked recessive trait. The AAV vector therapy delivers a functional copy of the F9 gene to the liver where functional factor IX is produced. Patients with high AAV5 antibody titers may not respond to therapy due to the neutralizing antibodies. Though the HOPE-B study did not exclude patients based on antibody titers, the trial had one non-responder to treatment whose antibody titer level was 1:700. It is important for providers to understand and be aware of the patient's antibody titer levels before administering treatment.

Symptoms of Hemophilia B can range from mild, going almost unnoticed to severe where patients have a factor level of less than 1% and often have bleeding for no known reason, especially in joints and muscles. Mild cases typically do not need prophylactic therapy and may only require on-demand factor for injuries or surgery while severe cases require preventative treatment. In its pivotal trial, participants were men of at least 18 years of age with inherited hemophilia B defined as severe with a factor IX activity level less than 1% or moderately severe with a factor IX activity level of 1 to 2%.

Standard of care for hemophilia B includes the use of factor IX replacement therapy. To have been enrolled in the HOPE-B trial, participants needed to be stable on factor IX therapy for 6 months prior to Hemgenix administration.

There is no data to support use of Hemgenix following prior use of Hemgenix or another AAV-based gene therapy.

References

1. Hemgenix [Package Insert]. Lexington, MA; uniQure, Inc.: 2022

2. Clinicaltrials.gov. HOPE-B: Trial of AMT-061 in severe or moderately severe hemophilia b patients (NCT03569891). Available at: https://clinicaltrials.gov/ct2/show/NCT03569891.

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Herceptin *(trastuzumab)*

Priority Health Part B Step Therapy Drug: Yes

Additional Priority Health Part B Criteria: No

Herceptin (trastuzumab) is the reference product for multiple trastuzumab biosimilars. Trastuzumab biosimilars include, but may not be limited to Ontruzant (trastuzumab-dttb), Ogivri (trastuzumab-dkst), Herzuma (trastuzumab-pkrb), and Trazimera (trastuzumab-qyyp).

The Food and Drug Administration (FDA) and current treatment guidelines including the National Comprehensive Cancer Network (NCCN) Guidelines support the use of FDA-approved trastuzumab biosimilars and do not favor one biosimilar or the reference product over another. Step therapy may be applied to certain Part B drugs, biologics, and biosimilars in a way that lowers costs and improves the quality of care for Medicare beneficiaries per the Centers for Medicare & Medicaid Services (CMS) guidance.

Priority Health also follows LCD L37205: Chemotherapy Drugs and their Adjuncts.

References

1. Herceptin [Package Insert]. South San Francisco, CA; Genentech, Inc.: 2010

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3. National Comprehensive Cancer Network. Gastric Cancer (Version 2.2024)

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6. Centers for Medicare & Medicaid Services. Local Coverage Determination (LCD) L37205: Chemotherapy Drugs and their Adjuncts.

Herceptin Hylecta *(trastuzumab and hyaluronidase)*

Priority Health Part B Step Therapy Drug: Yes

Additional Priority Health Part B Criteria: No

Herceptin Hylecta (trastuzumab and hyaluronidase) is a monoclonal antibody that targets HER2 receptors on tumor cells that overexpress the protein, preventing further cell growth, ultimately leading to programmed cell death. Both breast and gastric cancers can be positive for the HER2 receptor, representing nearly a third of all breast cancer cases.

The Food and Drug Administration (FDA) and current treatment guidelines including the National Comprehensive Cancer Network (NCCN) Guidelines support the use of trastuzumab (including biosimilars) in these conditions, and do not favor one biosimilar over another. Step therapy may be applied to certain Part B drugs, biologics, and biosimilars in a way that lowers costs and improves the quality of care for Medicare beneficiaries per the Centers for Medicare & Medicaid Services (CMS) guidance.

Priority Health follows LCD L37205: Chemotherapy Drugs and their Adjuncts.

References

1. Herceptin Hylecta [Package Insert]. South San Francisco, CA; Genentech, Inc.: 2019

2. National Comprehensive Cancer Network. Breast Cancer (Version 2.2024)

3. National Comprehensive Cancer Network. Gastric Cancer (Version 2.2024)

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6. Centers for Medicare & Medicaid Services. Local Coverage Determination (LCD) L37205: Chemotherapy Drugs and their Adjuncts.

Hercessi *(trastuzumab-strf)*
Priority Health Part B Step Therapy Drug: Yes
Additional Priority Health Part B Criteria: No
Hercessi is a trastuzumab biosimilar. Other trastuzumab biosimilars include Ontruzant (trastuzumab-dttb), Ogivri (trastuzumab-dkst), Kanjinti (trastuzumab-anns), and Trazimera (trastuzumab-qyyp). The Food and Drug Administration (FDA) and current treatment guidelines including the National Comprehensive Cancer Network (NCCN) Guidelines support the use of FDA-approved trastuzumab biosimilars and do not favor one product (biosimilar or reference biologic) over another. Step therapy may be applied to certain Part B drugs and biosimilars in a way that lowers costs and improves the quality of care for Medicare beneficiaries per the Centers for Medicare & Medicaid Services (CMS) guidance. Priority Health also follows LCD L37205: Chemotherapy Drugs and their Adjuncts
References 1. Hercessi [prescribing information]. Raleigh, NC: Accord BioPharma Inc.; April 2024. 2. National Comprehensive Cancer Network. Breast Cancer (Version 2.2024) 3. National Comprehensive Cancer Network. Gastric Cancer (Version 2.2024) 4. Centers for Medicare & Medicaid Services. Medicare Advantage Prior Authorization and Step Therapy for Part B Drugs. August 7, 2018. Retrieved from https://www.cms.gov/newsroom/fact-sheets/medicare-advantage-prior-authorization-and-step-therapy-part-b-drugs. 5. Centers for Medicare & Medicaid Services. (2018, August 7). Prior Authorization and Step Therapy for Part B Drugs in Medicare Advantage [Memorandum]. Retrieved from https://www.cms.gov/Medicare/Health-Plans/HealthPlansGenInfo/Downloads/MA_Step_Therapy_HPMS_Memo_8_7_2018.pdf 6. Centers for Medicare & Medicaid Services. Local Coverage Determination (LCD) L37205: Chemotherapy Drugs and their Adjuncts.
Herzuma *(trastuzumab-pkrb)*
Priority Health Part B Step Therapy Drug: Yes
Additional Priority Health Part B Criteria: No
Herzuma is a trastuzumab biosimilar. Other trastuzumab biosimilars include Ontruzant (trastuzumab-dttb), Ogivri (trastuzumab-dkst), Kanjinti (trastuzumab-anns), and Trazimera (trastuzumab-qyyp).

The Food and Drug Administration (FDA) and current treatment guidelines including the National Comprehensive Cancer Network (NCCN) Guidelines support the use of FDA-approved trastuzumab biosimilars and do not favor one biosimilar over another. Step therapy may be applied to certain Part B drugs and biosimilars in a way that lowers costs and improves the quality of care for Medicare beneficiaries per the Centers for Medicare & Medicaid Services (CMS) guidance.

Priority Health also follows LCD L37205: Chemotherapy Drugs and their Adjuncts

References

1. Herzuma [Package Insert]. Yeonsu-gu, Incheon; Celltrion, Inc.: 2019

2. National Comprehensive Cancer Network. Breast Cancer (Version 2.2024)

3. National Comprehensive Cancer Network. Gastric Cancer (Version 2.2024)

4. Centers for Medicare & Medicaid Services. Medicare Advantage Prior Authorization and Step Therapy for Part B Drugs. August 7, 2018. Retrieved from https://www.cms.gov/newsroom/fact-sheets/medicare-advantage-prior-authorization-and-step-therapy-part-b-drugs.

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6. Centers for Medicare & Medicaid Services. Local Coverage Determination (LCD) L37205: Chemotherapy Drugs and their Adjuncts.

Hympavzi *(marstacimab-hncq)*

Priority Health Part B Step Therapy Drug: Yes

Additional Priority Health Part B Criteria: Yes

Hympavzi is an anti-tissue factor pathway inhibitor (anti-TFPI) product indicated for the routine prophylaxis to prevent or reduce frequency of bleeding episodes in adults and pediatric patients ≥ 12 years of age with hemophilia A (congenital Factor VIII deficiency) without Factor VIII inhibitors or hemophilia B (congenital Factor IX deficiency) without Factor IX inhibitors. Hemophilia A is a genetic bleeding disorder caused by insufficient levels of factor VIII. Hemophilia B is a genetic bleeding disorder caused by insufficient levels of factor IX. Symptoms for both vary from mild to severe based on the level of factor activity with severe disease noted to have factor levels less than 1% and often have bleeding for no known reason, particularly in joints and muscles.

Other treatment options for hemophilia A include factor VIII replacement products, Hemlibra (a bi-specific Factor IXa- and Factor X-directed antibody), and gene therapy with Roctavian. Other treatment options for hemophilia B include factor IX replacement products and gene therapy with Beqvez and Hemgenix.

World Federation of Hemophilia guidelines recommends use of prophylaxis therapy in patients with moderate to severe hemophilia A or B. Both WFH and the CDC define moderate to severe as listed below:

- Mild hemophilia A: factor activity is 5-40 IU/dL (5 to <40% of normal)
- Moderate hemophilia A: factor activity is 1-5 IU/dL (1-5% of normal)
- Severe hemophilia A: factor activity is <1 IU/dL (<1% of normal)

For patients with hemophilia A with and without an inhibitor, the WFH recommends the use of Hemlibra for regular prophylaxis.

The National Bleeding Disorders Foundation Medical and Scientific Advisory Council (MASAC) recommends factor VIII and factor IX products as treatment of choice for patients with hemophilia A and B in whom such agents are necessary. MASAC also provides recommendations for the use of Hemlibra for patients with hemophilia A with and without inhibitors. Hympavzi is not yet addressed in current guidelines.

Hympavzi was approved based on results from phase III BASIS trial. This trial included patients ages 12 to under 75 years with severe hemophilia A or B (factor VIII or IX levels less than 1%) without factor VIII or IX inhibitors. This trial demonstrated superiority to on-demand based factor VIII or factor IX therapy and non-inferiority to routine prophylaxis with factor VIII or factor IX.

Step therapy is applied to certain Part B drugs, biologics, and biosimilars in a way that lowers costs and improves the quality of care for Medicare beneficiaries per the Centers for Medicare & Medicaid Services (CMS) guidance

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iDose TR *(travoprost intracameral implant)*

Priority Health Part B Step Therapy Drug: Yes

Additional Priority Health Part B Criteria: No

Glaucoma is a leading cause of blindness and is impacted by elevated intraocular pressure (IOP). iDose TR (travoprost intracameral implant) is indicated for open-angle glaucoma or ocular hypertension patients, working to lower IOP and slow disease progression. The goal of treatment is to maintain IOP in a target range to preserve visual function and overall quality of life.

Travoprost is one of several prostaglandin F receptor agonists, including another implant, Durysta (bimatoprost), and several topical agents (latanoprost, bimatoprost, tafluprost). The American Academy of Ophthalmology (AAO) recommends this class as first-line in IOP reduction due to the high efficacy, high tolerability, and convenient once-daily dosing. The AAO does not favor the use of one prostaglandin F receptor agonist over another.

iDose TR is implanted through a corneal incision and is not intended to be repeated following initial treatment. The titanium reservoir provides controlled and sustained release of travoprost. Two pivotal studies (GC-010 and GC-012) compared the results of iDose TR to another IOP treatment, timolol 0.5% ophthalmic solution. Results showed no significant change in vision between treatment arms. There are no studies comparing iDose TR with another prostaglandin, but the other prostaglandins were individually studied most often against timolol ophthalmic solution and found to be non-inferior. Durysta was also found to be non-inferior to timolol.

Currently, there are no compendia supported uses for this therapy outside the FDA-indication(s).

References

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2. American Academy of Ophthalmology: Primary Open-Angle Glaucoma Preferred Practice Pattern, 2020

Iheezo 3% *(chloroprocaine hcl/ pf gel eye drops)*

Priority Health Part B Step Therapy Drug: Yes

Additional Priority Health Part B Criteria: No

Iheezo is an ester anesthetic indicated for ocular surface anesthesia.

The most commonly used drugs for topical anesthesia during ophthalmic procedures are oxybuprocaine, proparacaine, tetracaine drops and lidocaine gel. The viscosity of gel formulations increases time on the ocular surface of the local anesthetics which results in increased drug exposure in the deeper tissues and reduces its systemic absorption, following topical administration. Iheezo is an ophthalmic gel 3% that has a viscosity not exceeding 2,000 cps. Topical anesthetic solutions with lower viscosity, such a tetracaine 0.5% ophthalmic solution have viscosity between 15 and 25 cps, are rapidly cleared from the surface of the cornea. A prospective randomized study compared the efficacy and safety of Iheezo 3% gel to tetracaine 0.5% eye drops in patients undergoing cataract surgery. Just before intraocular lens implantation) 150/163 patients (92.0%) in the chloroprocaine group and 153/169 patients (90.5%) in the tetracaine group achieved surface anesthesia with no supplementation. For both treatment groups median time to obtain surface anesthesia and mean duration of anesthesia was 1 and 22 min, respectively. The study established clinical equivalence between Iheezo 3% gel and tetracaine 0.5% eye drop and concluded that Iheezo is a valid therapeutic alternative cataract surgery and other less invasive ophthalmic procedures.

In 2 randomized studies chloroprocaine applied topically to the eye provided full conjunctival anesthesia in significantly more patients compared with placebo (study 1, 90% vs 12%; study 2, 95% vs 20%). The median time to onset of anesthesia was 0.67 minutes in both studies and the median duration of anesthesia was 14.3 and 19.3 minutes. All chloroprocaine-treated patients received 3 drops instilled to the eye and study 2 included single or multiple instillations.

References

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3. Figus M, Giansanti F, Villani E, et al. Chloroprocaine 3% Gel as a Novel Ocular Topical Anesthetic: Results from a Multicenter, Randomized Clinical Trial in Patients Undergoing Cataract Surgery.J Ocul Pharmacol Ther. 2024;40(2):117-12.

Ilaris *(canakinumab)*

Priority Health Part B Step Therapy Drug: Yes

Additional Priority Health Part B Criteria: Yes

Ilaris (canakinumba) is an interleukin-1 beta (IL-1B) monoclonal antibody. It blocks IL-1 receptor interaction and neutralizes overactive IL-1B activity which is present in disorders such as Cryopyrin-Associated Periodic Syndromes (CAPS), systemic juvenile idiopathic arthritis (SJIA), Still's disease, and gout.

Gout is the most common form of inflammatory arthritis. The 2020 American College of Rheumatology (ACR) guidelines strongly recommend initiating urate-lowering therapy (ULT) in patients with gout. The guidelines define gout patients as patients with any of the following: 1 or more subcutaneous tophi, evidence of radiographic damage (any modality) attributable to gout, or frequent gout flares (with frequent defined as 2 or more annually). Continuing concomitant anti-inflammatory prophylaxis therapy for 3 to 6 months over less than 3 months, with ongoing evaluation and continued prophylaxis as needed if the patient continues to experience gout flares, is strongly recommended. Continuing ULT indefinitely over stopping ULT is conditionally recommended. If therapy is well-tolerated and not burdensome, the Patient Panel expressed a preference to continue treatment.

For the treatment of acute gout flares, colchicine, NSAIDs, or glucocorticoids (oral, intraarticular, or intramuscular) are appropriate first-line therapies over interleukin-1 (IL-1) inhibitors or adrenocorticotropic hormone (ACTH). Using an IL-1 inhibitor over no therapy (beyond supportive/analgesic treatment) is conditionally recommended for patients experiencing a gout flare for whom anti-inflammatory therapies are either ineffective, poorly tolerated, or contraindicated. Treatment with glucocorticoids (intramuscular, intravenous, or intraarticular) over IL-1 inhibitors or ACTH is strongly recommended for patients who are unable to take oral medications.

The use of Ilaris in combination with other biologic agents or targeted disease-modifying antirheumatic drugs is not recommended due to a lack of clinical evidence to support the safety and efficacy of concurrent use.

References

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Ilumya *(tildrakizumab)*
Priority Health Part B Step Therapy Drug: Yes
Additional Priority Health Part B Criteria: Yes

Ilumya is an interleukin-23 (IL-23) antagonist indicated for Plaque Psoriasis (PsO).

Per the 2020 Joint AAD-NPF guidelines (non-biologic), recommended treatments include methotrexate, cyclosporine, and acitretin. Methotrexate and cyclosporine are category A recommendations, whereas acitretin is a category B recommendation. The 2019 Joint AAD-NPF guidelines (biologics) recommend (category A) the use of biologics in treating psoriasis but do not suggest one agent over another. Tumor necrosis factor (TNF) inhibitors, interleukin-12/23, IL-23, and IL-17 inhibitors have all shown efficacy in this condition. These include infliximab, adalimumab, Enbrel, Skyrizi, Cosentyx and Ilumya. Otezla is also a recommended treatment option included in the guidelines.

Ilumya has not been studied in combination with other biologic agents, Otezla, or JAK inhibitors due to an increased risk of infection and increased immunosuppression. As such, use of Ilumya in combination with these agents is not recommended.

The Food and Drug Administration (FDA) considers biosimilars to be highly similar with no clinically meaningful differences to the biologic reference product. Biosimilars are considered safe and effective and provide an option to increase access to lifesavings drugs at lower costs. The FDA and current treatment guidelines do not favor one product (biologic or biosimilar) over another.

Step therapy is applied to certain Part B drugs, biologics, or biosimilars in a way that lowers costs and improves the quality of care for Medicare beneficiaries per the Centers for Medicare & Medicaid Services (CMS) guidance.

References

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Iluvien *(fluocinolone acetonide intravitreal implant)*

Priority Health Part B Step Therapy Drug: No

Additional Priority Health Part B Criteria: Yes

Illuvien (fluocinolone acetonide intravitreal implant) contains a corticosteroid and is indicated for the treatment of diabetic macular edema in patients who have been previously treated with a course of corticosteroids and did not have a clinically significant rise in intraocular pressure.

Diabetic macular edema (DME) is defined as the presence of intraretinal fluid (edema) and thickening involving the macula, the part of the retina responsible for central vision. It is a vision-threatening complication of diabetes and can occur at any stage or severity of diabetic retinopathy. Edema that is centrally located within the macula can be associated with more substantial decreases in visual acuity.

The efficacy of Iluvien was assessed in two three-year, randomized (2:1, active: sham), multicenter, double-masked, parallel groups studies that enrolled patients with diabetic macular edema that had previously been treated with laser photocoagulation. The primary efficacy endpoint in both trials was the proportion of subjects in whom vision had improved by 15 letters or more from baseline after 24 months of follow-up. A 15-letter or more improvement in best corrected visual acuity score occurred in significantly more patients who received fluocinolone acetonide implants compared with sham injections or standard of care for the treatment of diabetic macular edema. A post hoc analysis investigated the long-term effects of intravitreal 0.19 mg fluocinolone acetonide implant on progression and regression of diabetic retinopathy. The data set found that intravitreal fluocinolone 0.2 and 0.5 mcg/day implants significantly delayed the development of proliferative diabetic retinopathy and the progression of diabetic retinopathy compared with placebo.

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Imaavy *(nipocalimab-aahu)*
Priority Health Part B Step Therapy: Yes
Additional Priority Health Part B Criteria: Yes

Imaavy is a neonatal fragment crystallizable receptor blocker indicated for treatment of generalized myasthenia gravis in adult and pediatric patients ages 12 and up who are anti-acetylcholine receptor (AChR) or anti-muscle-specific tyrosine kinase (MuSK) antibody positive (Ab+).

Myasthenia gravis is the most common primary disorder of neuromuscular transmission and can be characterized by ocular, bulbar, limb and respiratory muscle weakness. Muscle weakness can vary person to person and generally improves with rest and worsens with physical activity. Most patients who develop myasthenia gravis have autoantibodies that attack acetylcholine receptors (AChR) which reduces the number of these receptors over time at the postsynaptic neuromuscular junction.

There is no cure for myasthenia gravis but treatment can control symptoms. Life expectancy is near normal. Initial therapy for most patients with myasthenia gravis involves a cholinesterase inhibitor to increase acetylcholine at the neuromuscular junction. Glucocorticoids are also used due to their rapid onset of action. Up to 10-20% of patients are believed to have refractory disease. Biologics, neonatal fragment crystallizable receptor antagonists or complement inhibitors may be used for chronic immunotherapy. Most patients with refractory myasthenia gravis will require immunotherapy at some point during their illness to aid in maintaining disease stability.

Step therapy is applied to certain Part B drugs, biologics, and biosimilars in a way that lowers costs and improves the quality of care for Medicare beneficiaries per the Centers for Medicare & Medicaid Services (CMS) guidance.

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Imuldosa IV *(ustekinumab- srfl)*

Priority Health Part B Step Therapy: Yes

Additional Priority Health Part B Criteria: Yes

Imuldosa is a biosimilar to Stelara. It has been approved by the FDA for all indications of its reference biologic. The FDA has also provisionally determined Imuldosa to be interchangeable with Stelara. Ustekinumab (including the biosimilars and reference product) is a monoclonal antibody that inhibits interleukin (IL)-12 and IL-23 and is indicated in several inflammatory conditions including Ulcerative Colitis (UC) and Crohn's Disease (CD).

The Food and Drug Administration (FDA) considers biosimilars to be highly similar with no clinically meaningful differences to the biologic reference product. Biosimilars are considered safe and effective and provide an option to increase access to lifesavings drugs at lower costs. The FDA and current treatment guidelines do not favor one product (biologic or biosimilar) over another.

There is limited data on the concurrent use of ustekinumab with other biologic agents, targeted synthetic DMARDs (e.g., JAK inhibitors), and phosphodiesterase-4 (PDE4) inhibitors (Otezla). Given the absence of strong clinical evidence and the potential for increased infection risk, it is not recommended to use ustekinumab in combination with these agents.

Step therapy is applied to certain Part B drugs, biologics, and biosimilars in a way that lowers costs and improves the quality of care for Medicare beneficiaries per the Centers for Medicare & Medicaid Services (CMS) guidance

References

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Infliximab injection (J1745 - excludes biosimilar, 10 mg)

Priority Health Part B Step Therapy Drug: Yes

Additional Priority Health Part B Criteria: Yes

Infliximab is a tumor necrosis factor inhibitor (TNFi) indicated for several conditions including Crohn's Disease (CD), Ulcerative Colitis (UC), fistulizing CD, Rheumatoid Arthritis (RA), active ankylosing spondylitis (AS), psoriatic arthritis (PsA), and plaque psoriasis (PsO).

Ankylosing spondylitis 'AS' and non-radiographic axial spondyloarthritis 'NRAS' are related conditions. The 2019 American College of Rheumatology recommendations for AS and NRAS are similar. Recommended first-line agents include nonsteroidal anti-inflammatory drugs (NSAIDs) due to their well-known safety and efficacy profiles. For patients who have active disease despite treatment with NSAIDs, treatment with a TNFi is recommended. Guidelines do not favor one TNFi over another.

Hidradenitis suppurativa (HS) is a chronic, painful skin condition that varies in presentation. There are no established treatment guidelines for this condition, but the foundation for HS has put forth evidence-based recommendations. Initial treatment includes topical and systemic antibiotics with progression to biologics if refractory or unresponsive to initial treatment. Antibiotics have been used to treat HS for decades; there is robust evidence to show symptom improvement and patient tolerability. Biologic agents (e.g., TNFi, interleukin inhibitors) have shown some benefit in small studies but lack the robust support to make strong recommendations for dosing, appropriate goals of therapy, and duration of treatment.

The 2018 American College of Gastroenterology (ACG) guidelines recommend mercaptopurine, azathioprine, and methotrexate in symptomatic CD despite prior corticosteroid use. TNFi agents are effective in those with inadequate response to these initial therapies.

Per the 2020 American Gastroenterology Association guidelines, multiple agents effectively induce and maintain remission of UC, including corticosteroids, 5-aminosalicylates '5-ASA', and biologics. Treatment of mild-to-moderate UC is typically started with 5-ASA therapy. In those who do not respond to 5-ASA therapy, induction can be achieved through short-term corticosteroids. Once induction is achieved, maintenance can be managed with

thiopurines. Methotrexate is not recommended for induction or maintenance of remission in UC, whereas biologic agents do have support for use in these treatment areas. Guidelines do not favor one biologic over another, nor do they favor biologics over thiopurine monotherapy for those in remission.

For Rheumatoid Arthritis (RA), guidelines favor the use of biologic DMARDs (bDMARD) for moderate or high disease activity despite prior conventional synthetic DMARDs (csDMARD). Guidelines do not favor one bDMARD over another, however TNFi agents have the most documented safety and efficacy profiles.

Per the 2020 Joint AAD-NPF guidelines (non-biologic), recommended treatments include methotrexate, cyclosporine, and acitretin. Methotrexate and cyclosporine are category A recommendations, whereas acitretin is a category B recommendation. The 2019 Joint AAD-NPF guidelines (biologics) recommend (category A) the use of biologics in treating psoriasis but do not suggest one agent over another. TNFis, interleukin-12/23, IL-23, and IL-17 inhibitors have all shown efficacy in this condition.

Per the 2018 American College of Rheumatology (ACR)/National Psoriasis Foundation (NPF) guidelines, methotrexate, sulfasalazine, cyclosporine, and leflunomide may be used in patients with non-severe Psoriatic Arthritis (PsA) and have robust safety and efficacy evidence to support their use. If initial treatment is not sufficient, switching to a biologic is suggested.

There is limited data on the concurrent use of infliximab products with other biologic agents, targeted synthetic DMARDs (JAK inhibitors), and PDE4 inhibitors (Otezla). Given the absence of strong clinical evidence and the potential for increased infection risk, it is not recommended to use infliximab products in combination with these agents.

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Infugem *(gemcitabine hcl)*

Priority Health Part B Step Therapy Drug: Yes

Additional Priority Health Part B Criteria: No

Infugem is a gemcitabine injection. Gemcitabine is a nucleoside metabolic inhibitor indicated for multiple cancers including: a) in combination with carboplatin, for the treatment of advanced ovarian cancer that has relapsed at least 6 months after completion of platinum-based therapy, b) in combination with paclitaxel, for first-line treatment of metastatic breast cancer after failure of prior anthracycline-containing adjuvant chemotherapy, unless anthracyclines were clinically contraindicated, c) in combination with cisplatin for the treatment of non-small cell lung cancer, and d) as a single agent for the treatment of pancreatic cancer.

Priority Health also follows LCD (L37205) for Chemotherapy Drugs and their Adjuncts.

References

1. Centers for Medicare & Medicaid Services (CMS) Local Coverage Determination (LCD) L37205: Chemotherapy Drugs and their Adjuncts.

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Ivra *(melphalan hcl)*

Priority Health Part B Step Therapy Drug: Yes

Additional Priority Health Part B Criteria: No

Ivra (melphalan hcl) is an alkylating drug indicated for palliative treatment of patients with multiple myeloma for whom oral therapy is not appropriate. Ivra is a new injectable formulation of melphalan, differing from current formulations which are available as lyophilized powder for injection.

No new clinical efficacy trials were required for FDA approval of Ivra. Approval was based on an earlier randomized trial of intravenous melphalan compared to oral melphalan in the treatment of myeloma. One hundred seven patients were randomized to the oral melphalan arm and 203 patients to the intravenous melphalan arm. More patients had a poor-risk classification (58% versus 44%) and high tumor load (51% versus 34%) on the oral compared to the intravenous arm (P<0.04). Response rates at week 22 were 44% in the oral melphalan group and 38% in the intravenous melphalan group. Because of changes in

protocol design after week 22, other efficacy parameters such as response duration and survival could not be compared.

Step therapy is applied to certain Part B drugs, biologics, and biosimilars in a way that lowers costs and improves the quality of care for Medicare beneficiaries per the Centers for Medicare & Medicaid Services (CMS) guidance.

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Izervay (avacincaptad pegol sodium/PF)

Priority Health Part B Step Therapy Drug: No

Additional Priority Health Part B Criteria: Yes

Izervay (avacincaptad pegol) is a complement inhibitor indicated for the treatment of geographic atrophy (GA) secondary to age-related macular degeneration (AMD). Currently, there are no compendia supported uses for this therapy outside the FDA-indication(s).

The American Academy of Ophthalmology (AAO) state that an estimated 80% of patients with AMD have non-neovascular or atrophic AMD. The neovascular form is responsible for a large fraction of the severe central visual acuity (VA) loss associated with AMD.

Diagnostic testing such as optical coherence tomography (OCT) is important in diagnosing and managing AMD. OCT defines the cross-sectional architecture of the retina, which is not possible with any other imaging technology and can aid in determining the presence of subretinal and intraretinal fluid and in documenting the degree of retinal thickening. AAO also suggests that fundus autofluorescence is helpful to demonstrate areas of geographic atrophy and monitor their progression. Outcome goals are to reverse or minimize visual loss and improve visual function.

At this time, Izervay has not been studied and there is no data to support use in combination with other medications used to treat GA.

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Kanjinti *(trastuzumab-anns)*

Priority Health Part B Step Therapy Drug: Yes

Additional Priority Health Part B Criteria: No

Kanjinti is a trastuzumab biosimilar. Other trastuzumab biosimilars include Ontruzant (trastuzumab-dttb), Ogivri (trastuzumab-dkst), Herzuma (trastuzumab-pkrb), and Trazimera (trastuzumab-qyyp).

The Food and Drug Administration (FDA) and current treatment guidelines including the National Comprehensive Cancer Network (NCCN) Guidelines support the use of FDA-approved trastuzumab biosimilars and do not favor one biosimilar over another. Step therapy may be applied to certain Part B drugs, biologics, and biosimilars in a way that lowers costs and improves the quality of care for Medicare beneficiaries per the Centers for Medicare & Medicaid Services (CMS) guidance.

Priority Health also follows LCD L37205: Chemotherapy Drugs and their Adjuncts.

References

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2. Centers for Medicare & Medicaid Services. Medicare Advantage Prior Authorization and Step Therapy for Part B Drugs. August 7, 2018. Retrieved from https://www.cms.gov/newsroom/fact-sheets/medicare-advantage-prior-authorization-and-step-therapy-part-b-drugs.

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Kebilidi *(eladocagene exuparvovec-tneq)*

Priority Health Part B Step Therapy Drug: No

Additional Priority Health Part B Criteria: Yes

Aromatic L-amino acid decarboxylase (AADC) deficiency is an autosomal recessive rare disorder caused by a mutation on the DOPA decarboxylase (DDC) gene. AADC is characterized by a dysfunctional AADC enzyme which is responsible for the production of neurotransmitters including dopamine, serotonin, epinephrine, and norepinephrine. When this enzyme is not functional or has decreased activity, a smaller number of these neurotransmitters are produced leading to a lack of communication between neurons and signals being properly sent though the body.

Symptoms begin shortly after birth and can vary greatly between individuals. The two most common symptoms include hypotonia in the trunk and oculogyric crises. These are characterized by abnormal rotation of the eyeballs and gaze deviation, uncontrolled movements of the head, neck muscles, agitation and irritability. Other movement disorders may also be present and there may be dysfunction of the autonomic nervous system and gastrointestinal symptoms. Children have developmental delays and are not able to reach normal milestones such as walking and talking and experience failure to thrive.

Kebilidi is an adeno-associated virus (AAV) vector-based gene therapy that replaces the dysfunctional DDC gene in AADC patients with a functional copy of the gene. This is the first disease modifying therapy approved for the treatment of adult and pediatric patients with AADC deficiency. The vector is delivered to the patient's brain where the functional AADC enzyme is produced. Patients with high AAV2 antibody titers may not respond to therapy due to the antibody neutralizing Kebilidi before the gene can be properly incorporated into the genome.

Management has included a multidisciplinary approach to address specific needs of the affected individual. Various medications can help to manage symptoms and varies depending on the affected individual. First line options include dopamine agonists, MOA-B inhibitors and vitamin B6. Other medications may also be considered based on symptoms.

Kebilidi uses an adeno-associated virus serotype 2 (AAV2) vector to deliver a copy of a functional human DDC gene into the brain to promote expression of the AADC enzyme and thus enhanced dopamine production. However, patients with antibodies to an AAV may not respond to Kebildi or other gene therapies using a AAV2 vector due to the antibodies neutralizing the gene therapy before the functional gene is properly incorporated. Kebilidi's

pivotal study excluded patients from the trial based on antibody titers greater than 1200 fold.

References

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Kimyrsa *(oritavancin)*

Priority Health Part B Step Therapy Drug: Yes

Additional Priority Health Part B Criteria: Yes

Kimyrsa (oritavancin) is indicated for the treatment of acute bacterial skin and skin structure infections (SSTIs) caused by susceptible methicillin-resistant staphylococcus aureus (MRSA) isolates in adults for the treatment of acute bacterial skin and skin structure infections caused by susceptible isolates.

Clinical Practice Guidelines for the Diagnosis and Management of Skin and Soft Tissue Infections: 2014 Update by The Infectious Diseases Society of America (IDSA) advises that clinical evaluation of patients with SSTI aims to establish the cause and severity of infection and must take into account pathogen-specific and local antibiotic resistance patterns. There has been a significant increase in the frequency and severity of infections and the emergence of resistance to many of the antimicrobial agents commonly used to treat SSTIs in the past. Some of this increased frequency is related to the emergence of community-associated MRSA.

Gram stain and culture is recommended when evaluating purulent SSTIs (cutaneous abscesses, furuncles, carbuncles, and inflamed epidermoid cysts). Incision and drainage is the recommended treatment for inflamed epidermoid cysts, carbuncles, abscesses, and large furuncles. The decision to administer antibiotics directed against S. aureus as an adjunct to incision and drainage should be made based upon presence or absence of systemic inflammatory response syndrome (SIRS). For moderate purulent infections in patients with systemic signs of infections, empiric treatment with trimethoprim-

sulfamethoxazole (TMP/SMZ) or doxycycline is recommended. For MRSA infections TMP/SMX should be used and for MSSA infections dicloxacillin or cephalexin should be used. For severe purulent infections in patients who have failed incision and drainage plus oral antibiotics or those with systemic signs of infection, empiric treatment and/or confirmed MRSA should be treated with vancomycin, daptomycin, linezolid, telavancin or ceftaroline. If methicillin-sensitive staphylococcus aureus (MSSA) is confirmed, nafcillin, cefazolin or clindamycin are recommended.

Cultures of blood or cutaneous aspirates, biopsies, or swabs are not routinely recommended for non-purulent SSTI (necrotizing infection, cellulitis, erysipelas). For mild infections without systemic signs of infection, patients should receive an antimicrobial agent that is active against streptococci (penicillin VK, cephalosporin, dicloxacillin or clindamycin). For moderate infections with systemic signs of infection, intravenous treatment with penicillin, ceftriaxone, cefazolin or clindamycin is recommended. In severe infection, in patients who have failed oral antibiotic treatment or those with systemic signs of infection, emergent surgical inspection/debridement is recommended to rule out necrotizing process. Patients should also receive empiric treatment with vancomycin plus piperacillin/tazobactam. For treatment of streptococcal skin infections, in patients with a severe penicillin sensitivity, clindamycin, vancomycin, linezolid, daptomycin or telavancin are recommended. The guidelines do not mention oritavancin.

In adults with cellulitis/erysipelas, wound infection, or major cutaneous abscesses due to MRSA (n=405), single-dose oritavancin 1200 mg IV was associated with an early clinical response rate of 81.4% and a clinical success rate of 83.3%; these results were similar to those achieved with vancomycin 1 g or 15 mg/kg IV every 12 hours for 7 to 10 days (80.6% early clinical response rate and 84.1% clinical success rate).

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Kisunla *(donanemab-azbt)*

Priority Health Part B Step Therapy Drug: No

Additional Priority Health Part B Criteria: No

Kisunla is indicated for the treatment of Alzheimer's disease. It was studied in patients with confirmed presence of amyloid pathology and mild cognitive impairment (MCI) or mild dementia stage of disease, consistent with Stage 3 and Stage 4 Alzheimer's disease. Kisunla demonstrated substantial benefit compared to placebo in slowing Alzheimer's disease progression. The benefit was seen through several cognitive and function-based endpoints including the integrated Alzheimer's Disease Rating Scale (iADRS) and the Clinical Dementia Rating Scale – Sum of Boxes (CDR-SB). Dosing was continued or stopped based on observed effects on amyloid imaging. Reduction of brain amyloid plaque levels is considered a surrogate endpoint that is reasonably likely to predict clinical benefit. There was no data beyond the 76 weeks of Study 1 (NCT04437511) to determine whether additional dosing with Kisunla may be needed for longer-term clinical benefit.

The Centers for Medicare & Medicaid Services (CMS) released a national policy for coverage of monoclonal anti-amyloid antibodies approved by the Food and Drug Administration (FDA) for the treatment of Alzheimer's disease. Under this national policy, Medicare covers FDA-approved anti-amyloid antibodies under Coverage with Evidence Development (CED) when they are furnished in accordance with the prespecified coverage criteria for patients who have a clinical diagnosis of MCI due to Alzheimer's disease or mild Alzheimer's disease dementia, both with confirmed presence of amyloid beta pathology consistent with Alzheimer's disease. Monoclonal antibodies directed against amyloid that are approved based on evidence from a surrogate endpoint considered reasonably likely to predict clinical benefit may be covered in a randomized controlled trial conducted under an investigational new drug (IND) application. Monoclonal antibodies directed against amyloid that are approved based on evidence from a direct measure of clinical benefit may be covered in CMS-approved prospective comparative studies (study data may be collected in a registry). Refer to CMS's NCD: Monoclonal Antibodies Directed Against Amyloid for the Treatment of Alzheimer's Disease for a full description of criteria and evidence.

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Krystexxa *(pegloticase)*
Priority Health Part B Step Therapy Drug: Yes
Additional Priority Health Part B Criteria: No
Krystexxa (pegloticase) is a PEGylated uric acid specific enzyme indicated for the treatment of chronic gout in adult patients refractory to conventional therapy. The 2020 American College of Rheumatology Guideline for the Management of Gout strongly recommends either allopurinol or febuxostat over probenecid for patients with moderate-to-severe chronic kidney disease (CKD; stage ≥3). They also strongly recommended against the choice of Krystexxa as a first-line therapy due to cost, safety concerns, and favorable benefit-to-harm ratios of other available treatment options.
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Lamzede *(velmanase alfa-tycv)*
Priority Health Part B Step Therapy Drug: No
Additional Priority Health Part B Criteria: Yes
Alpha-mannosidosis is an ultra-rare genetic lysosomal storage disorder beginning in childhood and progressing through adulthood. The mutation of the MAN2B1 gene results in a deficiency of alpha-mannosidase which means the body is not able to break down alpha-mannosyl rich N-linked oligosaccharides. This can cause impaired cellular function an apoptosis. Complete absence of a functional enzyme can cause early childhood death due to deterioration of the central nervous system. Enzymes with low activity can lead to a milder form of disease which may include symptoms such as impaired hearing, cognitive impairment, susceptibility to bacterial infections and skeletal deformities. Lamzede is an enzyme replacement therapy used to treat non-central nervous system manifestations of the rare genetic disorder alpha-mannosidosis. This is a recombinant human lysosomal alpha-mannosidase enzyme. The enzyme catalyzes the degradation of accumulated mannose-containing oligosaccharides. Lamzede binds a mannose-6-phosphate receptor and gets transported into lysosomes where it can exert enzymatic breakdown of mannose-containing oligosaccharides. The 2019 diagnostic algorithm of alpha-mannosidosis states analysis of oligosaccharides in urine can be considered as an initial screening procedure. This can be suggestive of disease but not a definite diagnosis. Determination of enzymatic activity is considered the first choice for screening. Alpha-mannosidosis is confirmed when patients have a biochemical

assay showing alpha-mannosidase activity in white blood cells or skin fibroblasts less than 10% of normal and genotyping revealing two pathogenic mutations of the MAN2B1 gene.

Currently, there are no compendia supported uses for this therapy outside the FDA-indication(s).

References

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2. Lamzede [Package Insert]. Parma, Italy; Chiesi Farmaceutici S.p.A.: 2023

3. National Organization of Rare Diseases. Alpha-Mannosidosis. Accessed May 22, 2024. Available at Alpha-Mannosidosis - Symptoms, Causes, Treatment | NORD (rarediseases.org)

Lantidra *(donislecel-jujn)*

Priority Health Part B Step Therapy Drug: No

Additional Priority Health Part B Criteria: Yes

Lantidra (donislecel-jujn) for hepatic portal vein infusion is an allogeneic pancreatic islet cellular therapy indicated for the treatment of adults with Type 1 diabetes who are unable to approach target HbA1c because of current repeated episodes of severe hypoglycemia despite intensive diabetes management and education. Use in conjunction with concomitant immunosuppression. Currently, there are no compendia supported uses for this therapy outside the FDA-indication(s).

The American Diabetes Association (ADA) “Standards of Care in Diabetes—2024” recommend treating most adults with type 1 diabetes with insulin. The ADA categorizes level 1 hypoglycemia as a measurable glucose concentration <70 mg/dL (<3.9 mmol/L) but greater than or equal to 54 mg/dL (greater than or equal to 3.0 mmol/L)), level 2 hypoglycemia as a blood glucose concentration <54 mg/dL [<3.0 mmol/L]), and level 3 hypoglycemia as a severe event characterized by altered mental and/or physical functioning that requires assistance from another person for recovery, irrespective of glucose level. Continuous glucose monitoring (CGM) can be a valuable tool for detecting and preventing hypoglycemia in many individuals with diabetes, and it is recommended for individuals treated with insulin. Use of CGM can lead to improved glucose levels, decreased hypoglycemia, and enhanced self-efficacy.

The manufacturer of Lantidra advises when considering the risks associated with the infusion procedure and long-term immunosuppression, there is no evidence to show a benefit of administration of Lantidra in patients whose diabetes is well-controlled with insulin therapy or in patients with hypoglycemic unawareness who are able to prevent

repeated severe hypoglycemic events using intensive diabetes management (including insulin, devices, and education).

A second infusion of Lantidra may considered if the patient does not achieve independence from exogenous insulin within one year of infusion or within one year after losing independence from exogenous insulin after a previous infusion. Additionally, a third infusion may be performed using the same criteria as for the second infusion. However, there are no data regarding the effectiveness or safety for patients receiving more than three infusions.

References

1. Lantidra [Package Insert]. Chicago, Illinois; CellTrans Inc.: 2023

2. American Diabetes Association. Standards of Care in Diabetes—2024. January 2024.

Available at: https://diabetesjournals.org/care/issue/47/Supplement_1

3. Clinicaltrials.gov. Islet Transplantation in Type I Diabetic Patients Using the University of Illinois at Chicago (UIC) Protocol. NCT03791567 and NCT00679042

Lenmeldy *(atidarsagene autotemcel)*

Priority Health Part B Step Therapy Drug: No

Additional Priority Health Part B Criteria: Yes

Lenmeldy (atidarasagen autotemcel) is an autologous hematopoietic stem cell-based gene therapy for the treatment of children with metachromatic leukodystrophy (MLD) with presymptomatic late infantile (PSLI), presymptomatic early juvenile (PSEJ), or early symptomatic early juvenile (ESEJ) subtypes. Late infantile onset is the most common and severe form of the disease with symptoms starting before 30 months of age. Juvenile onset form is heterogenous in presentation with symptoms starting between 30 months to 6 years old for early juvenile and age 7 to 16 years for late juvenile.

Consensus guidelines for monitoring and management of MLD in the United States recommends that gene therapy be considered in early onset MLD including late infantile and early juvenile subtypes. In late-onset MLD, including late juvenile and adult subtypes, hematopoietic cell transplant should be considered for patients with no or minimal disease involvement.

Documentation of biochemical and molecular diagnosis of MLD is based on arylsulfatase A (ARSA) activity below the normal range and identification of two disease-causing ARSA alleles, either known or novel mutations. Novel mutations required a 24-hour urine collection to show elevated sulfatide levels for inclusion in the clinical trials. In the clinical trials, patients with ESEJ subtype were excluded if they had a Gross Motor Function Classification – MLD (GMFC-MLD) of 2 or greater indicating a loss of capacity of walking independently.

There is no data to support use of Lenmeldy following HSCT or after use of another MLD gene therapy.

References

1. Lenmeldy [package insert]. Boston, PA; Orchard Therapeutics NA; March 2024.

2. Clinicaltrials.gov. A Single Arm, Open Label, Clinical Study of Cryopreserved Autologous CD34+ Cells Transduced With Lentiviral Vector Containing Human ARSA cDNA (OTL-200), for the Treatment of Early Onset Metachromatic Leukodystrophy (MLD). (NCT03392987) Available at: https://clinicaltrials.gov/study/NCT03392987

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4. Adang LA, Bonkowsky JL, Boelens JJ, et al. Consensus guidelines for the monitoring and management of metachromatic leukodystrophy in the United States.Cytotherapy. 2024;26(7):739-748. doi:10.1016/j.jcyt.2024.03.487

5. Institute for Clinical and Economic Review. Atidarsagene Autotemcel for Metachromatic Leukodystrophy. October 30, 2023. Accessed June 2024. Available at: https://icer.org/wp-content/uploads/2023/10/MLD-Final-Evidence-Report_For-Publication_10302023.pdf

Leqembi *(lecanemab-irmb)*

Priority Health Part B Step Therapy Drug: No

Additional Priority Health Part B Criteria: No

Leqembi (lecanemab-irmb) is indicated for the treatment of Alzheimer's disease. It was studied in patients with confirmed presence of amyloid pathology and mild cognitive impairment (MCI) or mild dementia, consistent with Stage 3 and Stage 4 Alzheimer's disease. Leqembi significantly reduced decline in cognition and function compared to placebo from baseline to 18 months, with statistically significant changes starting around six months.

The Centers for Medicare & Medicaid Services (CMS) released a national policy for coverage of monoclonal anti-amyloid antibodies approved by the Food and Drug Administration (FDA) for the treatment of Alzheimer's disease. Under this national policy, Medicare covers FDA-approved anti-amyloid antibodies under Coverage with Evidence Development (CED) when they are furnished in accordance with the prespecified coverage criteria for patients who have a clinical diagnosis of MCI due to Alzheimer's disease or mild Alzheimer's disease dementia, both with confirmed presence of amyloid beta pathology consistent with Alzheimer's disease. Monoclonal antibodies directed against amyloid that are approved based on evidence from a surrogate endpoint considered reasonably likely to predict clinical benefit may be covered in a randomized controlled trial conducted under an investigational new drug (IND) application. Monoclonal antibodies directed against amyloid

that are approved based on evidence from a direct measure of clinical benefit may be covered in CMS-approved prospective comparative studies (study data may be collected in a registry). Refer to CMS's NCD: Monoclonal Antibodies Directed Against Amyloid for the Treatment of Alzheimer's Disease for a full description of criteria and evidence.

References

1. Centers for Medicare & Medicaid Services Medicare Coverage Database. National Coverage Determination (NCD) 200.3: Monoclonal Antibodies Directed Against Amyloid for the Treatment of ALZHEIMER's Disease (AD). April 7, 2022.

2. Leqembi [Package Insert]. Nutley, NJ; Eisai Inc.: 2023

3. Clinicaltrials.gov. A Study to Confirm Safety and Efficacy of Lecanemab in Participants With Early Alzheimer's Disease (Clarity AD) NCT03887455. Available at: https://clinicaltrials.gov/study/NCT03887455

Leqvio *(inclisiran)*

Priority Health Part B Step Therapy Drug: Yes

Additional Priority Health Part B Criteria: Yes

Leqvio (inclisiran) is a small interfering RNA (siRNA) directed to PCSK9 (proprotein convertase subtilisin kexin type 9) mRNA indicated as an adjunct to diet and maximally tolerated statin therapy for the treatment of adults with heterozygous familial hypercholesterolemia (HeFH) or clinical atherosclerotic cardiovascular disease (ASCVD), who require additional lowering of low density lipoprotein cholesterol (LDL-C).

The 2018 Guideline on the Management of Blood Cholesterol, by American College of Cardiology/American Heart Association, recommends treatment with high intensity or maximally tolerated statin therapy for adult patients with LDL-C levels > 190 mg/dL due to the increased risk of atherosclerotic cardiovascular disease (ASCVD) and both premature and recurrent coronary events. If with a high-intensity statin the patient experiences statin-associated side effects that are not severe (e.g., myalgias), the statin dose can be reduced or alternate statins can be trialed with the ultimate goal of treating with a guideline-recommended maximally tolerated statin. If maximally tolerated statin therapy fails to reduce LDL-C by at least 50% and/or the LDL-C level remains > 100 mg/dL, the guideline suggests that additional ASCVD risk reduction can be derived from the addition of ezetimibe to statin therapy. Should LDL-C remain > 100 mg/dL despite treatment with a maximally tolerated statin and ezetimibe, addition of a PCSK9 inhibitor may be considered. In patients at very high risk whose LDL-C level remains ≥70 mg/dL (≥1.8 mmol/L) on maximally tolerated statin and ezetimibe therapy, adding a PCSK9 inhibitor is reasonable.

In the 2022 American College of Cardiology (ACC) Expert Consensus Decision Pathway on the Role of Nonstatin Therapies for LDL-Cholesterol Lowering in the Management of Atherosclerotic Cardiovascular Disease Risk, PCSK9 monoclonal antibodies (i.e.,

evolocumab, alirocumab) are preferred as the initial PCSK9 inhibitor of choice in view of its demonstrated safety, efficacy, and benefits for cardiovascular outcomes in the FOURIER and ODYSSEY Outcomes trials. Inclisiran may be considered in patients with demonstrated poor adherence to PCSK9 monoclonal antibodies. Patients with adverse effects from both PSCK9 monoclonal antibodies or those who may be unable to self-inject may also be considered for therapy with Inclisiran.

There is currently no evidence or mechanistic plausibility for additional efficacy in LDL-C lowering or cardiovascular outcomes benefit for combination therapy with a PSCK9 monoclonal antibodies and inclisiran when added to maximally tolerated statin therapy with or without ezetimibe; therefore, if inclisiran is to be used, it should be used in place of a PCSK9 monoclonal antibodies.

References

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2. Grundy SM, et al. 2018 AHA/ACC/AACVPR/AAPA/ABC/ACPM/ADA/AGS/APhA/ASPC/NLA/PCNA Guideline on the Management of Blood Cholesterol: A Report of the American College of Cardiology/American Heart Association Task Force on Clinical Practice Guidelines. JACC Vol. 73, No. 24. 2019: e285-e350.

3. Lloyd-Jones D, Morris P, et al. 2022 ACC Expert Consensus Decision Pathway on the Role of Nonstatin Therapies for LDL-Cholesterol Lowering in the Management of Atherosclerotic Cardiovascular Disease Risk. J Am Coll Cardiol. 2022 Oct, 80 (14) 1366–1418.

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Lumizyme *(alglucosidase alfa)*

Priority Health Part B Step Therapy Drug: No

Additional Priority Health Part B Criteria: Yes

Lumizyme (alglucosidase alfa) for injection is a hydrolytic lysosomal glycogen-specific enzyme indicated for patients with Pompe disease (GAA deficiency). Lumizyme is dosed 20 mg per kg body weight and administered every 2 weeks. Currently, there are no compendia supported uses for this therapy outside the FDA-indication(s).

Common signs and symptoms of Pompe disease include cardiomegaly, cardiomyopathy, feeding difficulties, failure to thrive, hypotonia, muscle weakness, respiratory distress, and respiratory infections. Late-onset Pompe disease is characterized by a lack of severe cardiac involvement and patients present with symptoms related to skeletal muscle dysfunction affecting proximal lower limb and paraspinal trunk muscles, progressing to the diaphragm and accessory muscles of respiration. Patients with Pompe disease are typically managed by metabolic disease specialists/biochemical geneticists and neuromuscular experts. In the

'Pompe disease diagnosis and management guideline', experts recommend enzyme activity analysis with acid α-glucosidase (GAA) assay performed on skin fibroblasts (as the preferred tissue) or muscle biopsy, as the "gold standard" to confirm a diagnosis of Pompe disease. Mutation testing is also useful in identifying carriers when a familial mutation is known and can aid in confirmation of the diagnosis.

In the studies, treatment with Lumizyme IV for a median of 120 weeks demonstrated a reduction in the risk of requiring invasive ventilation by 58% and a reduced risk of death by 79% in infants (Infantile-Onset) compared with untreated historical controls. Studies also suggest correlation of treatment with Lumizyme and improvement in cardiac and skeletal muscle function in infants with glycogen storage disease type II (Pompe disease). In studies of treatment-naive patients with late-onset Pompe disease, Lumiqyme increased percent of predicted forced vital capacity (FVC) and significantly increased the distance walked on a 6-minute walk test at week 78 compared with placebo. Lumizyme has not been studied and there is no data to support use in combination with other enzyme replacement therapy (e.g., Nexviazyme, Pombiliti) used to treat late-onset Pompe disease.

References

1. Lumizyme [Package Insert]. Cambridge, MA; Genzyme Corporation: 2010

2. American College of Medical Genetics – Pompe Disease Diagnosis and Management Guideline, 2006. doi: 10.1097/01.gim.0000218152.87434.f

Lyfgenia *(lovotibeglogene autotemcel)*

Priority Health Part B Step Therapy Drug: Yes

Additional Priority Health Part B Criteria: Yes

Sickle cell disease (SCD) is a group of inherited disorders caused by a mutation in the beta globin gene, resulting in an abnormal hemoglobin called sickle hemoglobin (HbS). With SCD, these sickled red blood cells cannot bend or move easily through the rest of the body, blocking blood flow and causing severe episodes of pain, referred to as vaso-occlusive events (VOEs), and other serious health complications including stroke, deep vein thrombosis, and infections.

Several medications are available and effective in reducing the occurrence of VOEs. Hydroxyurea is the mainstay of therapy while other SCD medications like Endari are also recommended for patients either alone or in combination with hydroxyurea.

Safety and efficacy of Lyfgenia (Lovotibeglogene Autotemcel) in SCD were evaluated in the HGB-206 trial. Participants had severe SCD with documented βS/βS, βS/β0, and βS β+ genotypes, which represent more severe forms of the disease. Severe SCD was defined by having at least 4 VOEs each year during the previous 2 years despite appropriate supportive care (such as hydroxyurea). Key exclusion criteria included, but were not limited to: advanced liver disease, prior treatment with an allogenic stem cell transplant, and prior or

current malignancy or immunodeficiency disorder. There is currently no data supporting administration of Lyfgenia following administration of another gene therapy or a stem cell transplant. The American Society of Hematology (ASH) has not incorporated gene therapies (Lyfgenia, Casgevy) into guidelines, citing that more studies are needed to determine long-term benefits (reduced organ complications and prolonged survival rates) versus the current standard of care. There are no guidelines or head-to-head studies favoring one gene therapy over another.

Individuals are required to undergo hematopoietic stem cell (HSC) mobilization followed by apheresis to obtain CD34+ cells for Lyfgenia manufacturing. Therefore, adequate organ function is required to support the myeloablative conditioning regimen associated with Lyfgenia, and patients should be clinically stable to undergo this HSCT process.

Currently, there are no compendia supported uses for this therapy outside the FDA-indication(s).

References

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2. Centers for Disease Control and Prevention. Sickle cell disease (SCD). Available at: https://www.cdc.gov/ncbddd/sicklecell/index.html.

3. National Heart, Lung, and Blood Institute. Evidence-based management of sickle cell disease: expert panel report, 2014.

4. Clinicaltrials.gov. A study evaluating the safety and efficacy of the lentiGlobin BB305 drug product in severe sickle cell disease (NCT02140554).

5. 2019–2021 American Society of Hematology (ASH) Clinical Practice Guidelines on Sickle Cell Disease.

Margenza *(margetuximab-cmkb)*

Priority Health Part B Step Therapy Drug: Yes

Additional Priority Health Part B Criteria: No

Margenza (margetuximab-cmkb) is a receptor antagonist that targets HER2 receptors on tumor cells that overexpress the protein, preventing further cell growth, ultimately leading to programmed cell death. Both breast and gastric cancers can be positive for the HER2 receptor, representing nearly a third of all breast cancer cases.

The National Comprehensive Cancer Network (NCCN) Guidelines support the use of trastuzumab (and biosimilars) in these conditions. NCCN Guidelines do not favor one biosimilar over another and recommends any Food and Drug Administration (FDA)-approved biosimilar to be used to treat these conditions.

Step therapy may be applied to certain Part B drugs, biologics, and biosimilars in a way that lowers costs and improves the quality of care for Medicare beneficiaries per the Centers for Medicare & Medicaid Services (CMS) guidance.

Priority Health follows LCD L37205: Chemotherapy Drugs and their Adjuncts.

References

1. Margenza [Package Insert]. Rockville, MD; MacroGenics, Inc.: 2020

2. National Comprehensive Cancer Network. Breast Cancer (Version 2.2024)

3. National Comprehensive Cancer Network. Gastric Cancer (Version 2.2024

4. Centers for Medicare & Medicaid Services. Medicare Advantage Prior Authorization and Step Therapy for Part B Drugs. August 7, 2018. Retrieved from https://www.cms.gov/newsroom/fact-sheets/medicare-advantage-prior-authorization-and-step-therapy-part-b-drugs.

5. Centers for Medicare & Medicaid Services. (2018, August 7). Prior Authorization and Step Therapy for Part B Drugs in Medicare Advantage [Memorandum]. Retrieved from https://www.cms.gov/Medicare/Health-Plans/HealthPlansGenInfo/Downloads/MA_Step_Therapy_HPMS_Memo_8_7_2018.pdf

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Neupogen *(filgrastim)*

Priority Health Part B Step Therapy Drug: Yes

Additional Priority Health Part B Criteria: No

Hematopoietic growth factors are defined by their ability to promote proliferation and differentiation of hematopoietic progenitors into mature blood cells. Colony-stimulating factors (CSFs) are hematopoietic growth factors that regulate the growth and differentiation of cells towards the myeloid and erythroid lineages. Myeloid growth factors (MGFs), such as granulocyte colony-stimulating factors (G-CSF), are primarily used to reduce the incidence of febrile neutropenia (FN) in patients with non-myeloid malignancies receiving myelosuppressive chemotherapy.

Chemotherapy-induced neutropenia is a major risk factor for infection-related morbidity and mortality and also a significant dose-limiting toxicity in cancer treatment. Prophylactic treatment with granulocyte-colony stimulating factors (G-CSFs), such as filgrastim (including approved biosimilars) or pegfilgrastim is available to reduce the risk of chemotherapy-induced neutropenia. NCCN guideline recommends prophylactic G-CSF use if a patient's risk of developing FN is >20% (category 1). The American Society of Clinical Oncology (ASCO) and European Organization for Research and Treatment of Cancer (EORTC) guidelines have also adopted the 20% threshold for considering routine

prophylactic MGF support. The National Comprehensive Cancer Network (NCCN) Panel defines intermediate risk as a 10% to 20% probability of developing FN or a neutropenic event that would compromise treatment. For patients receiving intermediate-risk chemotherapy regimens, the panel recommends individualized consideration of prophylactic G-CSF use based on the presence of patient-specific risk factors.

Administration of CSFs to mobilize peripheral-blood progenitor cell (PBPC) often in conjunction with chemotherapy and their administration after autologous, but not allogeneic, PBPC transplantation is the current standard of care. Among autologous PBPC patients, post-transplant G-CSF use has been associated with savings in the duration of hospitalization and overall medical costs. The use of CSFs to mobilize peripheral blood progenitor cells (PBPC) and to shorten the period of neutropenia after cytoreduction and PBPC transplantation, is well established. Individuals receiving CSFs for mobilization should have their platelet counts monitored. Filgrastim is indicated for the mobilization of hematopoietic progenitor cells into the peripheral blood for collection by leukapheresis.

CSFs can increase the absolute neutrophil count in neutropenic patients with myelodysplastic syndromes (MDS). In the treatment of acute lymphocytic leukemia (ALL), CSFs are recommended after the initial first few days of chemotherapy of the initial induction or first post- remission course.

Current recommendations for the management of patients exposed to lethal doses of total body radiotherapy, but not doses high enough to lead to certain death due to injury to other organs, includes the prompt administration of CSF or pegylated G-CSF. Hematopoietic growth factors can increase the survival, proliferation, amplification, and differentiation of granulocyte progenitors to produce neutrophils.

Per NCCN guidelines on Hemopoietic growth Factors, an FDA-approved biosimilar is an appropriate substitute for filgrastim and pegfilgrastim.

References

1. Neupogen [Package Insert]. Thousand Oaks, CA; Amgen Inc.: 2013

2. Aapro MS, Bohlius J, Cameron DA, et al.; European Organization for Research and Treatment of Cancer. 2010 update of EORTC guidelines for the use of granulocyte-colony stimulating factor to reduce the incidence of chemotherapy-induced febrile neutropenia in adult patients with lymphoproliferative disorders and solid tumors. Eur J Cancer. 2011; 47 (1): 8-32. 2.

3. Bennett CL, Djulbegovic B, Norris LB, Armitage JO. Colony-stimulating factors for febrile neutropenia during cancer therapy. N Engl J Med. 2013; 368 (12): 1131-1139.

4. Smith TJ, Khatcheressian J, Lyman G, et al. 2006 update of recommendations for the use of white blood cell growth factors: an evidence-based clinical practice guideline. J Clin Oncol. 2006; 24 (19): 3187-3205.

5. National Comprehensive Cancer Network. Hematopoietic growth factors (Version 3.2024) 2024 Jan 30. Available at:

https://www.nccn.org/professionals/physician_gls/pdf/growthfactors.pdf. Accessed on May 20, 2024

Nexviazyme *(avalglucosidase alfangpt)*

Priority Health Part B Step Therapy Drug: No

Additional Priority Health Part B Criteria: Yes

Nexviazyme (avalglucosidase alfa-ngpt) for injection is a hydrolytic lysosomal glycogen-specific enzyme (enzyme replacement therapy) indicated for the treatment of patients 1 year of age and older with late-onset Pompe disease (lysosomal acid alpha-glucosidase [GAA] deficiency), to be administered 20 mg/kg in patients weighing ≥30 kg and 40 mg/kg in patients weighing < 30 kg. Currently, there are no compendia supported uses for this therapy outside the FDA-indication(s).

Common signs and symptoms of Pompe disease include cardiomegaly, cardiomyopathy, feeding difficulties, failure to thrive, hypotonia, muscle weakness, respiratory distress, and respiratory infections. Late-onset Pompe disease is characterized by a lack of severe cardiac involvement and patients present with symptoms related to skeletal muscle dysfunction affecting proximal lower limb and paraspinal trunk muscles, progressing to the diaphragm and accessory muscles of respiration. Patients with Pompe disease are typically managed by metabolic disease specialists/biochemical geneticists and neuromuscular experts. In the 'Pompe disease diagnosis and management guideline', experts recommend enzyme activity analysis with acid α-glucosidase (GAA) assay performed on skin fibroblasts (as the preferred tissue) or muscle biopsy, as the "gold standard" to confirm a diagnosis of Pompe disease. Mutation testing is also useful in identifying carriers when a familial mutation is known and can aid in confirmation of the diagnosis.

In the studies, Nexviazyme achieved non-inferiority, improved forced vital capacity, and significantly increased the distance walked in a 6 minute walk test in treatment-naïve patients with late-onset Pompe disease from baseline to week 49 compared to patients treated with alglucosidase alfa (Lumizyme). Nexviazyme has not been studied and there is no data to support use in combination with other enzyme replacement therapy (e.g. Lumizyme, Pombiliti) used to treat late-onset Pompe disease.

References

1. Nexviazyme [Package Insert]. Cambridge, MA; Genzyme Corporation

2. American College of Medical Genetics – Pompe Disease Diagnosis and Management Guideline, 2006. doi: 10.1097/01.gim.0000218152.87434.f3

Niktimvo *(axatilimab-csfr)*

Priority Health Part B Step Therapy Drug: Yes

Additional Priority Health Part B Criteria: Yes

Niktimvo is a colony stimulating factor-1 receptor-blocking antibody, for the treatment of chronic graft-versus-host disease (cGVHD) after failure of at least two prior lines of systemic therapy in adult and pediatric patients weighing at least 40 kg.

Chronic GVHD is a major complication of allogeneic hematopoietic cell transplantation and is associated with long-term morbidity, mortality, and impaired health-related quality of life. Chronic GVHD is a multisystem syndrome that occurs in 30% to 70% of patients following an allogeneic hematopoietic cell transplant. The skin (60% to 80%), oral (60%), ocular and mucosal surfaces (50%), and the genital area (20% to 50%) are frequently involved. Systemic corticosteroids are first-line medications for multisystemic chronic GVHD or moderate to severe skin-limited diseases. Other systemic therapies are utilized from various medication classes.

The efficacy of Niktimvo was evaluated in one, randomized, open-label, multicenter, multinational, Phase II pivotal study called AGAVE-201 that involved adult and pediatric patients with recurrent or refractory chronic GVHD who had received at least two lines of systemic therapy and required additional treatment. In all, 47% of patients reported being refractory to their last therapy. The overall response rate with Niktimvo through Cycle 7 Day 1 was 75%; all responses were partial.

Niktimvo has been addressed in the National Comprehensive Cancer Network (NCCN) hematopoietic cell transplantation guidelines (version 1.2024 – August 30, 2024). Options for first-line therapy for chronic GVHD include restarting, continuing, or escalating the original immunosuppressive agent(s) and/or administering systemic corticosteroids (0.5 to 1 mg/kg day of methylprednisolone or prednisone dose equivalent). Among the agents FDA-approved for use in chronic GVHD, Jakafi is the only agent given a category 1 recommendation for chronic GVHD. Niktimvo, Rezurock, and Imbruvica have a category 2A recommendation. The guidelines cite that each of these FDA-approved agents should be used following failure of one or two lines of systemic therapy (depending on the agent). Other medication alternatives are listed as options as well

Step therapy is applied to certain Part B drugs, biologics, and biosimilars in a way that lowers costs and improves the quality of care for Medicare beneficiaries per the Centers for Medicare & Medicaid Services (CMS) guidance

References

1. Niktimvo™ intravenous infusion [prescribing information]. Wilmington, DE: Incyte; August 2024

2. Wolff D, Cutler C, Lee SJ, et al. Axatilimab in recurrent or refractory chronic graft-versus-host disease. N Engl J Med. 2024;391(11):1002-1014.

3. Kitko CL, Arora M, DeFilipp Z, et al. Axatilimab for chronic graft-versus-host disease after failure of at least two prior systemic therapies: results of a Phase I/II study. J Clin Oncol. 2022;41:1864-1875.

4. The NCCN Hematopoietic Cell Transplantation Clinical Practice Guidelines in Oncology (version 2.2024 – August 30, 2024). © 2024 National Comprehensive Cancer Network. Available at: http://www.nccn.org. Accessed on September 9, 2024.

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6. Centers for Medicare & Medicaid Services. Medicare Advantage Prior Authorization and Step Therapy for Part B Drugs. August 7, 2018. Retrieved from https://www.cms.gov/newsroom/fact-sheets/medicare-advantage-prior-authorization-and-step-therapy-part-b-drugs.

7. Centers for Medicare & Medicaid Services. (2018, August 7). Prior Authorization and Step Therapy for Part B Drugs in Medicare Advantage [Memorandum]. Retrieved from https://www.cms.gov/Medicare/Health-Plans/HealthPlansGenInfo/Downloads/MA_Step_Therapy_HPMS_Memo_8_7_2018.pdf.

Nucala *(mepolizumab)*

Priority Health Part B Step Therapy Drug: Yes

Additional Priority Health Part B Criteria: Yes

Nucala (mepolizumab) is an interleukin-5 (IL-5) antagonist indicated for several conditions including severe eosinophilic asthma, eosinophilic granulomatosis with polyangiitis (EGPA) and hypereosinophilic syndrome (HES). IL-5 is responsible for the growth and survival of eosinophils which contribute to inflammation in the lungs.

The Global Initiative for Asthma (GINA) Guidelines on difficult-to-treat and severe asthma in adolescent and adult patients recommend using type 2-targeted biologic agents as add-on for patients with exacerbations and/or poor symptom control despite taking at least high-dose inhaled corticosteroids (ICS) and long-acting beta agonist (LABA) combinations, and who have allergic or eosinophilic biomarkers or need maintenance oral corticosteroids. Type 2-inflammation is defined as blood eosinophils of at least 150 microliters, a fractional exhaled nitric oxide (FeNO) of at least 20 parts per billion (ppb), sputum eosinophil level of at least 2%, and/or asthma that is clinically allergen driven. GINA guidelines also advise treatment should be optimized prior to initiating a biologic agent. For therapy optimization, consider trials of non-biologic medications in addition to medium/high dose ICS, such as LABA, long-acting muscarinic agonists (LAMA), and leukotriene receptor antagonists (LTRA).

HES is a condition where high (great than 1,500 cells/microliter) eosinophil levels lead to damage in the affected tissues (skin, lung, and GI tract). Treatment aims to reduce the total eosinophil count, decrease signs and symptoms, and prevent further disease progression. Initial treatment typically consists of either imatinib or glucocorticoids. The Guideline for the Investigation and Management of Eosinophilia in the British Journal of Hematology from January 2017 outlines further treatment strategies. In those who do not respond to initial steroid treatment or may respond but require chronic steroid use, DMARDs (azathioprine, cyclosporine) or other steroid-sparing drugs (hydroxyurea) should be considered. Nucala is another treatment consideration in this relapsed or refractory condition but is a category 2B recommendation per the guideline. Nucala's pivotal tried included patients with eosinophil counts >1,000 cells/mcL, had a history of 2 or more flares within the past 12 months, and had been stable on HES therapy for at least 4 weeks prior to start of study.

According to the 2021 American College of Rheumatology/Vasculitis Foundation Guideline for the Management of Antineutrophil Cytoplasmic Antibody–Associated Vasculitis, Nucala (in combination with glucocorticoids) is one of several recommended treatment options for the treatment of non-severe (vasculitis without life or organ-threatening manifestations) EGPA. Additional first-line options include methotrexate, azathioprine, and mycophenolate. In cases of relapse on Disease-Modifying Anti-Rheumatic Drugs 'DMARDs' (methotrexate, azathioprine, etc.), the guidelines recommend Nucala be added to treatment. The efficacy of mepolizumab in severe EGPA has not been established, and other therapies including rituximab and cyclophosphamide are recommended over mepolizumab in this setting.

The Joint Task Force on Practice Parameters GRADE guidelines for the medical management of chronic rhinosinusitis with nasal polyposis (CRSwNP) recommends inhaled topical corticosteroids (INCS) be used first-line to treat CRSwNP due to their extensive safety and efficacy profiles. The Guidelines recommend biologic agents be used after at least 4 weeks trial with INCS therapy.

The 2025 Global Initiative for Chronic Obstructive Lung Disease (GOLD) Guidelines recommend COPD treatment based on the assessment of symptoms history of exacerbations. Blood eosinophil counts are recommended by GOLD to guide the use of inhaled corticosteroids (ICS) as part of pharmacological management. Initial therapy should be selected according to the patient's GOLD group classification, which is based on airflow limitation severity measured by post-bronchodilator FEV_1. GOLD Grade 1 (mild) corresponds to $FEV_1 \geq 80\%$ predicted, while Grade 4 (very severe) is defined as $FEV_1 < 30\%$ predicted. First-line pharmacologic treatment typically includes a combination of a long-acting beta-agonist (LABA) and a long-acting muscarinic antagonist (LAMA). If the blood eosinophil count is ≥ 300 cells/μL, an ICS should be added to form triple therapy. If exacerbations persist despite triple therapy and the patient has a blood eosinophil count ≥ 300 cells/μL along with symptoms of chronic bronchitis, the guidelines now recommend adding dupilumab. As of the 2025 update, Nucala (mepolizumab) had not yet received approval for COPD with an eosinophilic phenotype.

Step therapy is applied to certain Part B drugs, biologics, and biosimilars in a way that lowers costs and improves the quality of care for Medicare beneficiaries per the Centers for Medicare & Medicaid Services (CMS) guidance.

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Nulojix *(belatacept)*

Priority Health Part B Step Therapy Drug: Yes

Additional Priority Health Part B Criteria: Yes

Nulojix is a selective T-cell co-stimulation blocker and is indicated for the prophylaxis of organ rejection in patient receiving kidney transplant, for patients who are Epstein-Barr virus (EBV) seropositive. This fusion protein contains a modified extracellular domain of CTLA-4 linked to a portion of the Fc domain of human immunoglobulin GI antibody. Stimulated T lymphocytes mediate immunologic rejection so belatacept binds to CD80 and CD86 on the antigen-presenting cell and prevents them from binding to CD28 on the T lymphocyte which prevents co-stimulation of T lymphocytes.

As per LCD L33824, immunosuppressive medications are covered only for the specific labeled indications. Prevention of renal rejection is most-commonly treated with tacrolimus

or cyclosporine and these are part of triple maintenance immunosuppressive therapy that includes a CNI (tacrolimus or cyclosporine), prednisone and an antimetabolite. Guideline recommendations note use of tacrolimus, cyclosporine or belatacept and may be used to initiate treatment.

Priority Health also follows LCD L33824 Immunosuppressive Drugs and LCA A52474 Immunosuppressive Drugs – Policy Article.

References

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Nuzyra (omadacycline)

Priority Health Part B Step Therapy Drug: Yes

Additional Priority Health Part B Criteria: Yes

Nuzyra (omadacycline) is a tetracycline-class antibiotic approved by the Food and Drug Administration (FDA) for the treatment of Community-Acquired Bacterial Pneumonia (CABP) and acute bacterial skin and skin structure infections (ABSSSIs) caused by susceptible microorganisms.

The Infectious Diseases Society of America (IDSA) divides SSTIs into purulent (including abscesses, furuncles, and carbuncles) and non-purulent (including cellulitis, erysipelas, and necrotizing fasciitis) infections. Treatment duration for most bacterial SSTIs is generally recommended to be 7-14 days. The choice of antibiotics depends on the type of infection, the suspected pathogens, and the patient's individual characteristics. For purulent infections, incision and drainage remain the standard of treatment. If systemic antibiotics are needed, especially when MRSA is suspected, agents such as trimethoprim-sulfamethoxazole, doxycycline, or clindamycin are recommended. For non-purulent cellulitis, which is often streptococcal in origin, cephalexin, amoxicillin, or penicillin VK are preferred. In cases of beta-lactam allergy, clindamycin or macrolides may be used, though resistance patterns should be considered.

The IDSA guidelines also emphasize aggressive treatment of necrotizing infections, recommending broad-spectrum empiric therapy such as vancomycin plus piperacillin-

tazobactam until specific pathogens are identified. For impetigo, mupirocin or retapamulin topical therapy is effective, with oral dicloxacillin or cephalexin for more extensive disease.

The 2025 Antimicrobial Agents and Chemotherapy review titled New Perspectives on Antimicrobial Agents provides insight on omadacycline's role in treating community-acquired pneumonia and skin and soft tissue infections (SSTIs). It highlights its broad-spectrum activity, including efficacy against MRSA and vancomycin-resistant Enterococcus, and tetracycline-resistant Streptococcus pneumoniae. The review notes that vancomycin remains a preferred first-line agent for many serious gram-positive infections and that other alternatives like linezolid, daptomycin, and clindamycin are also appropriate depending on the clinical scenario, resistance patterns, and patient-specific factors.

The most recent ATS/IDSA guidelines for community-acquired pneumonia (CAP), updated in 2019, provide a structured approach to diagnosis and treatment based on illness severity. For outpatients without comorbidities, amoxicillin or doxycycline is preferred. For outpatients with comorbidities, combination therapy (e.g., amoxicillin-clavulanate plus a macrolide) or monotherapy with a respiratory fluoroquinolone (like levofloxacin) is recommended. Hospitalized patients with non-severe CAP are typically treated with beta-lactam plus macrolide or a respiratory fluoroquinolone alone. In severe CAP, empiric coverage includes beta-lactam plus macrolide or beta-lactam plus fluoroquinolone, with additional agents like vancomycin or linezolid added if MRSA is suspected.

Step therapy is applied to certain Part B drugs, biologics, and biosimilars in a way that lowers costs and improves the quality of care for Medicare beneficiaries per the Centers for Medicare & Medicaid Services (CMS) guidance.

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Nypozi *(filgrastim-txid)*
Priority Health Part B Step Therapy Drug: Yes
Additional Priority Health Part B Criteria: No

Hematopoietic growth factors are defined by their ability to promote proliferation and differentiation of hematopoietic progenitors into mature blood cells. Colony-stimulating factors (CSFs) are hematopoietic growth factors that regulate the growth and differentiation of cells towards the myeloid and erythroid lineages. Myeloid growth factors (MGFs), such as granulocyte colony-stimulating factors (G-CSF), are primarily used to reduce the incidence of febrile neutropenia (FN) in patients with non-myeloid malignancies receiving myelosuppressive chemotherapy.

Chemotherapy-induced neutropenia is a major risk factor for infection-related morbidity and mortality and also a significant dose-limiting toxicity in cancer treatment. Prophylactic treatment with granulocyte-colony stimulating factors (G-CSFs), such as filgrastim (including approved biosimilars) or pegfilgrastim is available to reduce the risk of chemotherapy-induced neutropenia. NCCN guideline recommends prophylactic G-CSF use if a patient's risk of developing FN is >20% (category 1). The American Society of Clinical Oncology (ASCO) and European Organization for Research and Treatment of Cancer (EORTC) guidelines have also adopted the 20% threshold for considering routine prophylactic MGF support. The National Comprehensive Cancer Network (NCCN) Panel defines intermediate risk as a 10% to 20% probability of developing FN or a neutropenic event that would compromise treatment. For patients receiving intermediate-risk chemotherapy regimens, the panel recommends individualized consideration of prophylactic G-CSF use based on the presence of patient-specific risk factors.

Administration of CSFs to mobilize peripheral-blood progenitor cell (PBPC) often in conjunction with chemotherapy and their administration after autologous, but not allogeneic, PBPC transplantation is the current standard of care. Among autologous PBPC patients, post-transplant G-CSF use has been associated with savings in the duration of hospitalization and overall medical costs. The use of CSFs to mobilize peripheral blood progenitor cells (PBPC) and to shorten the period of neutropenia after cytoreduction and PBPC transplantation, is well established. Individuals receiving CSFs for mobilization should have their platelet counts monitored. Filgrastim is indicated for the mobilization of hematopoietic progenitor cells into the peripheral blood for collection by leukapheresis.

Several studies have shown that CSF administration can produce modest decreases in the duration of neutropenia when begun shortly after completion of the initial induction chemotherapy for the treatment of acute myeloid leukemia (AML). CSF use can be recommended after the completion of consolidation chemotherapy because of the potential to decrease the incidence of infection and eliminate the likelihood of hospitalization in some patients receiving intensive post-remission chemotherapy. CSFs can increase the absolute neutrophil count in neutropenic patients with myelodysplastic syndromes (MDS). In the treatment of acute lymphocytic leukemia (ALL), CSFs are

recommended after the initial first few days of chemotherapy of the initial induction or first post- remission course.

Current recommendations for the management of patients exposed to lethal doses of total body radiotherapy, but not doses high enough to lead to certain death due to injury to other organs, includes the prompt administration of CSF or pegylated G-CSF. Hematopoietic growth factors can increase the survival, proliferation, amplification, and differentiation of granulocyte progenitors to produce neutrophils.

Per NCCN guidelines on Hemopoietic growth Factors, an FDA-approved biosimilar is an appropriate substitute for filgrastim and pegfilgrastim.

Step therapy is applied to certain Part B drugs, biologics, and biosimilars in a way that lowers costs and improves the quality of care for Medicare beneficiaries per the Centers for Medicare & Medicaid Services (CMS) guidance.

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Ohtuvayre (*ensifentrine*)

Priority Health Part B Step Therapy Drug: Yes

Additional Priority Health Part B Criteria: Yes

Ohtuvayre is a nebulized phosphodiesterase inhibitor (PDE3/PDE4) indicated for the maintenance treatment of Chronic Obstructive Pulmonary Disease (COPD). Roflumilast is another phosphodiesterase inhibitor (PDE4). The safety and efficacy of using Ohtuvayre and roflumilast together has not been established.

The 2024 Global Initiative for Chronic Obstructive Lung Disease (GOLD) Guidelines recommend COPD treatment based on the assessment of airflow obstruction, symptoms, and exacerbation history.

Airway obstruction severity is classified into GOLD grades 1 through 4 using predicted forced expiratory volume or FEV1 (% predicted). Moderate COPD (GOLD Group 2) is characterized by a FEV1 between 50 to 79% and severe COPD (GOLD Group 3) by an FEV1 of 30-49% of what is expected. Ohtuvayre was approved based on the ENHANCE-1 and ENHANCE-2 trials, which included patients with moderate to severe COPD defined as a post-albuterol FEV1 > 30% and < 70%, corresponding to GOLD groups 2 and 3.

In addition to the FEV1 assessment and GOLD grades, guidelines utilize GOLD Groups to assess morbidity (exacerbations) and symptoms (dyspnea) and provide initial treatment recommendations. Exacerbations are considered moderate if treated with oral steroids and/or antibiotics without hospitalization, and severe if hospitalization or emergency room visits are required. Patients with 2 or more moderate or 1 or more severe exacerbations are GOLD Group E. Patients with 0 or 1 moderate exacerbations (without hospitalization) per year are either GOLD Group A or GOLD Group B based on symptoms. Symptoms are assessed through validated tools, the modified Medical Research Council (mMRC) and the COPD assessment test (CAT). Those without symptoms (mMRC 0 to 1 or CAT < 10) represent Group A and those with more disease burden are assigned to group B (mMRC 2+ or CAT 10+). Initial treatment for Group A is a single bronchodilator, Group B is dual therapy with a Long-Acting Beta Agonist (LABA) and Long-Acting Muscarinic Antagonist (LAMA), and Group E is dual therapy with a LABA/LAMA or triple therapy (LABA/LAMA/ICS) for elevated eosinophils (>300 cells/uL) or concomitant asthma.

Follow-up drug therapy is a stepped approach based on the initial therapy and the predominant trait of either dyspnea or exacerbations. If dyspnea is the predominant trait, follow-up therapy with a LAMA/LABA is recommended. If exacerbations are the predominant trait, follow-up therapy with a LABA/LAMA or LABA/LAMA/ICS is recommended. Addition of roflumilast (for those with FEV1< 50%) or azithromycin (preferred in former smokers) is also recommended. Current GOLD guidelines do not reference Ohtuvayre or its role in COPD management.

References

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2. Global Strategy for the Diagnosis, Management, and Prevention of Chronic Obstructive Pulmonary Disease (2024 Report). Global Initiative for Chronic Obstructive Lung Disease, 2024.

3. Clinicaltrials.gov. A Phase 3 Clinical Trial to Evaluate the Safety and Efficacy of Ensifentrine in Patients With COPD. Available at: https://clinicaltrials.gov/study/NCT04535986

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Omvoh *(mirikizumab-mrkz)* IV

Priority Health Part B Step Therapy Drug: Yes

Additional Priority Health Part B Criteria: Yes

Omvoh (mirkizumab-mrkz) is an interleukin-23 antagonist indicated for the treatment of moderately to severely active ulcerative colitis in adults. The intravenous solution is only indicated for induction treatment.

Ulcerative colitis (UC) is a chronic inflammatory disease that affects the colon in the gastrointestinal (GI) tract. UC-related inflammation can damage the lining in the colon. This inflammation can lead to symptoms—such as bowel urgency, blood in stool, and frequent bowel movements—that can get worse over time if left untreated. The pattern of disease activity is most often described as relapsing and remitting, with symptoms of active disease alternating with periods of clinical quiescence, which is called remission. Some patients with UC have persistent disease activity despite diagnosis and medical therapy, and a small number of patients present with the rapid-onset progressive type of colitis known as fulminant disease.

Ulcerative colitis is a chronic condition for which therapy is required to induce and maintain remission. Per the 2019 American College of Gastroenterology (ACG) Clinical Guideline: Ulcerative Colitis in Adults, therapeutic decisions should be categorized into those for induction and maintenance, with a goal of obtaining and maintaining a steroid-free remission. Selection of induction and maintenance therapies for UC should be based on disease extent, severity, and prognosis. Strategies for the management of the nonhospitalized patient with moderately to severely active UC include: 5-aminosalicaylate (5-ASA) therapy as monotherapy for induction of moderately but not severely active UC; non-systemic corticosteroids such as budesonide before the use of systemic therapy in patients with moderately active UC; and systemic corticosteroids rather than topical corticosteroids in patients with severely active UC. In patients with moderately to severely active UC, the guidelines recommend tumor necrosis factor inhibitor (TNFi) therapy (adalimumab, golimumab, or infliximab), vedolizumab, and tofacitinib for induction and maintenance of remission. The 2020 American Gastroenterological Association Institute Clinical Guideline on the Management of Moderate to Severe Ulcerative Colitis strongly recommends the same therapies as the ACG guidelines including ustekinumab as an additional option. The guidelines have not been updated with Omvoh.

In 2 randomized controlled trials in adults with moderate to severe active ulcerative colitis, mirkizumab-mrkz was associated with a significantly greater proportion of patients achieving clinical remission compared with placebo. Significantly more patients treated with mirkizumab-mrkz also experienced a decrease in stool frequency and rectal bleeding compared with placebo. In study UC-1, a greater proportion of patients treated with mirkizumab-mrkz compared with placebo achieved clinical response, defined as a 2-point or greater and 30% or less decrease from baseline in modified Mayo score (mMS), and a 1-point or more decrease from baseline in rectal bleeding (RB) subscore or an absolute RB subscore of 0 or 1 at Week 12 (65% vs 43%). Decreases in stool frequency (SF) and rectal

bleeding subscores were observed as early as Week 3 in patients treated with mirkizumab-mrkz compared with placebo. Of the patients who achieved clinical remission at week 12 in study UC-1 with mirkizumab-mrkz induction treatment, significantly more patients achieved clinical remission at week 40 with mirkizumab-mrkz compared with placebo in the maintenance study UC-2.

Omvoh has not been studied in combination with other biologic disease-modifying agents (tumor necrosis factor inhibitors, interleukin receptor antagonists, etc), targeted synthetic DMARDs (JAK inhibitors), or PDE4 inhibitors (Otezla) due to an increased risk of infection and increased immunosuppression. As such, use of Omvoh in combination with these agents is not recommended.

The Food and Drug Administration (FDA) considers biosimilars to be highly similar with no clinically meaningful differences to the biologic reference product. Biosimilars are considered safe and effective and provide an option to increase access to lifesavings drugs at lower costs. The FDA and current treatment guidelines do not favor one product (biologic or biosimilar) over another.

Step therapy is applied to certain Part B drugs, biologics, or biosimilars in a way that lowers costs and improves the quality of care for Medicare beneficiaries per the Centers for Medicare & Medicaid Services (CMS) guidance.

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Onpattro *(patisiran)*
Priority Health Part B Step Therapy Drug: No
Additional Priority Health Part B Criteria: Yes

Onpattro (patisiran) lipid complex injection contains a transthyretin-directed small interfering RNA and is indicated for the treatment of the polyneuropathy of hereditary transthyretin-mediated (hATTR) amyloidosis. The recommended dosage is 0.3 mg/kg (or 30 mg for patients weighing 100 kg or more) every 3 weeks by intravenous infusion.

Transthyretin (TTR) amyloidosis is caused by the extracellular deposition of amyloid fibrils composed of TTR. TTR is predominantly produced by the liver and is a plasma transport protein for thyroxine and vitamin A. TTR amyloidosis is caused by mutations that destabilize the TTR protein. The disease can present as an infiltrative cardiomyopathy (familial amyloid cardiomyopathy) or as a progressive, axonal sensory autonomic and motor neuropathy (familial amyloidotic polyneuropathy; TTR-FAP, also referred to as FAP or ATTR-PN). The disease induces peripheral neuropathy, initially affecting the lower limbs generally including toes, extending above the ankle, and moving toward the proximal lower limbs with motor deficits. Life-threatening autonomic dysfunction is also generally present as the disease progresses, which may include anhidrosis, sexual impotence, orthostatic hypotension, and neurogenic bladder.

Scoring systems for evaluating TTR-FAP include systems based on the stages of peripheral and autonomic neuropathies proposed by Coutinho, disease staging based on polyneuropathy disability (PND) score, the Portuguese classification to evaluate the severity of TTR-FAP, sensory impairment scoring, autonomic dysfunction scoring, and scoring of motor function for muscle weakness. Coutinho et al. divides clinical staging of TTR-FAP into stage 0 (no symptoms), stage I (unimpaired ambulation; mostly mild sensory, motor, and autonomic neuropathy in the lower limbs), stage II (assistance with ambulation required; mostly moderate impairment progression to the lower limbs, upper limbs, and trunk) and stage III (wheelchair-bound or bedridden; severe sensory, motor, and autonomic involvement of all limbs). The PND score divides neuropathic symptoms into stage 0 (no impairment), stage I (sensory disturbances but preserved walking capability), stage II (impaired walking capability but ability to walk without a stick or crutches), stage IIIA (walking only with the help of one stick or crutch), stage IIIB (walking with the help of two sticks or crutches), and stage IV (confined to a wheelchair or bedridden).

There is no data to support the efficacy and safety in use of disease-modifying therapies in liver transplant recipients or for use of pharmacotherapy in patients with stage 0 disease or with later-stage disease or cardiomyopathy. As such the 'Guideline of transthyretin-related hereditary amyloidosis for clinicians' recommends these populations should be treated only within the confines of a clinical trial.

Onpattro was studied in patients with polyneuropathy caused by hereditary transthyretin-mediated amyloidosis (hATTR amyloidosis) that were in Stage 1 or Stage 2 of the disease and had Val30Met mutation in the transthyretin gene or one of 38 other point mutations.

Onpattro improved multiple clinical manifestations over 18 months compared with placebo. There is a lack of evidence for use of Onpattro in combination with other TTR stabilizers or TTR-lowering agents. As such, use of Onpattro in combination with other TTR stabilizers or TTR-lowering agents is not recommended.

References

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Ontruzant *(trastuzumab-dttb)*

Priority Health Part B Step Therapy Drug: Yes

Additional Priority Health Part B Criteria: No

Ontruzant is a trastuzumab biosimilar. Other trastuzumab biosimilars include Kanjinti (trastuzumab-anns), Ogivri (trastuzumab-dkst), Herzuma (trastuzumab-pkrb), and Trazimera (trastuzumab-qyyp).

The Food and Drug Administration (FDA) and current treatment guidelines including the National Comprehensive Cancer Network (NCCN) Guidelines support the use of FDA-approved trastuzumab biosimilars and do not favor one biosimilar over another. Step therapy may be applied to certain Part B drugs, biologics, and biosimilars in a way that lowers costs and improves the quality of care for Medicare beneficiaries per the Centers for Medicare & Medicaid Services (CMS) guidance.

Priority Health also follows LCD L37205: Chemotherapy Drugs and their Adjuncts.

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Orbactiv (oritavancin)

Priority Health Part B Step Therapy Drug: Yes

Additional Priority Health Part B Criteria: Yes

Orbactiv (oritavancin) is indicated for the treatment of acute bacterial skin and skin structure infections caused by susceptible methicillin-resistant staphylococcus aureus (MRSA) isolates in adults for the treatment of acute bacterial skin and skin structure infections caused by susceptible isolates.

Clinical Practice Guidelines for the Diagnosis and Management of Skin and Soft Tissue Infections: 2014 Update by The Infectious Diseases Society of America (IDSA) advises that clinical evaluation of patients with SSTI aims to establish the cause and severity of infection and must take into account pathogen-specific and local antibiotic resistance patterns. There has been a significant increase in the frequency and severity of infections and the emergence of resistance to many of the antimicrobial agents commonly used to treat SSTIs in the past. Some of this increased frequency is related to the emergence of community-associated MRSA.

Gram stain and culture is recommended when evaluating purulent SSTIs (cutaneous abscesses, furuncles, carbuncles, and inflamed epidermoid cysts). Incision and drainage are the recommended treatments for inflamed epidermoid cysts, carbuncles, abscesses, and large furuncles. The decision to administer antibiotics directed against S. aureus as an adjunct to incision and drainage should be made based upon presence or absence of systemic inflammatory response syndrome (SIRS). For moderate purulent infections in patients with systemic sings of infections, empiric treatment with trimethoprim-sulfamethoxazole (TMP/SMZ) or doxycycline is recommended. For MRSA infections, TMP/SMX should be used and for MSSA infections dicloxacillin or cephalexin should be used. For severe purulent infections in patients who have failed incision and drainage plus oral antibiotics or those with systemic signs of infection, empiric treatment and/or confirmed MRSA should be treated with vancomycin, daptomycin, linezolid, telavancin or ceftaroline. If methicillin-sensitive staphylococcus aureus (MSSA) is confirmed, nafcillin, cefazolin or clindamycin are recommended.

Cultures of blood or cutaneous aspirates, biopsies, or swabs are not routinely recommended for non-purulent SSTI (necrotizing infection, cellulitis, erysipelas). For mild infections without systemic signs of infection, patients should receive an antimicrobial agent that is active against streptococci (penicillin VK, cephalosporin, dicloxacillin or clindamycin). For moderate infections with systemic signs of infection, intravenous treatment with penicillin, ceftriaxone, cefazolin or clindamycin is recommended. In severe infection, in patients who have failed oral antibiotic treatment or those with systemic signs of infection, emergent surgical inspection/debridement is recommended to rule out

necrotizing process. Patients should also receive empiric treatment with vancomycin plus piperacillin/tazobactam. For treatment of streptococcal skin infections, in patients with a severe penicillin sensitivity clindamycin, vancomycin, linezolid, daptomycin or telavancin are recommended. The guidelines do not mention oritavancin.

In adults with cellulitis/erysipelas, wound infection, or major cutaneous abscesses due to MRSA (n=405), single-dose oritavancin 1200 mg IV was associated with an early clinical response rate of 81.4% and a clinical success rate of 83.3%; these results were similar to those achieved with vancomycin 1 g or 15 mg/kg IV every 12 hours for 7 to 10 days (80.6% early clinical response rate and 84.1% clinical success rate).

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Orencia IV (abatacept)

Priority Health Part B Step Therapy Drug: Yes

Additional Priority Health Part B Criteria: Yes

Orencia is a biologic disease-modifying agent that functions as a selective T-cell co-stimulation blocker indicated for several inflammatory conditions including psoriatic arthritis (PsA) and rheumatoid arthritis (RA).

For rheumatoid arthritis, guidelines favor the use of biologic DMARDs (bDMARD) for moderate or high disease activity despite prior conventional synthetic DMARDs (csDMARD). Guidelines do not favor one bDMARD (e.g., Skyrizi, tocilizumab, Cosentyx, Orencia, infliximab) over another nor do they favor tsDMARD (e.g., Xeljanz, Rinvoq) over a bDMARD.

Per the 2018 American College of Rheumatology (ACR)/National Psoriasis Foundation (NPF) guidelines, methotrexate, sulfasalazine, cyclosporine, and leflunomide may be used in patients with non-severe psoriatic arthritis and have robust safety and efficacy evidence to support their use. If initial treatment is not sufficient, switching to a biologic (infliximab, adalimumab, Enbrel, Simponi Aria, Orencia, Skyrizi) or JAK inhibitor (Rinvoq, Xeljanz) is recommended.

Orencia has not been studied in combination with other biologic agents or Otezla due to an increased risk of infection and increased immunosuppression. Per current labeling, Orencia should not be used with other strong medicines that affect the immune system, such as biologic disease-modifying antirheumatic drugs (bDMARDs) and JAK inhibitors. As such, use of Orencia in combination with these agents is not recommended.

References

1. Orencia [Package Insert]. Princeton, NJ; Bristol-Myers Squibb Company: 2021

2. Fraenkel L, et al. 2021 American College of Rheumatology Guideline for the Treatment of Rheumatoid Arthritis. Arthritis Care & Research. 2021 Jul; 73 (7):924-939.

3. Singh JA, et al. 2018 American College of Rheumatology/National Psoriasis Foundation Guideline for the Treatment of Psoriatic Arthritis. Arthritis Rheumatol. 2019 Jan; 71 (1): 5-32.

Osenvelt *(denosumab-bmwo)*

Priority Health Part B Step Therapy Drug: Yes

Additional Priority Health Part B Criteria: Yes

Osenvelt is a biosimilar to Xgeva. It has been approved by the FDA for all indications of its reference biologic. The FDA has also provisionally determined Osenvelt to be interchangeable with Xgeva. Denosumab (including the biosimilars and reference product) is a monoclonal antibody that inhibits nuclear factor kappa-B ligand (RANKL), reducing osteoclast activity and bone resorption, which increases bone mass and strength. It also blocks RANKL from activating osteoclast-like giant cells. Denosumab is indicated for the prevention of skeletal-related events in patients with multiple myeloma or bone metastases from solid tumors as well as other cancer-related conditions involving bone loss.

The Food and Drug Administration (FDA) considers biosimilars to be highly similar with no clinically meaningful differences to the biologic reference product. Biosimilars are considered safe and effective and provide an option to increase access to lifesavings drugs at lower costs. The FDA and current treatment guidelines do not favor one product (biologic or biosimilar) over another.

Step therapy is applied to certain Part B drugs, biologics, and biosimilars in a way that lowers costs and improves the quality of care for Medicare beneficiaries per the Centers for Medicare & Medicaid Services (CMS) guidance.

References

1. Osenvelt [Package Insert]. Jersey City, NJ; Celltrion USA, Inc.: 2025

2. Centers for Medicare & Medicaid Services. Medicare Advantage Prior Authorization and Step Therapy for Part B Drugs. August 7, 2018. Retrieved from

https://www.cms.gov/newsroom/factsheets/medicare-advantage-prior-authorization-and-step-therapy-part-b-drugs.

3. Centers for Medicare & Medicaid Services. (2018, August 7). Prior Authorization and Step Therapy for Part B Drugs in Medicare Advantage [Memorandum]. Retrieved from https://www.cms.gov/Medicare/HealthPlans/HealthPlansGenInfo/Downloads/MA_Step_Therapy_HPMS_Memo_8_7_2018.pdf.

Otulfi IV *(ustekinumab-aauz)*

Priority Health Part B Step Therapy Drug: Yes

Additional Priority Health Part B Criteria: Yes

Otulfi is a biosimilar to Stelara. It has been approved by the FDA for all indications of its reference biologic. The FDA has also provisionally determined Otulfi to be interchangeable with Stelara. Ustekinumab (including the biosimilars and reference product) is a monoclonal antibody that inhibits interleukin (IL)-12 and IL-23 and is indicated in several inflammatory conditions including Ulcerative Colitis (UC) and Crohn's Disease (CD).

The Food and Drug Administration (FDA) considers biosimilars to be highly similar with no clinically meaningful differences to the biologic reference product. Biosimilars are considered safe and effective and provide an option to increase access to lifesavings drugs at lower costs. The FDA and current treatment guidelines do not favor one product (biologic or biosimilar) over another.

There is limited data on the concurrent use of ustekinumab with other biologic agents, targeted synthetic DMARDs (e.g., JAK inhibitors), and phosphodiesterase-4 (PDE4) inhibitors (Otezla). Given the absence of strong clinical evidence and the potential for increased infection risk, it is not recommended to use ustekinumab in combination with these agents.

Step therapy is applied to certain Part B drugs, biologics, and biosimilars in a way that lowers costs and improves the quality of care for Medicare beneficiaries per the Centers for Medicare & Medicaid Services (CMS) guidance.

References

1. Otulfi [Package Insert]. Lake Zurich, IL; Fresenius Kabi USA, LLC: 2024

2. Lichtenstein GR, Loftus EV, Isaacs KL, et al. ACG clinical guideline: management of crohn's disease in adults. AJG. 2018 April; 113 (4): 481-517

3. Feuerstein JD, Isaacs KL, Schneider Y, et al. AGA clinical practice guidelines on the management of moderate to severe ulcerative colitis. Gastroenterology. 2020; 158: 1450 – 6

4. Centers for Medicare & Medicaid Services. Medicare Advantage Prior Authorization and Step Therapy for Part B Drugs. August 7, 2018. Retrieved from

https://www.cms.gov/newsroom/fact-sheets/medicare-advantage-prior-authorization-and-step-therapy-part-b-drugs.

5. Centers for Medicare & Medicaid Services. (2018, August 7). Prior Authorization and Step Therapy for Part B Drugs in Medicare Advantage [Memorandum]. Retrieved from https://www.cms.gov/Medicare/Health-Plans/HealthPlansGenInfo/Downloads/MA_Step_Therapy_HPMS_Memo_8_7_2018.pdf.

Oxlumo *(lumasiran) injection*

Priority Health Part B Step Therapy Drug: No

Additional Priority Health Part B Criteria: Yes

Primary hyperoxalurias (PHs) are rare inborn errors of glyoxylate metabolism and are distinguished by the over-production of oxalate, which is poorly soluble and combines with calcium to form kidney and urinary stones. As a patient's glomerular filtration rate decreases throughout their lifetime, plasma oxalate levels will increase, and calcium oxalate will deposit into other areas of the body, such as the heart, bones, and retina. The increased production of oxalate leads to kidney injury, which could lead to kidney failure, necessitating a need for treatment of this condition. Symptoms may appear at any age. There are three notable types of PH that differ based on severity and the genetic mutation present. Primary hyperoxaluria type 1 (PH1) is the most common form, and patients with PH1 have mutation of the AGXT gene, which results in abnormal hepatic enzyme alanine-glyoxylate aminotransferase (AGT), which in turn causes the increase in glyoxylate and oxalate.

Oxlumo is an RNA interference (RNAi) therapy that indirectly lowers the amount of glyoxylate and oxalate. Conservative treatment is recommended initially after diagnosis and includes hyperhydration, alkalizing the urine and trialing pyridoxine. This is noted in The European Rare Kidney Disease Reference Network and OxalEurope developed clinical practice recommendations (2023) for primary hyperoxaluria. RNA interference (RNAi) therapies are briefly mentioned and, in general, are recommended for patients with a genetic diagnosis of PH1. Transplant of the liver and possibly the kidneys are an option to correct the AGXT mutation though recommendations around this area are also unclear.

Clinical trials have shown that Oxlumo and other RNAi therapies (e.g., Rivfloza) can effectively treat the underlying pathophysiology of oxalate overproduction. While RNAi therapies have the potential to improve patient outcomes, it should be noted that the clinical impact is not clear. It is also unclear to what extent these agents might replace a liver and/or kidney transplant.

There is no data or other supporting evidence for concomitant use of RNAi therapies.

References

1. OXLUMO (lumasiran) injection, for subcutaneous use [prescribing information]. Cambridge, MA: Alnylam Pharmaceuticals, Inc.; 2020.

2. Bacchetta J, Lieske JC. Primary hyperoxaluria type 1: novel therapies at a glance. Clin Kidney J. 2022;15(Suppl 1):i17-i22. Published 2022 May 17. doi:10.1093/ckj/sfab245

3. Groothoff JW, Metry E, Deesker L, et al. Clinical practice recommendations for primary hyperoxaluria: an expert consensus statement from ERKNet and OxalEurope. Nat Rev Nephrol. 2023;19:194-211.

4. Primary Hyperoxaluria: MedlinePlus Genetics. U.S. National Library of Medicine; National Institutes of Health; Department of Health and Human Services. Available at: https://medlineplus.gov/genetics/condition/primary-hyperoxaluria/#resources.

5. Garrelfs, SF, Frishberg Y, et al. Lumasiran, an RNAi Therapeutic for Primary Hyperoxaluria Type 1. N Engl J Med 2021; 384: 1216-1226. DOI: 10.1056/NEJMoa2021712. (ILLUMINATE-A; NCT03681184).

6. Clinicaltrials.gov. A Study of Lumasiran in Infants and Young Children With Primary Hyperoxaluria Type 1 (ILLUMINATE-B). Available at: https://clinicaltrials.gov/study/NCT03905694.

7. Clinicaltrials.gov. A Study to Evaluate Lumasiran in Patients With Advanced Primary Hyperoxaluria Type 1 (ILLUMINATE-C). Available at: https://clinicaltrials.gov/study/NCT04152200.

Ozurdex *(dexamethasone)* intravitreal implant

Priority Health Part B Step Therapy Drug: No

Additional Priority Health Part B Criteria: Yes

Ozurdex (dexamethasone intravitreal implant) is a corticosteroid indicated for: the treatment of macular edema following branch retinal vein occlusion (BRVO) or central retinal vein occlusion (CRVO); The treatment of non-infectious uveitis affecting the posterior segment of the eye; and The treatment of diabetic macular edema in patients who are pseudophakic or are phakic and scheduled for cataract surgery

The Diabetic Retinopathy Preferred Practice Pattern guideline advises that management options for diabetic retinopathy includes following a healthy diet and lifestyle, medical management, timely ophthalmic evaluation, and treatment under the care of an ophthalmologist. Cost-effective treatments with laser, anti–vascular endothelial growth factor (VEGF) agents, or intravitreal corticosteroids may also be considered. Regarding the use of steroids for diabetic macular edema (DME), the guideline references several studies that have evaluated the use of intravitreal administration of short- and long-acting corticosteroids for the treatment of DME. Topical corticosteroids and periocular steroid

injection demonstrated no significant benefit. The role of intravitreal triamcinolone acetonide was compared with focal laser photocoagulation surgery. Retinal thickness at 4 months, yet by 24 months, in patients randomized to focal/grid laser photocoagulation surgery had better mean visual acuity. A subsequent study showed that pseudophakic eyes treated with the combination of the intravitreal triamcinolone acetonide and focal laser had visual gains similar to eyes treated with anti-VEGF agents. The sustained-release dexamethasone implant for treatment naïve center-involved diabetic macular edema (CI-DME) improved visual acuity compared with sham treatment. The fluocinolone acetonide implant for DME treatment study revealed improved visual acuity relative to sham at 3 years. At three years, 75% of patients were treated with only one implant. Rates of cataract extraction of phakic eyes was 74.9% with an implant versus 23.1% for sham. Studies of intravitreal corticosteroids for DME have evaluated them as first-line agents only. Because of their side-effect profile, including cataract progression and elevated IOP, they are generally used as second-line agents for DME, especially for phakic patients.

Retinal vein occlusion (RVO) occurs when there is partial or complete obstruction of a retinal vein, and it is classified by the location of the occlusion. An obstruction of the retinal vein at or posterior to the optic nerve head is a central retinal vein occlusion (CRVO), and complete or partial obstruction at a branch or tributary of the central retinal vein is a branch retinal vein occlusion (BRVO). Vision loss associated with a vein occlusion usually occurs from macular ischemia or edema, retinal hemorrhages, vitreous hemorrhage, and epiretinal membrane formation.
The Retinal Vein Occlusions Preferred Practice Pattern guideline advises that in eyes with BRVO and macular edema, anti-VEGF injections, focal laser treatment, and intravitreal steroids all have demonstrated therapeutic benefit. In eyes with CRVO and macular edema, anti-VEGF and intravitreal steroids have demonstrated benefit. Intravitreal corticosteroids (triamcinolone and dexamethasone implant) are considered second line because of significant ocular side effects, such as secondary glaucoma and cataract formation.

References

1. Ozurdex [Package Insert]. Irvine, CA; Allergan, Inc.: 2014

2. Flaxel CJ, Adelman RA, Bailey ST, et al. Retinal Vein Occlusions Preferred Practice Pattern. Ophthalmology. Sept 2019; 127(2): PP288-P320.

3. Flaxel CJ, Adelman RA, Bailey ST, et al. Diabetic Retinopathy Preferred Practice Pattern. Ophthalmology. Jan 2020; 127(1): P66-P145.

Panzyga *(immune globulin)* intravenous

Priority Health Part B Step Therapy Drug: Yes

Additional Priority Health Part B Criteria: No

Intravenous immunoglobulin (IVIG) are human derived antibodies used to treat various autoimmune, infectious, and idiopathic diseases including, but not limited to: Chronic

Inflammatory Demyelinating Polyneuropathy (CIDP), Chronic Lymphocytic Leukemia (CLL), multiple myeloma, myasthenia gravis, and Immune Thrombocytopenia (ITP).

Primary immunodeficiency affects the body's natural immune system's ability to combat infection. These are genetic disorders that can be treated by undergoing hemopoietic stem cell transplantation, by receiving preventative medicine (like antibiotics to reduce infection risk) or managing with supportive care. IVIG plays a role in these patients' treatment by reducing infection risk and limiting the potential for disease complications.

Myasthenia gravis is a rare autoimmune disease that can lead to fatigue and generalized muscle weakness. Treatment options include corticosteroids and immunosuppressive therapies (azathioprine, mycophenolate, e.g.), but some patients will continue to show symptoms despite these treatments and are categorized as 'refractory' (per the 2016 International Consensus Guidance for Management of Myasthenia Gravis). These patients have functional impairment requiring further medical intervention. In severe cases, referred to as 'myasthenic crisis', patients experience a loss in respiratory muscle function requiring intubation or mechanical ventilation. The 2016 International Consensus recommends IVIG be used in these cases to allow the patient to recover from the crisis. IVIG acts to bridge myasthenia gravis patients from exacerbation to recovery while further immunosuppressive care is allowed time to take effect.

There are multiple IVIG products available. No clinical trials have been conducted comparing the efficacy of one therapy to another. For treatment of primary immune deficiency disorder, the following are some, but not all, FDA-approved IVIG products to treat these conditions: Asceniv, Bivigam, Carimune, Privigen, Gammagard Liquid, and Octagam. Certain patient specific factors may affect which IVIG product is selected. Diabetic patients may want to avoid products containing maltose or glucose (Gammagard S/D, Octagam, e.g.). Patients with low tolerance for increased intravascular volume may want to avoid products high in sodium or albumin content (Bivigam, e.g.).

Priority Health follows LCD L34771 for Immune Globulins.

References

1. Panzyga [Package Insert]. Lingolsheim, France; Octapharma SAS: 2021

2. Bonilla FA, et al. Practice parameter for the diagnosis and management of primary immunodeficiency. J Allergy Clin Immunol. 2015; 136 (5): 1186 – 205

3. Sanders DB, et al. International consensus guidance for management of myasthenia gravis: executive summary. Neurology. 2016 Jul 26; 87 (4): 419 - 25

4. Centers for Medicare & Medicaid Services. Local Coverage Determination (LCD) L34771: Immune Globulins

Pemfexy *(pemetrexed,* J9304*)*
Priority Health Part B Step Therapy Drug: Yes
Additional Priority Health Part B Criteria: No
Pemfexy is a pemetrexed injection. Step therapy is applied to certain Part B drugs in a way that lowers costs and improves the quality of care for Medicare beneficiaries per the Centers for Medicare & Medicaid Services (CMS) guidance.
References 1. Pemfexy [Package Insert]. Woodcliff Lake, NJ; Eagle Pharmaceuticals, Inc.: 2020 2. Pemetrexed [Package Insert]. Gujarat, India; Zydus Hospira Oncology Private Ltd.: 2022 3. Centers for Medicare & Medicaid Services. Medicare Advantage Prior Authorization and Step Therapy for Part B Drugs. August 7, 2018. Retrieved from https://www.cms.gov/newsroom/fact-sheets/medicare-advantage-prior-authorization-and-step-therapy-part-b-drugs 4. Centers for Medicare & Medicaid Services. (2018, August 7). *Prior Authorization and Step Therapy for Part B Drugs in Medicare Advantage* [Memorandum]. Retrieved from *https://www.cms.gov/Medicare/Health-Plans/HealthPlansGenInfo/Downloads/MA_Step_Therapy_HPMS_Memo_8_7_2018.pdf*
Pemrydi RTU *(pemetrexed disodium)*, J9324
Priority Health Part B Step Therapy Drug: Yes
Additional Priority Health Part B Criteria: No
Pemrydi RTU is a pemetrexed product. Current treatment guidelines including the National Comprehensive Cancer Network (NCCN) Guidelines support the use of pemetrexed and do not favor one product over another. Step therapy is applied to certain Part B drugs, biologics, and biosimilars in a way that lowers costs and improves the quality of care for Medicare beneficiaries per the Centers for Medicare & Medicaid Services (CMS) guidance.
References 1. Pemfexy [Package Insert]. Woodcliff Lake, NJ; Eagle Pharmaceuticals, Inc.: 2020 2. Pemetrexed [Package Insert]. Gujarat, India; Zydus Hospira Oncology Private Ltd.: 2022 3. Centers for Medicare & Medicaid Services. Medicare Advantage Prior Authorization and Step Therapy for Part B Drugs. August 7, 2018. Retrieved from https://www.cms.gov/newsroom/fact-sheets/medicare-advantage-prior-authorization-and-step-therapy-part-b-drugs

4. Centers for Medicare & Medicaid Services. (2018, August 7). *Prior Authorization and Step Therapy for Part B Drugs in Medicare Advantage* [Memorandum]. Retrieved from *https://www.cms.gov/Medicare/Health-Plans/HealthPlansGenInfo/Downloads/MA_Step_Therapy_HPMS_Memo_8_7_2018.pdf*

PiaSky (crovalimab-akkz)No

Priority Health Part B Step Therapy: No

Additional Priority Health Part B Criteria: Yes

PiaSky (crovalimab-akkz) is a complement C5 inhibitor indicated for the treatment of adult and pediatric patients 13 years and older with paroxysmal nocturnal hemoglobinuria (PNH) with a body weight of at least 40 kg. PiaSky has not been studied and there is no data to support use in combination with certain other medications used for PHN.

PNH is a hematopoietic stem cell disorder caused by a gene mutation that leads to abnormal red blood cells. Flow cytometry is the method of choice for identifying cells deficient in GPI-linked proteins and is the gold standard test to confirm the diagnosis of PNH. In PNH, thrombotic tendencies can occur in the extremities and atypical locations, such as hepatic portal (Budd-Chiari Syndrome), splenic, or mesenteric veins. Treatment options include supportive care (e.g. red blood cell transfusion), allogeneic hematopoietic stem cell transplantation, and complement therapy. Consider discontinuation of complement inhibitor treatment in the absence of clinical benefit.

References

1. PiaSky [Package Insert]. South San Francisco, CA; Genentech, Inc.: June 2024

2. Clinicaltrials.gov. Commodore 2. A Phase III Study Evaluating the Efficacy and Safety of Crovalimab Versus Eculizumab in Participants With Paroxysmal Nocturnal Hemoglobinuria (PNH) Not Previously Treated With Complement Inhibitors. NCT0443092. Available at: https://clinicaltrials.gov/study/NCT04434092

3. Clinicaltrials.gov. Commodore 1. A Study Evaluating The Safety, Pharmacokinetics, and Efficacy Of Crovalimab Versus Eculizumab In Participants With Paroxysmal Nocturnal Hemoglobinuria (PNH) Currently Treated With Complement Inhibitors. NCT04432584. Available at: https://clinicaltrials.gov/study/NCT04432584.

4. Borowitz MJ, Craig FE, DiGiuseppe JA, et al. Guidelines for the diagnosis and monitoring of paroxysmal nocturnal hemoglobinuria and related disorders by flow cytometry. Cytometry Part B (Clinical Cytometry). 2010; 78B: 211 – 30.

5. Cançado RD, da Silva Araújo A, Sandes AF, et al. Consensus statement for diagnosis and treatment of paroxysmal nocturnal haemoglobinuria. Hematol Transfus Cell Ther. 2021; 43:341- 348.

Pombiliti *(cipaglucosidase alfa-atga)*

Priority Health Part B Step Therapy: No

Additional Priority Health Part B Criteria: Yes

Pombiliti (cipaglucosidase alfa-atga) for injection is a hydrolytic lysosomal glycogen-specific enzyme indicated, in combination with Opfolda (an enzyme stabilizer) for the treatment of adult patients with late-onset Pompe disease (lysosomal acid alpha-glucosidase [GAA] deficiency) weighing ≥40 kg and who are not improving on their current enzyme replacement therapy (ERT). Pombiliti is dosed 20 mg/kg (of actual body weight) and administered every other week. Currently, there are no compendia supported uses for this therapy outside the FDA-indication(s).

Common signs and symptoms of Pompe disease include cardiomegaly, cardiomyopathy, feeding difficulties, failure to thrive, hypotonia, muscle weakness, respiratory distress, and respiratory infections. Late-onset Pompe disease is characterized by a lack of severe cardiac involvement and patients present with symptoms related to skeletal muscle dysfunction affecting proximal lower limb and paraspinal trunk muscles, progressing to the diaphragm and accessory muscles of respiration. Patients with Pompe disease are typically managed by metabolic disease specialists/biochemical geneticists and neuromuscular experts. In the 'Pompe disease diagnosis and management guideline', experts recommend enzyme activity analysis with acid α-glucosidase (GAA) assay performed on skin fibroblasts (as the preferred tissue) or muscle biopsy, as the "gold standard" to confirm a diagnosis of Pompe disease. Mutation testing is also useful in identifying carriers when a familial mutation is known and can aid in confirmation of the diagnosis.

In the studies, treatment with Pombiliti in combination with Opfolda (migLUstat) resulted in a numerically (although not significantly) greater increase in 6-minute walk distance from baseline and a significantly lower change in sitting FVC (% predicted) from baseline compared to treatment with alglucosidase alfa (Lumizyme) plus placebo in adult patients with late-onset Pompe disease. Pombiliti has not been studied and there is no data to support use in combination with other enzyme replacement therapy (such as Lumizyme or Nexviazyme) used to treat late-onset Pompe disease.

References

1. Pombiliti [package insert]. Philadelphia, PA: Amicus Therapeutics US, LLC; September 2023.

2. Opfolda [package insert]. Philadelphia, PA: Amicus Therapeutics US, LLC; September 2023.

3. American College of Medical Genetics – Pompe Disease Diagnosis and Management Guideline, 2006. doi: 10.1097/01.gim.0000218152.87434.f3

Pyzchiva IV *(ustekinumab-ttwe)*
Priority Health Part B Step Therapy: Yes
Additional Priority Health Part B Criteria: Yes
Pyzchiva is a biosimilar to Stelara. It has been approved by the FDA for all indications of its reference biologic. The FDA has also provisionally determined Pyzchiva to be interchangeable with Stelara. Ustekinumab (including the biosimilars and reference product) is a monoclonal antibody that inhibits interleukin (IL)-12 and IL-23 and is indicated in several inflammatory conditions including Ulcerative Colitis (UC) and Crohn's Disease (CD). The Food and Drug Administration (FDA) considers biosimilars to be highly similar with no clinically meaningful differences to the biologic reference product. Biosimilars are considered safe and effective and provide an option to increase access to lifesavings drugs at lower costs. The FDA and current treatment guidelines do not favor one product (biologic or biosimilar) over another. There is limited data on the concurrent use of ustekinumab with other biologic agents, targeted synthetic DMARDs (e.g., JAK inhibitors), and phosphodiesterase-4 (PDE4) inhibitors (Otezla). Given the absence of strong clinical evidence and the potential for increased infection risk, it is not recommended to use ustekinumab in combination with these agents. Step therapy is applied to certain Part B drugs, biologics, and biosimilars in a way that lowers costs and improves the quality of care for Medicare beneficiaries per the Centers for Medicare & Medicaid Services (CMS) guidance.
References 1. Pyzchiva [prescribing information]. Princeton, NJ: Sandoz; June 2024. 2. Lichtenstein GR, Loftus EV, Isaacs KL, et al. ACG clinical guideline: management of crohn's disease in adults. AJG. 2018 April; 113 (4): 481-517 3. Feuerstein JD, Isaacs KL, Schneider Y, et al. AGA clinical practice guidelines on the management of moderate to severe ulcerative colitis. Gastroenterology. 2020; 158: 1450 – 6 4. Centers for Medicare & Medicaid Services. Medicare Advantage Prior Authorization and Step Therapy for Part B Drugs. August 7, 2018. Retrieved from https://www.cms.gov/newsroom/fact-sheets/medicare-advantage-prior-authorization-and-step-therapy-part-b-drugs. 5. Centers for Medicare & Medicaid Services. (2018, August 7). Prior Authorization and Step Therapy for Part B Drugs in Medicare Advantage [Memorandum]. Retrieved from https://www.cms.gov/Medicare/Health-Plans/HealthPlansGenInfo/Downloads/MA_Step_Therapy_HPMS_Memo_8_7_2018.pdf

Qalsody *(tofersen)*
Priority Health Part B Step Therapy: No
Additional Priority Health Part B Criteria: Yes
Qalsody (tofersen) injection is an antisense oligonucleotide indicated for the treatment of amyotrophic lateral sclerosis (ALS) in adults who have a mutation in the superoxide dismutase 1 (SOD1) gene. Qalsody was studied in patients with weakness associated with ALS and a SOD1 mutation confirmed by laboratory testing. Study patients had a vital capacity (VC) ≥50% of predicted value as adjusted for gender, age, and height (from the sitting position). Study patients with stable VC <50% but ≥45%, were also considered for inclusion (at the discretion of the investigator) if their VC had not declined by more than 5% in the previous 6 months. Qalsody showed a nominally statistically significant plasma neurofilament light chain (NfL) decrease for all subgroups from baseline to Week 28. At this time, Qalsody is approved under an accelerated approval based on decrease in NfL from baseline observed in patients treated with tofersen (Qalsody). Continued approval for this indication may be contingent upon verification of clinical benefit in confirmatory trial(s).
References 1. Qalsody [Package Insert]. Cambridge, MA; Biogen MA Inc.: 2023 2. Clinicaltrials.gov. An Efficacy, Safety, Tolerability, Pharmacokinetics and Pharmacodynamics Study of BIIB067 (Tofersen) in Adults With Inherited Amyotrophic Lateral Sclerosis (ALS) (VALOR (Part C)) (NCT02623699). Available at: https://clinicaltrials.gov/study/NCT02623699
Qfitlia *(fitusiran)*
Priority Health Part B Step Therapy Drug: Yes
Additional Priority Health Part B Criteria: Yes
Qfitlia is the first antithrombin (AT)-directed small interfering ribonucleic acid (siRNA) approved for hemophilia. Unlike other hemophilia treatments, Qfitlia can be administered subcutaneously (SC) as infrequently as once every 2 months (Q2M). Dose/frequency is adjusted by AT activity, measured using Siemens' FDA-cleared Innovance AT companion diagnostic test. Qfitlia has the broadest indication (hemophilia A and B with and without inhibitors) and enters a crowded market of SC prophylactics. In hemophilia A, it will directly compete with Roche's Hemlibra (emicizumab-kxwh), Pfizer's Hympavzi (marstacimab-hncq), and Novo Nordisk's Alhemo (concizumab-mtci). In hemophilia B, it will directly compete with Hympavzi and Alhemo.

Qfitlia is not yet addressed in current guidelines. The National Bleeding Disorders Foundation Medical and Scientific Advisory Council (MASAC) recommends factor VIII and factor IX products as treatment of choice for patients with hemophilia A and B in whom such agents are necessary. MASAC also provides recommendations for the use of Hemlibra for patients with hemophilia A with and without inhibitors. The International Society on Thrombosis and Hemostasis practice guidelines state that in patients with severe hemophilia A with inhibitors, prophylaxis with Hemlibra is recommended over bypassing agents (conditional recommendation based on very low-certainty evidence). The World Federation of Hemophilia (WFH) 2020 guideline recommends ITI be considered for patients with hemophilia A that develop persistent low-responding inhibitors and recommends Hemlibra prophylaxis over bypassing agent prophylaxis in those that fail or never underwent ITI.

References

1. Qfitlia [prescribing information]. Cambridge, MA: Sanofi, Inc.; 2025

2. Clinicaltrials.gov. TITLE. (NCT 03417102) Available at: https://clinicaltrials.gov/study/NCT03417102

3. Clinicaltrials.gov. TITLE (NCT 03417245) Available at: https://clinicaltrials.gov/study/NCT03417245

4. The Centers for Disease Control (CDC). Diagnosing Hemophilia. May 2024. Available at: https://www.cdc.gov/hemophilia/testing/index.html.

5. National Bleeding Disorders Foundation (NBDF). MASAC (Medical and Scientific Advisory Council) recommendations concerning products licensed for the treatment of hemophilia and selected disorders of the coagulation system. MASAC Document #284. Endorsed by the NBDF Board of Directors on April 11, 2024. Available at: https://www.bleeding.org/sites/default/files/document/files/MASAC-Products-Licensed.pdf.

Qutenza *(capsaicin)* 8% patch

Priority Health Part B Step Therapy: Yes

Additional Priority Health Part B Criteria: No

The transient receptor potential vanilloid 1 (TRPV1) is an ion channel expressed on nociceptive nerve fibers in the skin. Qutenza is a TRPV1 channel agonist indicated for the management of neuropathic pain associated with postherpetic neuralgia (PHN) or diabetic peripheral neuropathy (DPN). It is a synthetic version of a substance found in chili peppers. This patch targets neuropathic pain peripherally and delivers medication directly to nerves and then selectively binds with the TRPV1 protein that resides in the pain and heat sensing neurons.

Medication therapy represents the foundation of first and second-line therapy in diabetic neuropathic pain and includes options such as lidocaine patch, duloxetine, venlafaxine, pregabalin, gabapentin, or a tricyclic antidepressant (e.g., amitriptyline, nortriptyline).

Recommendations for postherpetic neuralgia treatment present a broad range of options that include topicals, pregabalin, gabapentin or a tricyclic antidepressant.

References

1. Qutenza [Package Insert]. Morristown, NJ; Averitas Pharma, Inc.: 2020

2. Price R, Smith D, Franklin G, et al. Oral and Topical Treatment of Painful Diabetic Polyneuropathy: Practice Guideline Update Summary: Report of the AAN Guideline Subcommittee. Neurology 2022; 98:31.

3. Pop-Busui R, Boulton AJ, Feldman EL, et al. Diabetic Neuropathy: A Position Statement by the American Diabetes Association. Diabetes Care 2017; 40:136.

4. Johnson RW, Rice AS. Clinical practice. Postherpetic neuralgia. N Engl J Med 2014; 371:1526.

Quzyttir *(cetirizine)* intravenous

Priority Health Part B Step Therapy: Yes

Additional Priority Health Part B Criteria: No

Quzyttir is an intravenous formulation of cetirizine which is a histamine-1 (H1) receptor antagonist. The H1 receptors inhibited by cetirizine are primarily on respiratory smooth muscle, vascular endothelial, immune, and gastrointestinal cells. H1 antihistamines are typically divided into older, first generation and new, second-generation agents. Agent selection may be based on a variety of factors including potential side effect profile.

Cetirizine does not cross the blood-brain barrier, avoiding neurons of the central nervous system and causing minimal sedation compared with first generation antihistamines.

References

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Reblozyl *(luspatercept-aamt)*

Priority Health Part B Step Therapy: No

Additional Priority Health Part B Criteria: Yes

Reblozyl (luspatercept-aamt) is an erythroid maturation agent (EMA) indicated for the treatment of anemia in adults with beta thalassemia and myelodysplastic syndromes (MDS) who require red blood cell (RBC) infusions.

Beta thalassemia is an inherited blood disorder that can cause reduction of normal hemoglobin and red blood cells in the body. This can lead to insufficient delivery of oxygen throughout the body. Reduced levels of red blood cells (anemia) can lead to symptoms of dizziness, weakness, fatigue, shortness of breath and headaches. Blood transfusions are the mainstay of care for individuals with thalassemia. Guidelines define a patient as transfusion dependent when they are getting infusions of packed red blood cells every 2 to 5 weeks to maintain the pre-transfusion hemoglobin of 9 g/dL - 10.5 g/dL and the post-transfusion hemoglobin less than 14 - 15 g/dL. Repeated blood transfusions can cause iron overload in these patients because the body has no normal way to remove excess iron. Guidelines recommend use of Reblozyl in adult patients with beta thalassemia who require regular red blood cell transfusions. Reblozyl allows for significant improvement in hemoglobin levels and reduction in transfusion requirements, which decreases risk of iron overload.

Myelodysplastic syndromes (MDS) are clonal hematopoietic stem cell (HSC) disorders that cause blood cytopenias and can progress to acute myeloid leukemia (AML) in one-third of cases. The main risk factors, allowing an individual risk-adapted treatment strategy, are cytogenetic abnormalities, marrow blasts percentage and number and severity of cytopenias. Patients with MDS are stratified into five risk groups (very low-, low-, intermediate-, high- and very high-risk. Higher-risk MDS carries a major risk of progression to AML and short survival, and treatment should aim to modify the disease course, with options including allogeneic stem cell transplantation and hypomethylating agents. In lower-risk MDS, the risk of AML progression is lower. The main priority is generally the treatment of cytopenias, mainly of anemia, and improvement in quality of life. Chronic RBC transfusions can be considered as the sole treatment of anemia in lower-risk MDS. However, repeated RBC transfusions are associated with chronic anemia. Erythropoiesis-stimulating agents (ESAs), such as recombinant erythropoietin or darbepoetin, are the first-choice treatment of anemia in most lower-risk MDS without del(5q) cytogenetic abnormalities. Lenalidomide is the preferred treatment for anemia in lower-risk MDS with del(5q). NCCN recommends use of Rebloyzl for treating ring sideroblastic MDS in patients with no response to prior ESA treatment or for treating very low- to intermediate-risk MDS.

Reblozyl has not been studied and there is no data to support use in combination with imetelstat (Rytelo).

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Rebyota *(fecal microbiota, live-jslm)*

Priority Health Part B Step Therapy: Yes

Additional Priority Health Part B Criteria: Yes

Rebyota (fecal microbiota, live - jslm) suspension is indicated for the prevention of recurrence of Clostridioides difficile infection (CDI) in individuals 18 years of age and older, following antibiotic treatment for recurrent CDI. Currently, there are no compendia supported uses for this therapy outside the FDA-indication(s).

For the initial Clostridioides difficile infection (CDI) episode, the 2021 Clinical Practice Guideline by the Infectious Diseases Society of America (IDSA) and Society for Healthcare Epidemiology of America (SHEA) recommend fidaxomicin, oral vancomycin, or (in some cases) metronidazole. For the first recurrence, recommendations include fidaxomicin, oral vancomycin, and (in some cases) bezlotoxumab as adjunctive treatment.

For second or subsequent CDI recurrence, recommendations include fidaxomicin, vancomycin, fecal microbiota transplantation, and (in some cases) bezlotoxumab as adjunctive treatment. The panel recommends that appropriate antibiotic treatments should be tried for at least 2 recurrences (ie, 3 CDI episodes) before offering fecal microbiota transplantation.

Rebyota is given as a single dose of 150 mL administered rectally 24 to 72 hours after the last dose of antibiotics for CDI.

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Clinical Infectious Diseases, Volume 73, Issue 5, 1 September 2021, Pages e1029–e1044, https://doi.org/10.1093/cid/ciab549

Releuko *(filgrastim-ayow)*

Priority Health Part B Step Therapy: Yes

Additional Priority Health Part B Criteria: No

Hematopoietic growth factors are defined by their ability to promote proliferation and differentiation of hematopoietic progenitors into mature blood cells. Colony-stimulating factors (CSFs) are hematopoietic growth factors that regulate the growth and differentiation of cells towards the myeloid and erythroid lineages. Myeloid growth factors (MGFs), such as granulocyte colony-stimulating factors (G-CSF), are primarily used to reduce the incidence of febrile neutropenia (FN) in patients with nonmyeloid malignancies receiving myelosuppressive chemotherapy.

Chemotherapy-induced neutropenia is a major risk factor for infection-related morbidity and mortality and also a significant dose-limiting toxicity in cancer treatment. Prophylactic treatment with granulocyte-colony stimulating factors (G-CSFs), such as filgrastim (including approved biosimilars) or pegfilgrastim is available to reduce the risk of chemotherapy-induced neutropenia. NCCN guideline recommends prophylactic G-CSF use if a patient's risk of developing FN is >20% (category 1). The American Society of Clinical Oncology (ASCO) and European Organization for Research and Treatment of Cancer (EORTC) guidelines have also adopted the 20% threshold for considering routine prophylactic MGF support. The National Comprehensive Cancer Network (NCCN) Panel defines intermediate risk as a 10% to 20% probability of developing FN or a neutropenic event that would compromise treatment. For patients receiving intermediate-risk chemotherapy regimens, the panel recommends individualized consideration of prophylactic G-CSF use based on the presence of patient-specific risk factors.

Administration of CSFs to mobilize peripheral-blood progenitor cell (PBPC) often in conjunction with chemotherapy and their administration after autologous, but not allogeneic, PBPC transplantation is the current standard of care. Among autologous PBPC patients, post-transplant G-CSF use has been associated with savings in the duration of hospitalization and overall medical costs. The use of CSFs to mobilize peripheral blood progenitor cells (PBPC) and to shorten the period of neutropenia after cytoreduction and PBPC transplantation, is well established. Individuals receiving CSFs for mobilization should have their platelet counts monitored. Filgrastim is indicated for the mobilization of hematopoietic progenitor cells into the peripheral blood for collection by leukapheresis.

Several studies have shown that CSF administration can produce modest decreases in the duration of neutropenia when begun shortly after completion of the initial induction chemotherapy for the treatment of acute myeloid leukemia (AML). CSF use can be recommended after the completion of consolidation chemotherapy because of the potential to decrease the incidence of infection and eliminate the likelihood of

hospitalization in some patients receiving intensive post-remission chemotherapy. CSFs can increase the absolute neutrophil count in neutropenic patients with myelodysplastic syndromes (MDS). In the treatment of acute lymphocytic leukemia (ALL), CSFs are recommended after the completion of the initial first few days of chemotherapy of the initial induction or first post remission course.

Current recommendations for the management of patients exposed to lethal doses of total body radiotherapy, but not doses high enough to lead to certain death due to injury to other organs, includes the prompt administration of CSF or pegylated G-CSF. Hematopoietic growth factors can increase the survival, proliferation, amplification, and differentiation of granulocyte progenitors to produce neutrophils.

Per NCCN guidelines on Hemopoietic growth Factors, an FDA-approved biosimilar is an appropriate substitute for filgrastim and pegfilgrastim.

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Remicade *(infliximab)*

Priority Health Part B Step Therapy: Yes

Additional Priority Health Part B Criteria: Yes

Remicade (infliximab) is a tumor necrosis factor inhibitor (TNFi) indicated for several conditions including Crohn's Disease (CD), Ulcerative Colitis (UC), fistulizing CD, Rheumatoid Arthritis (RA), active ankylosing spondylitis (AS), psoriatic arthritis (PsA), and plaque psoriasis (PsO).

Ankylosing spondylitis 'AS' and non-radiographic axial spondyloarthritis 'NRAS' are related conditions. The 2019 American College of Rheumatology recommendations for AS and NRAS are similar. Recommended first-line agents include nonsteroidal anti-inflammatory drugs (NSAIDs) due to their well-known safety and efficacy profiles. For patients who have active disease despite treatment with NSAIDs, treatment with a TNFi is recommended. Guidelines do not favor one TNFi over another.

Hidradenitis suppurativa (HS) is a chronic, painful skin condition that varies in presentation. There are no established treatment guidelines for this condition, but the foundation for HS has put forth evidence-based recommendations. Initial treatment includes topical and systemic antibiotics with progression to biologics if refractory or unresponsive to initial treatment. Antibiotics have been used to treat HS for decades; there is robust evidence to show symptom improvement and patient tolerability. Biologic agents (e.g., TNFi, interleukin inhibitors) have shown some benefit in small studies but lack the robust support to make strong recommendations for dosing, appropriate goals of therapy, and duration of treatment.

The 2018 American College of Gastroenterology (ACG) guidelines recommend mercaptopurine, azathioprine, and methotrexate in symptomatic CD despite prior corticosteroid use. TNFi agents are effective in those with inadequate response to these initial therapies.

Per the 2020 American Gastroenterology Association guidelines, multiple agents effectively induce and maintain remission of UC, including corticosteroids, 5-aminosalicylates '5-ASA', and biologics. Treatment of mild-to-moderate UC is typically started with 5-ASA therapy. In those who do not respond to 5-ASA therapy, induction can be achieved through short-term corticosteroids. Once induction is achieved, maintenance can be managed with thiopurines. Methotrexate is not recommended for induction or maintenance of remission in UC, whereas biologic agents do have support for use in these treatment areas. Guidelines do not favor one biologic over another, nor do they favor biologics over thiopurine monotherapy for those in remission.

For Rheumatoid Arthritis (RA), guidelines favor the use of biologic DMARDs (bDMARD) for moderate or high disease activity despite prior conventional synthetic DMARDs (csDMARD). Guidelines do not favor one bDMARD over another, however TNFi agents have the most documented safety and efficacy profiles.

Per the 2020 Joint AAD-NPF guidelines (non-biologic), recommended treatments include methotrexate, cyclosporine, and acitretin. Methotrexate and cyclosporine are category A recommendations, whereas acitretin is a category B recommendation. The 2019 Joint AAD-NPF guidelines (biologics) recommend (category A) the use of biologics in treating psoriasis but do not suggest one agent over another. TNFis, interleukin-12/23, IL-23, and IL-17 inhibitors have all shown efficacy in this condition.

Per the 2018 American College of Rheumatology (ACR)/National Psoriasis Foundation (NPF) guidelines, methotrexate, sulfasalazine, cyclosporine, and leflunomide may be used in patients with non-severe Psoriatic Arthritis (PsA) and have robust safety and efficacy

evidence to support their use. If initial treatment is not sufficient, switching to a biologic is suggested.

There is limited data on the concurrent use of infliximab products with other biologic agents, targeted synthetic DMARDs (JAK inhibitors), and PDE4 inhibitors (Otezla). Given the absence of strong clinical evidence and the potential for increased infection risk, it is not recommended to use infliximab products in combination with these agents.

The Food and Drug Administration (FDA) supports the use of FDA-approved biosimilars and do not favor one biosimilar over another. Step therapy is applied to certain Part B drugs, biologics, and biosimilars in a way that lowers costs and improves the quality of care for Medicare beneficiaries per the Centers for Medicare & Medicaid Services (CMS) guidance.

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Rethymic *(allogeneic processed thymus tissue–agdc)*
Priority Health Part B Step Therapy Drug: No
Additional Priority Health Part B Criteria: Yes
Congenital athymia is a rare immune disorder where a child is born without a thymus, a gland that produces white blood cells and helps the immune system fight infections. Newborns with congenital athymia have severe immunodeficiency, making them susceptible to life-threatening infections, and many infants die from infections or autoimmune symptoms by 2 or 3 years of age. Congenital athymia is sometimes mistaken for Severe Combined Immunodeficiency (SCID). Patients with either disorder present with very low T-cell counts. Both congenital athymia and SCID are primary immunodeficiency disorders, but they are two separate conditions. Per Rethymic's Food and Drug Administration (FDA)-approved labeling, Rethymic is not indicated for the treatment of patients with SCID. Due to the condition, diagnostic and treatment requirements, patients are best managed by a specialist for the condition such as a pediatric immunologist.
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Retisert *(fluocinolone acetonide)* intravitreal implant
Priority Health Part B Step Therapy: Yes
Additional Priority Health Part B Criteria: Yes

Retisert (fluocinolone acetonide intravitreal implant) is indicated for the treatment of chronic non-infectious uveitis affecting the posterior segment of the eye. Retisert has also been studied for use in macular edema due to diabetes mellitus.

Uveitis is a group of eye diseases caused by inflammation (redness, swelling, pain, etc.) inside the eye, which can lead to vision loss. Uveitis can result from infections, or non-infectious causes. Non-infectious uveitis can result from a disease somewhere else in the body. The uvea (middle layer of the eye) has many blood vessels. If the immune system is fighting a problem in one area, the cells and chemicals it makes can travel through the bloodstream and enter the eye, leading to inflammation. Acute uveitis lasts less than three months; chronic uveitis lasts longer than three months. Chronic non-infectious uveitis is generally treated with steroids, applied near or inside the eye, or other medicines, taken either by mouth or injection, to control the inflammation.

Fluocinolone acetonide intravitreal implant effectively controlled ocular inflammation and significantly reduced uveitis recurrence rates over 3 years in patients with noninfectious posterior uveitis in a randomized trial. The preimplantation uveitis recurrence rate of 62% for the 0.59-mg implant group significantly dropped to 4%, 10%, and 20% in years 1, 2, and 3, respectively, following implantation. Recurrence rates for non-implanted eyes increased significantly from 44% in to 59% in 3 years. The need for adjunctive therapy decreased significantly 1 year (80% reduction in systemic medications and 95% reduction in periocular injections) after implantation for implanted eyes which continued for years 2 and 3. Topical corticosteroid use decreased by approximately 50% 1 year following implantation. Visual acuity for implanted eyes did not change significantly over the 3-year postimplantation period; however, visual acuity for non-implanted eyes declined significantly.

Diabetic macular edema (DME) is defined as the presence of intraretinal fluid (edema) and thickening involving the macula, the part of the retina responsible for central vision. It is a vision-threatening complication of diabetes and can occur at any stage or severity of diabetic retinopathy. Edema that is centrally located within the macula can be associated with more substantial decreases in visual acuity.

The 3-year efficacy and safety results of a 4-year study evaluating fluocinolone acetonide (FA) intravitreal implants in eyes with persistent or recurrent diabetic macular edema (DME) was studied prospectively. Patients were randomized 2:1 to receive 0.59-mg FA implant (n = 127) or standard of care (SOC additional laser or observation; n = 69). The primary efficacy outcome was ≥15-letter improvement in visual acuity (VA) at 6 months. Overall, VA improved ≥3 lines in 16.8% of implanted eyes at 6 months. Secondary outcomes included resolution of macular retinal thickening and Diabetic Retinopathy Severity Score (DRSS). The number of implanted eyes with no evidence of retinal thickening at the center of the macula was higher than SOC eyes at 6 months. A higher rate of improvement and lower rate of decline

in DRSS occurred in the implanted group versus the SOC group at 6 months. The study concluded that The 0.59-mg FA intravitreal implant may be an effective treatment for eyes with persistent or recurrent DME.

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Revcovi *(elapegademase-lvlr)* injection

Priority Health Part B Step Therapy: No

Additional Priority Health Part B Criteria: Yes

Revcovi (elapegademase-lvlr) injection is a recombinant adenosine deaminase indicated for the treatment of adenosine deaminase severe combined immune deficiency (ADA-SCID) in pediatric and adult patients. Currently, there are no compendia supported uses for this therapy outside the FDA-indication(s). Revcovi is given 0.2 mg/kg intramuscularly weekly in some patients transitioning from Adagen or 0.2 mg/kg twice a week (based on ideal body weight or actual weight, whichever is greater) in Adagen-naïve patients. Following the initial dosing recommendations, maintenance doses may be adjusted to maintain a target trough plasma ADA activity of at least 30 mmol/hr/L, a trough erythrocyte deoxyadenosine nucleotide (dAXP) below 0.02 mmol/L, and adequate immune reconstitution based on the clinical assessment of the patient.

The manufacturer recommends the optimal long-term dose and schedule of administration be established for each patient individually and may be adjusted based on the laboratory values for trough ADA activity, trough dAXP level, and/or according to the treating physician's medical assessment of the patient's clinical status above.

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Rezzayo *(rezafungin acetate)*

Priority Health Part B Step Therapy: No

Additional Priority Health Part B Criteria: No

Rezzayo (rezafungin) is indicated for the treatment of candidemia and invasive candidiasis (IC) in adult patients who have limited or no alternative options. Approval is based on

limited clinical safety and efficacy data. Rezafungin has not been studied in patients with endocarditis, osteomyelitis, or meningitis due to Candida.

Infections due to Candida species are major causes of morbidity and mortality, causing clinical disease ranging from superficial and mucosal infections to invasive disease associated with candidemia and metastatic organ involvement. Candidemia is one of the most common healthcare-associated bloodstream infections in US hospitals. Earlier intervention with appropriate antifungal therapy and removal of a contaminated central venous catheter (CVC) or drainage of infected material is generally associated with better overall outcomes

The 2016 Update by the Infectious Diseases Society of America for Clinical Practice Guideline for the Management of Candidiasis recommends systemic antifungals comprising azoles, amphotericin B, and echinocandins. The echinocandins are preferred agents for most episodes of candidemia and invasive candidiasis, with the exception of central nervous system (CNS), eye, and urinary tract infections due to these organisms. This preference is based on a strong safety profile, convenience, early fungicidal activity, a trend toward better outcomes based on data from individual studies and combined analyses of candidemia studies and the emergence of azole-resistant Candida species. Rezafungin is a newer echinocandin that is not addressed in the guidelines.

The Phase 3 ReSTORE trial in patients with candidemia and/or IC, on which FDA approval was based, compared weekly treatment with rezafungin vs daily treatment with caspofungin. Rezafungin was non-inferior to caspofungin for the efficacy endpoints of all-cause mortality at day 30 (primary endpoint for FDA) and global cure at day 14 (primary endpoint for European Medicines Agency), with a similar safety profile.

Currently, there are no compendia supported uses for this therapy outside the FDA-indication(s).

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Riabni *(rituximab-arrx)*
Priority Health Part B Step Therapy: Yes
Additional Priority Health Part B Criteria: No
Riabni (rituximab-aarx) is a monoclonal antibody that induces apoptosis in DHL 4 human B cell lymphoma cells and inhibits rheumatoid factor production, antigen presentation, T-cell activation and proinflammatory cytokine production in rheumatoid arthritis. Rituxan was the original rituximab product launched, but many biosimilars have since come to market including Riabni, Ruxience, Truxima, and Rituxan Hycela. NCCN and Rheumatoid Arthritis Guidelines do not favor one rituximab product over another. Priority Health also follows LCD L37205: Chemotherapy Drugs and their Adjuncts.
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Rituxan *(rituximab)*
Priority Health Part B Step Therapy: Yes
Additional Priority Health Part B Criteria: No
Rituxan (rituximab) is a monoclonal antibody that induces apoptosis in DHL 4 human B cell lymphoma cells and inhibits rheumatoid factor production, antigen presentation, T-cell activation and proinflammatory cytokine production in rheumatoid arthritis. Rituxan was the original rituximab product launched, but many biosimilars have since come to market including Riabni, Ruxience, Truxima, and Rituxan Hycela. NCCN and Rheumatoid Arthritis Guidelines do not favor one rituximab product over another. Priority Health also follows LCD L37205: Chemotherapy Drugs and their Adjuncts.
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Rituxan Hycela *(rituximab/ hyaluronidase)*
Priority Health Part B Step Therapy: Yes
Additional Priority Health Part B Criteria: No
Rituxan Hycela (rituximab/hyaluronidase) is a monoclonal antibody that induces apoptosis in DHL 4 human B cell lymphoma cells and inhibits rheumatoid factor production, antigen presentation, T-cell activation and proinflammatory cytokine production in rheumatoid arthritis. Hyaluronidase is an enzyme that serves to promote rituximab delivery under the skin so that rituximab can be given subcutaneously (versus intravenously). Rituxan was the original rituximab product launched, but many biosimilars have since come to market including Riabni, Ruxience, Truxima, and Rituxan Hycela. NCCN and Rheumatoid Arthritis Guidelines do not favor one rituximab product over another. Priority Health also follows LCD L37205: Chemotherapy Drugs and their Adjuncts.
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Rivfloza *(nedosiran)* injection solution
Priority Health Part B Step Therapy: No
Additional Priority Health Part B Criteria: Yes
Primary hyperoxalurias (PHs) are rare inborn errors of glyoxylate metabolism and are distinguished by the over-production of oxalate, which is poorly soluble and combines with calcium to form kidney and urinary stones. As a patient's glomerular filtration rate decreases throughout their lifetime, plasma oxalate levels will increase, and calcium oxalate will deposit into other areas of the body, such as the heart, bones, and retina. The increased production of oxalate leads to kidney injury, which could lead to kidney failure, necessitating a need for treatment of this condition. Symptoms may appear at any age. There are three notable types of PH that differ based on severity and the genetic mutation present. Primary hyperoxaluria type 1 (PH1) is the most common form, and patients with PH1 have mutation of the AGXT gene, which results in abnormal hepatic enzyme alanine-glyoxylate aminotransferase (AGT), which in turn causes the increase in glyoxylate and oxalate. Rivfloza is an RNA interference (RNAi) therapy that indirectly lowers the amount of glyoxylate and oxalate. Conservative treatment is recommended initially after diagnosis and includes hyperhydration, alkalizing the urine and trialing pyridoxine. This is noted in The

European Rare Kidney Disease Reference Network and OxalEurope developed clinical practice recommendations (2023) for primary hyperoxaluria. RNA interference (RNAi) therapies are briefly mentioned and, in general, are recommended for patients with a genetic diagnosis of PH1. Transplant of the liver and possibly the kidneys are an option to correct the AGXT mutation though recommendations around this area are also unclear.

Clinical trials have shown that Rivfloza and other RNAi therapies (e.g., Oxlumo) can effectively treat the underlying pathophysiology of oxalate overproduction. While RNAi therapies have the potential to improve patient outcomes, it should be noted that the clinical impact is not clear. It is also unclear to what extent these agents might replace a liver and/or kidney transplant.

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Roctavian *(valoctocogene roxaparvovc-rvox)*

Priority Health Part B Step Therapy: No

Additional Priority Health Part B Criteria: Yes

Roctavian is an adeno-associated virus (AAV) vector-based gene therapy product indicated for the treatment of adults with severe hemophilia A without antibodies to adeno-associated virus serotype 5 (AAV5). Roctavian consists of an AAV5 capsid that contains a DNA sequence that encodes the B-domain deleted SQ form of the human coagulation factor VIII. This is designed to introduce a functional copy of a transgene encoding the B-domain deleted SQ form of human coagulation factor VIII. Transcription of the gene occurs

within the liver and results in expression of this factor. The expressed factor replaced missing coagulation factor VIII needed for effective homeostasis.

Hemophilia A is a rare genetic bleeding disorder in which affected individuals have insufficient levels of factor VIII. It is the second most common type of hemophilia and caused by mutations in the F8 gene. The F8 gene is located on the X chromosome and thus the disease is inherited as an X-linked recessive trait.

Symptoms may vary from mild to severe based on the level of factor activity. Severe are noted to have a factor level less than 1% and often have bleeding for no known reason, particularly in joints and muscles.

The standard of care for Hemophilia A is the use of factor VIII replacement therapy. There are two types of products available which include plasma derived factor made from human donations and there is also recombinant factor made by genetically engineered technology. All factors have demonstrated similar efficacy and safety and reduce bleeding episodes.

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Rolvedon *(eflapegrastim-xnst)*

Priority Health Part B Step Therapy: Yes

Additional Priority Health Part B Criteria: No

Hematopoietic growth factors are defined by their ability to promote proliferation and differentiation of hematopoietic progenitors into mature blood cells. Colony-stimulating factors (CSFs) are hematopoietic growth factors that regulate the growth and differentiation of cells towards the myeloid and erythroid lineages. Myeloid growth factors (MGFs), such as granulocyte colony-stimulating factors (G-CSF), are primarily used to reduce the incidence of febrile neutropenia (FN) in patients with nonmyeloid malignancies receiving myelosuppressive chemotherapy.

Chemotherapy-induced neutropenia is a major risk factor for infection-related morbidity and mortality and also a significant dose-limiting toxicity in cancer treatment. Prophylactic treatment with granulocyte-colony stimulating factors (G-CSFs), such as filgrastim (including approved biosimilars) or pegfilgrastim is available to reduce the risk of chemotherapy-induced neutropenia. NCCN guideline recommends prophylactic G-CSF use if a patient's risk of developing FN is >20% (category 1). The American Society of Clinical Oncology (ASCO) and European Organization for Research and Treatment of Cancer (EORTC) guidelines have also adopted the 20% threshold for considering routine prophylactic MGF support. The National Comprehensive Cancer Network (NCCN) Panel defines intermediate risk as a 10% to 20% probability of developing FN or a neutropenic event that would compromise treatment. For patients receiving intermediate-risk chemotherapy regimens, the panel recommends individualized consideration of prophylactic G-CSF use based on the presence of patient-specific risk factors.

Administration of CSFs to mobilize peripheral-blood progenitor cell (PBPC) often in conjunction with chemotherapy and their administration after autologous, but not allogeneic, PBPC transplantation is the current standard of care. Among autologous PBPC patients, post-transplant G-CSF use has been associated with savings in the duration of hospitalization and overall medical costs. The use of CSFs to mobilize peripheral blood progenitor cells (PBPC) and to shorten the period of neutropenia after cytoreduction and PBPC transplantation, is well established. Individuals receiving CSFs for mobilization should have their platelet counts monitored. Filgrastim is indicated for the mobilization of hematopoietic progenitor cells into the peripheral blood for collection by leukapheresis.

Several studies have shown that CSF administration can produce modest decreases in the duration of neutropenia when begun shortly after completion of the initial induction chemotherapy for the treatment of acute myeloid leukemia (AML). CSF use can be recommended after the completion of consolidation chemotherapy because of the potential to decrease the incidence of infection and eliminate the likelihood of hospitalization in some patients receiving intensive post-remission chemotherapy. CSFs can increase the absolute neutrophil count in neutropenic patients with myelodysplastic syndromes (MDS). In the treatment of acute lymphocytic leukemia (ALL), CSFs are recommended after the completion of the initial first few days of chemotherapy of the initial induction or first post remission course.

Current recommendations for the management of patients exposed to lethal doses of total body radiotherapy, but not doses high enough to lead to certain death due to injury to other organs, includes the prompt administration of CSF or pegylated G-CSF. Hematopoietic growth factors can increase the survival, proliferation, amplification, and differentiation of granulocyte progenitors to produce neutrophils.

Per NCCN guidelines on Hemopoietic growth Factors, an FDA-approved biosimilar is an appropriate substitute for filgrastim and pegfilgrastim.

References

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Ryoncil *(remestemcel-L_rknd)*

Priority Health Part B Step Therapy Drug: Yes

Additional Priority Health Part B Criteria: Yes

Ryoncil is an allogeneic bone marrow-derived mesenchymal stromal cell therapy indicated for the treatment of steroid-refractory acute graft-versus-host disease (GVHD) in pediatric patients ≥ 2 months of age. The only other treatment option for aGVHD is Jakafi which is indicated for people 12 years and older. Jakafi and Ryoncil are the only agents approved for treatment of aGVHD.

The National Comprehensive Cancer Network (NCCN) guidelines for Hematopoietic Cell Transplantation (version 2.2024 – August 30, 2024) do not address Ryoncil.

Step therapy is applied to certain Part B drugs, biologics, and biosimilars in a way that lowers costs and improves the quality of care for Medicare beneficiaries per the Centers for Medicare & Medicaid Services (CMS) guidance.

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Ryplazim *(plasminogen, human-tvmh)*

Priority Health Part B Step Therapy: No

Additional Priority Health Part B Criteria: Yes

Ryplazim (plasminogen, human-tvmh) is plasma-derived human plasminogen indicated for the treatment of patients with plasminogen deficiency type 1 (hypoplasminogenemia), to be given 6.6 mg/kg body weight administered every 2 to 4 days.

Congenital type 1 plasminogen deficiency (PLGD) is caused by variants in the plasminogen (PLG) gene, which leads to a deficiency of the plasminogen enzyme and causes reductions in both the level of immunoreactive and functional plasminogen. Congenital type 2 PLGD (dysplasminogenemia) is characterized by a normal or near normal plasminogen immunoreactive plasminogen level with decreased activity. This patient population usually does not exhibit symptoms.

Individuals with PLGD type 1 develop thick growths on the mucous membranes of the body, often referred to as woody lesions or pseudomembranes. Symptoms include juvenile colloid milium, ligneous conjunctivitis, and ligneous gingivitis but lesions can also form in the mucous membranes of the middle ear (leading to chronic middle ear infection (otitis media) and hearing loss), nose, throat, vocal cords, larynx, respiratory tract (leading to recurrent pneumonia and obstruction of the airways), gastrointestinal tract (leading to ulcers or what appears as an inflammatory bowel disease), renal tubules of the kidney (leading to obstruction and poor kidney function), and the female genital tract (leading to pain with menses, intercourse and infertility).

Molecular genetic testing can detect variants in the PLG gene known to cause the disorder and can confirm the diagnosis.

Ryplazim was studied in patients with PLGD type 1 and a baseline plasminogen activity level between <5% and 45% of normal, and biallelic mutations in the PLG gene. Initial dosing frequency was determined based on the plasminogen activity level and was maintained for 12 weeks. If lesions did not resolve by 12 weeks, or there were new or recurrent lesions, the dosing frequency was increased. After 12 weeks, average absolute plasminogen activity in study patients reached physiological levels (70% to 130%) immediately after dosing, were sustained for approximately 24 hours, and continued to maintain an absolute 10% above baseline 96 hours after dosing. External and internal lesions were resolved by the end of week 48 in 75% or more of study patients. No recurrent or new external or internal lesions were observed in any patient through week 48.

References

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Rystiggo *(rozanolixizumab-noli)*

Priority Health Part B Step Therapy: Yes

Additional Priority Health Part B Criteria: Yes

Rystiggo (rozanolixizumab-noli) is a neonatal Fc receptor blocker indicated for the treatment of generalized myasthenia gravis (gMG) in adult patients who are anti-acetylcholine receptor (AChR-Ab+) or anti-muscle-specific tyrosine kinase (MuSK) antibody positive. Currently, there are no compendia supported uses for this therapy outside the FDA-indication(s). Rystiggo has not been studied and there is no data to support use in combination with other medications used to treat MG.

The International Consensus Guidance for Management of Myasthenia Gravis recommends a nonsteroidal immunosuppressive (IS) agent be used initially in conjunction with corticosteroids, be used alone, or be added to corticosteroids in certain patients. Nonsteroidal IS agents for MG include azathioprine, cyclosporine, mycophenolate mofetil, methotrexate, and tacrolimus. The effect of azathioprine may be delayed for 4 to 12 months but can reverse symptoms in most patients. Maximum improvement with cyclosporine is achieved 6 months or longer after starting treatment. More than half of patients treated with cyclophosphamide become asymptomatic after one year. Once treatment goals have been achieved and maintained for 6 months to 2 years, the IS dose should be tapered slowly to the minimal effective amount.

Rystiggo was studied in patients with an MG-Activities of Daily Living (MG-ADL) total score of at least 3 (with at least 3 points from non-ocular symptoms) and found to have significantly lower MG-ADL score at day 43 compared with placebo.

References

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Ryzneuta *(efbemalenograstim alfa-vuxw)*

Priority Health Part B Step Therapy Drug: Yes

Additional Priority Health Part B Criteria: No

Hematopoietic growth factors are defined by their ability to promote proliferation and differentiation of hematopoietic progenitors into mature blood cells. Colony-stimulating factors (CSFs) are hematopoietic growth factors that regulate the growth and differentiation of cells towards the myeloid and erythroid lineages. Myeloid growth factors (MGFs), such as granulocyte colony-stimulating factors (G-CSF), are primarily used to reduce the incidence of febrile neutropenia (FN) in patients with nonmyeloid malignancies receiving myelosuppressive chemotherapy. Chemotherapy-induced neutropenia is a major risk factor for infection-related morbidity and mortality and also a significant dose-limiting toxicity in cancer treatment. Prophylactic treatment with granulocyte-colony stimulating factors (G-CSFs), such as filgrastim (including approved biosimilars) or pegfilgrastim is available to reduce the risk of chemotherapy-induced neutropenia.

NCCN guideline recommends prophylactic G-CSF use if a patient's risk of developing FN is >20% (category 1). The American Society of Clinical Oncology (ASCO) and European Organization for Research and Treatment of Cancer (EORTC) guidelines have also adopted the 20% threshold for considering routine prophylactic MGF support. The National Comprehensive Cancer Network (NCCN) Panel defines intermediate risk as a 10% to 20% probability of developing FN or a neutropenic event that would compromise treatment. For patients receiving intermediate-risk chemotherapy regimens, the panel recommends individualized consideration of prophylactic G-CSF use based on the presence of patient-

specific risk factors. Per NCCN guidelines on Hemopoietic growth Factors, an FDA-approved biosimilar is an appropriate substitute for filgrastim and pegfilgrastim.

Step therapy is applied to certain Part B drugs, biologics, and biosimilars in a way that lowers costs and improves the quality of care for Medicare beneficiaries per the Centers for Medicare & Medicaid Services (CMS) guidance.

References

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Saphnelo *(anifrolumab-fnia)*

Priority Health Part B Step Therapy: Yes

Additional Priority Health Part B Criteria: Yes

Saphnelo (anifrolumab-fnia) is a type I interferon (IFN) receptor antagonist indicated for the treatment of adult patients with moderate to severe systemic lupus erythematosus (SLE), who are receiving standard therapy. Saphnelo has not been studied and there is no data to support use in combination with other biologic drug or Lupkynis.

In the absence of contraindications, the 2019 European League Against Rheumatism (EULAR) recommends hydroxychloroquine (HCQ) for all patients with SLE. Glucocorticoids (GC) can provide rapid symptom relief, but various detrimental effects limit its use. Consequent initiation of immunosuppressive (IS) drugs, however, facilitates a more rapid GC tapering and may prevent disease flares. IS options include methotrexate, azathioprine, mycophenolate mofetil, and cyclophosphamide.

Guidelines recommend belimumab should be considered in extrarenal disease with inadequate control (ongoing disease activity or frequent flares) to first-line treatments (typically including combination of HCQ and prednisone with or without IS agents), and inability to taper GC daily dose to acceptable levels. Benlysta (belimumab) is a B-lymphocyte stimulator (BLyS)-specific inhibitor also indicated for the treatment of active

systemic lupus erythematosus (SLE) in patients aged 5 years and older who are receiving standard therapy. Benlysta was studied in patients with active SLE disease with a SELENA-SLEDAI score ≥6 and positive autoantibody test results. Patients receiving Benlysta 10 mg/kg plus standard therapy achieved a significantly higher SRI-4 response than the group receiving placebo plus standard therapy. The SRI uses the SELENA-SLEDAI score as an objective measure of reduction in global disease activity; along with the British Isles Lupus Assessment Group (BILAG) and the Physician's Global Assessment (PGA) score. Guidelines do not include Saphnelo yet.

Guidelines do recommend treatment in SLE should aim at remission or at low disease activity in all organ systems (if remission cannot be achieved).

References

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Selarsdi IV *(ustekinumab-aekn)*

Priority Health Part B Step Therapy: Yes

Additional Priority Health Part B Criteria: Yes

Selarsdi IV is a biosimilar to Stelara, and has been approved by the FDA for all indications of its reference biologic. Ustekinumab (including the biosimilars and reference product) is a monoclonal antibody that inhibits interleukin (IL)-12 and IL-23 and is indicated in several inflammatory conditions including Ulcerative Colitis (UC) and Crohn's Disease (CD).

The Food and Drug Administration (FDA) considers biosimilars to be highly similar with no clinically meaningful differences to the biologic reference product. Biosimilars are considered safe and effective and provide an option to increase access to lifesavings drugs at lower costs. The FDA and current treatment guidelines do not favor one product (biologic or biosimilar) over another. In addition, effective May 1, 2025, Selarsdi has been approved by the FDA as interchangeable with Stelara.

The 2018 American College of Gastroenterology (ACG) guidelines recommend mercaptopurine, azathioprine, and methotrexate in symptomatic CD despite prior corticosteroid use. TNF inhibitors (e.g., adalimumab) are effective in those with inadequate response to these initial therapies. Other biologic or targeted synthetic disease-modifying

antirheumatic drugs are not addressed by the guidelines, however these agents have since been FDA-approved for use in this condition

There is limited data on the concurrent use of ustekinumab with other biologic agents, targeted synthetic DMARDs (e.g., JAK inhibitors), and phosphodiesterase-4 (PDE4) inhibitors (Otezla). Given the absence of strong clinical evidence and the potential for increased infection risk, it is not recommended to use ustekinumab in combination with these agents.

Step therapy is applied to certain Part B drugs, biologics, and biosimilars in a way that lowers costs and improves the quality of care for Medicare beneficiaries per the Centers for Medicare & Medicaid Services (CMS) guidance.

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Signifor LAR *(pasireotide)*

Priority Health Part B Step Therapy: Yes

Additional Priority Health Part B Criteria: No

Signifor LAR (pasireotide) is a somatostatin analog indicated for the treatment of Acromegaly and Cushing's disease in adults for whom surgery has not worked well enough or who cannot have surgery.

A Pituitary Society update to acromegaly management guidelines recommend Sandostatin LAR (octreotide) as a well-established treatment for acromegaly. This update further suggests several studies confirm efficacy of Signifor LAR (pasireotide) for some patients uncontrolled on octreotide LAR.

The Consensus on Diagnosis Management of Cushing's Disease: A Guideline Update recommends use of ketoconazole and other steroidogenesis inhibitors for rapid normalization of cortisol. Adrenal steroidogenesis inhibitors are used as first-line agents given their reliable effectiveness. In mild disease, if residual tumor is present and there is a potential for tumor shrinkage, pasireotide or cabergoline can be considered. Combination

therapy of ketoconazole plus cabergoline or pasireotide may be rational combinations if there is visible tumor present.

References

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Simponi Aria *(golimumab)* IV

Priority Health Part B Step Therapy: Yes

Additional Priority Health Part B Criteria: Yes

Simponi Aria is a tumor necrosis factor inhibitor (TNFi) indicated for several inflammatory conditions including Ulcerative Colitis (UC), Rheumatoid Arthritis (RA), ankylosing spondylitis (AS), and psoriatic arthritis (PsA).

Ankylosing spondylitis 'AS' and non-radiographic axial spondyloarthritis 'NRAS' are related conditions. The 2019 American College of Rheumatology recommendations for AS and NRAS are similar. Recommended first-line agents include nonsteroidal anti-inflammatory drugs (NSAIDs) due to their well-known safety and efficacy profiles. For patients who have active disease despite treatment with NSAIDs, treatment with a TNFi (adalimumab, Enbrel, Simponi Aria, infliximab) is recommended. Cosentyx has a role in those who do not respond to initial TNFi agent. Guidelines do not favor one TNFi over another, nor do they address JAK inhibitors (Rinvoq, Xeljanz), however these agents have since been FDA-approved for use in those who had previously had inadequate response to a TNFi.

For Rheumatoid Arthritis (RA), guidelines favor the use of biologic DMARDs (bDMARD) for moderate or high disease activity despite prior conventional synthetic DMARDs (csDMARD). Guidelines do not favor one bDMARD (e.g., infliximab, Skyrizi, tocilizumab, Cosentyx) over another nor do they favor tsDMARD (Xeljanz, Rinvoq) over bDMARD.

Per the 2018 American College of Rheumatology (ACR)/National Psoriasis Foundation (NPF) guidelines, methotrexate, sulfasalazine, cyclosporine, and leflunomide may be used in patients with non-severe Psoriatic Arthritis (PsA) and have robust safety and efficacy evidence to support their use. If initial treatment is not sufficient, switching to a biologic (infliximab, adalimumab, Enbrel, Simponi Aria, Skyrizi) or JAK inhibitor (Rinvoq, Xeljanz) is recommended.

Per the 2020 American Gastroenterology Association guidelines, multiple agents effectively induce and maintain remission of UC, including corticosteroids, 5-aminosalicylates '5-ASA',

and biologics. Treatment of mild-to-moderate UC is typically started with 5-ASA therapy. In those who do not respond to 5-ASA therapy, induction can be achieved through short-term corticosteroids. Once induction is achieved, maintenance can be managed with thiopurines. Methotrexate is not recommended for induction or maintenance of remission in UC, whereas biologic agents do have support for use in these treatment areas. Guidelines do not favor one biologic (e.g., adalimumab, infliximab) over another, nor do they favor biologics over thiopurine monotherapy for those in remission. The guidelines do not address tsDMARDs (Rinvoq, Xeljanz), however these agents have since been FDA-approved for use in this condition.

There is limited data on the concurrent use of Simponi Aria with other biologic agents, targeted synthetic DMARDs (JAK inhibitors), and PDE4 inhibitors (Otezla). Given the absence of strong clinical evidence and the potential for increased infection risk, it is not recommended to use Simponi Aria in combination with these agents.

References

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Sivextro *(tedizolid)*

Priority Health Part B Step Therapy: Yes

Additional Priority Health Part B Criteria: No

Sivextro (tedizolid) is indicated for the treatment of adult and pediatric patients (12 years or older) with acute bacterial skin and skin structure infections (SSTI) and acute bacterial skin and skin structure infections caused by susceptible methicillin-resistant staphylococcus aureus (MRSA) isolates.

Clinical Practice Guidelines for the Diagnosis and Management of Skin and Soft Tissue Infections: 2014 Update by The Infectious Diseases Society of America (IDSA) advises that clinical evaluation of patients with SSTI aims to establish the cause and severity of infection and must take into account pathogen-specific and local antibiotic resistance patterns. There has been a significant increase in the frequency and severity of infections and the

emergence of resistance to many of the antimicrobial agents commonly used to treat SSTIs in the past. Some of this increased frequency is related to the emergence of community-associated MRSA.

Gram stain and culture is recommended when evaluating purulent SSTIs (cutaneous abscesses, furuncles, carbuncles, and inflamed epidermoid cysts). Incision and drainage are the recommended treatments for inflamed epidermoid cysts, carbuncles, abscesses, and large furuncles. The decision to administer antibiotics directed against S. aureus as an adjunct to incision and drainage should be made based upon presence or absence of systemic inflammatory response syndrome (SIRS). For moderate purulent infections in patients with systemic signs of infections, empiric treatment with trimethoprim-sulfamethoxazole (TMP/SMZ) or doxycycline is recommended. For MRSA infections TMP/SMX should be used and for MSSA infections dicloxacillin or cephalexin should be used. For severe purulent infections in patients who have failed incision and drainage plus oral antibiotics or those with systemic signs of infection, empiric treatment and/or confirmed MRSA should be treated with vancomycin, daptomycin, linezolid, telavancin or ceftaroline. If methicillin-sensitive staphylococcus aureus (MSSA) is confirmed, nafcillin, cefazolin or clindamycin are recommended.

Cultures of blood or cutaneous aspirates, biopsies, or swabs are not routinely recommended for non-purulent SSTI (necrotizing infection, cellulitis, erysipelas). For mild infections without systemic signs of infection, patients should receive an antimicrobial agent that is active against streptococci (penicillin VK, cephalosporin, dicloxacillin or clindamycin). For moderate infections with systemic signs of infection, intravenous treatment with penicillin, ceftriaxone, cefazolin or clindamycin is recommended. In severe infection, in patients who have failed oral antibiotic treatment or those with systemic signs of infection, emergent surgical inspection/debridement is recommended to rule out necrotizing process. Patients should also receive empiric treatment with vancomycin plus piperacillin/tazobactam. For treatment of streptococcal skin infections, in patients with a severe penicillin sensitivity clindamycin, vancomycin, linezolid, daptomycin or telavancin are recommended. The guidelines mention tedizolid as an effective agent in SSTIs, including MRSA, but makes no recommendation regarding its use since it was not yet approved by the Food and Drug administration when they were published.

A 6-day course of oral tedizolid was noninferior to a 10-day course of oral linezolid for the treatment of acute complicated bacterial skin and skin structure infections (ABSSSI) in adults (N=667). Early clinical response (ECR; no increase in lesion surface area and an oral temperature of 37.6 degrees C or lower at 48 to 72 hours) was achieved in 79.5% of tedizolid recipients and in 79.4% of linezolid recipients. This included 42.1% and 43.1% of tedizolid and linezolid recipients with MRSA. Additionally, clinical response rate at the end of treatment (day 11) and posttherapy evaluation (days 7 to 14), failure rate, and adverse event profiles were similar among study arm.

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Skyrizi *(risankizumab-rzaa)* IV 600 mg/10 mL vial

Priority Health Part B Step Therapy: Yes

Additional Priority Health Part B Criteria: Yes

Skyrizi (risankizumab-rzaa) is an IL-23 antagonist indicated for multiple inflammatory conditions including moderate to severe active Crohn's disease (CD) and moderate to severely active ulcerative colitis (UC). Inhibition of IL-23 blocks the release of pro-inflammatory cytokines, disrupting the inflammation cascade. It is available as both an intravenous (IV) and subcutaneous (SC) formulation. The IV formulation is only approved for Crohn's disease and ulcerative colitis induction dosing and is not indicated for maintenance treatment or for other inflammatory conditions. Following induction-dosing, all patients being treat for active CD or UC should be transitioned to the SC formulation.

The 2018 American College of Gastroenterology guidelines recommend multiple agents in the treatment of active CD and induction of CD remission. Corticosteroids are primarily used to treat active flares but have been shown to induce/maintain remission in those with moderate-to-severe CD. These steroids are recommended for short-term use only. They should be discontinued through tapering and switched to steroid-sparing options within weeks of starting, should symptoms persist despite initial steroid treatment. The guidelines recommend mercaptopurine, azathioprine, and methotrexate as steroid-sparing options (other agents like cyclosporine, tacrolimus, and mycophenolate are not indicated for CD and should not be used). Biologics, such as tumor necrosis factor (TNF) inhibitors (e.g., infliximab, adalimumab, and certolizumab pegol) and Skyrizi are recommended to treat CD that does not respond adequately to treatment with corticosteroids, or the steroid-sparing treatments mentioned.

The 2020 American Gastroenterological Association (AGA) Clinical Practice Guidelines recommend multiple agents in the treatment of moderate to severe ulcerative colitis. Systemic oral glucocorticoids are used for inducing remission while thiopurine monotherapy can be considered for maintenance of remission. In hospitalized adult patients with acute severe ulcerative colitis refractory to intravenous corticosteroids, the AGA suggests using infliximab or cyclosporine. The AGA also recommends using infliximab, adalimumab, golimumab, vedolizumab, tofacitinib, or ustekinumab for induction and

maintenance of remission. Skyrizi is not mentioned in the 2020 AGA guidelines for management of moderate to severe ulcerative colitis. In the INSPIRE induction study, clinical remission was significantly greater in adults who received risankizumab-rzaa compared to placebo. In the COMMAND maintenance study, patients who achieved a clinical response in the induction study were randomized to receive maintenance treatment with risankizumab-rzaa. Clinical remission was significantly greater for patients receiving risankizumab-rzaa compared to placebo.

Skyrizi has not been studied in combination with other biologic disease-modifying agents (e.g., TNF inhibitors, interleukin receptor antagonists), targeted synthetic disease modifying anti-rheumatic drugs or DMARDs (JAK inhibitors), or phosphodiesterase-4 (PDE4) inhibitors (Otezla) due to an increased risk of infection and increased immunosuppression. As such, use of Skyrizi in combination with other biologic agents, targeted synthetic DMARDs, or Otezla is not recommended.

References

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2. Lichtenstein GR, Loftus EV, Isaacs KL, et al. ACG clinical guideline: management of Crohn's disease in adults. AJG. 2018 May; 113 (4): 481-517

3. Feuerstein, JD, Isaacs KL, Yecheskel Y, et al. AGA Clinical Practice Guidelines on the Management of Moderate to Severe Ulcerative Colitis. Gastroenterology. 2020 April; 158 (5):1450 - 1461

Skysona *(elivaldogene autotemcel)*

Priority Health Part B Step Therapy: No

Additional Priority Health Part B Criteria: Yes

Skysona is a lentiviral vector (LVV)-based autologous hematopoietic stem cell gene therapy indicated as a single dose per lifetime, to slow the progression of neurological dysfunction in pediatric patients who are assigned male at birth and diagnosed with cerebral adrenoleukodystrophy (CALD). CALD is a rare neurologic disease caused by mutations in the ABCD1 gene that leads to a buildup of VLCFA causing inflammation and damage to the brain.

The possibility of adrenoleukodystrophy (ALD) may be raised by clinical signs or symptoms, family history of ALD, or a positive newborn screen. The VLCFA panel is highly sensitive for detecting ALD and is the appropriate first step in the diagnosis. If VLCFA levels are elevated or if the ratios of VLCFA are abnormal, genetic testing for mutations of the ABCD1 gene should be performed to confirm the diagnosis. individuals with confirmed ALD should undergo neuroimaging of the brain using MRI at the time of diagnosis. In symptomatic males with cerebral disease, MRI demonstrates abnormal demyelination in cerebral white matter.

Allogeneic hematopoietic stem cell transplantation (HSCT) may delay progression of childhood CALD however, there are limitations. HSCT is only indicated for patients in early stages of disease who show evidence of central nervous system involvement but no neurological symptoms. The most successful outcomes are reported in patients who received cells from human leukocyte antigen (HLA)-identical, related donors unaffected with the disorder. Also note that allogeneic HCT is a major procedure that carries significant risks, including infection and graft-versus-host disease.

References:

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Soliris *(eculizumab)*

Priority Health Part B Step Therapy: Yes

Additional Priority Health Part B Criteria: Yes

Soliris (eculizumab) is a complement inhibitor indicated for the treatment of multiple indications involving the complement system including neuromyelitis optica spectrum disorder (NMOSD), generalized myasthenia gravis (gMG) in patients who are anti-acetylcholine receptor antibody positive (AChR-Ab+), atypical hemolytic uremic syndrome (aHUS), and paroxysmal nocturnal hemoglobinuria (PNH). Soliris has not been studied and there is no data to support use in combination with certain other medications used for NMOSD, MG, aHUS, or PHN (except danicopan).

The NMOSD diagnostic criteria for adults include at least 1 core clinical characteristic (optic neuritis, acute myelitis, area postrema syndrome, acute brainstem syndrome, symptomatic narcolepsy or acute diencephalic clinical syndrome with NMOSD-typical diencephalic MRI lesions, or symptomatic cerebral syndrome with NMOSD-typical brain lesions) and detection of AQP4-immunoglobulin G antibodies. Treatments for relapse prevention in NMOSD include immunosuppressants (corticosteroids, azathioprine, mycophenolate, methotrexate, cyclosporine, and tacrolimus), B cell depleting agents (rituximab and inebilizumab (Uplizna)), interleukin-6 signaling blocking agents (satralizumab (Enspryng)), and complement blocking agents (Soliris, Ultomiris). The European Federation of the Neurological Societies recommend azathioprine and rituximab as first-line therapy and cyclophosphamide or mycophenolate as second-line therapy for NMOSD. The NMOSD Delphi Consensus Statements recommend Enspryng, Uplizna, or Soliris following failure of

existing treatments. Soliris was studied in patients with at least 1 attack in the previous 12 months and with an Expanded Disability Status Scale score of 7 or less. Attacks were significantly reduced with Soliris compared with placebo.

The International Consensus Guidance for Management of MG recommends a nonsteroidal immunosuppressive (IS) agent (azathioprine, cyclosporine, e.g.) be used initially with or without corticosteroids in certain patients. Azathioprine can reverse symptoms in most patients, but the effect is delayed by 4 to 8 months. Maximum improvement with cyclosporine is achieved after 6 months. Most patients treated with cyclophosphamide become asymptomatic after 1 year. Once treatment goals are achieved and maintained for at least 6 months, the IS dose is tapered slowly to the minimal effective dose.

Vyvgart (efgartigimod) is a neonatal Fc receptor blocker also approved for the treatment of gMG in patients with AChR-Ab+ disease. Soliris was studied in patients with an MG-Activities of Daily Living (MG-ADL) total score of 6 or more and found to have significantly improved the MG-ADL score compared with placebo. The 2020 Update to the guidance recommends Soliris be considered in the treatment of severe, refractory, AChR-Ab+ gMG.

AHUS consists of acute hemolytic anemia with fragmented red blood cells (microangiopathic hemolytic anemia), thrombocytopenia, and acute kidney injury. Mutations in complement genes, or antibodies to their protein products, result in unregulated activity of the alternate complement pathway, endothelial injury, and TMA (lesions in the kidneys and other organs). Signs of TMA include increases in serum LDH and serum creatinine levels and a decrease in platelet count. aHUS is diagnosed with laboratory and clinical aspects along with exclusion of other causes of HUS and thrombotic thrombocytopenic purpura.

PNH is a hematopoietic stem cell disorder caused by a gene mutation that leads to abnormal red blood cells. Flow cytometry is the method of choice for identifying cells deficient in GPI-linked proteins and is the gold standard test to confirm the diagnosis of PNH. In PNH, thrombotic tendencies can occur in the extremities and atypical locations, such as hepatic portal (Budd-Chiari Syndrome), splenic, or mesenteric veins. Treatment options include supportive care (e.g. red blood cell transfusion), allogeneic hematopoietic stem cell transplantation, and complement therapy. Consider discontinuation of complement inhibitor treatment in the absence of clinical benefit.

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Spevigo *(spesolimab-sbzo)* 450 MG/7.5 ML VIAL

Priority Health Part B Step Therapy: Yes

Additional Priority Health Part B Criteria: Yes

There are various types of psoriasis including plaque, pustular, guttate, inverse and erythrodermic. Generalized pustular psoriasis (GPP) is a rare and potentially life-threatening subtype of pustular psoriasis characterized by flares of widespread, painful, neutrophil-containing pustules. Patients can appear ill with systemic symptoms such as fever, fatigue, nausea, and headache.

The European Rare and Severe Psoriasis Expert Network (ERASPEN) consensus criteria are used to help define and diagnose GPP. ERASPEN defines GPP as primary, sterile,

macroscopically visible pustules occurring on non-acral skin and not within psoriasis plaques. GPP can occur with or without systemic inflammation and with or without psoriasis vulgaris. ERASPEN states that GPP should only be diagnosed if it has relapsed at least once or when it persists for more than 3 months.

Goals of treatment of GPP are to improve pustules, alleviate systemic symptoms, and minimize risk of life-threatening complications. There are no standard guidelines for treatment of GPP. Oral retinoids (e.g., acitretin), cyclosporine, methotrexate, and various biologics including tumor necrosis factor (TNF) inhibitors such as infliximab are recommended first-line for GPP in the Japanese guidelines for the treatment of GPP (2018), a 2012 consensus statement from the NPF Medical Board, and joint guidelines on psoriasis from the American Academy of Dermatology and NPF (2019, 2020). More severe, acute GPP flares require faster-acting therapies including cyclosporine, infliximab, interleukin (IL-17) and (IL-23) biologics. Cyclosporine and infliximab have a long-standing history for the treatment of GPP and are supported by the above guidelines.

Spevigo for GPP flares was evaluated in the Effisayil-1 trial. Patients had a diagnosis of GPP per the ERASPEN diagnostic criteria and presented with a GPP flare of moderate to severe intensity defined by the following: a GPPPGA total score of 3 or more, new or worsening pustules, GPPPGA pustulation sub-score of 2 more, and 5% more of body-surface area with erythema and the presence of pustules. Participants received a single 900 mg intravenous (IV) dose of Spevigo. Participants could then receive an additional open-label, IV dose of Spevigo on day 8, an open-label, IV dose of Spevigo as a rescue medication after day 8, or both, and were followed to week 12. Subsequent flares were treated with standard of care therapy per the physician's discretion.

Per its prescribing information, the recommended dose of Spevigo is a single 900 mg dose administered by IV infusion to treat a GPP flare. If flare symptoms persist, an additional IV 900 mg dose may be given one week after the initial dose. There is no literature supporting the continued use of the Spevigo intravenous (IV) formulation as maintenance treatment for prevention or control of GPP flares.

References

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Spinraza *(nusinersen sodium)*

Priority Health Part B Step Therapy: Yes

Additional Priority Health Part B Criteria: Yes

Spinraza (nusinersen) intrathecal injection is a survival motor neuron-2 (SMN2)-directed antisense oligonucleotide indicated for the treatment of spinal muscular atrophy (SMA) in pediatric and adult patients. Currently, there are no compendia supported uses for this therapy outside the FDA-indication(s).

Currently, there are no guidelines regarding the treatment of spinal muscular atrophy. Evrysdi (risdiplam) for oral solution is a survival of motor neuron 2 (SMN2) splicing modifier also indicated for the treatment of SMA in pediatric and adult patients. It is a systemic therapy administered by mouth and is the least invasive treatment of SMA approved by the US Food and Drug Administration (FDA). In the study of Evrysdi, outcomes were better than those predicted from the natural history of SMA disease progression.

Spinraza was studied in presymptomatic SMA patients who had a genetic diagnosis of 5q SMA and 2 or 3 copies of SMN2.

References

1. Spinraza [Package Insert]. Cambridge, MA; Biogen Inc.: 2016

2. Evrysdi [Package Insert]. South San Francisco, CA; Genentech, Inc.: 2024

Spravato *(esketamine)*

Priority Health Part B Step Therapy: Yes

Additional Priority Health Part B Criteria: Yes

This policy was created after evaluating the Food and Drug Administration (FDA)-approved prescribing information and CMS-approved compendia which include:

- Micromedex DrugDex
- American Hospital Formulary Service- Drug Information (AHFS-DI)
- Lexi-Drugs
- Clinical Pharmacology

Spravato is a non-competitive N-methyl D-aspartate (NMDA) receptor antagonist approved for its role in certain depression indications, including treatment-resistant depression and major depressive disorder with acute suicidal ideation.

Although there is not an official consensus for the definition of treatment-resistant depression (TRD), many treatment models consider TRD as the inadequate response to at least 2 adequate trials of antidepressant pharmacotherapy. Initial treatment options include but are not limited to selective-serotonin reuptake inhibitors (SSRIs) [ex. sertraline,

fluoxetine, paroxetine], serotonin-norepinephrine reuptake inhibitors (SNRIs) [ex. venlafaxine, desvenlafaxine, duloxetine], norepinephrine-dopamine reuptake inhibitors (NDRIs) [bupropion], and tricyclic antidepressants (TCAs) [ex. amitriptyline, nortriptyline].

Antidepressants and psychotherapy are recommended first-line options to treat depression by The American Psychiatry Association guidelines for the treatment of depression (2010) and The American Psychological Association clinical practice guideline for the treatment of depression (2019). In general, guidelines confirm that adequate treatment with an antidepressant for at least 4 to 6 weeks is necessary before conclusion of inadequate or no response to the medication. A change in treatment should be considered for patients who have not fully responded to an adequate acute phase treatment over enough time which is generally 4 to 8 weeks. Changes in treatment can include optimizing the dose of the initial medication, changing to a different medication, or combining medications. Following any change in treatment, if at least a moderate improvement in symptoms is not observed after an additional 4 to 8 weeks of treatment, the diagnosis should be reappraised, side effects assessed, complicating comorbid conditions and psychosocial factors reviewed, and the treatment plan adjusted. For some patients with a partial response to treatment, extending the trial for 4 to 8 weeks could allow some patients to response more fully. For those with treatment-resistant depression, combined treatment is also recommended. Recommended augmentation strategies include addition of one of the following agents to a first-line antidepressant: antipsychotics [ex. aripiprazole, olanzapine, quetiapine, risperidone], lithium, or thyroid hormone (T3) [ex. liothyronine].

Support for the contents of the policy can be found in current and widely used treatment guidelines or clinical literature as well as the manufacturer's prescribing information.

References

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5. American Psychological Association. (2019). Clinical practice guideline for the treatment of depression across three age cohorts. 2019.

6. American Psychiatric Association. Arlington (VA): Practice Guidelines for the Assessment and Treatment of Patients With Suicidal Behaviors. November 2010

Stelara *(ustekinumab)* IV 130 mg/26 ml vial
Priority Health Part B Step Therapy: Yes
Additional Priority Health Part B Criteria: Yes

Stelara is a monoclonal antibody that inhibits interleukin (IL)-12 and IL-23 and is an IL-17 receptor A antagonist indicated for several inflammatory conditions including Plaque Psoriasis (PsO), Psoriatic Arthritis (PsA), Ulcerative Colitis (UC) and Crohn's Disease (CD).

Per the 2018 American College of Rheumatology (ACR)/National Psoriasis Foundation (NPF) guidelines, methotrexate, sulfasalazine, cyclosporine, and leflunomide may be used in patients with non-severe psoriatic arthritis and have robust safety and efficacy evidence to support their use. If initial treatment is not sufficient, switching to a biologic (infliximab, adalimumab, Enbrel, Simponi Aria, Skyrizi) or a Janus kinase (JAK) inhibitor (Rinvoq, Xeljanz) is recommended.

The 2020 Joint AAD-NPF guidelines (non-biologic) recommend methotrexate, cyclosporine, and acitretin. Methotrexate and cyclosporine are category A recommendations, whereas acitretin is a category B recommendation. The 2019 Joint AAD-NPF guidelines (biologics) recommend (category A) the use of biologics in treating psoriasis but do not suggest one agent over another. Tumor necrosis factor (TNF) inhibitors, interleukin-12/23, IL-23, and IL-17 inhibitors have all shown efficacy in this condition. These include infliximab, adalimumab, Enbrel, Skyrizi, Stelara and Cosentyx. Otezla is also a recommended treatment option included in the guidelines.

The 2018 American College of Gastroenterology (ACG) guidelines recommend mercaptopurine, azathioprine, and methotrexate in symptomatic CD despite prior corticosteroid use. TNF inhibitors (e.g., adalimumab) are effective in those with inadequate response to these initial therapies. Other biologic or targeted synthetic disease-modifying antirheumatic drugs (b/tsDMARDs) are not addressed by the guidelines, however these agents have since been FDA-approved for use in this condition.

The American Gastroenterological Association (AGA) guidelines for managing moderate to severe ulcerative colitis (UC) recommend that if a drug (excluding corticosteroids and cyclosporine) is effective in inducing remission or response, it should be continued for maintaining remission. For patients who have achieved remission, typically induced with corticosteroids, the panel suggests using thiopurine monotherapy rather than no treatment for maintenance. For induction of remission, the panel recommends biologic monotherapy over thiopurine. However, the panel does not make a specific recommendation for or against using biologic monotherapy over thiopurine monotherapy for maintaining remission.

There is limited data on the concurrent use of Stelara with other biologic agents, targeted synthetic DMARDs (e.g., JAK inhibitors), and phosphodiesterase-4 (PDE4) inhibitors (Otezla). Given the absence of strong clinical evidence and the potential for increased infection risk, it is not recommended to use Stelara in combination with these agents.

The Food and Drug Administration (FDA) considers biosimilars to be highly similar with no clinically meaningful differences to the biologic reference product. Biosimilars are considered safe and effective and provide an option to increase access to lifesavings drugs at lower costs. The FDA and current treatment guidelines do not favor one product (biologic or biosimilar) over another.

Step therapy is applied to certain Part B drugs, biologics, or biosimilars in a way that lowers costs and improves the quality of care for Medicare beneficiaries per the Centers for Medicare & Medicaid Services (CMS) guidance.

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Steqeyma IV *(ustekinumab- stba)*

Priority Health Part B Step Therapy: Yes

Additional Priority Health Part B Criteria: Yes

Steqeyma is a biosimilar to Stelara. It has been approved by the FDA for all indications of its reference biologic. The FDA has also provisionally determined Steqeyma to be interchangeable with Stelara. Ustekinumab (including the biosimilars and reference product) is a monoclonal antibody that inhibits interleukin (IL)-12 and IL-23 and is indicated in several inflammatory conditions including Ulcerative Colitis (UC) and Crohn's Disease (CD).

The Food and Drug Administration (FDA) considers biosimilars to be highly similar with no clinically meaningful differences to the biologic reference product. Biosimilars are considered safe and effective and provide an option to increase access to lifesavings drugs

at lower costs. The FDA and current treatment guidelines do not favor one product (biologic or biosimilar) over another.

There is limited data on the concurrent use of ustekinumab with other biologic agents, targeted synthetic DMARDs (e.g., JAK inhibitors), and phosphodiesterase-4 (PDE4) inhibitors (Otezla). Given the absence of strong clinical evidence and the potential for increased infection risk, it is not recommended to use ustekinumab in combination with these agents.

Step therapy is applied to certain Part B drugs, biologics, and biosimilars in a way that lowers costs and improves the quality of care for Medicare beneficiaries per the Centers for Medicare & Medicaid Services (CMS) guidance.

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Stimufend (pegfilgrastim-fpgk)

Priority Health Part B Step Therapy: Yes

Additional Priority Health Part B Criteria: No

Hematopoietic growth factors are defined by their ability to promote proliferation and differentiation of hematopoietic progenitors into mature blood cells. Colony-stimulating factors (CSFs) are hematopoietic growth factors that regulate the growth and differentiation of cells towards the myeloid and erythroid lineages. Myeloid growth factors (MGFs), such as granulocyte colony-stimulating factors (G-CSF), are primarily used to reduce the incidence of febrile neutropenia (FN) in patients with non-myeloid malignancies receiving myelosuppressive chemotherapy.

Chemotherapy-induced neutropenia is a major risk factor for infection-related morbidity and mortality and also a significant dose-limiting toxicity in cancer treatment. Prophylactic

treatment with granulocyte-colony stimulating factors (G-CSFs), such as filgrastim (including approved biosimilars) or pegfilgrastim is available to reduce the risk of chemotherapy-induced neutropenia. NCCN guideline recommends prophylactic G-CSF use if a patient's risk of developing FN is >20% (category 1). The American Society of Clinical Oncology (ASCO) and European Organization for Research and Treatment of Cancer (EORTC) guidelines have also adopted the 20% threshold for considering routine prophylactic MGF support. The National Comprehensive Cancer Network (NCCN) Panel defines intermediate risk as a 10% to 20% probability of developing FN or a neutropenic event that would compromise treatment. For patients receiving intermediate-risk chemotherapy regimens, the panel recommends individualized consideration of prophylactic G-CSF use based on the presence of patient-specific risk factors.

Administration of CSFs to mobilize peripheral-blood progenitor cell (PBPC) often in conjunction with chemotherapy and their administration after autologous, but not allogeneic, PBPC transplantation is the current standard of care. Among autologous PBPC patients, post-transplant G-CSF use has been associated with savings in the duration of hospitalization and overall medical costs. The use of CSFs to mobilize peripheral blood progenitor cells (PBPC) and to shorten the period of neutropenia after cytoreduction and PBPC transplantation, is well established. Individuals receiving CSFs for mobilization should have their platelet counts monitored. Filgrastim is indicated for the mobilization of hematopoietic progenitor cells into the peripheral blood for collection by leukapheresis.

Several studies have shown that CSF administration can produce modest decreases in the duration of neutropenia when begun shortly after completion of the initial induction chemotherapy for the treatment of acute myeloid leukemia (AML). CSF use can be recommended after the completion of consolidation chemotherapy because of the potential to decrease the incidence of infection and eliminate the likelihood of hospitalization in some patients receiving intensive post-remission chemotherapy. CSFs can increase the absolute neutrophil count in neutropenic patients with myelodysplastic syndromes (MDS). In the treatment of acute lymphocytic leukemia (ALL), CSFs are recommended after the initial first few days of chemotherapy of the initial induction or first post- remission course.

Current recommendations for the management of patients exposed to lethal doses of total body radiotherapy, but not doses high enough to lead to certain death due to injury to other organs, includes the prompt administration of CSF or pegylated G-CSF. Hematopoietic growth factors can increase the survival, proliferation, amplification, and differentiation of granulocyte progenitors to produce neutrophils.

References

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3. Bennett CL, Djulbegovic B, Norris LB, Armitage JO. Colony-stimulating factors for febrile neutropenia during cancer therapy. N Engl J Med. 2013; 368 (12): 1131-1139.

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Stoboclo *(denosumab-bmwo)*

Priority Health Part B Step Therapy Drug: Yes

Additional Priority Health Part B Criteria: Yes

Stoboclo is a biosimilar to Prolia. It has been approved by the FDA for all indications of its reference biologic. The FDA has also provisionally determined Stoboclo to be interchangeable with Prolia. Denosumab (including the biosimilars and reference product) is a monoclonal antibody that inhibits nuclear factor kappa-B ligand (RANKL), reducing osteoclast activity and bone resorption, which increases bone mass and strength. It also blocks RANKL from activating osteoclast-like giant cells. Denosumab is indicated for the treatment of postmenopausal women with osteoporosis at high risk for fracture as well as other conditions involving excessive bone loss, such as those caused by hormone therapy in cancer patients.

The Food and Drug Administration (FDA) considers biosimilars to be highly similar with no clinically meaningful differences to the biologic reference product. Biosimilars are considered safe and effective and provide an option to increase access to lifesavings drugs at lower costs. The FDA and current treatment guidelines do not favor one product (biologic or biosimilar) over another.

Step therapy is applied to certain Part B drugs, biologics, and biosimilars in a way that lowers costs and improves the quality of care for Medicare beneficiaries per the Centers for Medicare & Medicaid Services (CMS) guidance.

References

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2. Centers for Medicare & Medicaid Services. Medicare Advantage Prior Authorization and Step Therapy for Part B Drugs. August 7, 2018. Retrieved from

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Supprelin LA *(histrelin acetate)* implant

Priority Health Part B Step Therapy: Yes

Additional Priority Health Part B Criteria: No

Supprelin LA (histrelin acetate) is a gonadotropin releasing hormone (GnRH) agonist indicated for the treatment of children with central precocious puberty (CPP).

CPP is a condition characterized by typical biochemical and physical features of puberty, but occurs at an abnormally early age. The current standard of care for the treatment of CPP is the initiation of a GNRH agonist. This includes leuprolide monthly or every 3 month injection and histrelin implant. There are currently no clinical studies available suggesting the use of one GnRH agonist product over the other.

References

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Susvimo *(ranibizumab)*

Priority Health Part B Step Therapy: Yes

Additional Priority Health Part B Criteria: Yes

Susvimo (ranibizumab) ocular implant, a vascular endothelial growth factor (VEGF) inhibitor, is indicated for the treatment of patients with neovascular (wet) age-related macular degeneration (AMD) who have previously responded to at least two intravitreal injections of a VEGF inhibitor.

Age-related macular degeneration (AMD) is a disorder of the macula characterized by one or more of the following:

presence of at least intermediate-size drusen (≥63 µm in diameter), retinal pigment epithelium (RPE) abnormalities such as hypopigmentation or hyperpigmentation, and presence of any of the following features: geographic atrophy of the RPE, choroidal neovascularization ([CNV] exudative, wet), polypoidal choroidal vasculopathy (PCV), reticular pseudodrusen, or retinal angiomatous proliferation. Age-related macular degeneration is a

leading cause of severe, irreversible vision impairment in developed countries. The main risk factors for the development of advanced AMD are increasing age, ethnicity (i.e., Caucasian) and family history. The Age-Related Macular Degeneration Preferred Practice Pattern Guideline supports the use of antioxidant vitamins and minerals for slowing the progression to later stages of AMD, intravitreal injection of anti-VEGF agents, photodynamic therapy (PDT), and laser photocoagulation surgery to treat neovascular AMD. The VEGF inhibitors have demonstrated improved visual and anatomic outcomes compared with other therapies. Anti-VEGF therapies have become first-line therapy for treating and stabilizing most cases of neovascular AMD and a Cochrane systematic review demonstrates the effectiveness of these agents to maintain visual acuity. Guidelines recommend EyleaTM, Avastin®, VabysmoTM, or Lucentis for treatment. The guidelines have not been updated with Beovu®, Byooviz, and Susvimo.

Ranibizumab intravitreal injection implant (n=248) was equivalent to ranibizumab intravitreal injection (n=167) for the change from baseline in distance Best Corrected Visual Acuity (BCVA) score averaged over weeks 36 and 40 measured using the Early Treatment Diabetic Retinopathy Study (ETDRS) visual acuity chart at a starting distance of 4 meters (0.2 vs 0.5; treatment difference, -0.3 [95% CI, -1.7 to 1.1]) in the randomized ARCHWAY trial in patients with neovascular age-related macular degeneration. The study included patients who had received a median of 4 doses of anti-VEGF intravitreal agents in the study eye with demonstrated response prior to study treatment.

References

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2. Flaxel CJ, Adelman RA, Bailey ST, et al. Age-related macular degeneration preferred practice pattern. Ophthalmology. 2020 Jan (updated March 2022); 127 (1): P1 - P65.

3. Clinicaltrials.gov. A Phase III Study to Evaluate the Port Delivery System With Ranibizumab Compared With Monthly Ranibizumab Injections in Participants With Wet Age-Related Macular Degeneration (Archway) (NCT04429503).

Syfovre *(pegcetacoplan)* intravitreal injection

Priority Health Part B Step Therapy: No

Additional Priority Health Part B Criteria: Yes

Syfovre (pegcetacoplan) is a complement inhibitor indicated for the treatment of geographic atrophy (GA) secondary to age-related macular degeneration (AMD). Currently, there are no compendia supported uses for this therapy outside the FDA-indication(s).

The American Academy of Ophthalmology (AAO) state that an estimated 80% of patients with AMD have non-neovascular or atrophic AMD. The neovascular form is responsible for a large fraction of the severe central visual acuity (VA) loss associated with AMD.

Diagnostic testing such as optical coherence tomography (OCT) is important in diagnosing and managing AMD. OCT defines the cross-sectional architecture of the retina, which is not possible with any other imaging technology and can aid in determining the presence of subretinal and intraretinal fluid and in documenting the degree of retinal thickening. AAO also suggests that fundus autofluorescence is helpful to demonstrate areas of geographic atrophy and monitor their progression. Outcome goals are to reverse or minimize visual loss and improve visual function.

Syfovre, given monthly or every other month (EOM), was evaluated in two Phase 3 trials, DERBY and OAKS. In these trials, reductions in geographic lesion growth ranged from 16% to 22% from baseline to 24 months with modest differences between monthly and EOM administration. In OAKS, reductions in overall geographic lesion growth ranged from 16% to 18% in the EOM group compared to 21% to 22% in the monthly group. In DERBY, reductions ranged from 11% to 16% in the EOM group versus 12% to 19% in the monthly group. In addition, Syfovre did not meet its primary outcome of change in lesion growth compared to sham at 12 months in the DERBY trial. There were no differences between the Syfovre and sham groups in outcomes measuring visual function. Adverse reactions occurred more frequently in the monthly Syfovre treatment group compared with the EOM Syfovre group with fewer rates of neovascular (wet) AMD reported with the EOM regimen (7%) compared to the monthly regimen (12%).

At this time, Syfovre has not been studied and there is no data to support use in combination with other medications used to treat GA.

References

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Tepezza *(teprotumumab-trbw)*
Priority Health Part B Step Therapy: Yes
Additional Priority Health Part B Criteria: No
Tepezza (teprotumumab-trbw) for injection is an insulin-like growth factor-1 receptor inhibitor indicated for the treatment of Thyroid Eye Disease (TED). Thyroid eye disease is also known as thyroid-associated orbitopathy or Graves' orbitopathy (GO). The 2021 European Group on Graves' orbitopathy (EUGOGO) clinical practice guidelines for the medical management of Graves' orbitopathy recommend a combination of i.v. methylprednisolone and mycophenolate sodium (or mofetil) as first-line treatment for moderate-to-severe and active GO with the optimal regimen being a cumulative dose of 4.5 g of i.v. methylprednisolone given in 12 weekly infusions (six infusions of 0.5 g, followed by six infusions of 0.25 g). Alternatively, in most severe cases and constant/inconstant diplopia, monotherapy with higher cumulative doses not exceeding 8 g can be used. Second-line treatment options include a second course of i.v. methylprednisolone monotherapy, oral prednisone/prednisolone combined with either cyclosporine or azathioprine, orbital radiotherapy combined with oral or i.v. glucocorticoids, teprotumumab, rituximab, and tocilizumab. If treated with oral glucocorticoids, treatment is recommended to start with either with a fixed dose of 100 mg prednisone/prednisolone or 1 mg/kg bodyweight and tapered down by 5 to 10 mg each week until withdrawal (over 4 to 6 months).
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Testopel *(testosterone)* implant
Priority Health Part B Step Therapy: Yes
Additional Priority Health Part B Criteria: Yes
Testopel is an androgen indicated for testosterone replacement therapy in adult males for conditions associated with a deficiency or absence of endogenous testosterone: primary hypogonadism (congenital or acquired) and hypogonadotropic hypogonadism (congenital or acquired). Per the 2018 Endocrine Society Clinical Practice guideline, testosterone therapy is recommended in hypogonadal men to induce and maintain secondary sex characteristics and correct symptoms of testosterone deficiency. After treatment initiation, patients should

be evaluated for compliance and response to testosterone treatment, as well as adverse effects.

Testosterone levels vary diurnally and can also vary based on several factors. In accordance with FDA label and clinical practice guidelines, hypogonadism should be confirmed by ensuring serum testosterone concentrations are below the normal range on 2 or more separate mornings. Per the American Urological Association (AUA) Guideline on Evaluation and Management of Testosterone Deficiency, a total testosterone level below 300 nanograms per deciliter (ng/dL) is a reasonable cut-off to support the diagnosis of low testosterone. However, references ranges may vary per lab. In addition, the clinical diagnosis of testosterone deficiency should only be made when a patient has low total testosterone levels combined with symptoms and/or signs of low testosterone.

Per the Clinical Guideline from the American College of Physicians Testosterone Treatment in Adult Men With Age-Related Low Testosterone, clinicians should consider intramuscular rather than transdermal formulations when initiating testosterone treatment as costs are considerably lower and clinical effectiveness and harms are similar. Evidence from 20 observational studies with a mean follow-up ranging from 0.73 to 10.3 years showed no increased risk for mortality, cardiovascular events, prostate cancer, or pulmonary embolism or deep venous thrombosis. No consistent differences were observed in harms according to transdermal versus intramuscular formulations in the included observational studies that addressed the comparison. Evidence from indirect comparisons suggests no substantial differences in clinical effectiveness, benefits, or harms between intramuscular and transdermal testosterone applications, although very little evidence exists from direct comparisons of the 2 formulations.

Per the Endocrine Treatment of Gender-Dysphoric/Gender-Incongruent Persons: An Endocrine Society Clinical Practice Guideline transgender and gender diverse (TGD) persons may require medically necessary gender-affirming hormone therapy (GAHT) to achieve changes consistent with their embodiment goals, gender identity, or both. Masculinizing GAHT typically consists of testosterone. Clinical studies have demonstrated the efficacy of several different androgen preparations to induce masculinization in transgender males. Regimens to change secondary sex characteristics follow the general principle of hormone replacement treatment of male hypogonadism. Clinicians can use either parenteral or transdermal preparations to achieve testosterone values in the normal male range. The guidelines do not recommend one testosterone product over another. In general, the goal is to target serum levels of the sex steroids to match the levels associated with the individual's gender identity, although optimal target ranges have not been established

Step therapy is applied to certain Part B drugs, biologics, or biosimilars in a way that lowers costs and improves the quality of care for Medicare beneficiaries per the Centers for Medicare & Medicaid Services (CMS) guidance.

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Tezspire *(tezepelumab-ekko)*

Priority Health Part B Step Therapy: Yes

Additional Priority Health Part B Criteria: Yes

Tezspire (tezepelumab-ekko) is a thymic stromal lymphopoietin (TSLP) blocker, human monoclonal antibody (IgG2λ), indicated for the add-on maintenance treatment of severe asthma. TSLP is a cytokine involved in the asthma immune response and is over-expressed in asthma patients.

The Global Initiative for Asthma (GINA) Guidelines on difficult-to-treat and severe asthma in adolescent and adult patients recommend using type 2-targeted biologic agents as add-on for patients with exacerbations and/or poor symptom control despite taking at least high-dose inhaled corticosteroids (ICS) and long-acting beta agonist (LABA) combinations, and who have allergic or eosinophilic biomarkers or need maintenance oral corticosteroids. Type 2-inflammation is defined as blood eosinophils at least 150 microliters, fractional exhaled nitric oxide (FeNO) at least 20 parts per billion (ppb), sputum eosinophils of at least 2%, and/or asthma that is clinically allergen driven. GINA guidelines also advise treatment should be optimized prior to initiating a biologic agent. For therapy optimization, consider trials of non-biologic medications in addition to medium/high dose ICS, such as LABA, long-acting muscarinic agonists (LAMA), and leukotriene receptor antagonists (LTRA).

Tezspire has not been studied in combination with other biologic agents due to an increased risk of infection and increased immunosuppression. As such, use of Tezspire in combination with other biologic agents is not recommended.

References

1. Tezspire [Package Insert]. Sodertalje, Sweden; AstraZeneca: 2023

2. Global Initiative for Asthma. Difficult-To-Treat & Severe Asthma in adolescents and adult patients, 2023.

3. Global Initiative for Asthma. Global Strategy for Asthma Management and Prevention, 2023

Tofidence *(tocilizumab-bavi)*
Priority Health Part B Step Therapy Drug: Yes
Additional Priority Health Part B Criteria: Yes

Tofidence (tocilizumab-bavi) and Tyenne (tocilizumab-aazg) are biosimilars to Actemra (tocilizumab). Tocilizumab is an interleukin-6 inhibitor (IL-6i) indicated for multiple inflammatory conditions.

A randomized double-blind, single-dose, three-arm, parallel phase I study compared the pharmacokinetics, safety and immunogenicity of Tofidence with reference tocilizumab in healthy volunteers. A randomized, double-blind, multi-dose, three-arm parallel phase III study compared Tofidence with tocilizumab to establish equivalent efficacy and comparable pharmacokinetic, safety and immunogenicity profiles, in subjects with rheumatoid arthritis inadequately controlled by methotrexate.

The Food and Drug Administration (FDA) has determined the biosimilars to be highly similar to the reference product (Actemra) and supports the use of approved biosimilars.

Tocilizumab has not been studied in combination with other biologics or Janus Kinase (JAK) inhibitors due to an increased risk of infection and increased immunosuppression. As such, use of tocilizumab in combination with other biologic agents or JAK inhibitors is not recommended. Tocilizumab has not been studied with Otezla and has no studies to support coadministration.

Step therapy is applied to certain Part B drugs, biologics, or biosimilars in a way that lowers costs and improves the quality of care for Medicare beneficiaries per the Centers for Medicare & Medicaid Services (CMS) guidance.

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3. Clinicaltrials.gov. Comparative Study to Evaluate the Pharmacokinetics of BAT1806 vs Actemra® in Healthy Subjects. (NCT03606876) Available at: https://clinicaltrials.gov/study/NCT03606876

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https://www.cms.gov/Medicare/Health-Plans/HealthPlansGenInfo/Downloads/MA_Step_Therapy_HPMS_Memo_8_7_2018.pdf

Tremfya *(guselkumab)* IV vial

Priority Health Part B Step Therapy: Yes

Additional Priority Health Part B Criteria: Yes

Tremfya is an interleukin-23 (IL-23) inhibitor and is available in both a subcutaneous (SC) injection and an intravenous (IV) infusion. The IV formulation is currently indicated for the induction phase of ulcerative colitis treatment in adults. The SC formulation is indicated in the maintenance phase of treatment in ulcerative colitis, as well as other inflammatory conditions such as psoriatic arthritis and plaque psoriasis.

The 2019 American College of Gastroenterology (ACG) guidelines for ulcerative colitis (UC) recommend that management of UC be guided by the specific diagnosis, disease activity, and disease prognosis.

Both the 2019 ACG guidelines and the 2020 American Gastroenterological Association (AGA) guidelines have recommendations for the induction of remission in moderate to severely active UC that include tumor necrosis factor (TNF) inhibitors, oral 5-aminisalicylates, oral budesonide, and oral systemic corticosteroids. Recommendation for maintenance of remission for moderate to severe disease also include several drug classes including interleukin 12/23 therapies (ustekinumab), vedolizumab, TNF inhibitors, Janus kinase (JAK) inhibitors, and immunomodulators (thiopurines, methotrexate).

Per the 2020 AGA guidelines for managing moderate to severe ulcerative colitis (UC), if a drug (excluding corticosteroids and cyclosporine) is effective in inducing remission or response, it should be continued for maintaining remission. For patients who have achieved remission, typically induced with corticosteroids, the panel suggests using thiopurine monotherapy rather than no treatment for maintenance. For induction of remission, the panel recommends biologic monotherapy over thiopurine. However, the panel does not make a specific recommendation for or against using biologic monotherapy over thiopurine monotherapy for maintaining remission.

There is limited data on the concurrent use of Tremfya with other biologic agents, targeted synthetic DMARDs (e.g., JAK inhibitors), and phosphodiesterase-4 (PDE4) inhibitors (Otezla). Given the absence of strong clinical evidence and the potential for increased infection risk, it is not recommended to use Tremfya in combination with these agents.

The Food and Drug Administration (FDA) considers biosimilars to be highly similar with no clinically meaningful differences to the biologic reference product. Biosimilars are considered safe and effective and provide an option to increase access to lifesavings drugs at lower costs. The FDA and current treatment guidelines do not favor one product (biologic or biosimilar) over another.

Step therapy is applied to certain Part B drugs, biologics, or biosimilars in a way that lowers costs and improves the quality of care for Medicare beneficiaries per the Centers for Medicare & Medicaid Services (CMS) guidance.

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2. Feuerstein JD, Isaacs KL, Schneider Y, et al. AGA clinical practice guidelines on the management of moderate to severe ulcerative colitis. Gastroenterology. 2020; 158: 1450 - 61. 29.

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Tyenne *(tocilizumab-aazg)*

Priority Health Part B Step Therapy Drug: Yes

Additional Priority Health Part B Criteria: Yes

Tyenne (tocilizumab-aazg) is a biosimilar to Actemra (tocilizumab).

Tocilizumab (including biosimilars) is an interleukin-6 inhibitor (IL-6i) indicated for multiple inflammatory conditions, including rheumatoid arthritis (RA), giant cell arteritis, and juvenile idiopathic arthritis (JIA). The Food and Drug Administration (FDA) has determined Tyenne to be highly similar to its reference product, and supports the use of approved biosimilars.

Guidelines favor the use of biologic DMARDs (bDMARD) in those with moderate or high disease activity despite previous conventional synthetic (csDMARD) trials for RA and JIA. Guidelines do not currently favor one bDMARD class over another, however tumor necrosis factor inhibitors (TNFis) have the most documented safety and efficacy profiles. Infliximab agents (including Inflectra and Renflexis) are TNFis that work to block the activity of TNF, a cytokine that causes inflammation. It is this inflammation that is the primary target in the treatment of conditions like RA and JIA.

For patients with severe COVID-19 requiring high-flow oxygen or more intensive respiratory

support, the National Institutes of Health (NIH) recommends the use of tocilizumab in combination with dexamethasone (or an equivalent glucocorticoid). While other immunomodulatory agents have shown potential benefit in severely or critically ill patients, their routine use is not currently recommended due to a lack of clear advantage over established therapies such as JAK inhibitors (e.g., baricitinib) or IL-6 inhibitors (e.g., tocilizumab). However, in cases where baricitinib or tocilizumab are unavailable, the NIH COVID-19 Treatment Guidelines Panel suggests abatacept or infliximab as reasonable alternatives for patients who meet the appropriate clinical criteria.

The European League Against Rheumatism (EULAR) recommendations for the management of large vessel vasculitis (LVV) include immediate initiation of high dose glucocorticoid therapy for induction of remission in active giant cell arteritis (GCA). Adjunctive therapy using tocilizumab is recommended in selected patients with GCA (refractory or relapsing disease, presence of an increased risk for glucocorticoid-related adverse events or complications).

Although giant cell arteritis (GCA) is characterized by granulomatous inflammation, tumor necrosis factor (TNF) inhibitors were initially considered a rational therapeutic option. However, multiple small randomized controlled trials have demonstrated that TNF inhibitors—including infliximab—do not confer clinical benefit in GCA. These agents failed to improve remission rates or provide corticosteroid-sparing effects in patients with newly diagnosed disease

In patients experiencing moderate to severe cytokine release syndrome (CRS), with or without concurrent immune effector cell–associated neurotoxicity syndrome (ICANS), the standard therapeutic approach involves administration of tocilizumab in combination with glucocorticoids. This regimen has become foundational in the management of CAR T-cell–associated toxicities, particularly in cases marked by escalating inflammatory responses. While several investigational strategies aimed at targeting inflammatory cytokines are currently under evaluation, their impact on CAR T-cell efficacy and the progression of ICANS remains uncertain.

Tocilizumab has not been studied in combination with other biologics or Janus Kinase (JAK) inhibitors due to an increased risk of infection and increased immunosuppression. As such, use of tocilizumab in combination with other biologic agents or JAK inhibitors is not recommended. Tocilizumab has not been studied with Otezla and has no studies to support coadministration.

Step therapy is applied to certain Part B drugs, biologics, or biosimilars in a way that lowers costs and improves the quality of care for Medicare beneficiaries per the Centers for Medicare & Medicaid Services (CMS) guidance.

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Tyvaso *(treprostinil)* inhalation

Priority Health Part B Step Therapy: Yes

Additional Priority Health Part B Criteria: Yes

Tyvaso (treprostinil) is a prostacyclin mimetic indicated for the treatment of pulmonary arterial hypertension (PAH; WHO Group 1) and pulmonary hypertension associated with interstitial lung disease (PH-ILD; WHO Group 3). Studies with Tyvaso establishing effectiveness in PAH predominately included patients with NYHA Functional Class III symptoms and etiologies of idiopathic or heritable PAH or PAH associated with connective tissue diseases (CTD). The study with Tyvaso establishing effectiveness in PH-ILD predominately included patients with etiologies of idiopathic interstitial pneumonia (IIP) inclusive of idiopathic pulmonary fibrosis (IPF), combined pulmonary fibrosis and emphysema (CPFE), and WHO Group 3 connective tissue disease (CTD).

The 2022 European Society of Cardiology and the European Respiratory Society (ESC/ERS) Guidelines for the diagnosis and treatment of pulmonary hypertension (PH) recommend right heart catheterization as the gold standard for diagnosing and classifying PH as well as assessing cardiopulmonary hemodynamics during exercise. Patients with PH are classified based upon etiology and mechanism into groups including group 1 (pulmonary arterial hypertension), group 2 (pulmonary hypertension associated with left heart disease), group 3 (pulmonary hypertension associated with lung diseases and/or hypoxia), group 4 (pulmonary hypertension associated with chronic pulmonary artery obstruction), and group 5 (pulmonary hypertension with unclear and/or multifactorial mechanisms).

For patients with PAH presenting at low or intermediate risk, the guidelines recommend initial combination therapy with a phosphodiesterase 5 inhibitor (PDE5i) and an endothelin receptor antagonist (ERA). PDE5is include sildenafil and tadalafil. ERAs include ambrisentan, bosentan, and macitentan. Initial treatment with oral triple-combination therapy in patients who present at low or intermediate risk is not recommended due to the current lack of evidence supporting this strategy.

For patients with WHO Group 3 PH, the guidelines recommend initially optimizing the treatment of the underlying lung disease. This includes the use of supplementary oxygen and non-invasive ventilation when necessary, as well as participation in pulmonary rehabilitation programs. For those with ILD and PH, inhaled treprostinil may be considered based on the INCREASE study findings. However, studies on the use of drugs approved for PAH in patients with PH associated with chronic obstructive pulmonary disease (COPD) or emphysema have shown mixed results. Due to the lack of large randomized trials, there is insufficient evidence to support the general use of medication approved for PAH in patients with COPD and PH.

The most widely used measure of exercise capacity in PH centers is the 6-minute walking test (6MWT). The 6MWT is easy to perform, inexpensive, and widely accepted by many as an important and validated variable in assessment of PH; and the change in the 6-minute walking distance (6MWD) is one of the most commonly used parameters in PAH clinical trials. In the studies of adults with pulmonary hypertension due to interstitial lung disease, inhaled treprostinil significantly improved the change in 6 minute walk distance (6WMD) from baseline to week 16 compared with placebo.

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Tzield *(teplizumab-mzww)* vial
Priority Health Part B Step Therapy: No
Additional Priority Health Part B Criteria: Yes
Tzield (teplizumab-mzwv) injection is a CD3-directed antibody indicated to delay the onset of Stage 3 type 1 diabetes (T1D) in adults and pediatric patients aged 8 years and older with Stage 2 T1D, to be given with dosing based on body surface area and administered once daily for 14 days. Currently, there are no compendia supported uses for this therapy outside the FDA-indication(s). The manufacturer recommends Stage 2 T1D be confirmed by documenting at least two positive pancreatic islet autoantibodies in those who have dysglycemia without overt hyperglycemia using an oral glucose tolerance test (OGTT) or alternative method if appropriate and OGTT is not available. In patients who meet criteria for Stage 2 type 1 diabetes diagnosis, the patient's clinical history should be confirmed to not suggest type 2 diabetes. Tzield was studied in patients 8 to 49 years of age with Stage 2 T1D. The American Diabetes Association (ADA) “Standards of Care in Diabetes” defines stage 2 as individuals with both dysglycemia on OGTT and at least two listed pancreatic islet autoantibodies. Pancreatic islet autoantibodies of study patients include: glutamic acid decarboxylase 65 (GAD) autoantibodies, insulin autoantibody (IAA), insulinoma-associated antigen 2 autoantibody (IA-2A), zinc transporter 8 autoantibody (ZnT8A), and islet cell autoantibody (ICA). Dysglycemia in the study included fasting blood glucose greater than 110mg/dL and less than 126 mg/dL (5.6–6.9 mmol/L), 2 hour glucose greater or equal to 140 mg/dL and less than 200 mg/dL (7.8–11.0 mmol/L), or 30, 60, or 90 minute value on OGTT greater than or equal to 200 mg/dL (11.1 mmol/L or greater). ADA guidelines state that unless there is a clear clinical diagnosis, diagnosis requires two abnormal screening test results.
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Udenyca *(pegfilgrastim-cbqv)*
Priority Health Part B Step Therapy: Yes
Additional Priority Health Part B Criteria: No
Hematopoietic growth factors are defined by their ability to promote proliferation and differentiation of hematopoietic progenitors into mature blood cells. Colony-stimulating

factors (CSFs) are hematopoietic growth factors that regulate the growth and differentiation of cells towards the myeloid and erythroid lineages. Myeloid growth factors (MGFs), such as granulocyte colony-stimulating factors (G-CSF), are primarily used to reduce the incidence of febrile neutropenia (FN) in patients with non-myeloid malignancies receiving myelosuppressive chemotherapy.

Chemotherapy-induced neutropenia is a major risk factor for infection-related morbidity and mortality and also a significant dose-limiting toxicity in cancer treatment. Prophylactic treatment with granulocyte-colony stimulating factors (G-CSFs), such as filgrastim (including approved biosimilars) or pegfilgrastim is available to reduce the risk of chemotherapy-induced neutropenia. NCCN guideline recommends prophylactic G-CSF use if a patient's risk of developing FN is >20% (category 1). The American Society of Clinical Oncology (ASCO) and European Organization for Research and Treatment of Cancer (EORTC) guidelines have also adopted the 20% threshold for considering routine prophylactic MGF support. The National Comprehensive Cancer Network (NCCN) Panel defines intermediate risk as a 10% to 20% probability of developing FN or a neutropenic event that would compromise treatment. For patients receiving intermediate-risk chemotherapy regimens, the panel recommends individualized consideration of prophylactic G-CSF use based on the presence of patient-specific risk factors.

Administration of CSFs to mobilize peripheral-blood progenitor cell (PBPC) often in conjunction with chemotherapy and their administration after autologous, but not allogeneic, PBPC transplantation is the current standard of care. Among autologous PBPC patients, post-transplant G-CSF use has been associated with savings in the duration of hospitalization and overall medical costs. The use of CSFs to mobilize peripheral blood progenitor cells (PBPC) and to shorten the period of neutropenia after cytoreduction and PBPC transplantation, is well established. Individuals receiving CSFs for mobilization should have their platelet counts monitored. Filgrastim is indicated for the mobilization of hematopoietic progenitor cells into the peripheral blood for collection by leukapheresis.

Several studies have shown that CSF administration can produce modest decreases in the duration of neutropenia when begun shortly after completion of the initial induction chemotherapy for the treatment of acute myeloid leukemia (AML). CSF use can be recommended after the completion of consolidation chemotherapy because of the potential to decrease the incidence of infection and eliminate the likelihood of hospitalization in some patients receiving intensive post-remission chemotherapy. CSFs can increase the absolute neutrophil count in neutropenic patients with myelodysplastic syndromes (MDS). In the treatment of acute lymphocytic leukemia (ALL), CSFs are recommended after the initial first few days of chemotherapy of the initial induction or first post- remission course.

Current recommendations for the management of patients exposed to lethal doses of total body radiotherapy, but not doses high enough to lead to certain death due to injury to other organs, includes the prompt administration of CSF or pegylated G-CSF.

Hematopoietic growth factors can increase the survival, proliferation, amplification, and differentiation of granulocyte progenitors to produce neutrophils.

References

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2. Aapro MS, Bohlius J, Cameron DA, et al.; European Organization for Research and Treatment of Cancer. 2010 update of EORTC guidelines for the use of granulocyte-colony stimulating factor to reduce the incidence of chemotherapy-induced febrile neutropenia in adult patients with lymphoproliferative disorders and solid tumors. Eur J Cancer. 2011; 47 (1): 8-32. 2.

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Ultomiris (ravulizumab-cqvz)

Priority Health Part B Step Therapy: Yes

Additional Priority Health Part B Criteria: Yes

Ultomiris (ravulizumab) is a complement inhibitor indicated for the treatment of multiple indications involving the complement system including neuromyelitis optica spectrum disorder (NMOSD) in patients who are anti-aquaporin-4 (AQP4) antibody positive, generalized myasthenia gravis (gMG) in patients who are anti-acetylcholine receptor antibody-positive (AChR-Ab+), atypical hemolytic uremic syndrome (aHUS) and paroxysmal nocturnal hemoglobinuria (PNH). Ultomiris has not been studied and there is no data to support use in combination with Soliris, Uplizna, Enspryng, Vyvgart, Rystiggo, Zilbrysq and similar therapies for these conditions.

The NMOSD diagnostic criteria for adults include at least 1 core clinical characteristic (optic neuritis, acute myelitis, area postrema syndrome, acute brainstem syndrome, symptomatic narcolepsy or acute diencephalic clinical syndrome with NMOSD-typical diencephalic MRI lesions, or symptomatic cerebral syndrome with NMOSD-typical brain lesions) and detection of AQP4-immunoglobulin G antibodies. Treatments for relapse prevention in NMOSD include immunosuppressants (corticosteroids, azathioprine, mycophenolate, methotrexate, cyclosporine, and tacrolimus), B cell depleting agents (rituximab and inebilizumab (Uplizna)), interleukin-6 signaling blocking agents (satralizumab (Enspryng)),

and complement blocking agents (Soliris, Ultomiris). The European Federation of the Neurological Societies recommend azathioprine and rituximab as first-line therapy and cyclophosphamide or mycophenolate as second-line therapy for NMOSD. The NMOSD Delphi Consensus Statements recommend Enspryng, Uplizna, or Soliris following failure of existing treatments. Ultomiris did not have the NMOSD indication at the time of this publication. Ultomiris was studied in patients with at least 1 relapse in the previous 12 months and an Expanded Disability Status Scale score ≤ 7. The time to first adjudicated relapse was significantly improved with Ultomiris compared with placebo.

The International Consensus Guidance for Management of MG recommends a nonsteroidal immunosuppressive (IS) agent (azathioprine, cyclosporine, mycophenolate, methotrexate, or tacrolimus) be used initially with or without corticosteroids in certain patients. Azathioprine can reverse symptoms in most patients but the effect is delayed by 4 to 8 months. Maximum improvement with cyclosporine is achieved after 6 months. Once treatment goals are achieved and maintained for at least 6 months, taper the IS dose slowly to the minimal effective dose.

Vyvgart is a neonatal Fc receptor blocker also approved for the treatment of AChR-Ab+ gMG. Ultomiris was studied in patients with an MG-Activities of Daily Living (MG-ADL) total score ≥6 and found to have significantly improved MG-ADL score compared with placebo. The 2020 Update to the guidance recommends complement inhibitor (Soliris) be considered in the treatment of severe, refractory, AChR-Ab+ gMG.

AHUS consists of acute hemolytic anemia with fragmented red blood cells, thrombocytopenia, and acute kidney injury. Mutations or antibodies to their protein products result in unregulated activity of the alternate complement pathway, endothelial injury, and TMA (lesions in the kidneys and other organs). Signs of TMA include increases in serum LDH and serum creatinine levels and decrease in platelet count. aHUS is diagnosed with laboratory and clinical aspects along with exclusion of other causes of HUS and thrombotic thrombocytopenic purpura.

PNH is caused by a gene mutation that leads to a red blood cell deficiency. Flow cytometry is the gold standard diagnostic test for PNH. PNH causes thrombotic tendencies in the extremities and atypical locations. Treatment options may include supportive care (e.g. red blood cell transfusion) and complement therapy. Consider discontinuation of complement inhibitor treatment with no clinical benefit.

References

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Uplizna *(inebilzumab-cdon)*

Priority Health Part B Step Therapy: Yes

Additional Priority Health Part B Criteria: Yes

Uplizna (inebilizumab-cdon) is a CD19-directed cytolytic antibody indicated for the treatment of neuromyelitis optica spectrum disorder (NMOSD) in adult patients who are anti-aquaporin-4 (AQP4) antibody positive. It is also indicated for the treatment of immunoglobulin G4-related disease (IgG4-RD) in adult patients.

Treatments for relapse prevention in neuromyelitis optica spectrum disorders (NMOSD) include conventional immunosuppressants (corticosteroids, azathioprine, mycophenolate mofetil, methotrexate, cyclosporine A, tacrolimus, and mitoxantrone), B cell depleting agents (rituximab and inebulizumab), interleukin-6 signaling blocking agents (tocilizumab and satralizumab (Enspryng)), complement blocking agents (eculizumab), and intravenous immunoglobulins. The European Federation of the Neurological Societies (EFNS) guidelines on diagnosis and management of neuromyelitis optica recommend azathioprine and rituximab (a chimeric anti-CD20 monoclonal antibody) as first-line therapy.

Cyclophosphamide, mitoxantrone, or mycophenolate mofetil are recommended as second-line therapy. The NMOSD Delphi Consensus Statements recommend that eculizumab (Soliris), inebilizumab (Uplizna), or satralizumab (Enspryng) may be initiated at diagnosis, after first attack, or after relapse due to failure of existing treatments.

The goal of treatment in IgG4-RD is to reduce disease activity and prevent irreversible damage. All symptomatic patients, especially those with organ-threatening features (e.g., pancreatic pain, obstructive jaundice), should receive treatment—urgently if organ function is compromised. Treatment can also be proposed to asymptomatic patients in case of: (1) persistence of a pancreatic mass in imaging to rule out cancer, (2) persistence of liver test abnormalities (cholestasis) in case of associated IgG4-related cholangitis, and (3) in subclinical situations that could lead to severe or irreversible organ failure. Glucocorticoids are the preferred first-line medication for active IgG4-related disease, with response rates around 97–100% and a significant decrease of serum IgG4 levels. Response to initial treatment should be assessed at week 2–4 with clinical, biochemical, and morphological markers. Glucocorticoid therapy should gradually be tapered by 5 mg every two weeks. Adding immunosuppressive agents should be considered in case of disease relapse as maintenance of remission strategy, and in patients with a high risk of disease relapse, particularly in the case of multi-organ involvement. If there is no change in disease activity or the disease relapsed during the 3 months of treatment (during glucocorticoid taper or discontinuation), then immunosuppressive drugs should be added. Rituximab should be considered if patients are resistant or intolerant to high-dose glucocorticoids to maintain remission or have failed to respond to immunosuppressive therapies. Uplizna is not yet addressed in current guidelines.

Uplizna has not been studied and there is no data to support combination use with rituximab, eculizumab, Ultomiris or other similar medications.

Step therapy is applied to certain Part B drugs, biologics, or biosimilars in a way that lowers costs and improves the quality of care for Medicare beneficiaries per the Centers for Medicare & Medicaid Services (CMS) guidance.

References

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Ustekinumab IV *(unbranded)*

Priority Health Part B Step Therapy: Yes

Additional Priority Health Part B Criteria: Yes

Ustekinumab is a biosimilar to Stelara. It has been approved by the FDA for all indications of its reference biologic. The FDA has also provisionally determined ustekinumab to be interchangeable with Stelara. Ustekinumab (including the biosimilars and reference product) is a monoclonal antibody that inhibits interleukin (IL)-12 and IL-23 and is indicated in several inflammatory conditions including Ulcerative Colitis (UC) and Crohn's Disease (CD).

The Food and Drug Administration (FDA) considers biosimilars to be highly similar with no clinically meaningful differences to the biologic reference product. Biosimilars are considered safe and effective and provide an option to increase access to lifesavings drugs at lower costs. The FDA and current treatment guidelines do not favor one product (biologic or biosimilar) over another.

There is limited data on the concurrent use of ustekinumab with other biologic agents, targeted synthetic DMARDs (e.g., JAK inhibitors), and phosphodiesterase-4 (PDE4) inhibitors (Otezla). Given the absence of strong clinical evidence and the potential for increased infection risk, it is not recommended to use ustekinumab in combination with these agents.

Step therapy is applied to certain Part B drugs, biologics, and biosimilars in a way that lowers costs and improves the quality of care for Medicare beneficiaries per the Centers for Medicare & Medicaid Services (CMS) guidance.

References

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Ustekinumab-ttwe IV

Priority Health Part B Step Therapy: Yes

Additional Priority Health Part B Criteria: Yes

Ustekinumab-ttwe is a biosimilar to Stelara. It has been approved by the FDA for all indications of its reference biologic. The FDA has also provisionally determined ustekinumab-ttwe to be interchangeable with Stelara. Ustekinumab (including the biosimilars and reference product) is a monoclonal antibody that inhibits interleukin (IL)-12 and IL-23 and is indicated in several inflammatory conditions including Ulcerative Colitis (UC) and Crohn's Disease (CD).

The Food and Drug Administration (FDA) considers biosimilars to be highly similar with no clinically meaningful differences to the biologic reference product. Biosimilars are considered safe and effective and provide an option to increase access to lifesavings drugs at lower costs. The FDA and current treatment guidelines do not favor one product (biologic or biosimilar) over another.

There is limited data on the concurrent use of ustekinumab with other biologic agents, targeted synthetic DMARDs (e.g., JAK inhibitors), and phosphodiesterase-4 (PDE4) inhibitors (Otezla). Given the absence of strong clinical evidence and the potential for increased infection risk, it is not recommended to use ustekinumab in combination with these agents.

Step therapy is applied to certain Part B drugs, biologics, and biosimilars in a way that lowers costs and improves the quality of care for Medicare beneficiaries per the Centers for Medicare & Medicaid Services (CMS) guidance.

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Vegzelma *(bevacizumab-abcd)*

Priority Health Part B Step Therapy: Yes

Additional Priority Health Part B Criteria: No

Vegzelma (bevacizumab-adcd) is biosimilar to Avastin® (bevacizumab). Bevacizumab is a vascular endothelial growth factor inhibitor indicated for the treatment of multiple cancers including a) metastatic colorectal cancer, in combination with intravenous fluorouracil-based chemotherapy for first- or second-line treatment; b) metastatic colorectal cancer, in combination with fluoropyrimidine-irinotecan- or luoropyrimidine oxaliplatin-based chemotherapy for second-line treatment in patients who have progressed on a first-line bevacizumab product-containing regimen; c) Unresectable, locally advanced, recurrent or metastatic non-squamous non-small cell lung cancer, in combination with carboplatin and paclitaxel for first-line treatment; d) recurrent glioblastoma in adult; e) metastatic renal cell carcinoma in combination with interferon alfa, and more.

Myvasi (bevacizumab-awwb) is biosimilar to Avastin® (bevacizumab). Zirabev (bevacizumab-bvzr) is biosimilar to Avastin® (bevacizumab). Per NCCN guidelines, an FDA-approved biosimilar is an appropriate substitute for bevacizumab.

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Ventavis *(iloprost)* inhalation

Priority Health Part B Step Therapy: Yes

Additional Priority Health Part B Criteria: Yes

Ventavis (iloprost) inhalation solution is a prostacyclin mimetic indicated for the treatment of pulmonary arterial hypertension (PAH) (WHO Group 1) to improve a composite endpoint consisting of exercise tolerance, symptoms (NYHA Class), and lack of deterioration. Studies establishing effectiveness included predominately patients with NYHA Functional Class III-IV symptoms and etiologies of idiopathic or heritable PAH or PAH associated with connective tissue diseases.

The 2022 European Society of Cardiology and the European Respiratory Society (ESC/ERS) Guidelines for the diagnosis and treatment of pulmonary hypertension (PH) recommend right heart catheterization as the gold standard for diagnosing and classifying PH as well as assessing cardiopulmonary hemodynamics during exercise. Patients with PH are classified based upon etiology and mechanism into groups: group 1 (pulmonary arterial hypertension), group 2 (pulmonary hypertension associated with left heart disease), group 3 (pulmonary hypertension associated with lung diseases and/or hypoxia), group 4 (pulmonary hypertension associated with chronic pulmonary artery obstruction), and group 5 (pulmonary hypertension with unclear and/or multifactorial mechanisms).

For patients with PAH presenting at low or intermediate risk, the guidelines recommend initial combination therapy with a phosphodiesterase 5 inhibitor (PDE5i) and an endothelin receptor antagonist (ERA). PDE5is include sildenafil and tadalafil. ERAs include ambrisentan and bosentan. Initial treatment with oral triple-combination therapy is not recommended due to the current lack of evidence supporting this strategy.

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Veopoz *(pozelimab-bbfg)* 400 MG/2 ML vial

Priority Health Part B Step Therapy: No

Additional Priority Health Part B Criteria: Yes

Veopoz (pozelimab-bbfg) injection is a complement inhibitor indicated for the treatment of adult and pediatric patients 1 year of age and older with CD55-deficient protein-losing enteropathy (PLE), also known as CHAPLE disease to be administered 30 mg/kg once followed by 10 mg/kg as a subcutaneous injection once weekly starting on day 8. Currently, there are no compendia supported uses for this therapy outside the FDA-indication(s).

Veopoz was studied in patients with protein-losing enteropathy (PLE) with a confirmed genotype of biallelic CD55 loss-of-function mutation. Active CD55-deficient PLE was defined as low serum albumin (also referred to as hypoalbuminemia with a serum albumin concentration of ≤3.2 g/dL) with one or more of the following signs or symptoms within the previous six months: diarrhea, abdominal pain, peripheral edema, or facial edema. All study patients achieved normalization by week 12 and maintained serum albumin concentrations within normal range and throughout treatment at week 72.

Veopoz has not been studied and there is no data to support use in combination with eculizumab used to treat CD55-deficient PLE.

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Vibativ *(telavancin)*

Priority Health Part B Step Therapy: Yes

Additional Priority Health Part B Criteria: Yes

Vibativ (telavancin) is indicated for the treatment of adult patients with complicated skin and skin structure infections (SSTIs), hospital-acquired pneumonia (HAP), and ventilator-associated pneumonia (VAP) caused by susceptible methicillin-resistant staphylococcus aureus (MRSA) isolates. In hospital-acquired and ventilator-associated bacterial pneumonia, it should be reserved for use when alternative treatments are not appropriate.

The 2016 Clinical Practice Guidelines for management of adults with hospital-acquired and ventilator-associated pneumonia recommend that MRSA HAP/VAP be treated with either vancomycin or linezolid rather than other antibiotics or antibiotic combinations. Their systematic review identified 7 randomized trials that addressed the selection of antibiotics for HAP/VAP caused by MRSA. Four trials compared linezolid to vancomycin. The remaining 3 trials compared telavancin, quinupristin plus dalfopristin, or vancomycin plus rifampin to vancomycin alone.

None of the other trials demonstrated a clear superiority of an alternative antibiotic or regimen over vancomycin alone. The study comparing telavancin to vancomycin combined 2 smaller trials conducted in patients with gram-positive nosocomial pneumonia. In the combined population of 1503 patients, there were no differences in clinical cure rate, mortality, or adverse effects, although there was a trend toward increased all-cause mortality with telavancin in one of the component studies. This primarily occurred among patients with creatinine clearance values <30 mL/minute, prompting an FDA advisory panel to recommend limiting the use of telavancin to patients with creatinine clearance levels above this threshold]. Increases in serum creatinine were more common in the telavancin group.

Clinical Practice Guidelines for the Diagnosis and Management of Skin and Soft Tissue Infections: 2014 Update by The Infectious Diseases Society of America (IDSA) recommend telavancin as an option to treat streptococcal skin infections for patients with severe penicillin hypersensitivity, surgical site Infections, and cellulitis due to MRSA. For patients with severe penicillin hypersensitivity other treatment options include clindamycin, vancomycin, linezolid, daptomycin. For the management of surgical site infections, if the institution in which the operation was performed has a significant proportion of infections with MRSA or the patient has had prior MRSA infection, nasal colonization or was previously on antibiotics, the initial antibiotic should include vancomycin, linezolid, daptomycin, telavancin, or ceftaroline for MRSA coverage. Coverage for MRSA is advised in cellulitis associated with penetrating trauma, especially from illicit drug use, purulent drainage, or with concurrent evidence of MRSA infection elsewhere. Options for treatment of MRSA in those circumstances include intravenous drugs (vancomycin, daptomycin, linezolid, or telavancin) or oral therapy with doxycycline, clindamycin, or trimethoprim-sulfamethoxazole.

Telavancin was noninferior to twice-daily vancomycin based on pooled results from 2 randomized noninferiority trials in patients (n=1867) with complicated skin and skin structure infections due gram-positive bacteria, including MRSA. Overall clinical cure rates were 88.3% and 87.1% for telavancin and vancomycin, respectively, and 90.6% and 84.4% among patients with MRSA. Clinical cure rates among patients with Staphylococcus aureus bacteremia were 57.1% for telavancin compared with 54.6% for vancomycin. Upon post hoc analysis, cure rates were similar between treatment groups for specific types of complicated skin and skin structure infections (eg, abscesses, extensive cellulitis, ulcers).

References

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4. Stryjewski ME, Barriere SL, O'Riordan W, et al: Efficacy of telavancin in patients with specific types of complicated skin and skin structure infections. J Antimicrob Chemother 2012; 67(6):1496-1502.

Vivimusta *(Bendamustine)* IV

Priority Health Part B Step Therapy: Yes

Additional Priority Health Part B Criteria: No

Bendamustine is an alkylating agent with a unique mechanism indicated for the treatment of chronic lymphocytic leukemia (CLL) and indolent B-cell non-Hodgkin lymphoma (NHL) that has progressed during or within six months of treatment with rituximab or a rituximab-containing regimen.

Current National Comprehensive Cancer Network (NCCN) guidelines for the treatment of CLL recommend bendamustine (category 2A) as a viable consideration for those without del(17p)/TP53 mutation, both as a first-line and refractory treatment. TP53 deletions are associated with worse prognosis and worse outcomes on many treatment options, including bendamustine.

Bendamustine also carries a category 2A recommendation for use in NCCN B-Cell lymphoma guidelines. NCCN Guidelines do not favor one biosimilar over another and recommend any FDA-approved biosimilar can be used to treat these conditions.

Priority Health also follows LCD L37205: Chemotherapy Drugs and their Adjuncts.

References

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2. National Comprehensive Cancer Network. Chronic lymphocytic leukemia/small lymphocytic lymphoma (Version 3.2024). 2024 Mar 26.

3. National Comprehensive Cancer Network. B-Cell lymphomas (Version 2.2024). 2024 April 30.

Vyalev *(foscarbidopa and foslevodopa)*

Priority Health Part B Step Therapy Drug: Yes

Additional Priority Health Part B Criteria: Yes

Vyalev (foscarbidopa and foslevodopa) injection is a combination of prodrugs foscarbidopa and foslevodopa and is indicated for the treatment of motor fluctuations in adults with advanced Parkinson's disease (PD).

The International Parkinson and Movement Disorder Society recommends non-ergot dopamine agonists (e.g. pramipexole, ropinirole), oral levodopa preparations, selegiline, and rasagiline for early PD. Non-ergot dopamine agonists, rasagiline, and zonisamide may also be considered for adjunct therapy in early/stable PD. There are many options for treating motor fluctuations, and there is a hierarchical approach to these treatments in clinical practice. First-line options include oral and transdermal therapies (levodopa, dopamine agonists, etc.,) followed by parenteral and surgical techniques as the disease advances. All non-ergot oral and transdermal dopamine agonists, COMT and/or MAO-B inhibitors are clinically useful and remain effective options for treating motor fluctuations.

In the pivotal study with Vyalev, participants in the study were required to have a diagnosis of idiopathic PD that is levodopa-responsive, have recognizable/identifiable "Off" and "On" states (motor fluctuations), be taking a minimum of 400 milligrams per day of levodopa equivalents, and have motor symptoms inadequately controlled by current therapy (as judged by the investigator). Vyalev showed a significantly greater increase from baseline to week 12 in "on" time without troublesome dyskinesia and also a greater reduction in "off" time as compared with the oral carbidopa/levodopa treatment arm.

Vyalev also follows LCD L33794 for External Infusion Pumps.

References

1. VYALEV™ [prescribing information]. North Chicago, IL: AbbVie Inc.; October 2024

2. Clinicaltrials.gov. Study Comparing Continuous Subcutaneous Infusion Of ABBV-951 With Oral Carbidopa/Levodopa Tablets For Treatment Of Motor Fluctuations In Adult Participants With Advanced Parkinson's Disease (NCT04380142). Available at: https://clinicaltrials.gov/study/NCT04380142.

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4. Fox, S.H., Katzenschlager, R., Lim, S.-Y., et al. International Parkinson and movement disorder society evidence-based medicine review: Update on treatments for the motor symptoms of Parkinson's disease. Mov Disord. 2018; 33: 1248-1266. https://doi.org/10.1002/mds.27372.

5. Centers for Medicare & Medicaid Services. Local Coverage Determination (LCD) L33794 External Infusion Pumps

Vyepti *(eptinezumab-jjmr)*

Priority Health Part B Step Therapy: Yes

Additional Priority Health Part B Criteria: Yes

Vyepti (eptinezumab-jjmr) is indicated for the preventive treatment of migraine in adults. It is a humanized monoclonal antibody (mAb) that binds to calcitonin gene-related peptide (CGRP) ligand and blocks its binding to the receptor. Currently, there are no compendia supported uses for this therapy outside the FDA-indication(s).

The American Headache Society (AHS) states that those with migraine and poorly controlled attacks are at risk of medication overuse and are more likely to develop medication-overuse headache and chronic migraine. The overuse of medications for the acute treatment of headache may reduce the effectiveness of some preventive treatments. Measures to ensure appropriate use of acute treatments and education and lifestyle modifications should be implemented before developing a preventive treatment plan.

The AHS revised Consensus Statement (June 2021) continues to recommend adequate trials of established acute and/or preventive treatments before initiating use of newer migraine-specific acute and preventive therapies. This is in part due to cost considerations, and no published evidence supports or refutes this hierarchical approach. Additionally, there is also no robust evidence either to support or discard the combination of different migraine preventatives.

Multiple commercial CGRP antagonist products are currently available: erenumab (Aimovig), fremanezumab (Ajovy), galcanezumab (Emgality), and eptinezumab (Vyepti). Ajovy, Emgality, and Vyepti target the CGRP ligand, and Aimovig targets the CGRP receptor. A significant proportion of patients who do not achieve a 50% reduction in migraine headaches in the first 4 weeks following the initial subcutaneous (SC) dose of a CGRP mAb may achieve a response in the 4 weeks following the second dose. A smaller proportion of patients may also respond in the 4 to 8 weeks following the third consecutive SC dose.

The European Headache Federation guidelines suggest most individuals with migraine considered to be responders can be identified after 3 to 6 months. Treatment can be stopped if it does not demonstrate even partial efficacy. In patients with a partial response, cumulative benefits may occur over 6 to 12 months of continued use.

References

1. Ailani J, Burch RC, Robbins MS, the Board of Directors of the American Headache Society (2021) The American Headache Society Consensus Statement: update on integrating new migraine treatments into clinical practice. Headache 61(7):1021–1039. DOI: 10.1111/head.14153

2. Vyepti [Package Insert]. Bothell, WA; Lundbeck Seattle BioPharmaceuticals, Inc.: 2020

3. Sacco S, Amin FM, Ashina M, et al: European Headache Federation guideline on the use of monoclonal antibodies targeting the calcitonin gene related peptide pathway for migraine prevention - 2022 update. J Headache Pain 2022; 23(1):67. DOI: 10.1186/s10194-022-01431-x

Vyjuvek *(beremagene geperpavec-svdt)* Gel topical

Priority Health Part B Step Therapy: No

Additional Priority Health Part B Criteria: Yes

Vyjuvek is indicated for the treatment of wounds in patients with Dystrophic Epidermolysis Bullosa (DEB), provided those patients have mutations in the *COL7A1* gene. This *COL7A1* gene is responsible for binding the dermis to the epidermis to promote wound healing. Patients with DEB lack the collagen needed to maintain the skin's integrity during even small incidents. Skin is prone to blistering or tearing which can lead to scarring or increase exposure to infection.

The Dystrophic Epidermolysis Bullosa Research Association (DEBRA) International (2020) Guideline recommends all EB patients undergo genetic testing to confirm or rule out DEB.

The safety and effectiveness of Vyjuvek was established in a Phase III, multicenter, randomized, double-blind, placebo-controlled, intra-patient GEM-3 trial. Key exclusion criteria: current evidence or history of squamous cell carcinoma, active infection in the area being treated, or those who had received a skin graft within the past 3 months. The study found statistically significant responses (proportion of complete wound close at 24 weeks) in the treatment group vs placebo (39% more wounds were able to be closed).

Currently, there are no compendia supported uses for this therapy outside the FDA-indication(s).

References

1. Vvyjuvek [Package Insert]. Pittsburgh, PA; Krystal Biotech, Inc.: 2023

2. Krystal Biotech, Inc. A phase III double blinded, placebo-controlled, efficacy and safety study of beremagene geperpavec (B-VEC, previously "KB103") for the treatment of dystrophic epidermolysis bullosa (DEB). ClinicalTrials.gov identifier: NCT04491604.

3. Has C, et al. Clinical practice guidelines for laboratory diagnosis of epidermolysis bullosa. Br J Dermatol (2020); 182: 574-592

Vyvgart *(efgartigimod alfa-fcab)*

Priority Health Part B Step Therapy: Yes

Additional Priority Health Part B Criteria: Yes

Vyvgart (efgartigimod) is a neonatal Fc receptor blocker indicated for the treatment of generalized myasthenia gravis (gMG) in adult patients who are anti-acetylcholine receptor antibody positive (AChR-Ab+). Vyvgart has not been studied and there is no data to support use in combination with other medications used to treat MG.

The International Consensus Guidance for Management of Myasthenia Gravis recommends a nonsteroidal immunosuppressive (IS) agent be used initially in conjunction with corticosteroids, be used alone, or be added to corticosteroids in certain patients. Nonsteroidal IS agents for MG include azathioprine, cyclosporine, mycophenolate mofetil, methotrexate, and tacrolimus. The effect of azathioprine is delayed by 4 to 8 months but can reverse symptoms in most patients. Maximum improvement with cyclosporine is achieved 6 months or longer after starting treatment. More than half of patients treated with cyclophosphamide become asymptomatic after one year. Once treatment goals have been achieved and maintained for 6 months to 2 years, the IS dose should be tapered slowly to the minimal effective amount.

Vyvgart was studied in patients with an MG-Activities of Daily Living (MG-ADL) total score of 5 or more and found greater improvement in MG-ADL score compared with placebo.

References

1. Narayanaswami P, Sanders DB, Wolfe GI, et al. International consensus guidance for management of myasthenia gravis: 2020 update. Neurology. 2021; 96: 114 - 22. DOI: 10.1212/WNL.0000000000011124

2. Skeie GO, Apostolski S, Evoli A, et al. Guidelines for treatment of autoimmune neuromuscular transmission disorders. European J Neurol. 2010 Jul; 17 (7): 893 - 902. DOI: 10.1111/j.1468-1331.2010.03019.x

3. Vyvgart [Package Insert]. Zwijnaarde, Belgium; argenx BV: 2021

4. Sanders DB, Wolfe GI, Benatar M, et al. International consensus guidance for management of myasthenia gravis: executive summary. Neurology. 2016 Jul 26; 87 (4): 419 - 25. DOI: 10.1212/WNL.0000000000002790

5. Howard JF Jr. Clinical Overview of MG. Myasthenia Gravis Foundation of America (MGFA). Published June 2015. https://myasthenia.org/Professionals/Clinical-Overview-of-MG

Vyvgart Hytrulo *(efgartigimod alfa and hyaluronidase-qvfc)*

Priority Health Part B Step Therapy: Yes

Additional Priority Health Part B Criteria: Yes

Vyvgart Hytrulo (efgartigimod alfa and hyaluronidase-qvfc) is a combination of efgartigimod alfa, a neonatal Fc receptor blocker, and hyaluronidase, an endoglycosidase, indicated for the treatment of generalized myasthenia gravis (gMG) in adult patients who are anti-acetylcholine receptor antibody positive (AChR-Ab+) and for the treatment of chronic inflammatory demyelinating polyradiculoneuropathy (CIDP). Vyvgart Hytrulo has not been studied and there is no data to support use in combination with other medications used to treat MG or CIDP.

The International Consensus Guidance for Management of Myasthenia Gravis recommends a nonsteroidal immunosuppressive (IS) agent be used initially in conjunction with corticosteroids, be used alone, or be added to corticosteroids in certain patients. Nonsteroidal IS agents for MG include azathioprine, cyclosporine, mycophenolate mofetil, methotrexate, and tacrolimus. The effect of azathioprine is delayed by 4 to 8 months but can reverse symptoms in most patients. Maximum improvement with cyclosporine is achieved 6 months or longer after starting treatment. More than half of patients treated with cyclophosphamide become asymptomatic after one year. Once treatment goals have been achieved and maintained for 6 months to 2 years, the IS dose should be tapered slowly to the minimal effective amount.

Vyvgart was studied in patients with an MG-Activities of Daily Living (MG-ADL) total score of 5 or more and a significantly greater proportion of patients responded to efgartigimod compared with placebo.

The European Academy of Neurology/Peripheral Nerve Society guideline for diagnosing and treating CIDP highlights that diagnosis relies on a combination of clinical, electrodiagnostic, and laboratory features, while excluding other disorders that may mimic CIDP. The criteria for CIDP are most closely linked to electrodiagnostic detection of peripheral nerve demyelination. The guideline strongly recommends first-line treatment with either corticosteroids or immunoglobulin, with no preference for either treatment based on the level of evidence. For patients with contraindications to long-term high-dose corticosteroids, intravenous immunoglobulin (IVIg) or subcutaneous immunoglobulin (SCIg) may be preferred. Additionally, for patients with motor CIDP, who may deteriorate with corticosteroids, IVIg should be considered as the first-line treatment. Plasma exchange may be also an acceptable option for chronic treatment. If the objective response is inadequate or the maintenance doses of the initial treatment (IVIg, corticosteroids, or plasma exchange) result in significant side-effects, the other first-line treatment alternatives should be tried before considering combination treatments. Adding an immunosuppressant or immunomodulatory drug may be considered, but there is no sufficient evidence to recommend any particular drug. If the first-line treatment is effective, continuation should be considered until the maximum benefit has been achieved. The guidelines do not mention Vyvgart Hytrulo.

Treatment with Vyvgart Hytrulo resulted in a significantly longer time to clinical deterioration, as indicated by an increase in 1 or more points in the adjusted Inflammatory Neuropathy Case and Treatment (aINCAT) disability score compared with placebo in a randomized withdrawal study of adults with chronic inflammatory demyelinating polyneuropathy (CIDP) that initially experienced clinical benefit with treatment.

References

1. Narayanaswami P, Sanders DB, Wolfe GI, et al. International consensus guidance for management of myasthenia gravis: 2020 update. Neurology. 2021; 96: 114 - 22. DOI: 10.1212/WNL.0000000000011124

2. Skeie GO, Apostolski S, Evoli A, et al. Guidelines for treatment of autoimmune neuromuscular transmission disorders. European J Neurol. 2010 Jul; 17 (7): 893 - 902. DOI: 10.1111/j.1468-1331.2010.03019.x

3. Vyvgart Hytrulo [Package Insert]. Zwijnaarde, Belgium; argenx BV: 2024

4. Howard JF Jr. Clinical Overview of MG. Myasthenia Gravis Foundation of America (MGFA). Published June 2015. https://myasthenia.org/Professionals/Clinical-Overview-of-MG.

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Wezlana IV *(ustekinumab-auub)*

Priority Health Part B Step Therapy: Yes

Additional Priority Health Part B Criteria: Yes

Wezlana is a biosimilar to Stelara. It has been approved by the FDA for all indications of its reference biologic. The FDA has also provisionally determined Wezlana to be interchangeable with Stelara. Ustekinumab (including the biosimilars and reference product) is a monoclonal antibody that inhibits interleukin (IL)-12 and IL-23 and is indicated in several inflammatory conditions including Ulcerative Colitis (UC) and Crohn's Disease (CD).

The Food and Drug Administration (FDA) considers biosimilars to be highly similar with no clinically meaningful differences to the biologic reference product. Biosimilars are considered safe and effective and provide an option to increase access to lifesavings drugs at lower costs. The FDA and current treatment guidelines do not favor one product (biologic or biosimilar) over another.

There is limited data on the concurrent use of ustekinumab with other biologic agents, targeted synthetic DMARDs (e.g., JAK inhibitors), and phosphodiesterase-4 (PDE4) inhibitors (Otezla). Given the absence of strong clinical evidence and the potential for increased infection risk, it is not recommended to use ustekinumab in combination with these agents.

Step therapy is applied to certain Part B drugs, biologics, and biosimilars in a way that lowers costs and improves the quality of care for Medicare beneficiaries per the Centers for Medicare & Medicaid Services (CMS) guidance.

References

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2. Lichtenstein GR, Loftus EV, Isaacs KL, et al. ACG clinical guideline: management of crohn's disease in adults. AJG. 2018 April; 113 (4): 481-517

3. Feuerstein JD, Isaacs KL, Schneider Y, et al. AGA clinical practice guidelines on the management of moderate to severe ulcerative colitis. Gastroenterology. 2020; 158: 1450 – 6

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Winrevair *(sotatercept)*

Priority Health Part B Step Therapy Drug: Yes

Additional Priority Health Part B Criteria: Yes

Winrevair (sotatercept) subcutaneous powder for solution is an activin signaling inhibitor indicated for the treatment of adults with pulmonary arterial hypertension (PAH, World Health Organization [WHO] Group 1) to increase exercise capacity, improve WHO functional class (FC), and reduce the risk of clinical worsening events. Studies establishing effectiveness included patients with NYHA Functional Class II-III symptoms and who had been receiving stable background PAH therapy.

The 2022 European Society of Cardiology and the European Respiratory Society (ESC/ERS) Guidelines for the diagnosis and treatment of pulmonary hypertension (PH) recommend right heart catheterization as the gold standard for diagnosing and classifying PH as well as assessing cardiopulmonary hemodynamics during exercise. Patients with PH are classified based upon etiology and mechanism into group 1 (pulmonary arterial hypertension), group

2 (pulmonary hypertension associated with left heart disease), group 3 (pulmonary hypertension associated with lung diseases and/or hypoxia), group 4 (pulmonary hypertension associated with chronic pulmonary artery obstruction), and group 5 (pulmonary hypertension with unclear and/or multifactorial mechanisms).

For patients with PAH presenting at low or intermediate risk, the guidelines recommend initial combination therapy with a phosphodiesterase 5 inhibitor (PDE5i) and an endothelin receptor antagonist (ERA). PDE5is include sildenafil and tadalafil. ERAs include ambrisentan and bosentan.

The most widely used measure of exercise capacity in PH centers is the 6-minute walking test (6MWT). The 6MWT is easy to perform, inexpensive, and widely accepted by many as an important and validated variable in assessment of PH; and the change in the 6-minute walking distance (6MWD) is one of the most used parameters in PAH clinical trials. In the studies of adults with WHO group 1 pulmonary arterial hypertension, Winrevair significantly improved the change in 6WMD from baseline to week 24 compared with placebo.

References

1. Winrevair™ subcutaneous injection [prescribing information]. Rahway, NJ: Merck; March 2024.

2. Hoeper M, Badesch D, Ghofrani A, et al. Phase 3 trial of sotatercept for treatment of pulmonary arterial hypertension. N Engl J Med. 2023;388:1478-1490.

3. 2022 ESC/ERS Guidelines for the Diagnosis and Treatment of Pulmonary Hypertension: Developed by the Task Force for the Diagnosis and Treatment of Pulmonary Hypertension of the European Society of Cardiology (ESC) and the European Respiratory Society (ERS). Eur Heart J 2022;Aug 26. DOI: 10.1183/13993003.00879-2022

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Xenleta *(lefamulin)*

Priority Health Part B Step Therapy: Yes

Additional Priority Health Part B Criteria: No

Xenleta (lefamulin) is indicated for the treatment of community-acquired bacterial pneumonia (CABP) in adults caused by the following microorganisms, if susceptible: Streptococcus pneumoniae, Staphylococcus aureus (methicillin-susceptible isolates), Haemophilus influenzae, Legionella pneumophila, Mycoplasma pneumoniae, Chlamydophila pneumoniae.

Antibiotic recommendations for the empiric treatment of community-acquired bacterial pneumonia (CAP) are based on selecting agents effective against the major treatable bacterial causes of CAP. Traditionally, these bacterial pathogens include Streptococcus pneumoniae, Haemophilus influenzae, Mycoplasma pneumoniae, Staphylococcus aureus, Legionella species, Chlamydia pneumoniae, and Moraxella catarrhalis. The Clinical Practice Guideline of the American Thoracic Society and Infectious Diseases Society of America on Diagnosis and Treatment of Adults with Community-acquired Pneumonia recommends obtaining sputum for gram stain and culture in hospitalized patients with severe CAP, and when strong risk factors for MRSA and P. aeruginosa are identified, unless local etiological data have already shown these pathogens are very infrequently identified in patients with CAP.

For healthy outpatient adults without comorbidities or risk factors for antibiotic resistant pathogens, the committee recommends amoxicillin, doxycycline, or a macrolide (azithromycin or clarithromycin) only in areas with pneumococcal resistance to macrolides <25% (conditional recommendation, moderate quality of evidence). For outpatient adults with comorbidities such as chronic heart, lung, liver, or renal disease; diabetes mellitus; alcoholism; malignancy; or asplenia they recommend combination therapy of amoxicillin/clavulanate or a cephalosporin with a macrolide or doxycycline. Monotherapy with respiratory fluoroquinolone (levofloxacin, moxifloxacin, or gemifloxacin) is a treatment option. Both sets of treatment recommendations contain multiple antibiotic options without specifying a preference order. The choice between these options requires a risk–benefit assessment for each individual patient, weighing local epidemiological data against specific risk factors that increase the risk of individual choices, such as documented β-lactam or macrolide allergy, cardiac arrhythmia (macrolides), vascular disease (fluoroquinolones), and history of infection with Clostridium difficile. The guidelines state there is a need for research on new therapeutic agents for adults with CAP and lefamulin, a new pleuromutilin antibiotic that was recently demonstrated to be noninferior to moxifloxacin in hospitalized adult patients with CAP. In inpatient adults with nonsevere CAP without risk factors for MRSA or P. aeruginosa they recommend combination therapy with a β-lactam (ampicillin + sulbactam, cefotaxime, ceftriaxone, or ceftaroline) and a macrolide. Monotherapy with respiratory fluoroquinolone is also a treatment option.

In the LEAP 1 randomized, double-blind trial in 551 adult patients with community-acquired bacterial pneumonia (CABP), lefamulin was noninferior to moxifloxacin (with or without linezolid, depending on possibility of MRSA involvement) with regard to early clinical response (ECR) rate at 72 to 120 hours after the first dose of study drug. Lefamulin ECR rate was 87.3% compared with an ECR rate of 90.2% for moxifloxacin (treatment difference, -2.9%; 95% CI, -8.5% to 2.8%). In the LEAP 2 randomized, double-blind trial in 738 adult patients with CAPB, lefamulin was noninferior to moxifloxacin with regard to ECR rate at 72 to 120 hours after the first dose of study drug. ECR rates for both treatment groups was 90.8% (treatment difference, 0.1%; 1-sided 97.5% CI, -4.4% to infinity). ECR was achieved if improvement in at least 2 signs/symptoms of CABP occurred, no signs/symptoms of CABP worsened, and no additional non-study antibiotic CABP treatment was administered.

References

1. Xenleta [Package Insert]. Dublin, Ireland; Nabriva therapeutics Ireland DAC: 2019

2. Clinicaltrials.gov. Study to Compare Lefamulin to Moxifloxacin (With or Without Linezolid) for the Treatment of Adults With Pneumonia (LEAP). (NCT02559310). Available at: https://clinicaltrials.gov/study/NCT02559310

3. Clinicaltrials.gov. Study to Compare Lefamulin to Moxifloxacin for the Treatment of Adults With Pneumonia (LEAP2). (NCT02813694). Available at: https://clinicaltrials.gov/study/NCT02813694

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Xenpozyme *(olipudase-alfa-rpcp)* 20 MG vial

Priority Health Part B Step Therapy: No

Additional Priority Health Part B Criteria: Yes

Xenpozyme (olipudase alfa-rpcp) for injection is a hydrolytic lysosomal sphingomyelin-specific enzyme indicated for treatment of non–central nervous system manifestations of acid sphingomyelinase deficiency (ASMD) in adult and pediatric patients. The dosing is to be initiated at 0.1 mg/kg in adults or 0.03 mg/kg in pediatrics, with dosing based on adjusted body weight (kg) in patients with a body mass index (BMI) greater than 30 kg/m2.

Acid sphingomyelinase deficiency (ASMD) is also called Niemann-Pick disease (NPD). ASMD is divided into 3 phenotypes: infantile neurovisceral ASMD (NPD type A), chronic neurovisceral ASMD (intermediate; NPD type A/B), and chronic visceral ASMD (NPD type B). Patients with ASMD are typically managed by metabolic disease specialists/medical geneticists. In the 'Consensus recommendation for a diagnostic guideline for acid sphingomyelinase deficiency', the advisory panel recommends that when ASMD is suspected, an enzyme assay for ASM activity should be completed first, with diagnosis confirmed by demonstration of decreased ASM activity. The National Organization for Rare Disorders (NORD) states the diagnosis is confirmed with a sample that demonstrates less than 10% that of a control sample.

Xenpozyme was studied in patients with a clinical diagnosis of acid sphingomyelinase deficiency (ASMD) type B and A/B. Adults studied also had diffusion capacity of the lungs for carbon monoxide (DLco) ≤70% of the predicted normal value and a spleen volume ≥6 multiples of normal (MN). Pediatrics studied had a spleen volume ≥5 MN. In the studies, Xenpozyme demonstrated improvements in spleen and liver volumes, predicted diffusion capacity of the lungs for carbon monoxide (DLco), and platelet counts in adults and

pediatrics. However, two patients with ASMD type A that received a version of olipudase alfa manufactured from a different process developed anaphylaxis.

References

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3. Xenpozyme [Package Insert]. Cambridge, MA; Genzyme Corporation: 2022

Xolair *(omalizumab)* vial/prefilled syringe

Priority Health Part B Step Therapy: Yes

Additional Priority Health Part B Criteria: Yes

Xolair (omalizumab) is a monoclonal antibody that specifically targets immunoglobulin E (IgE). Xolair is indicated for the treatment of moderate to severe asthma inadequately controlled by inhaled corticosteroids and presence of a positive skin test or in vitro reactivity to a perennial aeroallergen, chronic urticaria (CU) refractory to H1 antihistamine treatment, chronic rhinosinusitis with nasal polyps (CRSwNP) inadequately controlled with nasal corticosteroids as add-on maintenance treatment, and IgE-mediated food allergy. According to current labeling, the dose and dosing frequency of Xolair for asthma, nasal polyps, and food allergies are based on the serum IgE level (IU/ml) measured before treatment begins, along with the patient's body weight. Dosage recommendations start at a minimum pretreatment serum IgE level of 30 IU/ml.

The Global Initiative for Asthma (GINA) Guidelines on difficult-to-treat and severe asthma in adolescent and adult patients recommend using type 2-targeted biologic agents as add-on for patients with exacerbations and/or poor symptom control despite taking at least high-dose inhaled corticosteroids (ICS) and long-acting beta agonist (LABA) combinations, and who have allergic or eosinophilic biomarkers or need maintenance oral corticosteroids. Type 2-inflammation is defined as blood eosinophils of at least 150 microliters, a fractional exhaled nitric oxide (FeNO) of at least 20 parts per billion (ppb), sputum eosinophils at least 2%, and/or asthma that is clinically allergen driven. GINA guidelines also advise treatment should be optimized prior to initiating a biologic agent. For therapy optimization, consider trials of non-biologic medications in addition to medium/high dose ICS, such as LABA, long-acting muscarinic agonists (LAMA), and leukotriene receptor antagonists (LTRA).

The European Academy of Allergology and Clinical Immunology (EAACI), the Global Allergy and Asthma European Network (GA²LEN) and its Urticaria and Angioedema Centers of Reference and Excellence (UCAREs and ACAREs), the European Dermatology Forum (EDF; EuroGuiDerm), and the Asia Pacific Association of Allergy, Asthma and Clinical Immunology

guideline for the definition, classification, diagnosis, and management of urticaria defines chronic urticaria as the occurrence of wheals, angioedema, or both for more than 6 weeks. The guideline recommends second generation H1-antihistamine as first-line treatment for all types of urticaria. Typical doses can be increased up to four times in patients with chronic urticaria unresponsive to a standard-dosed second generation H1-antihistamine. Xolair is recommended as a second line agent for the treatment of patients with chronic urticaria unresponsive to high dose second generation H1-antihistamines. Alternative therapies include but are not limited to H2 antihistamines (e.g., famotidine), oral steroids, or leukotriene modifiers.

The Joint Task Force on Practice Parameters GRADE guidelines for the medical management of chronic rhinosinusitis with nasal polyposis (CRSwNP) recommends inhaled topical corticosteroids (INCS) be used first-line to treat CRSwNP due to their extensive safety and efficacy profiles. The Guidelines recommend biologic agents be used after at least 4 weeks with INCS therapy. In the clinical trials that evaluated Xolair safety and efficacy for CRSwNP, all patients were required to have previously tried at least 4 weeks of INCS to be eligible for the studies. Once enrolled, all patients had to complete an additional 4-week run-in with intranasal mometasone prior to start date. All patients continued to receive background intranasal mometasone throughout the study (24 weeks).

Xolair was evaluated in a phase 3 study for the reduction of allergic reactions (Type I), including anaphylaxis, that may occur with accidental exposure to one or more foods in adult and pediatric patients aged 1 year and older with IgE-mediated food allergy. Patients were included in the study if they had a clinical history of allergic reaction following consumption of peanuts and two additional foods, either milk, eggs, wheat, cashews, hazelnuts, or walnuts. Patients were additionally required to have a positive skin prick test (≥4 mm wheal greater than saline control), and positive food specific IgE (≥6 kUA/L) to the specified foods.

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Yesintek IV *(ustekinumab-kfce)*

Priority Health Part B Step Therapy: Yes

Additional Priority Health Part B Criteria: Yes

Yesintek is a biosimilar to Stelara. It has been approved by the FDA for all indications of its reference biologic. Effective May 1, 2025, Yesintek has been approved by the FDA as interchangeable with Stelara. Ustekinumab (including the biosimilars and reference product) is a monoclonal antibody that inhibits interleukin (IL)-12 and IL-23 and is indicated in several inflammatory conditions including Ulcerative Colitis (UC) and Crohn's Disease (CD).

The Food and Drug Administration (FDA) considers biosimilars to be highly similar with no clinically meaningful differences to the biologic reference product. Biosimilars are considered safe and effective and provide an option to increase access to lifesavings drugs at lower costs. The FDA and current treatment guidelines do not favor one product (biologic or biosimilar) over another.

The 2018 American College of Gastroenterology (ACG) guidelines recommend mercaptopurine, azathioprine, and methotrexate in symptomatic CD despite prior corticosteroid use. TNF inhibitors (e.g., adalimumab) are effective in those with inadequate response to these initial therapies. Other biologic or targeted synthetic disease-modifying antirheumatic drugs are not addressed by the guidelines, however these agents have since been FDA-approved for use in this condition

There is limited data on the concurrent use of ustekinumab with other biologic agents, targeted synthetic DMARDs (e.g., JAK inhibitors), and phosphodiesterase-4 (PDE4) inhibitors (Otezla). Given the absence of strong clinical evidence and the potential for increased infection risk, it is not recommended to use ustekinumab in combination with these agents.

Step therapy is applied to certain Part B drugs, biologics, and biosimilars in a way that lowers costs and improves the quality of care for Medicare beneficiaries per the Centers for Medicare & Medicaid Services (CMS) guidance.

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Yupelri *(revefenacin)*

Priority Health Part B Step Therapy: Yes

Additional Priority Health Part B Criteria: No

Yupelri (revefenacin) is an anticholinergic indicated for the maintenance treatment of patients with chronic obstructive pulmonary disease (COPD). Revefenacin (Yupelri), tiotropium (Spiriva), and umeclidinium (Incruse) are long-acting muscarinic antagonists (LAMA), also referred to as anticholinergics.

The Global Initiative for Chronic Obstructive Lung Disease recommend LAMA treatments as they have shown to improve symptoms, including cough and sputum and health status. LAMA treatment has also shown to improve the effectiveness of pulmonary rehabilitation and reduce exacerbations and related hospitalizations.

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Yutiq *(fluocinolone)* implant

Priority Health Part B Step Therapy: No

Additional Priority Health Part B Criteria: Yes

Yutiq (fluocinolone acetonide intravitreal implant) is approved for the treatment of chronic non-infectious uveitis affecting the posterior segment of the eye.

Uveitis is a group of eye diseases caused by inflammation (redness, swelling, pain, etc.) inside the eye, which can lead to vision loss. Uveitis can result from infections, or non-infectious causes. Non-infectious uveitis can result from a disease somewhere else in the body. The uvea (middle layer of the eye) has many blood vessels. If the immune system is fighting a problem in one area, the cells and chemicals it makes can travel through the bloodstream and enter the eye, leading to inflammation. Acute uveitis lasts less than three months; chronic uveitis lasts longer than three months. Chronic non-infectious uveitis is generally treated with steroids, applied near or inside the eye, or other medicines, taken either by mouth or injection, to control the inflammation.

In 2 randomized studies, the proportion of patients who experienced a recurrence of uveitis in the treated eye within 6 months was significantly lower with fluocinolone acetonide intravitreal implant versus sham injection (recurrence rate, 18% vs 79% in study 1 and 22% vs 54% in study 2). Within 12 months, the recurrence rate was 28% versus 86% in study 1 and 33% versus 60% in study 2 for active treatment compared with sham injection, respectively. Recurrence was defined as either deterioration in visual acuity, vitreous haze attributable to non-infectious uveitis or need for rescue medications.

A Cochrane Review of Corticosteroid implants for chronic non-infectious uveitis included randomized controlled trials comparing either fluocinolone acetonide (FA) or dexamethasone (DEX) intravitreal implants with standard-of-care therapy or sham procedures, with at least six months of follow-up after treatment. Two trials compared corticosteroid implants with sham injection. One trial evaluated a short-acting implant (0.7 mg dexamethasone) that released corticosteroid for approximately three months, while the other evaluated a long-acting implant (0.18 mg fluocinolone acetonide [FA]) that released corticosteroid for approximately 36 months. Low-certainty evidence suggested that these corticosteroid implants were likely to reduce the risk of uveitis recurrence and to improve best-corrected distance visual acuity (BCVA) at the six-month primary time point compared with sham injection.

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Zevaskyn *(prademagene zamikeracel)*

Priority Health Part B Step Therapy: No

Additional Priority Health Part B Criteria: Yes

Zevaskyn (prademagene zamikeracel; pz-cel) is a topically applied autologous cell-based gene therapy composed of keratinocytes genetically modified using a retroviral vector carrying the functional COL7A1 gene. Zevaskyn is indicated for the treatment of wounds in adult and pediatric patients with recessive dystrophic epidermolysis bullosa (RDEB). EB is classified into four major types: EB simplex (EBS), dystrophic EB (DEB), junctional EB (JEB), and Kindler EB(KEB; also known as Kindler syndrome).

Zevaskyn uses the patient's own skin cells, genetically modified to produce type VII collagen. These genecorrected cells are applied topically to wound areas in a single surgical session. Up to 12 sheets, each approximately credit card-sized, can be applied per procedure—either combined to cover large areas or applied across multiple smaller lesions.

Zevaskyn is the third product approved for EB. Krystal Biotech's Vyjuvek (beremagene geperpavec-svdt) is a topically applied gene therapy that was approved in May 2023 for DEB. Chiesi Global Rare Diseases' Filsuvez (birch triterpenes) is a topical product approved for DEB and JEB in December 2023; it works by promoting wound healing in general. These therapies have not been evaluated for concurrent use on the same treatment areas as Zevaskyn.

Approval of Zevaskyn was supported by results from the Phase 3, randomized, open-label, intrapatient-controlled VIITAL study (NCT04227106). At one month post-application, 20 out of 24 grafts (83%) demonstrated at least 75% wound healing, while at 12 months, this level of healing was observed in 12 out of 24 grafts (50%). All grafts were well tolerated, with no serious adverse events reported. In a long-term follow-up study, seven adults with severe recessive dystrophic epidermolysis bullosa (RDEB) each received six sheets of autologous gene-corrected keratinocyte grafts applied to chronic wounds. The patients were monitored for an average of 5.9 years. At six months, 93% of grafted sites achieved at least 50% wound healing. By five years, 70% of sites maintained ≥50% healing, and 63% achieved ≥75% healing.

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Zevtara *(ceftobiprole medocaril sodium for injection)*

Priority Health Part B Step Therapy: Yes

Additional Priority Health Part B Criteria: Yes

Zevtera (ceftobiprole medocaril Sodium) is a fifth-generation cephalosporin with broad-spectrum bactericidal activity against a wide range of gram-positive bacteria. It is indicated for the treatment of staphylococcus aureus bloodstream infection (bacteremia) (SAB), community-acquired bacterial pneumonia, and acute bacterial skin and skin structure infections (ABSSSI).

The Infectious Diseases Society of America (IDSA) divides SSTIs into purulent (including abscesses, furuncles, and carbuncles) and non-purulent (including cellulitis, erysipelas, and necrotizing fasciitis) infections. Treatment duration for most bacterial SSTIs is generally recommended to be 7-14 days. The choice of antibiotics depends on the type of infection, the suspected pathogens, and the patient's individual characteristics. For purulent infections, incision and drainage remain the standard of treatment. If systemic antibiotics are needed, especially when MRSA is suspected, agents such as trimethoprim-sulfamethoxazole, doxycycline, or clindamycin are recommended. For non-purulent cellulitis, which is often streptococcal in origin, cephalexin, amoxicillin, or penicillin VK are preferred. In cases of beta-lactam allergy, clindamycin or macrolides may be used, though resistance patterns should be considered. The IDSA guidelines also emphasize aggressive treatment of necrotizing infections, recommending broad-spectrum empiric therapy such as vancomycin plus piperacillin-tazobactam until specific pathogens are identified. For impetigo, mupirocin or retapamulin topical therapy is effective, with oral dicloxacillin or cephalexin for more extensive disease.

The most recent ATS/IDSA guidelines for community-acquired pneumonia (CAP), updated in 2019, provide a structured approach to diagnosis and treatment based on illness severity. For outpatients without comorbidities, amoxicillin or doxycycline is preferred. For outpatients with comorbidities, combination therapy (e.g., amoxicillin-clavulanate plus a macrolide) or monotherapy with a respiratory fluoroquinolone (like levofloxacin) is recommended. Hospitalized patients with non-severe CAP are typically treated with beta-lactam plus macrolide or a respiratory fluoroquinolone alone. In severe CAP, empiric

coverage includes beta-lactam plus macrolide or beta-lactam plus fluoroquinolone, with additional agents like vancomycin or linezolid added if MRSA is suspected.

Staphylococcus aureus bacteremia (SAB) is a serious cause of bloodstream infection associated with significant morbidity and mortality. All patients with uncomplicated SAB are recommended to receive at least two weeks of intravenous antibiotic therapy. For complicated SAB, therapy with intravenous antibiotics for four to six weeks has been the standard practice. The selection of antibiotic is dependent on methicillin susceptibility. Agents used for treatment of MSSA include penicillinase-resistant semisynthetic penicillins, first-generation cephalosporins, vancomycin and daptomycin. A beta-lactam is the preferred drug of choice for MSSA bacteremia. Anti-staphylococcal penicillins such as nafcillin are often utilized as first line agents. In the case of MRSA bacteremia, vancomycin or daptomycin monotherapy is recommended as first line agents. IDSA guidelines recommend an assessment for foci of infection that may need surgical attention and/or consideration of high dose daptomycin in combination with another agent such as gentamicin, rifampin, linezolid, or a beta-lactam antibiotic.

Approval of Zevtera was supported by clinical efficacy and safety data from the Phase 3 studies ERADICATE (SAB), TARGET (ABSSSI), and two Phase 3 studies in CABP, all showing noninferiority versus the comparator arm.

Step therapy is applied to certain Part B drugs, biologics, and biosimilars in a way that lowers costs and improves the quality of care for Medicare beneficiaries per the Centers for Medicare & Medicaid Services (CMS) guidance.

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Ziextenzo *(pegfilgrastim-bmez)*

Priority Health Part B Step Therapy: Yes

Additional Priority Health Part B Criteria: No

Hematopoietic growth factors are defined by their ability to promote proliferation and differentiation of hematopoietic progenitors into mature blood cells. Colony-stimulating factors (CSFs) are hematopoietic growth factors that regulate the growth and differentiation of cells towards the myeloid and erythroid lineages. Myeloid growth factors (MGFs), such as granulocyte colony-stimulating factors (G-CSF), are primarily used to reduce the incidence of febrile neutropenia (FN) in patients with non-myeloid malignancies receiving myelosuppressive chemotherapy.

Chemotherapy-induced neutropenia is a major risk factor for infection-related morbidity and mortality and also a significant dose-limiting toxicity in cancer treatment. Prophylactic treatment with granulocyte-colony stimulating factors (G-CSFs), such as filgrastim (including approved biosimilars) or pegfilgrastim is available to reduce the risk of chemotherapy-induced neutropenia. NCCN guideline recommends prophylactic G-CSF use if a patient's risk of developing FN is >20% (category 1). The American Society of Clinical Oncology (ASCO) and European Organization for Research and Treatment of Cancer (EORTC) guidelines have also adopted the 20% threshold for considering routine prophylactic MGF support. The National Comprehensive Cancer Network (NCCN) Panel defines intermediate risk as a 10% to 20% probability of developing FN or a neutropenic event that would compromise treatment. For patients receiving intermediate-risk chemotherapy regimens, the panel recommends individualized consideration of prophylactic G-CSF use based on the presence of patient-specific risk factors.

Administration of CSFs to mobilize peripheral-blood progenitor cell (PBPC) often in conjunction with chemotherapy and their administration after autologous, but not allogeneic, PBPC transplantation is the current standard of care. Among autologous PBPC patients, post-transplant G-CSF use has been associated with savings in the duration of hospitalization and overall medical costs. The use of CSFs to mobilize peripheral blood progenitor cells (PBPC) and to shorten the period of neutropenia after cytoreduction and PBPC transplantation, is well established. Individuals receiving CSFs for mobilization should have their platelet counts monitored. Filgrastim is indicated for the mobilization of hematopoietic progenitor cells into the peripheral blood for collection by leukapheresis.

Several studies have shown that CSF administration can produce modest decreases in the duration of neutropenia when begun shortly after completion of the initial induction chemotherapy for the treatment of acute myeloid leukemia (AML). CSF use can be recommended after the completion of consolidation chemotherapy because of the potential to decrease the incidence of infection and eliminate the likelihood of

hospitalization in some patients receiving intensive post-remission chemotherapy. CSFs can increase the absolute neutrophil count in neutropenic patients with myelodysplastic syndromes (MDS). In the treatment of acute lymphocytic leukemia (ALL), CSFs are recommended after the initial first few days of chemotherapy of the initial induction or first post- remission course.

Current recommendations for the management of patients exposed to lethal doses of total body radiotherapy, but not doses high enough to lead to certain death due to injury to other organs, includes the prompt administration of CSF or pegylated G-CSF. Hematopoietic growth factors can increase the survival, proliferation, amplification, and differentiation of granulocyte progenitors to produce neutrophils.

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Zilbrysq *(zilucoplan injection, solution)*

Priority Health Part B Step Therapy: Yes

Additional Priority Health Part B Criteria: Yes

Zilbrysq (zilucoplan) is a complement inhibitor indicated for the treatment of generalized myasthenia gravis (gMG) in adult patients who are antiacetylcholine receptor antibody positive (AChR-Ab+). Zilbrysq has not been studied and there is no data to support use in combination with other medications used to treat MG.

Vyvgart (efgartigimod) and Rystiggo (rozanolixizumab-noli) are both neonatal Fc receptor blockers also approved for the treatment of gMG in adult patients who are AChR-Ab+. Similar to Zilbrysq, Ultomiris (ravulizumab) is another complement inhibitor indicated for

the treatment of adult patients with gMG who are AChR-Ab+. Guidelines currently do not include recommendations regarding Vyvgart, Rystiggo, Ultomiris, and Zilbrysq.

Zilbrysq was studied in patients with an MG-Activities of Daily Living (MG-ADL) total score of 6 or more and produced a significantly greater and clinically meaningful change at week 12 compared with placebo.

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Zymfentra *(infliximab-dyyb)*

Priority Health Part B Step Therapy: Yes

Additional Priority Health Part B Criteria: Yes

Zymfentra is a tumor necrosis factor inhibitor (TNFi) currently indicated for maintenance treatment of moderately to severe Crohn's disease (CD) and Ulcerative Colitis (UC) in those who have completed induction therapy with an intravenous infliximab product. Zymfentra is only available as a subcutaneous (SC) formulation.

The 2018 American College of Gastroenterology (ACG) guidelines recommend biologics including TNFi agents (infliximab, adalimumab, Enbrel) and interleukin (IL)-23 inhibitors (e.g., Skyrizi) in patients with an inadequate response to corticosteroids, thiopurines, and

methotrexate. Guidelines do not favor one biologic over another for treatment of CD. Janus-kinase (JAK) inhibitors (e.g., Xeljanz, Rinvoq), otherwise known as targeted synthetic disease-modifying antirheumatic drugs (tsDMARDs), are small molecules that can be taken orally. These agents disrupt cytokine signaling that leads to the inflammation cascade. Rinvoq was approved after the guidelines were published but was found safe and effective in the management of CD during two clinical trials (U-EXCEL and U-EXCEED).

Per the 2020 American Gastroenterology Association guidelines, multiple agents effectively maintain remission of UC, including thiopurines (azathioprine, mercaptopurine) and biologics. Methotrexate is not recommended for induction or maintenance of remission in UC, whereas biologics (including TNFis) do have support for use in these treatment areas. Guidelines do not favor one biologic over another for treatment of UC. Xeljanz is recommended as one of the many first-line options in the induction and maintenance of UC remission. Rinvoq was also found to be safe and effective in the management of UC during two clinical trials (U-ACHIEVE and U-ACCOMPLISH).

Zymfentra has not been studied in combination with other biologic disease-modifying agents, tsDMARDs, or PDE4 inhibitors (e.g., Otezla) due to an increased risk of infection and increased immunosuppression. As such, use of Zymfentra in combination with other biologic agents, targeted synthetic DMARDs, or Otezla is not recommended.

The Food and Drug Administration (FDA) considers biosimilars to be highly similar with no clinically meaningful differences to the biologic reference product. Biosimilars are considered safe and effective and provide an option to increase access to lifesavings drugs at lower costs. The FDA and current treatment guidelines do not favor one product (biologic or biosimilar) over another.

Step therapy is applied to certain Part B drugs, biologics, or biosimilars in a way that lowers costs and improves the quality of care for Medicare beneficiaries per the Centers for Medicare & Medicaid Services (CMS) guidance.

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Zynteglo *(onasemnogene abeparvovec)*

Priority Health Part B Step Therapy: No

Additional Priority Health Part B Criteria: Yes

Beta thalassemia is a type of inherited blood disorder that can cause reduction of normal hemoglobin and reg blood cells in the body though mutations in a beta-globin subunit. This can lead to insufficient delivery of oxygen though the body. Reduced levels of red blood cells can lead to several health issues including dizziness, weakness, fatigue, bone abnormalities and other complications. Patients often require lifelong blood transfusions for survival and treatment for iron overload due to these transfusions as well as other health complications including heart, liver or other organ problems.

Zynteglo is a autologous hematopoietic stem cell-based gene therapy for treatment of adult and pediatric patients with beta-thalassemia who require regular red blood cell (RBC) transfusions. Zynteglo is a one-time therapy. It is administered as a single dose and is a customized treatment created using an individual's own cells that are genetically modified to produce functional beta-globin.

Treatment options are limited for beta-thalassemia but do include allogeneic hematopoietic stem cell transplantation (HSCT) which is a curative treatment in up to 80-90% of individuals. Donors may be limited, and some are not optimal candidates due to age or iron related complications and there is also a risk of graft-versus-host disease with transplant. Otherwise, blood transfusions are the mainstay of care.

Blood transfusions are the mainstay of care for individuals with thalassemia. Guidelines define a patient as transfusion dependent when they are getting infusions of packed red blood cells every 2 to 5 weeks to maintain the pre-transfusion hemoglobin of 9 g/dL - 10.5 g/dL and the post-transfusion hemoglobin less than 14 - 15 g/dL. This translates to approximately 100 mL/kg/year of packed red blood cells.

There is a lack of data around safety and efficacy in supporting administration of Zynteglo following previous gene therapy or with a previous HSCT.

References

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