Gold Coast Health Plan Medicare Part B

References & Clinical Criteria

For Part B Prior Authorization

This document is updated frequently.
Last revised: **06/16/2026**

References & Clinical Criteria

For Medicare Part B Prior Authorization

Gold Coast Health Plan 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, Gold Coast Health Plan 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, Gold Coast Health Plan 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.

Abecma (*idecabtagene icleucel-avwa)*

Additional Gold Coast Health Plan Part B Criteria: No

Abecma is a B-cell maturation antigen (BCMA)-directed genetically modified autologous T cell immunotherapy indicated for the treatment of adult patients with relapsed or refractory multiple myeloma after two or more prior lines of therapy, including an immunomodulatory agent, a proteasome inhibitor, and an anti-CD38 monoclonal antibody.

Gold Coast Health Plan follows NCD 110.24 for Chimeric Antigen Receptor (CAR) T-Cell Therapy.

References

1. Abecma [Package Insert]. Summit, NJ; Bristol-Myers Squibb: 2021
2. Centers for Medicare & Medicaid Services. National Coverage Determination (NCD) 110.24 Chimeric Antigen Receptor (CAR) T-cell Therapy. https://www.cms.gov/medicare-coverage-database/view/ncd.aspx?ncdid=374

Actemra IV (*tocilizumab)*

Additional Gold Coast Health Plan 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.

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)*

Additional Gold Coast Health Plan 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.

Adzynma *(ADAMTS13, recombinant-krhn)*

Additional Gold Coast Health Plan 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.

Persistent severe deficiency (less than 10%) of ADAMTS13 activity is required to confirm TTP diagnosis. For differentiation from aTTP/iTTP from cTTP, identification of ADAMTS13 autoantibodies is needed. Samples for ADAMTS13 activity and autoantibody testing should be collected and gene analysis should be pursued to confirm the diagnosis of cTTP.

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/

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

Additional Gold Coast Health Plan 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.

Gold Coast Health Plan 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 https://www.cms.gov/medicare-coverage-database/view/lcd.aspx?lcdid=34771&ver=49&=

Alymsys *(bevacizumab-maly)*

Additional Gold Coast Health Plan Part B Criteria: No

Gold Coast Health Plan follows Centers for Medicare & Medicaid Services Medicare Coverage Database. Local Coverage Determination (LCD) L37205: Chemotherapy Drugs and their Adjuncts.

Alymsys (bevacizumab-maly) is biosimilar to Avastin® (bevacizumab). Bevacizumab is a vascular endothelial growth factor inhibitor indicated for the treatment of multiple cancers including:

1. metastatic colorectal cancer, in combination with intravenous fluorouracil-based chemotherapy for first- or second-line treatment;
2. 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;
3. unresectable, locally advanced, recurrent or metastatic non-squamous non-small cell lung cancer, in combination with carboplatin and paclitaxel for first-line treatment;
4. recurrent glioblastoma in adult;
5. 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.https://www.cms.gov/medicare-coverage-database/view/lcd.aspx?lcdId=37205&ver=15
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 3.2025 – January 14, 2025)
6. National Comprehensive Cancer Network. Colon Cancer (Version 1.2025 – February 7, 2025)
7. National Comprehensive Cancer Network. Kidney Cancer (Version 3.2025 – January 9, 2025)
8. National Comprehensive Cancer Network. Non-Small Cell Lung Cancer (Version 3.2025 – January 14, 2025)

Amvuttra *(vutrisiran)*

Additional Gold Coast Health Plan 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.

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.

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. 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.

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

Apretude *(cabotegravir)*

Additional Gold Coast Health Plan Part B Criteria: No

Apretude is an HIV-1 integrase strand transfer inhibitor (INSTI) indicated for PrEP to reduce the risk of sexually acquired HIV-1 infection in adults and adolescents weighing at least 35 kg who are at risk for HIV-1 acquisition.

Gold Coast Health Plan follows Centers for Medicare and Medicaid Services National Coverage Determination Pre-Exposure Prophylaxis (PrEP) for Human Immunodeficiency Virus (HIV) Prevention
(210.15), which covers drugs used for HIV PrEP under Part B.

References

1. Apretude (prescribing information). Durham, NC: ViiV Healthcare; 2024
2. Centers for Medicare & Medicaid Services Medicare Coverage Database National Coverage Determination Pre-Exposure Prophylaxis (PrEP) for Human Immunodeficiency Virus (HIV) Prevention (210.15)https://www.cms.gov/medicare-coverage-database/view/ncd.aspx?ncdid=377&ncdver=1

Aucatzyl *(obecabtagene autoleucel)*

Additional Gold Coast Health Plan Part B Criteria: No

Gold Coast Health Plan follows NCD 110.24 for Chimeric Antigen Receptor (CAR) T-Cell Therapy.

Aucatzyl is a CD19-directed genetically modified autologous T cell immunotherapy indicated for the treatment of adults with relapsed or refractory B-cell precursor acute lymphoblastic leukemia.

References

1. Aucatzyl (obecabtagene autoleucel)[Package Insert]. Autolous Inc. Gaithersburg, MD. 2024.
2. Clinicaltrials.gov. A study of CD19 targeted CAR-T cell therapy in adult patients with relapsed or refractory b-cell acute lymphoblastic leukemia (NCT04404660). Available at: https://clinicaltrials.gov/study/NCT04404660.
3. Centers for Medicare & Medicaid Services. National Coverage Determination (NCD) 110.24 Chimeric Antigen Receptor (CAR) T-cell Therapy. https://www.cms.gov/medicare-coverage-database/view/ncd.aspx?ncdid=374

Avastin *(bevacizumab)*

Additional Gold Coast Health Plan Part B Criteria: No

Gold Coast Health Plan follows Centers for Medicare & Medicaid Services Medicare Coverage Database. Local Coverage Determination (LCD) L37205: Chemotherapy Drugs and their Adjuncts.

Avastin is bevacizumab injection. Bevacizumab is a vascular endothelial growth factor inhibitor indicated for the treatment of multiple cancers including:

1. metastatic colorectal cancer, in combination with intravenous fluorouracil-based chemotherapy for first- or second- line treatment;
2. 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;
3. Unresectable, locally advanced, recurrent or metastatic non-squamous non-small cell lung cancer, in combination with carboplatin and paclitaxel for first-line treatment;
4. recurrent glioblastoma in adult;
5. 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 Medicare Coverage Database. Local Coverage Determination (LCD) L37205: Chemotherapy Drugs and their Adjuncts.https://www.cms.gov/medicare-coverage-database/view/lcd.aspx?lcdId=37205&ver=15
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 3.2025 – January 14, 2025)
6. National Comprehensive Cancer Network. Colon Cancer (Version 1.2025 – February 7, 2025)
7. National Comprehensive Cancer Network. Kidney Cancer (Version 3.2025 – January 9, 2025)
8. National Comprehensive Cancer Network. Non-Small Cell Lung Cancer (Version 3.2025 – January 14, 2025)

Avsola *(infliximab-axxq)*

Additional Gold Coast Health Plan 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.

References

1. Alikhan A, Sayed C, Alavi A, et al. North American clinical management guidelines for hidradenitis suppurativa: A publication from the United States and Canadian Hidradenitis Suppurativa Foundations: Part I: Diagnosis, evaluation, and the use of complementary and

procedural management. J Am Acad Dermatol. 2019;81(1):76-90. doi:10.1016/j.jaad.2019.02.067

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
3. 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.
4. Avsola (infliximab-axxq) [Package Insert]. Thousand Oaks, CA,;Amgen, Inc: 2019
5. 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
6. 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.
7. Ward, MM, Deodhar, A, Akl, EA, et al. 2019 Update of the American College of Rheumatology/Spondylitis Association of America/Spondyloarthritis Research and Treatment Network Recommendations for the Treatment of Ankylosing Spondylitis and Nonradiographic Axial Spondyloarthritis. Arthritis Rheumatol. 2019 Oct;71(10):1599-16

BEIZRAY (docetaxel + albumin) injection, for IV use
DOCIVYX (docetaxel) injection, for IV use

Additional Gold Coast Health Plan Part B Criteria: YES – LCD L37205

Docetaxel is a CYP3A4 substrate. *In vitro* studies have shown that the metabolism of docetaxel may be modified by the concomitant administration of compounds that induce, inhibit, or are metabolized by cytochrome P450 3A4.

In vivo studies showed that the exposure of docetaxel increased 2.2-fold when it was coadministered with ketoconazole, a potent inhibitor of CYP3A4. Protease inhibitors, particularly ritonavir, may increase the exposure of docetaxel. Concomitant use of BEIZRAY and drugs that inhibit CYP3A4 may increase exposure to docetaxel and should be avoided. In patients receiving treatment with BEIZRAY, close monitoring for toxicity and a BEIZRAY dose reduction could be considered if systemic administration of a potent CYP3A4 inhibitor cannot be avoided.

Docetaxel is an antineoplastic agent that acts by disrupting the microtubular network in cells that is essential for mitotic and interphase cellular functions. Docetaxel binds to free tubulin and promotes the assembly of tubulin into stable microtubules while simultaneously inhibiting their disassembly. This leads to the production of microtubule bundles without normal function and to the stabilization of microtubules, which results in the inhibition of mitosis in cells. Docetaxel's binding to microtubules does not alter the number of protofilaments in the bound microtubules, a feature which differs from most spindle poisons currently in clinical use.

Most common adverse reactions across all docetaxel indications are infections, neutropenia, anemia, febrile neutropenia, hypersensitivity, thrombocytopenia, neuropathy, dysgeusia, dyspnea, constipation, anorexia, nail disorders, fluid retention, asthenia, pain, nausea, diarrhea, vomiting, mucositis, alopecia, skin reactions, and myalgia.

References:

1. BEIZRAY Prescribing Information. Pennington, NJ: Zydus Pharmaceuticals Inc.; 2024. Available at: https://dailymed.nlm.nih.gov/dailymed/fda/fdaDrugXsl.cfm?setid=8fb7d980-d6c7-468b-a9f0-adff16101a4b&type=display. Accessed on 1/15/26.
2. Centers for Medicare & Medicaid Services. Local Coverage Determination (LCD) L37205: Chemotherapy Drugs and their Adjuncts. Available at: https://www.cms.gov/medicare-coverage-database/view/lcd.aspx?lcdid=37205&ver=15&keyword=chemotherapy&keywordType=starts&areaId=s6&docType=NCA,CAL,NCD,MEDCAC,TA,MCD,6,3,5,1,F,P&contractOption=all&sortBy=relevance&bc=1.
3. DOCIVYX Prescribing Information. Orlando, FL: Ingenus Pharmaceuticals, LLC; 2022. Available at: https://www.accessdata.fda.gov/drugsatfda_docs/label/2024/215813s001s002lbl.pdf. Accessed on 1/15/26.
4. National Comprehensive Cancer Network. Breast Cancer Version 1.2026.
5. National Comprehensive Cancer Network. Gastric Cancer Version 1.2026.
6. National Comprehensive Cancer Network. Head and Neck Cancers Version 1.2026.
7. National Comprehensive Cancer Network. Non-Small Cell Lung Cancer Version 3.2026.

Benlysta IV *(belimumab)*

Additional Gold Coast Health Plan Part B Criteria: Yes

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.

References

1. Aringer M, Costenbader K, Daikh D, et al. 2019 European League Against Rheumatism/American College of Rheumatology classification criteria for systemic lupus erythematosus. Annals of the Rheumatic Diseases 2019;78:1151-1159. DOI: 10.1002/art.40930
2. Benlysta [Package Insert]. Rockville, MD; Human Genome Sciences, Inc.: 2018
3. Fanouriakis A, Kostopoulou M, Alunno A, et al. Ann Rheum Dis. 2019;78:736–745. DOI: 10.1136/annrheumdis-2019-215089
4. Fanouriakis A, Kostopoulou M , Cheema K, et al. 2019 update of the Joint European League Against Rheumatism and European Renal Association– European Dialysis and Transplant Association (EULAR/ ERA–EDTA) recommendations for the management of lupus nephritis. Ann Rheum Dis. 2020; 79: 713 –23. DOI: 10.1136/annrheumdis-2020-216924
5. Tunnicliffe DJ, Singh-Grewal D, Kim S, at al. Diagnosis, monitoring, and treatment of systemic lupus erythematosus: a systematic review of clinical practice guidelines. 2015 Oct; 67 (10): 1440 – 52. DOI: 10.1002/acr.22591
6. Wallace D.J., Stohl W., Furie R.A., et al. A phase II, randomized, double-blind, placebo- controlled, dose-ranging study of belimumab in patients with active systemic lupus erythematosus. Arthritis Rheum, 61 (9) (2009), pp. 1168-1178

Bevacizumab Biosimilars

Additional Gold Coast Health Plan Part B Criteria: YES – LCD L37205

Brand Name: Avastin®

Bevacizumab binds VEGF and prevents the interaction of VEGF to its receptors (Flt-1 and KDR) on the surface of endothelial cells. The interaction of VEGF with its receptors leads to endothelial cell proliferation and new blood vessel formation in in-vitro models of angiogenesis.

Bevacizumab is indicated for the treatment of:

- Metastatic colorectal cancer, in combination with IV fluorouracil-based chemotherapy for first- or second-line treatment.
- 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.
- Unresectable, locally advanced, recurrent or metastatic non-squamous non-small cell lung cancer, in combination with carboplatin and paclitaxel for first-line treatment.
- Recurrent glioblastoma in adults.
- Metastatic renal cell carcinoma in combination with interferon alfa.
- Persistent, recurrent, or metastatic cervical cancer, in combination with paclitaxel and cisplatin, or paclitaxel and topotecan.
- Epithelial ovarian, fallopian tube, or primary peritoneal cancer:
    - in combination with carboplatin and paclitaxel, followed by Avastin as a single agent, for stage III or IV disease following initial surgical resection.
    - in combination with paclitaxel, pegylated liposomal doxorubicin, or topotecan for platinum-resistant recurrent disease who received no more than 2 prior chemotherapy regimens.
    - in combination with carboplatin and paclitaxel or carboplatin and gemcitabine, followed by Avastin as a single agent, for platinum-sensitive recurrent disease.
- Hepatocellular Carcinoma (HCC): in combination with atezolizumab for the treatment of patients with unresectable or metastatic HCC who have not received prior systemic therapy

Most common adverse reactions related to bevacizumab (incidence > 10%) are epistaxis, headache, hypertension, rhinitis, proteinuria, taste alteration, dry skin, hemorrhage, lacrimation disorder, back pain and exfoliative dermatitis.

References:

1. ALYMSYS Prescribing Information. Bridgewater, NJ: Amneal Pharmaceuticals LLC; 2022.
2. AVASTIN Prescribing Information. South San Francisco, CA: Genentech, Inc; 2004.
3. Centers for Medicare & Medicaid Services. Local Coverage Determination (LCD) L37205: Chemotherapy Drugs and their Adjuncts.
4. JOBEVNE Prescribing Information. Cambridge, MA: Biocon Biologics Inc; 2025.
5. MVASI Prescribing Information. Thousand Oaks, CA: Amgen, Inc; 2017.

6. National Comprehensive Cancer Network. Breast Cancer Version 1.2026
7. National Comprehensive Cancer Network. Central Nervous System Cancers Version 3.2025.
8. National Comprehensive Cancer Network. Cervical Cancer Version 2.2026.
9. National Comprehensive Cancer Network. Colon Cancer Version 5.2025.
10. National Comprehensive Cancer Network. Hepatocellular Carcinoma Version 2.2025.
11. National Comprehensive Cancer Network. Kidney Cancer Version 1.2026.
12. National Comprehensive Cancer Network. Mesothelioma: Pleural Version 2.2026.
13. National Comprehensive Cancer Network. Non-Small Cell Lung Cancer Version 3.2026.
14. National Comprehensive Cancer Network. Ovarian Cancer/Fallopian Tube Cancer/Primary Peritoneal Cancer Version 3.2025.
15. National Comprehensive Cancer Network. Soft Tissue Sarcoma Version 1.2026.
16. National Comprehensive Cancer Network. Uterine Neoplasms Version 2.2026.
17. National Comprehensive Cancer Network. Vulvar Cancer Version 2.2026.
18. VEGZELMA Prescribing Information. Jersey City, NJ: Celltrion USA Inc; 2022.
19. ZIRABEV Prescribing Information. New York, NY: Pfizer, Inc; 2019.

Bivigam *(immune globulin)*

Additional Gold Coast Health Plan Part B Criteria: Yes

Gold Coast Health Plan follows LCD L34771 for Immune Globulins.

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.).

References

1. Bivigam [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 https://www.cms.gov/medicare-coverage-database/view/lcd.aspx?lcdid=34771&ver=49&=

BIZENGRI® (zenocutuzumab-zbco) injection, for IV use

Additional Gold Coast Health Plan Part B Criteria: No

The FDA has granted accelerated approval for the use of BIZENGRI®, a bispecific HER2- and HER3-directed antibody, for the treatment of patients with advanced, unresectable or metastatic non-small cell lung cancer (NSCLC) or pancreatic adenocarcinoma harboring a neuregulin 1 (NRG1) gene fusion with disease progression on or after prior systemic therapy.

Pancreatic adenocarcinoma: Accelerated FDA approval was based on an open-label, multi-cohort, multicenter phase II basket trial (eNRGy) that included 36 patients with advanced or metastatic NRG1 fusion-positive pancreatic adenocarcinoma who progressed on prior systemic therapy (either FOLFIRINOX, gemcitabine plus taxane-based therapy, or both), responses were seen in 15 patients

(ORR of 42%). The median duration of response was seven months (ranging from 2 to 21 months). *Non-small cell lung cancer (NCSLC):* Accelerated FDA approval was based on an open-label, multi-cohort, multicenter phase II basket trial (eNRGy). The study enrolled adult patients with advanced or metastatic NRG1 fusion-positive NSCLC who had disease progression following standard of care treatment for their disease. In the subset of 93 patients with NSCLC, the response rate was 29% with a median duration of response of 12.7 months.

The safety of zenocutuzumab was evaluated in 204 patients with *NRG1*-positive cancers; grade 3 or 4 adverse events occurred in 35%, with fatal adverse events in 4%, although these were not considered to be treatment-related. Treatment-related grade 3 or 4 events occurred in 7% including anemia, nausea, diarrhea, vomiting, abdominal pain, and elevated aspartate transaminase or alanine transaminase (1% or less for each). Other toxicities of concern with zenocutuzumab include infusion-related reactions, interstitial lung disease, and left ventricular dysfunction.

References:

1. Bizengri Prescribing Information. Cambridge, MA: Merus US, Inc.; 2025. Available at: https://bizengri.com/pdf/BIZENGRI_Full_Prescribing_Information_2025.pdf. Accessed September 9, 2025.
2. National Comprehensive Cancer Network Guidelines. Non-Small Cell Lung Cancer Version 2.2025. Available at: https://www.nccn.org/professionals/physician_gls/pdf/nscl.pdf. Accessed September 9, 2025.
3. National Comprehensive Cancer Network Guidelines. Pancreatic Adenocarcinoma Version 2.2025. Available at: https://www.nccn.org/professionals/physician_gls/pdf/pancreatic.pdf. Accessed September 9, 2025.
4. Neal, J, Lovely, C. Personalized, genotype-directed therapy for advanced non-small cell lung cancer. In: UpToDate, Connor RF (Ed), Wolters Kluwer. (Accessed on September 9, 2025.)
5. Singh, H, Cardin, D. Second- and later-line systemic therapy for metastatic exocrine pancreatic cancer. In: UpToDate, Connor RF (Ed), Wolters Kluwer. (Accessed on September 9, 2025.)

Boniva IV *(ibandronate sodium)*

Additional Gold Coast Health Plan Part B Criteria: Yes

Gold Coast Health Plan follows Local Coverage Dtermination (LCD) L34648-bisphosphonate Drug Therapy.

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.

References

1. Boniva [Package Insert]. South San Francisco, CA; Genentec USA, Inc.: 2011
2. Camacho PM, Petak SM, Binkley N, et al. American Association of Clinical Endocrinologists/American College of Endocrinology clinical practice guidelines for the diagnosis and treatment of postmenopausal osteoporosis-2020 update. Endocr Pract. 2020;26:1–46. DOI: 10.4158/GL-2020-0524SUPPL
3. Centers for Medicare & Medicaid Services. Local Coverage Determination (LCD) L34648: bisphosphonate Drug Therapy https://www.cms.gov/medicare-coverage-database/view/lcd.aspx?lcdid=34648&ver=29&keyword=Multiple+Myeloma&keywordType=starts&areaId=all&docType=F&contractOption=all&sortBy=relevance&bc=1

BLENREP (belantamab mafodotin-blmf) injection, for IV use

Additional Gold Coast Health Plan Part B Criteria: YES – LCD L37205

The safety of BLENREP with bortezomib and dexamethasone (n = 242) compared with daratumumab with bortezomib, and dexamethasone (n = 246) was evaluated in DREAMM-7 in patients with relapsed or refractory multiple myeloma who received at least one prior line of therapy [see Clinical Studies (14)]. Patients received BLENREP 2.5 mg/kg of actual body weight once every 3 weeks in combination with bortezomib and dexamethasone (BVd) for the first 8 cycles, followed by BLENREP as a single agent or daratumumab in combination with bortezomib and dexamethasone (DVd) for the first 8 cycles, followed by daratumumab as a single agent. Among patients who received BLENREP, 69% were exposed for 6 months or longer and 55% were exposed for greater than one year. The safety of BLENREP in combination with bortezomib and dexamethasone in patients who received only one prior line of therapy (n = 125) has not been established.

The most common adverse reactions (≥20%) with BLENREP in combination with bortezomib and dexamethasone are reduction in best-corrected visual acuity (BCVA), corneal exam findings, blurred vision, dry eye, photophobia, foreign body sensation in eyes, eye irritation, upper respiratory tract infection, hepatotoxicity, eye pain, diarrhea, fatigue, pneumonia, cataract, and COVID19.

BLENREP causes ocular toxicity, defined as changes in the corneal epithelium and changes in BCVA based on ophthalmic exam (including slit lamp exam), or other ocular adverse reactions as defined by the CTCAE [see Adverse Reactions (6.1)]. In DREAMM-7, ocular toxicity occurred in 92% of patients, including Grade 3 or 4 in 77% of patients. The most common ocular toxicities (>25%) were reduction in BCVA (89%) and corneal exam findings (86%) based on ophthalmic exam findings, blurred vision (66%), dry eye (51%), photophobia (47%), foreign body sensation in eyes (44%), eye irritation (43%), and eye pain (33%).

BLENREP is available only through a restricted program called the BLENREP REMS because of the risk of ocular toxicity. Further information is available at www.BLENREPREMS.com and 1-855-690-9572.

References:

1. BLENREP Billing and Coding Guide. Philadelphia, PA: GlaxoSmithKline LLC; 2025..
2. BLENREP Prescribing Information. Philadelphia, PA: GlaxoSmithKline LLC; 2025.
3. Centers for Medicare & Medicaid Services. Local Coverage Determination (LCD) L37205
4. National Comprehensive Cancer Network. Multiple Myeloma Version 5.2026.

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

Additional Gold Coast Health Plan Part B Criteria: Yes

Gold Coast Health Plan follows the Centers for Medicare & Medicaid Services. Local Coverage Determination (LCD) **L35170** Botulinum Toxins.

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

1. Botox [Package Insert]. Irvine, CA; Allergen, Inc.: 2017
2. Daxxify [Package Insert]. Newark, CA; Revance Theraputics, Inc.: 2022
3. Dysport [Package Insert]. Wrexham, UK; Ipsen Biopharm Ltd.: 2016
4. Myobloc [Package Insert]. Rockville, MD; Solstice Neurosciences.: 2020
5. S.D. Silberstein, S. Holland, F. Freitage, et al. Evidence-based guideline update: pharmacologic treatment for episodic migraine prevention in adults: report of the Quality Standards Subcommittee of the American

Academy of Neurology and the American Headache Society. Neurology 2012: 78(17), 1337–1345. https://doi.org/10.1212/WNL.0b013e3182535d20

6. S.D. Silberstein(2015). Preventive Migraine Treatment. Continuum (Minneapolis, Minn.), 21(4 Headache), 973–989. https://doi.org/10.1212/CON.0000000000000199
7. Xeomin [Package Insert]. Frankfurt, Germany; Merz Pharmaceuticals: 2018
8. The Centers for Medicare & Medicaid Services. Local Coverage Determination (LCD) L33646 Botulinum Toxins https://www.cms.gov/medicare-coverage-database/view/lcd.aspx?LCDId=33646
9. Lightner DJ, Gomelsky A, Souter L, Vasavada SP. Diagnosis and Treatment of Overactive Bladder (Non-Neurogenic) in Adults: AUA/SUFU Guideline Amendment 2019. J Urol. 2019;202(3):558-563. doi:10.1097/JU.0000000000000309
10. Arbouw ME, Movig KL, Koopmann M, et al. Glycopyrrolate for sialorrhea in Parkinson disease: a randomized, double-blind, crossover trial. Neurology 2010; 74:1203
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

BORUZU® (bortezomib) injection, for IV or subcutaneous use

Additional Gold Coast Health Plan Part B Criteria: No

BORUZU is a newly approved ready-to-use formulation for the brand drug VELCADE (bortezomib), a drug which was originally FDA approved in 2003. VELCADE requires reconstitution prior to injecting. BORUZU is a proteosome inhibitor approved for the treatment of adult patients with multiple myeloma or mantle cell lymphoma. It is for subcutaneous (SC) or intravenous (IV) administration only. Because each route of administration has a different final concentration, caution should be used when calculating the volume to be administered.

BORUZU is contraindicated in patients with hypersensitivity to bortezomib, boron or mannitol, including anaphylactic reactions. It is also contraindicated for intrathecal administration.
The most commonly reported adverse reactions (≥ 20%) in clinical studies include nausea, diarrhea, thrombocytopenia, neutropenia, peripheral neuropathy, fatigue, neuralgia, anemia, leukopenia, constipation, vomiting, lymphopenia, rash, pyrexia, and anorexia.

BORUZU is a major substrate for cytochrome P450 3A4; patients will have to be monitored for concurrent drug-drug interactions. Concurrent use with strong 3A4 inducers is NOT recommended and should be avoided as it can decrease patient exposure to BORUZU. Patients on concurrent strong 3A4 inhibitors should be monitored closely for any signs of BORUZU toxicity, as it can increase exposure to BORUZU.

References:

1. *Boruzu* Prescribing Information. Telangana, India: Amneal Oncology Private Limited; 2024. Available at: https://doc-isolation-prod.prod.fire.glass/api/wopi/downloads/docisolation-viewer/v2/?fileAccessId=g_b98d244c-c904-4582-b2e9-23ac5c4c1577&statusCode=1000&operationRestriction=3. Accessed September 10, 2025.
2. National Comprehensive Cancer Network Guidelines. Multiple Myeloma Version 2.2026. Available at: https://www.nccn.org/professionals/physician_gls/pdf/myeloma.pdf. Accessed September 10, 2025.
3. National Comprehensive Cancer Network Guidelines. B-Cell Lymphomas Version 3.2025. Available at: https://www.nccn.org/professionals/physician_gls/pdf/b-cell.pdf. Accessed September 10, 2025.
4. *Velcade* Prescribing Information. Cambridge, MA. Millennium Pharmaceuticals, Inc. 2008. Available at: https://www.accessdata.fda.gov/drugsatfda_docs/label/2008/021602s015lbl.pdf. Accessed September 22, 2025.

Breyanzi *(lisocabtagene maraleucel)*

Additional Gold Coast Health Plan Part B Criteria: No

Gold Coast Health Plan follows NCD 110.24 for Chimeric Antigen Receptor (CAR) T-Cell Therapy.

References

1. Breyanzi [Package Insert]. Bothell, WA; Bristol-Myers Squibb: 2022
2. Centers for Medicare & Medicaid Services. National Coverage Determination (NCD) 110.24 Chimeric Antigen Receptor (CAR) T-cell Therapy. https://www.cms.gov/medicare-coverage-database/view/ncd.aspx?ncdid=374

Carvykti *(ciltacabtagene autoleucel)*

Additional Gold Coast Health Plan Part B Criteria: No

Gold Coast Health Plan follows NCD 110.24 for Chimeric Antigen Receptor (CAR) T-Cell Therapy.

References

1. Carvykti [Package Insert]. Horsham, PA; Janssen Biotech, Inc.: 2023
2. Centers for Medicare & Medicaid Services. National Coverage Determination (NCD) 110.24 Chimeric Antigen Receptor (CAR) T-cell Therapy. https://www.cms.gov/medicare-coverage-database/view/ncd.aspx?ncdid=374

Casgevy *(exagamglogene autotemcel)*

Additional Gold Coast Health Plan Part B Criteria: Yes

Casgevy is indicated for the treatment of patients aged 12 years and older with:

- sickle cell disease (SCD) with recurrent vaso-occlusive crises (VOCs)
- transfusion-dependent β-thalassemia (TDT)

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.
5. 2019–2021 American Society of Hematology (ASH) Clinical Practice Guidelines on Sickle Cell Disease.
6. Cappellini MD, Cohen A, Porter J, et al. Guidelines for the management of transfusion dependent thalassemia. 2021. Available at: https://issuu.com/internationalthalassaemiafederation/docs/final_guideline_4th
7. Clinicaltrials.gov. A safety and efficacy study evaluating CTX001 in subjects with transfusion- dependent βthalassemia (NCT03655678). Available at: https://clinicaltrials.gov/study/NCT03655678.

Cimzia *(certolizumab pegol)*

Additional Gold Coast Health Plan 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.

References

1. Cimzia [Package Insert]. Smyrna, GA; UCB, Inc.: 2016
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. 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
4. 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.
5. Ward, MM, Deodhar, A, Akl, EA, et al. 2019 Update of the American College of Rheumatology/Spondylitis Association of America/Spondyloarthritis Research and Treatment Network Recommendations for the Treatment of Ankylosing Spondylitis and Nonradiographic Axial Spondyloarthritis. Arthritis Rheumatol. 2019 Oct;71(10):1599-1613

Cinqair *(reslizumab)*

Additional Gold Coast Health Plan 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

1. Cinqair [Package Insert]. West Chester, PA; Teva Respiratory, LLC: 2020
2. Global Initiative for Asthma. Global Strategy for Asthma Management and Prevention, 2024
3. Global Initiative for Asthma. Difficult-To-Treat & Severe Asthma in adolescents and adult patients, 2024.

Cinryze *(C1 esterase inhibitor [human])*

Additional Gold Coast Health Plan Part B Criteria: Yes

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.

References

1. Busse, P. J., Christiansen, S. C., Riedl, M. A., Banerji, A., Bernstein, J. A., Castaldo, A. J., Craig, T., Davis-Lorton, M., Frank, M. M., Li, H. H., Lumry, W. R., & Zuraw, B. L. (2021). US HAEA Medical Advisory Board 2020 Guidelines for the Management of Hereditary Angioedema. The journal of allergy and clinical immunology. In practice, 9(1), 132–150.e3. https://doi.org/10.1016/j.jaip.2020.08.046
2. Cinryze [Package Insert]. Lexington, MA; ViroPharm Biologics, LLC.: 2022.

Cosentyx IV *(secukinumab)*

Additional Gold Coast Health Plan 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

1. COSENTYX [prescribing information]. East Hanover, New Jersey: Novartis
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.
4. Ward, MM, Deodhar, A, Akl, EA, et al. 2019 Update of the American College of Rheumatology/Spondylitis Association of America/Spondyloarthritis Research and Treatment Network Recommendations for the Treatment of Ankylosing Spondylitis and Nonradiographic Axial Spondyloarthritis. Arthritis Rheumatol. 2019 Oct;71(10):1599-1613

Cytogam (cytomegalovirus immune globulin) injection, for IV use

Additional Gold Coast Health Plan Part B Criteria: YES

Gold Coast Health Plan must follow LCD L34771 – Immune Globulins

Cytomegalovirus Immune Globulin Intravenous (Human) is indicated for the prophylaxis of cytomegalovirus disease associated with transplantation of kidney, lung, liver, pancreas and heart. In transplants of these organs other than kidney from CMV seropositive donors into seronegative recipients, prophylactic CMV-IGIV should be considered in combination with ganciclovir.

Clinical studies have shown a 50% reduction in primary CMV disease in renal transplant patients given CMV-IGIV and a 56% reduction in serious CMV disease in liver transplant patients given CMV-IGIV. CMV-IGIV prophylaxis was associated with increased survival in liver transplant recipients. Recent studies of combined prophylaxis with CMV-IGIV and ganciclovir have shown reductions in the incidence of serious CMV associated disease in CMV seronegative recipients of CMV seropositive organs below that expected from one drug alone.

CMV-IGIV is made from human plasma and, like other plasma products, carries the possibility for transmission of blood-borne viral agents and theoretically, the Creutzfeldt-Jakob disease (CJD) agent. Immune Globulin Intravenous (Human) products have been reported to be associated with renal dysfunction, acute renal failure, osmotic nephrosis and death. Patients predisposed to acute renal failure include patients with any degree of pre-existing renal insufficiency, diabetes mellitus, age greater than 65, volume depletion, sepsis, paraproteinemia or patients receiving known nephrotoxic drugs. Especially in such patients, IGIV products should be administered at the minimum concentrations available and the minimum rate of infusion practicable. While these reports of renal dysfunction and acute renal failure have been associated with the use of many IGIV products, those containing sucrose as a stabilizer (and given at daily doses of 350 mg/kg or greater) account for a disproportionate share of the total number. CytoGam® contains sucrose as a stabilizer.
During administration, the patient's vital signs should be monitored continuously and careful observation made for any symptoms throughout the infusion. Epinephrine should be available for the treatment of an acute anaphylactic reaction.

References:

1. Centers for Medicare & Medicaid Services. Local Coverage Determination (LCD) L34771. Available at: https://www.cms.gov/medicare-coverage-database/view/lcd.aspx?lcdid=34771&ver=51&keyword=cytogam&keywordType=starts&areaId=all&docType=NCA,CAL,NCD,MEDCAC,TA,MCD,6,3,5,1,F,P&contractOption=all&sortBy=relevance&bc=1

2. Cytogam. [Prescribing Information]. Roswell, GA; Saol Therapeutics, Inc.: 2020. Available at: https://www.fda.gov/media/77671/download

DATROWAY® (datopotamab deruxtecan-dlnk) injection, for IV use

Additional Gold Coast Health Plan Part B Criteria: No

The FDA has granted accelerated approval for the use of Datroway®, a Trop-2-directed antibody and topoisomerase inhibitor conjugate, for the treatment of patients with locally advanced or metastatic epidermal growth factor receptor (*EGFR*)-positive non-small cell lung cancer (NSCLC) who have received prior *EGFR*-directed therapy and platinum-based chemotherapy.

Approval is based on objective response rate (44 percent) and duration of response (7 months) in a phase II study in such patients, but it may be contingent on results of a confirmatory trial. The most common grade ≥3 treatment related adverse event with this agent is stomatitis (which occurred in 9.5 percent in the trial). For those with *EGFR*-positive NSCLC who have progressed on both platinum-based chemotherapy and a next-generation tyrosine kinase inhibitor, we consider Datroway® to be an appropriate option.

Datroway® is also approved for the treatment of unresectable or metastatic, hormone receptor (HR) positive, human epidermal growth factor receptor 2 (HER2) negative (IHC 0, IHC 1+ or IHC 2+/ISH-) breast cancer in adults who have received prior endocrine-based therapy and chemotherapy for unresectable or metastatic disease.

References:

1. Datroway Coding and Reimbursement Guide. Basking Ridge, NJ: Daiichi Sankyo, Inc.; Available at: https://www.datroway4u.com/hcp/coding-and-reimbursement. Accessed August 28, 2025.
2. Datroway Prescribing Information. Basking Ridge, NJ: Daiichi Sankyo, Inc.; June 2025. Available at: https://daiichisankyo.us/prescribing-information-portlet/getPIContent?productName=Datroway&inline=true. Accessed August 28, 2025.
3. Eichler, AF. What's New in Oncology. In: UpToDate, Connor RF (Ed), Wolters Kluwer. (Accessed on September 5, 2025.)
4. National Comprehensive Cancer Network (NCCN) Guidelines. Breast Cancer Version 4.2025. Available at https://www.nccn.org/professionals/physician_gls/pdf/breast.pdf. Accessed August 28, 2025.
5. National Comprehensive Cancer Network (NCCN) Guidelines. Non-Small Cell Lung Cancer Version 8.2025. Available at https://www.nccn.org/professionals/physician_gls/pdf/nscl.pdf. Accessed August 28, 2025.

Denosumab Biosimilars (Prolia, Xgeva) subcutaneous injection

Additional Gold Coast Health Plan Part B Criteria: YES

Gold Coast Health Plan must follow LCD L34648 – Bisphosphonate Drug Therapy.

Prolia (denosumab) is a RANK ligand (RANKL) inhibitor indicated for multiple skeletal related conditions including a) the treatment of postmenopausal women with osteoporosis at high risk for fracture, b) to increase bone mass in men with osteoporosis at high risk for fracture, c) the treatment of glucocorticoid-induced osteoporosis in men and women at high risk for fracture, d) to increase bone mass in men at high risk for fracture receiving androgen deprivation therapy for nonmetastatic prostate cancer, and e) to increase bone mass in women at high risk for fracture receiving adjuvant aromatase inhibitor therapy for breast cancer.

Xgeva (denosumab) is a RANK ligand (RANKL) indicated for a) prevention of skeletal-related events in patients with multiple myeloma and in patients with bone metastases from solid tumors, b) treatment of adults and skeletally mature adolescents with giant cell tumor of bone that is unresectable or where surgical resection is likely to result in severe morbidity, and c) treatment of hypercalcemia of malignancy refractory to bisphosphonate therapy.

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.

AACE Guidelines suggest that a significant decrease in Bone Mineral Density (BMD) or recurrent fractures in a patient who is compliant to therapy may indicate a treatment failure. Rebound bone loss and fractures can occur following discontinuation of denosumab therapy. It is therefore recommended that patients be transitioned to an alternative antiresorptive therapy to prevent rebound bone loss and possible rebound fracture.

References:

1. Centers for Medicare & Medicaid Services. Local Coverage Determination (LCD) L34648: Bisphosphonate Drug Therapy https://www.cms.gov/medicare-coverage-database/view/lcd.aspx?lcdid=34648&ver=29&keyword=Multiple+Myeloma&keywordType=starts&areaId=all&docType=F&contractOption=all&sortBy=relevance&bc=1
2. National Comprehensive Cancer Network. Multiple Myeloma (Version 5.2026).
3. National Comprehensive Cancer Network. Breast Cancer (Version 1.2026).
4. National Comprehensive Cancer Network. Bone Cancer (Version 2.2026).
5. National Comprehensive Cancer Network. Prostate Cancer (Version 4.2026).
6. Prolia [Package Insert]. Thousand Oaks, CA; Amgen, Inc.: 2010. Available at: https://www.pi.amgen.com/-/media/Project/Amgen/Repository/pi-amgen-com/Prolia/prolia_pi.pdf. Accessed on 1/16/26.
7. Xgeva [Package Insert]. Thousand Oaks, CA; Amgen, Inc.: 2010. Available at: https://www.pi.amgen.com/-/media/Project/Amgen/Repository/pi-amgen-com/Xgeva/xgeva_pi.pdf. Accessed on 1/16/26.

Docivyx *(docetaxel)*

Additional Gold Coast Health Plan Part B Criteria: Yes

Gold Coast Health Plan follows Centers for Medicare & Medicaid Services Local Coverage Determination (LCD) L37205: Chemotherapy Drugs and their Adjuncts.

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).

References

1. Docivyx [Package Insert]. New Jersey; Avyxa LLC: 2023.
2. Docetaxel intravenous injection [Package Insert]. Durham, NC; Accord Healthcare, Inc: 2013.
3. Schwartzberg, LS and Navari, RM. (2018). Safety of Polysorbate 80 in the Oncology Setting. Advances in therapy, 35(6), 754–767.
4. Centers for Medicare & Medicaid Services. Local Coverage Determination (LCD) L37205: Chemotherapy Drugs and their Adjuncts. https://www.cms.gov/medicare-coverage-database/view/lcd.aspx?lcdId=37205&ver=15

Durysta *(bimatoprost intraocular implant)*

Additional Gold Coast Health Plan Part B Criteria: Yes

Durysta is a prostaglandin analog indicated for the reduction of intraocular pressure (IOP) in patients with open angle glaucoma (OAG) or ocular hypertension (OHT).

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

1. Durysta [Package Insert]. Madison, NJ; Allergan USA, INC.: 2020
2. American Academy of Ophthalmology: Primary Open-Angle Glaucome Preferred Practice Pattern, 2020.

Elevidys *(delandistrogene moxeparvovec-rokl)*

Additional Gold Coast Health Plan 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.

References

1. Elevidys [package insert]. Cambridge, MA; Sarepta Therapeutic Inc. June 2024, Accessed August 2024.
2. Clinicaltrials.gov. A Gene Transfer Therapy Study to Evaluate the Safety and Efficacy of Delandistrogene Moxeparvovec (SRP-9001) in patients with Duchenne Muscular Dystrophy (DMD) (EMBARK) (NCT05096221). Available at: https://clinicaltrials.gov/study/NCT05096221
3. Clinicaltrials.gov. A Gene Transfer Study to Evaluate the Safety of

Delandistrogene Moxeparvovec (SRP-9001) in Participants With Duchenne Muscular Dystrophy (DMD) (NCT03375164). Available at: https://clinicaltrials.gov/study/NCT03375164

4. Clinicaltrials.gov. A Randomized, Double-blind, Placebo-controlled Study of Delandistrogene Moxeparvovec (SRP-9001) for Duchenne Muscular Dystrophy (DMD). Available at: https://clinicaltrials.gov/study/NCT03769116

EMRELIS™ (telisotuzumab vedotin-tllv) injection, for IV use

Additional Gold Coast Health Plan Part B Criteria: No

EMRELIS is a c-Met-directed antibody and microtubule inhibitor conjugate indicated for the treatment of adult patients with locally advanced or metastatic non-squamous non-small cell lung cancer (NSCLC) with high c-Met protein overexpression (defined as ≥50% of tumor cells) with strong (3+) staining, as determined by an FDA-approved test, who have received a prior systemic therapy.
This indication is FDA approved under accelerated approval based on overall response rate (ORR) and duration of response (DOR). Continued approval for this indication may be contingent upon verification and description of clinical benefit in a confirmatory trial(s).

EMRELIS was studied in the LUMINOSITY trial, a multicenter, open-label, non-randomized, single-arm, muti-cohort phase 2 study. It evaluated EMRELIS monotherapy in 84 patients with locally advanced or metastatic EGFR wild-type non-squamous NSCLC with high c-Met protein overexpression who received prior systemic therapy.

The most common adverse reactions (≥20%) were peripheral neuropathy, fatigue, decreased appetite, and peripheral edema. (6.1) The most common Grade 3 or 4 laboratory abnormalities (≥2%) were decreased lymphocytes, increased glucose, increased alanine aminotransferase, increased gamma glutamyl transferase, decreased phosphorus, decreased sodium, decreased hemoglobin and decreased calcium.

Concomitant use with strong CYP3A inhibitors may increase unconjugated MMAE AUC, which may increase the risk of EMRELIS adverse reactions. Monitor patients for adverse reactions when EMRELIS is given concomitantly with strong CYP3A inhibitors.

References:

1. *Emrelis* Billing and Coding Guide. North Chicago, IL. AbbVie, Inc. Available at: https://www.emrelishcp.com/content/dam/emrelishcp/docs/emr-billing-coding-guide.pdf. Accessed September 12, 2025.
2. *Emrelis* Prescribing Information. North Chicago, IL. AbbVie, Inc. 2025. Available at: https://www.rxabbvie.com/pdf/emrelis_pi.pdf. Accessed September 12, 2025.

National Comprehensive Cancer Network (NCCN) Guidelines. Non-Small Cell Lung Cancer Version 8.2025. Available at https://www.nccn.org/professionals/physician_gls/pdf/nscl.pdf. Accessed

September 12, 2025.

ENCELTO™ (revakinagene taroretcel-lwey) implant, for intravitreal use

Additional Gold Coast Health Plan Part B Criteria: No

ENCELTO™ is an allogeneic encapsulated cell-based gene therapy indicated for the treatment of adults with idiopathic macular telangiectasia type 2 (MacTel). It is intended for surgical intravitreal implantation under aseptic conditions by a qualified ophthalmologist.

ENCELTO secretes recombinant human ciliary neurotrophic factor (rhCNTF), which is one of several neurotrophic factors endogenously produced by neurons and supporting glial cells. Exogenous CNTF is though to initially target Müller glia to trigger a cascade of signaling events that may promote photoreceptor survival. The exact mechanism of action of ENCELTO, however, is not completely understood.

The efficacy of ENCELTO was evaluated in 2 studies: Study NTMT-03-A and Study NTMT-03-B. The most common adverse reactions (incidence ≥ 2%) were conjunctival hemorrhage, delayed dark adaptation, foreign body sensation, eye pain, suture related complications, miosis, conjunctival hyperemia, eye pruritus, ocular discomfort, vitreous hemorrhage, blurred vision, headache, dry eye, eye irritation, cataract progression or formation, vitreous floaters, severe vision loss, eye discharge, anterior chamber cell and iridocyclitis.

ENCELTO is contraindicated in patients with active or suspected ocular or periocular infections, and in patients with known hypersensitivity to Endothelial Serum Free Media (Endo-SFM). There is currently no data on the use of ENCELTO in pregnant women or during lactation.

References:

1. *Encelto* Billing and Coding Guide. Cumberland, RI. Neurotech Pharmaceuticals, Inc. Available at: https://www.encelto.com/ecp/Billing-And-Coding-Guide.pdf. Accessed September 17, 2025.
2. *Encelto* Prescribing Information. Cumberland, RI. Neurotech Pharmaceuticals, Inc. 2025. Available at: https://www.neurotechpharmaceuticals.com/wp-content/uploads/ENCELTO-PRESCRIBING-INFORMATION.pdf. Accessed September 17, 2025.

Enjaymo *(sutimlimab-jome)*

Additional Gold Coast Health Plan 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 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

1. Enjaymo [Package Insert]. Waltham, MA; Bioverative USA Inc.: 2022
2. Jäger, U., Barcellini, W., et al. (2020). "Diagnosis and treatment of autoimmune hemolytic anemia in adults: Recommendations from the First International Consensus Meeting." Blood Rev 41: 100648. https://doi.org/10.1016/j.blre.2019.100648

Entyvio *(vedolizumab)*

Additional Gold Coast Health Plan 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

1. Entyvio [Package Insert]. Lexington, MA; Takeda Pharmaceuticals U.S.A. Inc: 2022
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

3. 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

Erzofri *(paliperidone palmitate)*

Additional Gold Coast Health Plan Part B Criteria: Yes

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.

References

1. Erzofri (Package Insert]. Yantai, Shandong Province, China; Shandong Luye Pharmaceutical Co., Ltd: 2024

2. Keepers GA, Fochtmann LJ, Anzia JM, et al. The American Psychiatric Association Practice Guideline for the Treatment of Patients With Schizophrenia. *Am J Psychiatry*. 2020;177(9):868-872. doi:10.1176/appi.ajp.2020.177901

Evenity *(romosozumab-aqqg)*

Additional Gold Coast Health Plan 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.

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 (e.g., bisphosphonates).

References

1. Camacho PM, Petak SM, Binkley N, et al. American Association of Clinical Endocrinologists/American College of Endocrinology Clinical Practice Guidelines for the Diagnosis and Treatment of

Postmenopausal Osteoporosis-2020 Update. Endocrine practice: official journal of the American College of Endocrinology and the American Association of Clinical Endocrinologists. 2020;26:1-46. DOI: 10.4158/GL-2020-0524SUPPL

2. Evenity [Package Insert]. Thousand Oaks, CA; Amgen Inc.: 2019

Evkeeza *(evinacumab-dgnb)*

Additional Gold Coast Health Plan Part B Criteria: Yes

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.

References

1. Evkeeza [Package Insert]. Tarrytown, NY; Regeneron Pharmaceuticals, Inc.: 2021
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. Raal FJ et al. Familial hypercholesterolemia treatments: Guidelines and new therapies. Atherosclerosis 277 (2018) 483-492

EXDENSUR (depemokimab-ulaa) injection, for subcutaneous use
Additional Gold Coast Health Plan Part B Criteria: No

EXDENSUR is an interleukin-5 (IL-5) antagonist, a monoclonal antibody (humanized immunoglobulin G [IgG]1 kappa) indicated for add-on maintenance treatment of severe asthma characterized by an eosinophilic phenotype in adult and pediatric patients aged 12 years and older.

The safety of EXDENSUR was based on a pooled safety population from 2 replicate, randomized, double-blind, parallel-group, placebo-controlled, multicenter clinical trials (SWIFT-1 and SWIFT-2) of 52 weeks duration. The 2 trials included 762 adult and pediatric patients 12 years of age and older with asthma, who received either EXDENSUR 100 mg or placebo administered subcutaneously once every 6 months in addition to their existing background medications for asthma [see Clinical Studies (14)]. A total of 475 patients received 2 doses of EXDENSUR 100 mg in these trials.

The efficacy of EXDENSUR for the add-on maintenance treatment of severe asthma characterized by an eosinophilic phenotype was evaluated in 2 replicate, randomized (2:1 to EXDENSUR or placebo), double-blind, parallel-group, placebo-controlled, multicenter clinical trials (SWIFT-1 [NCT04719832] and SWIFT-2 [NCT04718103]) of 52 weeks duration.

The trials enrolled adult and pediatric patients aged 12 years and older with asthma characterized by an

eosinophilic phenotype, defined as a blood eosinophil count ≥150 cells/mcL at screening or ≥300 cells/mcL documented in the year prior to study entry. Patients were required to have 2 or more asthma exacerbations requiring treatment with systemic corticosteroids (SCS) in the prior year while on background asthma therapy consisting of a medium- to high-dose ICS plus at least one additional asthma controller with or without maintenance oral corticosteroids (OCS). Patients were also required to have reduced lung function at baseline (pre-bronchodilator forced expiratory volume in 1 second [FEV1].

In SWIFT-1 and SWIFT-2, the annualized rate of asthma exacerbations was significantly lower in patients receiving EXDENSUR compared to placebo (Table 3). During the 52-week treatment period, fewer patients experienced exacerbations in the EXDENSUR group (32% and 32%) compared to the placebo group (46% and 50%) in SWIFT-1 and SWIFT-2, respectively.

The most common adverse reactions (incidence ≥4%) were upper respiratory tract infection, allergic rhinitis, influenza, arthralgia, and pharyngitis.

In women with poorly or moderately controlled asthma, evidence demonstrates that there is an increased risk of preeclampsia in the mother, and prematurity, low birth weight, and small for gestational age in the neonate. The level of asthma control should be closely monitored in pregnant women and treatment adjusted as necessary to maintain optimal control. EXDENSUR can cross the placenta during pregnancy and the presence of the YTE modification may prolong and increase exposure to the infant exposed in utero. The impact of EXDENSUR transmission to the fetus should be considered.

References**:**
1. EXDENSUR Prescribing Information. Philadelphia, PA: GlaxoSmithKline LLC; 2025.

EYLEA (aflibercept) intravitreal injection
EYLEA HD (aflibercept) intravitreal injection
PAVBLU (aflibercept-ayyj) biosimilar, intravitreal injection

Additional Gold Coast Health Plan Part B Criteria: No

Because clinical trials are conducted under widely varying conditions, adverse reaction rates observed in the clinical trials of a drug cannot be directly compared to rates in other clinical trials of the same or another drug and may not reflect the rates observed in practice.

A total of 2980 adult patients treated with EYLEA constituted the safety population in eight phase 3 studies. Among those, 2379 patients were treated with the recommended dose of 2 mg. Serious adverse reactions related to the injection procedure have occurred in <0.1% of intravitreal injections with EYLEA including endophthalmitis and retinal detachment. The most common adverse reactions (≥5%) reported in patients receiving EYLEA were conjunctival hemorrhage, eye pain, cataract, vitreous detachment, vitreous floaters, and intraocular pressure increased.

A total of 1755 patients were treated with EYLEA HD and 804 patients were treated with EYLEA 2 mg in three clinical studies. The most common adverse reactions reported in ≥3% of patients treated with EYLEA HD were cataract, conjunctival hemorrhage, corneal epithelium defect, intraocular pressure increased, ocular discomfort/eye pain/eye irritation, retinal hemorrhage, vision blurred, vitreous

detachment and vitreous floaters.

A total of 2980 adult patients treated with aflibercept constituted the safety population in eight phase 3 studies. Among those, 2379 patients were treated with the recommended dose of 2 mg. Serious adverse reactions related to the injection procedure have occurred in <0.1% of intravitreal injections with aflibercept including endophthalmitis and retinal detachment. The most common adverse reactions (≥5%) reported in patients receiving aflibercept were conjunctival hemorrhage, eye pain, cataract, vitreous detachment, vitreous floaters, and intraocular pressure increased.

References**:**

1. EYLEA Prescribing Information. Tarrytown, NY: Regeneron Pharmaceuticals, Inc.; 2024. Available at: https://www.regeneron.com/downloads/eylea_fpi.pdf. Accessed on 1/19/26.
2. EYLEA HD Prescribing Information. Tarrytown, NY: Regeneron Pharmaceuticals, Inc.; 2024. Available at: https://www.regeneron.com/downloads/eyleahd_fpi.pdf. Accessed on 1/19/26.
3. PAVBLU Prescribing Information. Thousand Oaks, CA: Amgen, Inc.; 2024. Available at: https://www.pi.amgen.com/-/media/Project/Amgen/Repository/pi-amgen-com/pavblu/pavblu_fpi_english.pdf. Accessed on 1/19/26.

Fasenra *(benralizumab)*

Additional Gold Coast Health Plan 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.

References

1. Fasenra [Package Insert]. Sodertalje, Sweden; AstraZeneca AB: 2024
2. Global Initiative for Asthma. Global Strategy for Asthma Management and

Prevention, 2023

3. Global Initiative for Asthma. Difficult-To-Treat & Severe Asthma in adolescents and adult patients, 2024.
4. Bleecker ER, Fitzgerald JM, Chanez P, et al. Efficacy and safety of Fasenra for patients with severe asthma uncontrolled with high-dosage inhaled corticosteroids and long-acting β2- agonists (SIROCCO): a randomized, multicenter, placebo-controlled phase 3 trial. Lancet. 2016;388:2115-2127
5. Agache I, Akdis CA, Akdis M, et al. EAACI Biologicals Guidelines-Recommendations for severe asthma. *Allergy*. 2021;76(1):14-44
6. Chung SA, et al. 2021 American College of Rheumatology/Vasculitis Foundation Guideline for the Management of Antineutrophil Cytoplasmic Antibody-Associated Vasculitis., 2021.

Fylnetra *(pegfilgrastim-pbbk)*

Additional Gold Coast Health Plan Part B Criteria: Yes

Fylnetra is a leukocyte growth factor indicated to decrease the incidence of infection, as manifested by febrile neutropenia, in patients with nonmyeloid malignancies receiving myelosuppressive anti-cancer drugs associated with a clinically significant incidence of febrile neutropenia.

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

1. Fylnetra [Package Insert]. Piscataway, NJ; Kashiv Biosciences, LLC: 2022
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 1.2025 — October 11, 2024. Available at: https://www.nccn.org/professionals/physician_gls/pdf/growthfactors.pdf

Gel-One *(hyaluronan/ hyaluronic acid)* for intra-articular injection

Additional Gold Coast Health Plan Part B Criteria: Yes

Gold Coast Health Plan follows LCD L39529 (Intraarticular Knee Injections of Hyaluronan).

Hyaluronic acid injections are indicated to treat osteoarthritis pain of the knee when conservative nonpharmacologic therapy and non-steroidal anti-inflammatory drugs (NSAIDs) or simple analgesics, such as acetaminophen, have failed.

The 2019 American College of Rheumatology (ACR)/Arthritis Foundation (AF) Guideline for the Management of Osteoarthritis of the Hand, Hip, and Knee recommends a comprehensive plan for the management of osteoarthritis (OA) in an individual patient that may include educational, behavioral, psychosocial, and physical interventions, as well as topical, oral, and intraarticular medications. The guidelines strongly recommend exercise, weight loss in patients with knee A who are overweight or obese, self-efficacy and self-management programs, tai chi, cane use, hand orthoses for first

carpometacarpal (CMC) joint OA, tibiofemoral bracing for tibiofemoral knee OA, topical nonsteroidal anti-inflammatory drugs (NSAIDs) for knee OA, oral NSAIDs, and intraarticular glucocorticoid injections for knee OA.

Intraarticular hyaluronic acid injections are conditionally recommended against in patients with knee and/or first CMC joint OA and strongly recommended against in patients with hip OA. In prior systematic reviews, apparent benefits of hyaluronic acid injections in OA have been reported. These reviews have not, however, considered the risk of bias of the individual primary studies. The conditional recommendation against is consistent with the use of hyaluronic acid injections, in the context of shared decision-making that recognizes the limited evidence of benefit of this treatment, when other alternatives have been exhausted or failed to provide satisfactory benefit.

The 2021 American Academy of Orthopaedic Surgeons (AAOS) Evidence-Based Clinical Practice Guideline for the Management of OA of the Knee (Non-Arthroplasty) does not recommend hyaluronic acid (HA) intra-articular injection(s) for routine use in the treatment of symptomatic osteoarthritis of the knee. Some studies demonstrated a statistical benefit with the use of HA but could not reach the significance for a minimally clinical meaningful difference, leading to the conclusion that viscosupplementation can represent a viable option for some patients that failed other treatments when appropriately indicated. Analyses of these studies also demonstrated no significant differences among different viscosupplementation formulations.

References

1. Gel-One [Package Insert]. Warsaw, IN; Zimmer Biomet. 2011
2. Bannuru RR, Osani, MC, et al. OARSI guidelines for the non-surgical management of knee, hip, and polyarticular osteoarthritis.Osteoarth Cart 2019: 27: 1578-1589.
3. American Academy of Orthopaedic Surgeons Management of Osteoarthritis of the Knee (NonArthroplasty) Evidence-Based Clinical Practice Guideline. https://www.aaos.org/oak3cpg. Published 08/31/2021
4. Centers for Medicare & Medicaid Services Medicare Coverage Database. Local Coverage Determination (LCD) L39529: Intraarticular Knee Injections of Hyaluronan. https://www.cms.gov/medicare-coverage-database/view/lcd.aspx?lcdid=39529

Additional Gold Coast Health Plan Part B Criteria: Yes

Gold Coast Health Plan follows LCD L39529 (Intraarticular Knee Injections of Hyaluronan).

Hyaluronic acid injections are indicated to treat osteoarthritis pain of the knee when conservative nonpharmacologic therapy and non-steroidal anti-inflammatory drugs (NSAIDs) or simple analgesics, such as acetaminophen, have failed.

The 2019 American College of Rheumatology (ACR)/Arthritis Foundation (AF) Guideline for the Management of Osteoarthritis of the Hand, Hip, and Knee recommends a comprehensive plan for the management of osteoarthritis (OA) in an individual patient that may include educational, behavioral, psychosocial, and physical interventions, as well as topical, oral, and intraarticular medications. The guidelines strongly recommend exercise, weight loss in patients with knee A who are overweight or obese, self-efficacy and self-management programs, tai chi, cane use, hand orthoses for first carpometacarpal (CMC) joint OA, tibiofemoral bracing for tibiofemoral knee OA, topical nonsteroidal anti-inflammatory drugs (NSAIDs) for knee OA, oral NSAIDs, and intraarticular glucocorticoid injections for knee OA.

Intraarticular hyaluronic acid injections are conditionally recommended against in patients with knee and/or first CMC joint OA and strongly recommended against in patients with hip OA. In prior systematic reviews, apparent benefits of hyaluronic acid injections in OA have been reported. These reviews have not, however, considered the risk of bias of the individual primary studies. The conditional recommendation against is consistent with the use of hyaluronic acid injections, in the context of shared decision-making that recognizes the limited evidence of benefit of this treatment, when other alternatives have been exhausted or failed to provide satisfactory benefit.
The 2021 American Academy of Orthopedic Surgeons (AAOS) Evidence-Based Clinical Practice Guideline for the Management of OA of the Knee (Non-Arthroplasty) does not recommend hyaluronic acid (HA) intra-articular injection(s) for routine use in the treatment of symptomatic osteoarthritis of the knee. Some studies demonstrated a statistical benefit with the use of HA but could not reach the significance for a minimally clinical meaningful difference, leading to the conclusion that viscosupplementation can represent a viable option for some patients that failed other treatments when appropriately indicated. Analyses of these studies also demonstrated no significant differences among different viscosupplementation formulations.

References

1. GenVisc 850 [Package Insert]. Madrid, Spain; Tedec Meiji Farma
2. Bannuru RR, Osani, MC, et al. OARSI guidelines for the non-surgical management of knee, hip, and polyarticular osteoarthritis.Osteoarth Cart 2019: 27: 1578-1589.
3. American Academy of Orthopaedic Surgeons Management of Osteoarthritis of the Knee (NonArthroplasty) Evidence-Based Clinical Practice Guideline. https://www.aaos.org/oak3cpg. Published 08/31/2021
4. Centers for Medicare & Medicaid Services Medicare Coverage Database. Local Coverage Determination (LCD) L39529: Intraarticular Knee Injections of Hyaluronan. https://www.cms.gov/medicare-coverage-database/view/lcd.aspx?lcdid=39529

Granix *(tbo-filgrastim)*

Additional Gold Coast Health Plan Part B Criteria: Yes

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

1. Granix [Package Insert] Vilnius, Lithuania; Sicor Biotech UAB: 2014
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 1.2025 — October 11, 2024. Available at: https://www.nccn.org/professionals/physician_gls/pdf/growthfactors.pdf

Hemgenix *(etranacogene dezaparvovec-drlb)*

Additional Gold Coast Health Plan 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.
3. Shapiro AD. Hemophilia b. 2018. Available at: https://rarediseases.org/rare-diseases/hemophilia-b/.

Herceptin *(trastuzumab)*

Additional Gold Coast Health Plan Part B Criteria: Yes

Gold Coast Health Plan also follows LCD L37205: Chemotherapy Drugs and their Adjuncts.

Herceptin is a HER2/neu receptor antagonist indicated in adults for:

- The treatment of HER2-overexpressing breast cancer.
- The treatment of HER2-overexpressing metastatic gastric or gastroesophageal junction adenocarcinoma.

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.

References

1. Herceptin [Package Insert]. South San Francisco, CA; Genentech, Inc.: 2010
2. National Comprehensive Cancer Network. Breast Cancer Version 1.2025 — January 31, 2025
3. National Comprehensive Cancer Network. Gastric Cancer Version 5.2024 — December 20, 2024
4. Centers for Medicare & Medicaid Services. Local Coverage Determination (LCD) L37205: Chemotherapy Drugs and their Adjuncts. https://www.cms.gov/medicare-coverage-database/view/lcd.aspx?lcdId=37205&ver=15

Herceptin Hylecta *(trastuzumab and hyaluronidase)*

Additional Gold Coast Health Plan Part B Criteria: Yes

Gold Coast Health Plan also follows LCD L37205: Chemotherapy Drugs and their Adjuncts.

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.

References

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

2. National Comprehensive Cancer Network. Breast Cancer Version 1.2025 — January 31, 2025

3. National Comprehensive Cancer Network. Gastric Cancer Version 5.2024 — December 20, 2024

4. Centers for Medicare & Medicaid Services. Local Coverage Determination (LCD) L37205: Chemotherapy Drugs and their Adjuncts. https://www.cms.gov/medicare-coverage-database/view/lcd.aspx?lcdId=37205&ver=15

Hercessi *(trastuzumab-strf)*

Additional Gold Coast Health Plan Part B Criteria: Yes

Gold Coast Health Plan also follows LCD L37205: Chemotherapy Drugs and their Adjuncts.

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.

References

1. Hercessi [prescribing information]. Raleigh, NC: Accord BioPharma Inc.; April 2024.

2. National Comprehensive Cancer Network. Breast Cancer Version 1.2025 — January 31, 2025

3. National Comprehensive Cancer Network. Gastric Cancer Version 5.2024 — December 20, 2024

4. Centers for Medicare & Medicaid Services. Local Coverage Determination (LCD) L37205: Chemotherapy Drugs and their Adjuncts. https://www.cms.gov/medicare-coverage-database/view/lcd.aspx?lcdId=37205&ver=15

Herzuma *(trastuzumab-pkrb)*

Additional Gold Coast Health Plan Part B Criteria: Yes

Gold Coast Health Plan also follows LCD L37205: Chemotherapy Drugs and their Adjuncts.

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.

References

1. Herzuma [Package Insert]. Yeonsu-gu, Incheon; Celltrion, Inc.: 2019
2. National Comprehensive Cancer Network. Breast Cancer Version 1.2025 — January 31, 2025
3. National Comprehensive Cancer Network. Gastric Cancer Version 5.2024 — December 20, 2024
4. Centers for Medicare & Medicaid Services. Local Coverage Determination (LCD) L37205: Chemotherapy Drugs and their Adjuncts. https://www.cms.gov/medicare-coverage-database/view/lcd.aspx?lcdId=37205&ver=15

Hyalgen *(hyaluronan/ hyaluronic acid) for intra-articular injection*

Additional Gold Coast Health Plan Part B Criteria: Yes

Gold Coast Health Plan follows LCD L39529 (Intraarticular Knee Injections of Hyaluronan).

Hyaluronic acid injections are indicated to treat osteoarthritis pain of the knee when conservative nonpharmacologic therapy and non-steroidal anti-inflammatory drugs (NSAIDs) or simple analgesics, such as acetaminophen, have failed.

The 2019 American College of Rheumatology (ACR)/Arthritis Foundation (AF) Guideline for the Management of Osteoarthritis of the Hand, Hip, and Knee recommends a comprehensive plan for the management of osteoarthritis (OA) in an individual patient that may include educational, behavioral, psychosocial, and physical interventions, as well as topical, oral, and intraarticular medications. The guidelines strongly recommend exercise, weight loss in patients with knee A who are overweight or obese, self-efficacy and self-management programs, tai chi, cane use, hand orthoses for first carpometacarpal (CMC) joint OA, tibiofemoral bracing for tibiofemoral knee OA, topical nonsteroidal anti-inflammatory drugs (NSAIDs) for knee OA, oral NSAIDs, and intraarticular glucocorticoid injections for knee OA.

Intraarticular hyaluronic acid injections are conditionally not recommended in patients with knee and/or first CMC joint OA and strongly not recommended in patients with hip OA. In prior systematic reviews, apparent benefits of hyaluronic acid injections in OA have been reported. These reviews have not, however, considered the risk of bias of the individual primary studies. The conditional recommendation against is consistent with the use of hyaluronic acid injections, in the context of shared decision-making that recognizes the limited evidence of benefit of this treatment, when other alternatives have been exhausted or failed to provide satisfactory benefit.

The 2021 American Academy of Orthopaedic Surgeons (AAOS) Evidence-Based Clinical Practice Guideline for the Management of OA of the Knee (Non-Arthroplasty) does not recommend hyaluronic acid (HA) intra-articular injection(s) for routine use in the treatment of symptomatic osteoarthritis of the knee. Some studies demonstrated a statistical benefit with the use of HA but could not reach the significance for a minimally clinical meaningful difference, leading to the conclusion that viscosupplementation can represent a viable option for some patients that failed other treatments when appropriately indicated. Analyses of these studies also demonstrated no significant differences among different viscosupplementation formulations.

References

1. Hyalgen [Package Insert]. Abano Terme, Padua; Fidia Farmaceutici S.p.A.: 1997
2. Bannuru RR, Osani, MC, et al. OARSI guidelines for the non-surgical management of knee, hip, and polyarticular osteoarthritis. Osteoarth Cart 2019: 27: 1578-1589.
3. American Academy of Orthopaedic Surgeons Management of Osteoarthritis of the Knee (NonArthroplasty) Evidence-Based Clinical

Practice Guideline. https://www.aaos.org/oak3cpg. Published 08/31/2021

4. Centers for Medicare & Medicaid Services Medicare Coverage Database. Local Coverage Determination (LCD) L39529: Intraarticular Knee Injections of Hyaluronan. https://www.cms.gov/medicare-coverage-database/view/lcd.aspx?lcdid=39529

Hymovis *(hyaluronan/ hyaluronic acid) for intra-articular injection*

Additional Gold Coast Health Plan Part B Criteria: Yes

Gold Coast Health Plan follows LCD L39529 (Intraarticular Knee Injections of Hyaluronan).

Hyaluronic acid injections are indicated to treat osteoarthritis pain of the knee when conservative nonpharmacologic therapy and non-steroidal anti-inflammatory drugs (NSAIDs) or simple analgesics, such as acetaminophen, have failed.

The 2019 American College of Rheumatology (ACR)/Arthritis Foundation (AF) Guideline for the Management of Osteoarthritis of the Hand, Hip, and Knee recommends a comprehensive plan for the management of osteoarthritis (OA) in an individual patient that may include educational, behavioral, psychosocial, and physical interventions, as well as topical, oral, and intraarticular medications. The guidelines strongly recommend exercise, weight loss in patients with knee A who are overweight or obese, self-efficacy and self-management programs, tai chi, cane use, hand orthoses for first carpometacarpal (CMC) joint OA, tibiofemoral bracing for tibiofemoral knee OA, topical nonsteroidal anti-inflammatory drugs (NSAIDs) for knee OA, oral NSAIDs, and intraarticular glucocorticoid injections for knee OA.

Intraarticular hyaluronic acid injections are conditionally not recommended in patients with knee and/or first CMC joint OA and strongly not recommended in patients with hip OA. In prior systematic reviews, apparent benefits of hyaluronic acid injections in OA have been reported. These reviews have not, however, considered the risk of bias of the individual primary studies. The conditional recommendation against is consistent with the use of hyaluronic acid injections, in the context of shared decision-making that recognizes the limited evidence of benefit of this treatment, when other alternatives have been exhausted or failed to provide satisfactory benefit.

The 2021 American Academy of Orthopaedic Surgeons (AAOS) Evidence-Based Clinical Practice Guideline for the Management of OA of the Knee (Non-Arthroplasty) does not recommend hyaluronic acid (HA) intra-articular injection(s) for routine use in the treatment of symptomatic osteoarthritis of the knee. Some studies demonstrated a statistical benefit with the use of HA but could not reach the significance for a minimally clinical meaningful difference, leading to the conclusion that viscosupplementation can represent a viable option for some patients that failed other treatments when appropriately indicated. Analyses of these studies also demonstrated no significant differences among different viscosupplementation formulations.

References

1. Hymovis [Package Insert]. Abano Terme, Padua; Fidia Farmaceutici S.p.A
2. Bannuru RR, Osani, MC, et al. OARSI guidelines for the non-surgical management of knee, hip, and polyarticular osteoarthritis.Osteoarth Cart 2019: 27: 1578-1589.
3. American Academy of Orthopaedic Surgeons Management of Osteoarthritis of the Knee (NonArthroplasty) Evidence-Based Clinical Practice Guideline. https://www.aaos.org/oak3cpg. Published 08/31/2021
4. Centers for Medicare & Medicaid Services Medicare Coverage Database. Local Coverage Determination (LCD) L39529: Intraarticular Knee Injections of Hyaluronan. https://www.cms.gov/medicare-coverage-database/view/lcd.aspx?lcdid=39529

Hympavzi *(marstacimab-hncq)*

Additional Gold Coast Health Plan 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. WFH defines 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.

References

1. Hympavzi™ subcutaneous injection [prescribing information]. New York, NY: Pfizer; October 2024.

2. Clinicaltrials.gov. Study of the Efficacy and Safety PF-06741086 in Adult and Teenage Participants With Severe Hemophilia A or Moderately Severe to Severe Hemophilia B. (NCT 03938792) Available at: https://clinicaltrials.gov/study/NCT03938792?tab=history&a=46

3. 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.

4. Matino D, Acharya S, Palladino A, et al. Efficacy and safety of the anti-tissue factor pathway inhibitor marstacimab in participants with severe hemophilia A without inhibitors. Results from the BASIS trial. Presented at: American Society of Hematology; San Diego, CA: December 7-12, 2023.
5. Acharya SS, Matino D, Palladino A, et al. Safety and efficacy of the anti-tissue factor pathway inhibitor marstacimab in participants with severe hemophilia without inhibitors: results from the Phase 3 BASIS trial and ongoing long-term extension study. Presented at: Thrombosis and Hemostasis Societies of North America Summit; Chicago, IL; April 4-6, 2024.
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

iDose TR *(travoprost intracameral implant)*

Additional Gold Coast Health Plan Part B Criteria: Yes

iDose TR is a prostaglandin analog indicated for the reduction of intraocular pressure (IOP) in patients with open-angle glaucoma (OAG) or ocular hypertension (OHT).

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

1. IDOSE TR (travoprost implant) [prescribing information]. San Clemente, CA: Glaukos Corp.; 2023
2. American Academy of Ophthalmology: Primary Open-Angle Glaucoma Preferred Practice Pattern, 2020

Ilaris *(canakinumab)*

Additional Gold Coast Health Plan 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

1. Ilaris [prescribing information]. East Hanover, NJ: Novartis. August 2023
2. Fitzgerald JD, et al. 2020 American College of Rheumatology Guideline for the Management of Gout. Arthritis Care and Research. Vol. 72, No. 6, June 2020:744-760

Ilumya *(tildrakizumab)*

Additional Gold Coast Health Plan 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.

References

1. Ilumya [Package Insert]. Whitehouse Station, NJ; Merck & CO., Inc.: 2018
2. Menter A, et al. Joint American Academy of Dermatology-National Psoriasis Foundation guidelines of care for the management of psoriasis with systemic nonbiologic therapies. J Am Acad Dermatol. 2020;82(6):1445-1486.
3. Menter A, et al. Joint AAD-NPF guidelines of care for the management and treatment of psoriasis with biologics. J Am Acad Dermatol. 2019;80(4):1029-1072.

IMAAVY™ (nipocalimab-aahu) injection, for IV use

Additional Gold Coast Health Plan Part B Criteria: No

IMAAVY™ is a neonatal Fc receptor blocker indicated for the treatment of generalized myasthenia gravis (gMG) in adult and pediatric patients 12 years of age and older who are anti-acetylcholine receptor (AChR) or anti-muscle-specific tyrosine kinase (MuSK) antibody positive.

The efficacy of IMAAVY for the treatment of gMG in adults who are anti-AChR or anti-MuSK antibody positive was established in a 24-week, multicenter, randomized, double-blind, placebo-controlled study (Study 1; NCT04951622). Patients were treated with IMAAVY with the recommended dosage regimen. Study 1 enrolled patients with gMG who met the following criteria: Myasthenia Gravis Foundation of America (MGFA) Clinical Classification Class II to IV, Myasthenia Gravis-Activities of Daily Living (MG-ADL) total score of at least 6, and on stable dose of standard of care MG therapy prior to baseline that included acetylcholinesterase (AChE) inhibitors, steroids or non-steroidal immunosuppressive therapies (NSISTs), either in combination or alone.

In Study 1 and its extension study the safety of IMAAVY was evaluated in 186 patients with gMG who received at least one dose of IMAAVY. Of those patients, 168 patients were exposed to IMAAVY every 2 weeks for at least 6 months, and 140 patients were exposed for at least 12 months. The most common adverse reactions (reported in at least 10% of patients treated with IMAAVY) were respiratory tract infection, peripheral edema, and muscle spasms.

IMAAVY is contraindicated in patients with a history of serious hypersensitivity reaction to nipocalimab or to any of the excipients in IMAAVY.

References:

1. Antozzi C, Vu T, Ramchandren S, et al. Safety and efficacy of nipocalimab in adults with generalized myasthenia gravis (Vivacity-MG3): a phase 3, randomized, double-blind, placebo-controlled study. Lancet Neurol. 2025;24:105-116.

2. Bird, SJ. Overview of the treatment of myasthenia gravis. In: UpToDate, Connor RF (Ed), Wolters Kluwer. (Accessed on September 18, 2025.)
3. Hibberd, PL, Kotton CN. Immunizations in adults with cancer: live-virus vaccines. In: UpToDate, Connor RF (Ed), Wolters Kluwer. (Accessed on September 18, 2025.)
4. *Imaavy* Billing and Coding Guide. Horsham, PA. Janssen Biotech, Inc. Available at: https://asset.jnjwithme.com/document/imaavy-billing-and-coding-guide.pdf. Accessed September 18, 2025.
5. Imaavy Prescribing Information. Horsham, PA. Janssen Biotech, Inc. 2025. Available at: https://www.janssenlabels.com/package-insert/product-monograph/prescribing-information/IMAAVY-pi.pdf. Accessed September 18, 2025.
6. Narayanaswami P, Sanders DB, Wolfe G, et al. International Consensus Guidance for Management of Myasthenia Gravis: 2020 Update. Neurology. 2021;96(3):114-122.

Infliximab injection brand only (J1745 - excludes biosimilar, 10 mg)

Additional Gold Coast Health Plan 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.

References

1. Alikhan A, Sayed C, Alavi A, et al. North American clinical management guidelines for hidradenitis suppurativa: A publication from the United States and Canadian Hidradenitis Suppurativa Foundations: Part I: Diagnosis, evaluation, and the use of complementary and procedural management. J Am Acad Dermatol. 2019;81(1):76-90. doi:10.1016/j.jaad.2019.02.067
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
3. 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.
4. Infliximab injection [Package Insert]. Horsham, PA; Janssen Biotech, Inc.: 1998
5. 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
6. 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.
7. Ward, MM, Deodhar, A, Akl, EA, et al. 2019 Update of the American College of Rheumatology/Spondylitis Association of America/Spondyloarthritis Research and Treatment Network Recommendations for the Treatment of Ankylosing Spondylitis and Nonradiographic Axial Spondyloarthritis. Arthritis Rheumatol. 2019 Oct;71(10):1599-1613

Immune Globulins (IVIG) injection, for IV use

Additional Gold Coast Health Plan Part B Criteria: YES

Gold Coast Health Plan must follow LCD **L34314** - Immune Globulin Intravenous (IVIG)
Immunoglobulin is used to treat a wide variety of diseases, including primary and secondary immunodeficiency states and hematologic and autoimmune disorders. Immunoglobulin is increasingly recognized as a treatment of a variety of medical conditions, not only for its ability to fight infection as a replacement therapy but also for its anti-inflammatory and immunomodulating effects.

Indications for use of IVIG include **primary immunodeficiency** (including but not limited to Common Variable Immunodeficiency (CVID), X-linked Agammaglobulinemia, Congenital Agammaglobulinemia, Wiskott-Aldrich Syndrome and Severe Combined Immunodeficiencies), **Idiopathic Thrombocytopenic Purpura (ITP), Multifocal Motor Neuropathy, B-cell chronic lymphocytic leukemia (CLL), Kawasaki syndrome, chronic inflammatory demyelinating polyneuropathy (CIDP)** and **dermatomyositis**.

Other uses include:
Infection: Immunoglobulins play a role in the treatment and prevention of infection in a variety of clinical scenarios. NCCN recommends IG to prevent infections in certain individuals with chronic lymphocytic leukemia and multiple myeloma. The CDC continues to recommend IG to some children with HIV as well as in the post-exposure prophylaxis of measles, tetanus, and varicella. IG remains first line therapy for Kawasaki disease, a syndrome affecting children which involves fever, rash, and systemic inflammation and vasculitis. The cause of the disease is unknown but may have an infectious origin. IG is used in the acute phase of the disease to reduce the prevalence of coronary artery abnormalities. While it should ideally be administered within 10 days of onset, the American Heart Association recommends use beyond 10 days in the setting of persistent severe manifestations of the disease.

Transplant: IG has also been used in individuals undergoing blood, bone marrow, or solid organ transplant. The consensus guidelines for infection complications in hematopoietic cell transplant suggest that, while IG should not be routinely used, it may be considered pre- and post- transplant when the patient is hypogammaglobulinemic. For solid organ transplant recipients, IG has been used routinely in desensitization prior to transplant. IG may also be considered in antibody-mediated rejection (AMR). AMR remains a significant problem with lack of standardized treatment and limited therapeutic options. Relevant specialists support this indication; and some transplant centers include IG in protocol for AMR. There are literature and guidelines recommending IG in the setting of AMR as well.

Autoimmune diseases: The anti-inflammatory and immunomodulating effects of IG have shown benefit in many autoimmune conditions such as ITP, autoimmune encephalitis, fetal alloimmune thrombocytopenia, autoimmune neutropenia, skin blistering disease, and dermatomyositis. Polymyositis is a very rare condition but is thought to be similar to dermatomyositis. In autoimmune encephalitis, the autoimmune response may be triggered by tumors, and it is important to detect tumors promptly for appropriate overall management. Symptoms of AE may also precede the appearance of a tumor, so continued cancer screening is recommended, especially in individuals who have an incomplete response to medical therapy.

Neurologic conditions: IG is also recommended in several neurologic conditions such as Lambert-Eaton myasthenic syndrome (LEMS), myasthenia gravis (MG), chronic inflammatory demyelinating polyneuropathy (CIDP), and multifocal motor neuropathy (MMN). Several of these conditions require electrodiagnostic tests to confirm diagnosis. These tests include nerve conduction studies (NCS) measuring compound muscle action potential (CMAP), repetitive nerve stimulation (RNS), or single fiber electromyography (SFEMG) (see table below). Stiff person syndrome, a rare condition involving progressive muscle stiffness, is thought to have an autoimmune component. First line treatments are often benzodiazepines or baclofen, but IG is recommended in refractory cases. In some individuals with mild to moderate myasthenia gravis, symptoms may be well controlled on acetylcholinesterase inhibition alone (i.e., pyridostigmine), even though it does not treat the underlying cause. However, the cholinergic adverse effects of pyridostigmine are usually dose-limiting. Addition of steroidal and non-steroidal immunosuppressants is the typical clinical course for individuals whose symptoms are not well

controlled on pyridostigmine alone, with sufficient trial given to the non-steroidal immunosuppressants due to the lengthy onset of action.

All immune globulins have a boxed warning for thrombosis. Risk factors include advanced age, prolonged immobilization, hypercoagulable conditions, history of venous or arterial thrombosis, use of estrogens, indwelling vascular catheters, hyperviscosity, and cardiovascular risk factors. There is a boxed warning for renal dysfunction, acute renal failure and osmotic nephrosis and death. Patients predisposed to renal dysfunction include those with any degree of preexisting renal insufficiency, diabetes mellitus, age greater than 65, volume depletion, sepsis, paraproteinemia, overweight or in patients receiving known nephrotoxic drugs. Renal dysfunction and acute renal failure occur more commonly in patients receiving IVIG products containing sucrose.

Adverse events of immune globulin therapy can be difficult to classify due to the diversity of components in the formulation. Mild adverse events are common and may include low grade fever, headache, nausea, malaise, and myalgia. Infusion related reactions such as urticaria and fever can be prevented by pre-medicating patients with diphenhydramine and acetaminophen. Tension headache is the most common adverse event associated with immune globulin use and ranges in frequency from 26%-61%. Migraine headaches also occur.

Aseptic meningitis has been reported in patients receiving immune globulin administered intravenously and subcutaneously. It typically begins within several hours to two days following treatment. It may occur more frequently in females than males. Discontinuation of immune globulin treatment has resulted in remission of AMS within several days without sequelae. Immunoglobulin A-deficient patients with antibodies to IgA are at greater risk of developing severe hypersensitivity and anaphylactic reactions Because immune globulin products are derived from donor plasma, the transmission of infectious particles is possible.

References:

1. Alyglo prescribing information. GC Biopharma Corp. December 2023.
2. American Academy of Allergy Asthma & Immunology. Primary Immunodeficiency. Accessed at https://www.aaaai.org/conditions-and-treatments/primary-immunodeficiency-disease
3. Asceniv prescribing information. ADMA Biologics. March 2024.
4. Bivigam prescribing information. ADMA Biologics. March 2024.
5. Centers for Medicare & Medicaid Services. Local Coverage Determination (LCD) L34771. Available at: https://www.cms.gov/medicare-coverage-database/view/lcd.aspx?lcdid=34771&ver=51&keyword=cytogam&keywordType=starts&areaId=all&docType=NCA,CAL,NCD,MEDCAC,TA,MCD,6,3,5,1,F,P&contractOption=all&sortBy=relevance&bc=1
6. Flebogamma 10% DIF prescribing information. Grifols Biologicals, Inc. September 2019.
7. Flebogamma 5% DIF prescribing information. Grifols Biologicals, Inc. November 2024.
8. Gammagard Liquid prescribing information. Takeda Pharmaceuticals America, Inc. September 2024.
9. Gammaked prescribing information. Kedrion Biopharma Inc. January 2020.
10. Gammaplex prescribing information. Bio Products Laboratory. May 2024.
11. Gamunex-C prescribing information. Grifols USA Inc. January 2020.

12. Immune Deficiency Foundation Diagnostic & Clinical Care Guidelines for Primary Immunodeficiency Diseases Third Edition. 2015.
13. National Organization for Rare Disorders (NORD) Rare Disease Database. Dermatomyositis. Accessed at https://rarediseases.org/rare-diseases/dermatomyositis/.
14. National Organization for Rare Disorders (NORD) Rare Disease Database. Multifocal Motor Neuropathy. Accessed at https://rarediseases.org/rare-diseases/multifocal-motor-neuropathy/
15. National Institute of Neurological Disorders and Stroke. Multifocal Motor Neuropathy. Accessed at https://www.ninds.nih.gov/health-information/disorders/multifocal-motor-neuropathy
16. Octagam prescribing information. Octapharma USA, Inc. January 2024.
17. Panzyga Prescribing information. Octapharma USA Inc. February 2021.
18. Privigen prescribing information. CSL Behring AG. April 2022.
19. Qivigy prescribing information. Kedrion Biopharma Inc. September 2025.
20. Yimmugo prescribing information. Kedrion Biopharma. July 2024.

Infugem *(gemcitabine hcl)*

Additional Gold Coast Health Plan Part B Criteria: Yes

Gold Coast Health Plan also follows LCD (L37205) for Chemotherapy Drugs and their Adjuncts.

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.

References

1. Centers for Medicare & Medicaid Services (CMS) Local Coverage Determination (LCD) L37205: Chemotherapy Drugs and their Adjuncts. https://www.cms.gov/medicare-coverage-database/view/lcd.aspx?lcdId=37205&ver=15
2. Infugem [Package Insert]. Gujarat, India; Sun Pharmaceutical Ind. Ltd.:

2018

INLEXZO™ (gemcitabine intravesical system)
Additional Gold Coast Health Plan Part B Criteria: YES – LCD L37205

The safety of INLEXZO monotherapy was evaluated in Cohort 2 of SunRISe-1, a multi-center, open-label study in 85 adult patients with BCG-unresponsive NMIBC with CIS, with or without papillary tumors. Patients received INLEXZO (225 mg of gemcitabine) inserted into the bladder every 3 weeks for 6 months, followed by once every 12 weeks for up to 18 months, or until unacceptable toxicity, disease persistence, recurrence, or progression. The median number of doses of INLEXZO administered to patients was 9 (range: 1 to 14) doses. The median duration of exposure to INLEXZO was 41 weeks (range: 1 to 108 weeks).

The most common (>15%) adverse reactions, including laboratory abnormalities, are urinary frequency, urinary tract infection, dysuria, micturition urgency, decreased hemoglobin, increased lipase, urinary tract pain, decreased lymphocytes, hematuria, increased creatinine, increased potassium, increased AST, decreased sodium, bladder irritation, and increased ALT.

The efficacy of INLEXZO was evaluated in Cohort 2 of SunRISe-1 (NCT04640623), a single-arm, multi-center trial in 83 adults with BCG-unresponsive, NMIBC with CIS, with or without papillary tumors (T1, or high-grade Ta) following transurethral resection. BCG-unresponsive NMIBC CIS was defined as persistent or recurrent CIS alone or with Ta/T1 disease within 12 months of adequate BCG therapy. Adequate BCG therapy was defined as a minimum administration of at least five of six doses of an initial induction course plus either of: at least two of three doses of maintenance therapy or at least two of six doses of a second induction course. Prior to treatment, all patients had undergone transurethral resection of bladder tumor (TURBT) to remove all resectable disease (Ta and T1 components). Residual CIS (Tis components) not amenable to complete resection was permitted. The trial included patients who were ineligible for or who had elected not to undergo radical cystectomy and excluded patients with extra-vesical (i.e., urethra, ureter, or renal pelvis), muscle invasive (T2-T4), locally advanced, or metastatic urothelial carcinoma.

References:

1. Centers for Medicare & Medicaid Services. Local Coverage Determination (LCD) L37205: Chemotherapy Drugs and their Adjuncts. Available at: https://www.cms.gov/medicare-coverage-database/view/lcd.aspx?lcdid=37205&ver=15&keyword=chemotherapy&keywordType=starts&areaId=s6&docType=NCA,CAL,NCD,MEDCAC,TA,MCD,6,3,5,1,F,P&contractOption=all&sortBy=relevance&bc=1.
2. INLEXZO Billing and Coding Guide. Horsham, PA: Janssen Biotech, Inc.; 2025. Available at: https://www.inlexzohcp.com/pdf/Access_and_Reimbursement_Guide.pdf. Accessed on 1/12/26.
3. INLEXZO Prescribing Information. Horsham, PA: Janssen Biotech, Inc.; 2025. Available at: https://www.jnjlabels.com/package-insert/product-monograph/prescribing-information/INLEXZO-pi.pdf. Accessed on 1/12/26.
4. National Comprehensive Cancer Network. Bladder Cancer Version 3.2025. Available at:

https://www.nccn.org/professionals/physician_gls/pdf/bladder.pdf. Accessed on 1/12/26.

ITVISMA® (onasemnogene abeparvovec-brve) suspension, for intrathecal injection

Additional Gold Coast Health Plan Part B Criteria: No

ITVISMA is indicated for the treatment of spinal muscular atrophy (SMA) in adult and pediatric patients 2 years of age and older with confirmed mutation in survival motor neuron 1 (SMN1) gene.

The safety data reflects exposure of ITVISMA in two clinical studies, Study 1, a randomized, sham-controlled study which evaluated the safety of ITVISMA in 126 patients with spinal muscular atrophy (SMA) and Study 2, an open-label-single arm study which evaluated safety of ITVISMA in 27 patients with SMA who were previously treated with nusinersen (at least 4 months washout) or risdiplam (at least 15 days washout). In Study 1, a total of 75 patients received a single intrathecal injection of ITVISMA at a fixed dose of 1.2×10^{14} vg and 51 patients underwent a sham-procedure. In Study 2, a total of 27 patients received a single intrathecal injection of ITVISMA at a fixed dose of 1.2×10^{14} vg. The patients were followed for a duration of 52 weeks for both studies.

The efficacy of ITVISMA was evaluated in a randomized, double-blind, sham-controlled study (Study 1; NCT05089656). The study enrolled patients with spinal muscular atrophy (SMA) who were treatment-naive, and able to sit but never able to walk independently. Patients with elevated (reference to > 1:50) baseline serum anti-AAV9 antibody titer were excluded. A total of 136 patients were randomized in 3:2 ratio to receive either ITVISMA at a dose of 1.2×10^{14} vg by single lumbar intrathecal injection or sham procedure. Randomization was stratified by age and pre-treatment Hammersmith Functional Motor Scale – Expanded (HFMSE) score at screening. A total of 126 patients received the assigned treatment and were included in the efficacy evaluation.

The most common adverse reactions that occurred in at least 10% of patients were upper respiratory tract infection, upper gastrointestinal symptoms, pyrexia, and headache.

References:

1. ITVISMA Billing and Coding Guide. Bannockburn, IL: Novartis Gene Therapies, Inc.; 2025
2. ITVISMA Prescribing Information. Bannockburn, IL: Novartis Gene Therapies, Inc.; 2025

Izervay (avacincaptad pegol sodium/PF)

Additional Gold Coast Health Plan 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.

References

1. Clinicaltrials.gov. A Phase 3 Safety and Efficacy Study of Intravitreal Administration of Zimura (Complement C5 Inhibitor). NCT04435366 (GATHER2).
2. Clinicaltrials.gov. Zimura in Participants with Geographic Atrophy Secondary to Dry AgeRelated Macular Degeneration NCT02686658) (GATHER1).
3. Izervay [Package Insert]. Parsippany, NJ: IVERIC bio, Inc.; August 2023
4. Flaxel CJ, Adelman RA, Bailey ST, et al. Age-related macular degeneration preferred practice pattern. Ophthalmology. 2020 Jan (updated March 2022); 127 (1): 1 - 65. DOI: 10.1016/j.ophtha.2019.09.024

Kanjinti *(trastuzumab-anns)*

Additional Gold Coast Health Plan Part B Criteria: Yes

Gold Coast Health Plan also follows LCD L37205: Chemotherapy Drugs and their Adjuncts.

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.

References

1. Kanjinti (trastuzumab-anns) [package insert]. Thousand Oaks, CA: Amgen Inc.; 2019.
2. National Comprehensive Cancer Network. Breast Cancer Version 1.2025 — January 31, 2025
3. National Comprehensive Cancer Network. Gastric Cancer Version 5.2024 — December 20, 2024
4. Centers for Medicare & Medicaid Services. Local Coverage Determination (LCD) L37205: Chemotherapy Drugs and their Adjuncts. https://www.cms.gov/medicare-coverage-database/view/lcd.aspx?lcdId=37205&ver=15

KEBILIDI™ (eladocagene exuparvovec-tneq) suspension, for intraputaminal infusion

Additional Gold Coast Health Plan Part B Criteria: No

KEBILIDI is a gene therapy indicated for the treatment of adult and pediatric patients with aromatic L-amino acid decarboxylase (AADC) deficiency. Eladocagene exuparvovec gene therapy was previously available in Europe and the UK under the brand name Upstaza. The FDA has granted KEBILIDI accelerated approval based on a change from baseline in gross motor milestone achievement at 48 weeks post-treatment. Continued approval for this indication may be contingent upon verification and description of clinical benefit in a confirmatory clinical trial.

The efficacy of Kebilidi was evaluated in a 48-week, Phase 2, open-label, single arm study (NCT04903288). The trial consisted of a trial phase (8 weeks), an extension phase (to 48 weeks), and an ongoing long-term extension phase (to 260 weeks). All patients (n = 13) received a total dose of 1.8 x 1011 vector genome given as 4 intraputaminal infusions in a single stereotactic neurosurgical procedure. Select outcomes were compared to an external untreated natural history cohort of 44 pediatric patients with severe AADC deficiency with ≥ 1 motor milestone assessment after 2 years of age. Included patients were ages 1 to < 18 years old with genetically confirmed, severe AADC deficiency, decreased AADC enzyme activity in the plasma, and skull maturity appropriate for the procedure. Patients were also required to have persistent neurological defects secondary to AADC deficiency despite standard medical therapy and be unable to ambulate independently.

The most common adverse reactions (≥ 15%) were dyskinesia, pyrexia, hypotension, anemia, salivary hypersecretion, hypokalemia, hypophosphatemia, insomnia, hypomagnesemia, and procedural complications.

References:

1. *Kebilidi* Prescribing Information. Warren, NJ. PTC Therapeutics, Inc. 2024. Available at: https://www.kebilidi.com/prescribing-information.pdf. Accessed September 19, 2025.
2. Wassenberg T, Molero-Luis M, Jeltsch K, et al. Consensus guideline for the diagnosis and treatment of aromatic l-amino acid decarboxylase (AADC) deficiency. Orphanet Journal of Rare Diseases. 2017 Jan 18;12(1):12.

KEYTRUDA QLEX™ (pembrolizumab and berahyaluronidase alfa-pmph) subcutaneous injection

Additional Gold Coast Health Plan Part B Criteria: YES – LCD L37205

Because clinical trials are conducted under widely varying conditions, adverse reaction rates observed in the clinical trials of a drug cannot be directly compared to rates in the clinical trials of another drug and may not reflect the rates observed in practice. The data reflect exposure to intravenous pembrolizumab as a single agent in 2799 patients in three randomized, open-label, active-controlled trials (KEYNOTE-002, KEYNOTE-006, and KEYNOTE-010), which enrolled 912 patients with melanoma and 682 patients with NSCLC, and one single-arm trial (KEYNOTE-001), which enrolled 655 patients with melanoma and 550 patients with NSCLC.

In addition to the 2799 patients, certain subsections in the WARNINGS AND PRECAUTIONS describe adverse reactions observed with exposure to KEYTRUDA QLEX in combination with platinum doublet chemotherapy in a randomized, open-label, active-controlled trial (Study MK-3475A-D77), which enrolled 251 patients with NSCLC; intravenous pembrolizumab as a single agent in a randomized, placebo-controlled trial (KEYNOTE-091), which enrolled 580 patients with resected NSCLC; a non-randomized, open-label, multi-cohort trial (KEYNOTE-012), a non-randomized, open-label, single-cohort trial (KEYNOTE-055), and two randomized, open-label, active-controlled trials (KEYNOTE-040 and KEYNOTE-048 single agent arms), which enrolled 909 patients with HNSCC; in a randomized, open-label, active-controlled trial (KEYNOTE-048 combination arm), which enrolled 276 patients with HNSCC; in combination with axitinib in a randomized, active-controlled trial (KEYNOTE-426), which enrolled 429 patients with RCC; and in post-marketing use. Across all trials, 20 patients were administered either KEYTRUDA QLEX 790 mg/9,600 units every 6 weeks or intravenous pembrolizumab at doses of 2 mg/kg every 3 weeks, 10 mg/kg every 2 weeks, 10 mg/kg every 3 weeks, or 200 mg every 3 weeks. Among the 2799 patients who received intravenous pembrolizumab, 41% were exposed for 6 months or more and 21% were exposed for 12 months or more.

The most common adverse reactions (≥20%) in patients who received KEYTRUDA QLEX in combination with chemotherapy were nausea (25%), fatigue (25%), and musculoskeletal pain (21%). The safety of KEYTRUDA QLEX for the approved indications is also based on the safety of intravenous pembrolizumab given as a single agent or in combination with other antitumor medicines. The most common adverse reactions (≥20%) in patients who received intravenous pembrolizumab were:

- As a single agent: fatigue, musculoskeletal pain, rash, diarrhea, pyrexia, cough, decreased appetite, pruritus, dyspnea, constipation, pain, abdominal pain, nausea, and hypothyroidism.
- In combination with chemotherapy or chemoradiotherapy: fatigue/asthenia, nausea,

constipation, diarrhea, decreased appetite, rash, vomiting, cough, dyspnea, pyrexia, alopecia, peripheral neuropathy, mucosal inflammation, stomatitis, headache, weight loss, abdominal pain, arthralgia, myalgia, insomnia, palmar-plantar erythrodysesthesia, urinary tract infection, hypothyroidism, radiation skin injury, dysphagia, dry mouth, and musculoskeletal pain.

- In combination with chemotherapy and bevacizumab: peripheral neuropathy, alopecia, anemia, fatigue/asthenia, nausea, neutropenia, diarrhea, hypertension, thrombocytopenia, constipation, arthralgia, vomiting, urinary tract infection, rash, leukopenia, hypothyroidism, and decreased appetite.
- In combination with axitinib: diarrhea, fatigue/asthenia, hypertension, hepatotoxicity, hypothyroidism, decreased appetite, palmar-plantar erythrodysesthesia, nausea, stomatitis/mucosal inflammation, dysphonia, rash, cough, and constipation.
- In combination with lenvatinib: hypothyroidism, hypertension, fatigue, diarrhea, musculoskeletal disorders, nausea, decreased appetite, vomiting, stomatitis, weight loss, abdominal pain, urinary tract infection, proteinuria, constipation, headache, hemorrhagic events, palmar-plantar erythrodysesthesia, dysphonia, rash, hepatotoxicity, and acute kidney injury.
- In combination with enfortumab vedotin: rash, peripheral neuropathy, fatigue, pruritus, diarrhea, alopecia, weight loss, decreased appetite, dry eye, nausea, constipation, dysgeusia, and urinary tract infection.

References:

1. Centers for Medicare & Medicaid Services. Local Coverage Determination (LCD) L37205: Chemotherapy Drugs and their Adjuncts. Available at: https://www.cms.gov/medicare-coverage-database/view/lcd.aspx?lcdid=37205&ver=15&keyword=chemotherapy&keywordType=starts&areaId=s6&docType=NCA,CAL,NCD,MEDCAC,TA,MCD,6,3,5,1,F,P&contractOption=all&sortBy=relevance&bc=1.
2. KEYTRUDA QLEX Billing Codes and NDCs. Rashway, NJ: Merck Sharp & Dohme LLC; 2025.
3. KEYTRUDA QLEX Prescribing Information. Rashway, NJ: Merck Sharp & Dohme LLC; 2025.
4. National Comprehensive Cancer Network. Biliary Tract Cancers Version 3.2025.
5. National Comprehensive Cancer Network. Bladder Cancer Version 3.2025.
6. National Comprehensive Cancer Network. Breast Cancer Version 1.2026.
7. National Comprehensive Cancer Network. Cervical Cancer Version 2.2026.
8. National Comprehensive Cancer Network. Colon Cancer Version 5.2025.
9. National Comprehensive Cancer Network. Cutaneous Melanoma Version 2.2025.
10. National Comprehensive Cancer Network. Esophageal and Esophagogastric Junction Cancers. Version 2.2026.
11. National Comprehensive Cancer Network. Gastric Cancer Version 2.2026.
12. National Comprehensive Cancer Network. Head and Neck Cancers Version 1.2026.

13. National Comprehensive Cancer Network. Hepatocellular Carcinoma Version 2.2025.
14. National Comprehensive Cancer Network. Kidney Cancer Version 1.2026.
15. National Comprehensive Cancer Network. Merkel Cell Carcinoma Version 2.2026.
16. National Comprehensive Cancer Network. Non-Small Cell Lung Cancer Version 3.2026.
17. National Comprehensive Cancer Network. Pleural Mesothelioma Version 2.2026.
18. National Comprehensive Cancer Network. Squamous Cell Skin Cancer Version 1.2026.
19. National Comprehensive Cancer Network. Uterine Neoplasms Version 2.2026.

Kisunla *(donanemab-azbt)*

Additional Gold Coast Health Plan Part B Criteria: Yes

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.

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). https://www.cms.gov/medicare-coverage-database/view/ncacal-decision-memo.aspx?proposed=N&ncaid=305
2. Kisunla [Package Insert]. Indianapolis, IN; Eli Lilly and Company: 2024
3. Clinicaltrials.gov. A Study of Donanemab (LY3002813) in Participants With Early Alzheimer's Disease (TRAILBLAZER-ALZ 2. Available at: https://clinicaltrials.gov/study/NCT04437511

Kymriah *(tisagenlecleucel)*

Additional Gold Coast Health Plan Part B Criteria: No

Kymriah is a CD19-directed genetically modified autologous T-cell immunotherapy indicated for the treatment of:

1. Patients up to 25 years of age with B-cell precursor acute lymphoblastic leukemia (ALL) that is refractory or in second or later relapse.
2. Adult patients with relapsed or refractory (r/r) large B-cell lymphoma after two or more lines of systemic therapy, including diffuse large B-cell lymphoma (DLBCL) not otherwise specified, high grade B-cell lymphoma and DLBCL arising from follicular lymphoma.

Gold Coast Health Plan follows NCD 110.24 for Chimeric Antigen Receptor (CAR) T-Cell Therapy.

References

1. Centers for Medicare & Medicaid Services. National Coverage Determination (NCD) 110.24 Chimeric Antigen Receptor (CAR) T-cell Therapy. https://www.cms.gov/medicare-coverage-database/view/ncd.aspx?ncdid=374
2. Kymriah [Package Insert]. East Hanover, NJ; Novartis Pharmaceuticals Corporation: 2022

Lamzede *(velmanase alfa-tycv)*

Additional Gold Coast Health Plan Part B Criteria: Yes

Lamzede is indicated for the treatment of non-central nervous system manifestations of alpha-mannosidosis in adult and pediatric patients.

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

1. Guffon N, Tylki-Szymanska A, Borgwardt L, et al. Recognition of alpha-mannosidosis in pediatric and adult patients: presentation of a diagnostic algorithm from an international working group. Mole Gen & Metab. 2019; 126: 470 – 4
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)*

Additional Gold Coast Health Plan 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—2025" 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. Clinicaltrials.gov. Islet Transplantation in Type I Diabetic Patients Using the University of Illinois at Chicago (UIC) Protocol. NCT03791567 and NCT00679042
3. Rickels MR, et al. Islet Transplantation Versus Standard of Care for Type 1 Diabetes Complicated by Severe Hypoglycemia From the Collaborative Islet Transplant Registry and the T1D Exchange Registry. Diabetes Care 2025; dc241915. https://doi.org/10.2337/dc24-1915

Leqembi *(lecanemab-irmb)*

Additional Gold Coast Health Plan Part B Criteria: No

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

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). https://www.cms.gov/medicare-coverage-database/view/ncd.aspx?ncdid=375&ncdver=1
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)*

Additional Gold Coast Health Plan 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

1. Leqvio [Package Insert]. East Hanover, NJ; Novartis Pharmaceuticals Corporation: 2023
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.
4. McGowan MP, et al. Diagnosis and Treatment of Heterozygous Familial Hypercholesterolemia. Journal of the American Heart Association. 2019; 8:e013225

Loargys (pegzilarginase-nbln) injection, for IV use

Additional Gold Coast Health Plan Part B Criteria: NO

LOARGYS is an arginine specific enzyme indicated for the treatment of hyperargininemia in adult and

pediatric patients 2 years of age and older with Arginase 1 Deficiency (ARG1-D), in conjunction with dietary protein restriction. This indication is approved under accelerated approval based on reduction of plasma arginine. Continued approval for this indication may be contingent upon verification and description of clinical benefit in a confirmatory trial.

The safety and effectiveness of LOARGYS for the treatment of hyperargininemia in adult and pediatric patients with ARG1-D was evaluated in Trial 1 (NCT03921541) which was a multicenter, double-blind, 24-week placebo-controlled trial with a long-term open-label extension period of up to 150 weeks. A total of 32 patients were randomized 2:1 to receive intravenous LOARGYS (n=21) or placebo (n=11) once weekly for 24 weeks. Additional safety information was derived from Trial 2, a Phase 1 open-label trial that evaluated 16 patients between the ages of 5 to 31 years to assess safety, PK and PD of LOARGYS, and Trial 3, an open-label extension including 14 patients from Trial 2. A total of 21 patients between the ages of 2 and 28 years of age, at enrollment, received intravenous LOARGYS dosages up to 0.2 mg/kg once weekly and 11 patients received placebo for 24 weeks.

Most common adverse reactions (>10%) were vomiting, pyrexia, infusion associated reactions and constipation. Across Trials 1, 2, and 3, in patients with ARG1-D, the incidence of hypersensitivity reactions was 42% (5/12) in LOARGYS-treated patients who developed anti-drug antibodies (ADA) (i.e., anti-pegzilarginase-nbln antibodies and/or anti-PEG antibodies) and 3% (1/36) in those who were ADA-negative. Hypersensitivity reactions with symptoms including facial swelling, rash, flushing and dyspnea were reported in 13% (6/48) of LOARGYS-treated patients during clinical trials. Injection site reactions were reported in 14% (6/44) of patients after subcutaneous LOARGYS administration during the open-label extension periods in Trial 1 and Trial 3. Signs and symptoms included pain, erythema, swelling, irritation, and rash at the injection site.

References:

1. Loargys. [Prescribing Information]. Chicago, IL; Immedica Pharma US Inc.: February 2026. Available at: https://www.accessdata.fda.gov/drugsatfda_docs/label/2026/761211Orig1s000lbl.pdf.

Lumizyme *(alglucosidase alfa)*

Additional Gold Coast Health Plan 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)*

Additional Gold Coast Health Plan Part B Criteria: Yes

Lyfgenia is an autologous hematopoietic stem cell-based gene therapy indicated for the treatment of patients 12 years of age or older with sickle cell disease and a history of vaso-occlusive events.

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

1. Lyfgenia [prescribing information]. Somerville, MA: Bluebird Bio, Inc.; 2023
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.

LYMPHIR™ (denileukin diftitox-cxdl) injection, for IV use

Additional Gold Coast Health Plan Part B Criteria: YES – LCD L37205

The safety of LYMPHIR was evaluated in Study 302, an open-label, single-arm, multicenter trial that included 69 patients with relapsed or refractory Stage I-III. Patients received treatment with LYMPHIR 9 mcg/kg daily from Day 1 through Day 5 of each 21-day cycle. Treatment was administered until disease progression or unacceptable toxicity. The median number of LYMPHIR cycles was 6 (range: 1 to 42).

Serious adverse reactions occurred in 38% of patients who received LYMPHIR. Serious adverse reactions in > 2% of patients included capillary leak syndrome (10%), infusion-related reaction (9%), sepsis (7%), skin infection (2.9%), pyrexia (2.9%), and rash (2.9%).

LYMPHIR can cause capillary leak syndrome (CLS), including life-threatening or fatal reactions. CLS was defined in the clinical trials as the occurrence of at least 2 of the following symptoms at any time during LYMPHIR therapy: hypotension, edema, and serum albumin.

The most common adverse reactions (≥20%), including laboratory abnormalities, were increased transaminases, albumin decreased, nausea, edema, hemoglobin decreased, fatigue, musculoskeletal pain, rash, chills, constipation, pyrexia, and capillary leak syndrome.

References:

1. Centers for Medicare & Medicaid Services. Local Coverage Determination (LCD) L37205: Chemotherapy Drugs and their Adjuncts. Available at: https://www.cms.gov/medicare-coverage-database/view/lcd.aspx?lcdid=37205&ver=15&keyword=chemotherapy&keywordType=starts&areaId=s6&docType=NCA,CAL,NCD,MEDCAC,TA,MCD,6,3,5,1,F,P&contractOption=all&sortBy=relevance&bc=1.
2. LYMPHIR Prescribing Information. Cranford, NJ: Citius Oncology, Inc.; 2024. Available at: https://www.lymphirhcp.com/pdf/prescribing-information.pdf. Accessed on 1/12/26.
3. National Comprehensive Cancer Network. T-Cell Lymphomas Version 1.2026. Available at: https://www.nccn.org/professionals/physician_gls/pdf/t-cell.pdf. Accessed on 1/12/26.

LYNOZYFIC™ (linvoseltamab-gcpt) injection, for IV use

Additional Gold Coast Health Plan Part B Criteria: No

LYNOZYFIC is indicated for the treatment of adult patients with relapsed or refractory multiple myeloma (MM) who have received at least four prior lines of therapy, including a proteasome inhibitor, an immunomodulatory agent, and an anti-CD38 monoclonal antibody. This indication was FDA approved under accelerated approval based on response rate and durability of response. Continued approval for this indication may be contingent upon verification and description of clinical benefit in confirmatory

trial(s).

Support for LYNOZYFIC comes from an open-label, phase 2 multicenter study (LINKER-MM1) that evaluated linvoseltamab 200 mg in 117 patients with relapsed or refractory MM who had received at least three prior therapies, including an anti-CD38 monoclonal antibody, a proteasome inhibitor, and an immunomodulatory agent, or were triple-class refractory. Patients could not have received prior BCMA-targeted therapy.

The study ***excluded*** patients with known multiple myeloma brain lesions or meningeal involvement, history of a neurodegenerative condition, history of seizure within 12 months prior to study enrollment, active infection, a history of an allogeneic or autologous stem cell transplantation within 12 weeks, prior BCMA-directed bispecific antibody therapy, prior bispecific T-cell engaging therapy, or prior BCMA CAR-T cell therapy. After a median follow-up of 14.3 months, the overall response rate was 71 percent, with one-half of patients achieving a complete response (CR) or better. The estimated median duration of response was 29.4 months.

The most common adverse reactions (≥20%) were musculoskeletal pain, cytokine release syndrome, cough, upper respiratory tract infection, diarrhea, fatigue, pneumonia, nausea, headache, and dyspnea. The most common Grade 3 to 4 laboratory abnormalities (≥30%) were decreased lymphocyte count, decreased neutrophil count, decreased hemoglobin, and decreased white blood cell count.
Serious adverse reactions occurred in 74% of patients who received LYNOZYFIC. Serious adverse reactions that occurred in >5% of patients included cytokine release syndrome (27%), pneumonia (13%), COVID-19 (7%), and acute kidney injury (5%). Fatal adverse reactions occurred in 7% of patients, and included sepsis (3.4%), chronic kidney disease (0.9%), pneumonia (0.9%), tumor lysis syndrome (0.9%), and encephalopathy (0.9%).

LYNOZYFIC is available only through the LYNOZYFIC REMS program because of the risks of CRS and neurologic toxicity, including ICANS.

References:

1. *Lynozific* Prescribing Information. Tarrytown, NY. Regeneron Pharmaceuticals, Inc. Available at: https://www.regeneron.com/downloads/lynozyfic_fpi.pdf. Accessed September 19, 2025.
2. National Comprehensive Cancer Network. Multiple Myeloma Version 2.2026. Available at: https://www.nccn.org/professionals/physician_gls/pdf/myeloma.pdf. Accessed September 19, 2025.

Margenza *(margetuximab-cmkb)*

Additional Gold Coast Health Plan Part B Criteria: Yes

Gold Coast Health Plan follows LCD **L37205**: Chemotherapy Drugs and their Adjuncts.

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.

References

1. Margenza [Package Insert]. Rockville, MD; MacroGenics, Inc.: 2020
2. National Comprehensive Cancer Network. Breast Cancer Version 1.2025 — January 31, 2025
3. National Comprehensive Cancer Network. Gastric Cancer Version 5.2024 — December 20, 2024
4. Centers for Medicare & Medicaid Services. Local Coverage Determination (LCD) L37205: Chemotherapy Drugs and their Adjuncts. https://www.cms.gov/medicare-coverage-database/view/lcd.aspx?lcdId=37205&ver=15

Monovisc *(hyaluronan/ hyaluronic acid) for intra-articular injection*

Additional Gold Coast Health Plan Part B Criteria: Yes

Gold Coast Health Plan follows LCD L39529 (Intraarticular Knee Injections of Hyaluronan).

Hyaluronic acid injections are indicated to treat osteoarthritis pain of the knee when conservative nonpharmacologic therapy and non-steroidal anti-inflammatory drugs (NSAIDs) or simple analgesics, such as acetaminophen, have failed.

The 2019 American College of Rheumatology (ACR)/Arthritis Foundation (AF) Guideline for the Management of Osteoarthritis of the Hand, Hip, and Knee recommends a comprehensive plan for the management of osteoarthritis (OA) in an individual patient that may include educational, behavioral, psychosocial, and physical interventions, as well as topical, oral, and intraarticular medications. The guidelines strongly recommend exercise, weight loss in

patients with knee A who are overweight or obese, self-efficacy and self-management programs, tai chi, cane use, hand orthoses for first carpometacarpal (CMC) joint OA, tibiofemoral bracing for tibiofemoral knee OA, topical nonsteroidal anti-inflammatory drugs (NSAIDs) for knee OA, oral NSAIDs, and intraarticular glucocorticoid injections for knee OA.

Intraarticular hyaluronic acid injections are conditionally recommended against in patients with knee and/or first CMC joint OA and strongly recommended against in patients with hip OA. In prior systematic reviews, apparent benefits of hyaluronic acid injections in OA have been reported. These reviews have not, however, considered the risk of bias of the individual primary studies. The conditional recommendation against is consistent with the use of hyaluronic acid injections, in the context of shared decision-making that recognizes the limited evidence of benefit of this treatment, when other alternatives have been exhausted or failed to provide satisfactory benefit.

The 2021 American Academy of Orthopaedic Surgeons (AAOS) Evidence-Based Clinical Practice Guideline for the Management of OA of the Knee (Non-Arthroplasty) does not recommend hyaluronic acid (HA) intra-articular injection(s) for routine use in the treatment of symptomatic osteoarthritis of the knee. Some studies demonstrated a statistical benefit with the use of HA but could not reach the significance for a minimally clinical meaningful difference, leading to the conclusion that viscosupplementation can represent a viable option for some patients that failed other treatments when appropriately indicated. Analyses of these studies also demonstrated no significant differences among different viscosupplementation formulations.

References

1. Monovisc [Package Inesrt]. Bedfored, MA; Anika Therapeutics, Inc.
2. Bannuru RR, Osani, MC, et al. OARSI guidelines for the non-surgical management of knee, hip, and polyarticular osteoarthritis. Osteoarth Cart 2019: 27: 1578-1589.
3. American Academy of Orthopaedic Surgeons Management of Osteoarthritis of the Knee (NonArthroplasty) Evidence-Based Clinical Practice Guideline. https://www.aaos.org/oak3cpg. Published 08/31/2021
4. Centers for Medicare & Medicaid Services Medicare Coverage Database. Local Coverage Determination (LCD) L39529: Intraarticular Knee Injections of Hyaluronan. https://www.cms.gov/medicare-coverage-database/view/lcd.aspx?lcdid=39529

Neupogen *(filgrastim)*
Additional Gold Coast Health Plan Part B Criteria: Yes

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 1.2025) October 11, 2024, Available at: growthfactors.pdf

Nexviazyme *(avalglucosidase alfangpt)*

Additional Gold Coast Health Plan 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

Nucala *(mepolizumab)*

Additional Gold Coast Health Plan 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.

References

1. Nucala [Package Insert]. Philadelphia, PA; GlaxoSmithKline LLC: 2019
2. Global Initiative for Asthma. Global Strategy for Asthma Management and Prevention, 2024
3. Global Initiative for Asthma. Difficult-To-Treat & Severe Asthma in adolescents and adult patients, 2024.
4. Chung SA, et al. 2021 American College of Rheumatology/Vasculitis Foundation Guideline for the Management of Antineutrophil Cytoplasmic Antibody-Associated Vasculitis., 2021.
5. Butt NM, Lambert J, Ali S, et. al. Guideline for the investigation and management of eosinophilia. Br J Haematol. 2017;176:553-572

Nulojix *(belatacept)*

Additional Gold Coast Health Plan Part B Criteria: Yes

Gold Coast Health Plan also follows LCD L33824 Immunosuppressive Drugs and LCA A52474 Immunosuppressive Drugs – Policy Article.

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.

References

1. Centers for Medicare & Medicaid Services. Local Coverage Determination (LCD) L33824: Immunosuppressive Drugs. https://www.cms.gov/medicare-coverage-database/view/lcd.aspx?lcdid=33824
2. Nulojix [Package Insert]. Princeton, NJ; Bristol-Myers Squibb Company: 2014
3. Nelson, J., Alvey, N., Bowman, L., Schulte, J., Segovia, M. C., McDermott, J., Te, H. S., Kapila, N., Levine, D. J., Gottlieb, R. L., Oberholzer, J., & Campara, M. (2022). Consensus recommendations for use of maintenance

immunosuppression in solid organ transplantation: Endorsed by the American College of Clinical Pharmacy, American Society of Transplantation, and International Society for Heart and Lung Transplantation: An executive summary. Pharmacotherapy, 42(8), 594–598

Nypozi *(filgrastim-txid)*

Additional Gold Coast Health Plan Part B Criteria: Yes

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

1. Nypozi [Package Insert] San Diego, CA; Tanvex BioPharma USA, Inc: June 2024
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 1.2025) 2024 Oct 11. Available at: https://www.nccn.org/professionals/physician_gls/pdf/growthfactors.pdf.

Ohtuvayre (*ensifentrine*)

Additional Gold Coast Health Plan 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

1. Ohtuvayre [Package Insert]. Raleigh, NC; Verona Pharma, Inc: 2024
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
4. Clinicaltrials.gov. A Phase 3 Trial to Evaluate the Safety and Efficacy of Ensifentrine in Patients With COPD. Available at: https://clinicaltrials.gov/study/NCT04542057

Omvoh *(mirikizumab-mrkz)* IV

Additional Gold Coast Health Plan 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.

References

1. Omvoh™ intravenous infusion and subcutaneous injection [prescribing information]. Indianapolis, IN: EliLilly; October 2023
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.
3. Rubin DT, Ananthakrishnan AN, Siegel CA, et al. ACG clinical guideline: ulcerative colitis in adults. Am J Gastroenterol. 2019; 114: 384–413.

Onpattro *(patisiran)*

Additional Gold Coast Health Plan 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

1. Onpattro [Package Insert]. Cambrdige, MA; Alnylam Pharmaceuticals, Inc.: 2018

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.

Ontruzant *(trastuzumab-dttb)*

Additional Gold Coast Health Plan Part B Criteria: Yes

Gold Coast Health Plan also follows LCD L37205: Chemotherapy Drugs and their Adjuncts.

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.

References

1. Ontruzant [Package Insert]. Incheon, Korea; Samsung Bioepis Co., Ltd.: 2019
2. National Comprehensive Cancer Network. Breast Cancer Version 1.2025 — January 31, 2025
3. National Comprehensive Cancer Network. Gastric Cancer Version 5.2024 — December 20, 2024
4. Centers for Medicare & Medicaid Services. Local Coverage Determination (LCD) L37205: Chemotherapy Drugs and their Adjuncts. https://www.cms.gov/medicare-coverage-database/view/lcd.aspx?lcdId=37205&ver=15

Orencia IV (abatacept)

Additional Gold Coast Health Plan 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.

Orthovisc (hyaluronan/ hyaluronic acid) for intra-articular injection

Additional Gold Coast Health Plan Part B Criteria: Yes

Gold Coast Health Plan follows LCD L39529 (Intraarticular Knee Injections of Hyaluronan).

Hyaluronic acid injections are indicated to treat osteoarthritis pain of the knee when conservative nonpharmacologic therapy and non-steroidal anti-inflammatory drugs (NSAIDs) or simple analgesics, such as acetaminophen, have failed.

The 2019 American College of Rheumatology (ACR)/Arthritis Foundation (AF) Guideline for the Management of Osteoarthritis of the Hand, Hip, and Knee recommends a comprehensive plan for the management of osteoarthritis (OA) in an individual patient that may include educational, behavioral, psychosocial, and physical interventions, as well as topical, oral, and intraarticular medications. The guidelines strongly recommend exercise, weight loss in patients with knee A who are overweight or obese, self-efficacy and self-management programs, tai chi, cane use, hand orthoses for first carpometacarpal (CMC) joint OA, tibiofemoral bracing for tibiofemoral knee OA, topical nonsteroidal anti-inflammatory drugs (NSAIDs) for knee OA, oral NSAIDs, and intraarticular glucocorticoid injections for knee OA.

Intraarticular hyaluronic acid injections are conditionally recommended against in patients with knee and/or first CMC joint OA and strongly recommended against in patients with hip OA. In prior systematic reviews, apparent benefits of hyaluronic acid injections in OA have been reported. These reviews have not, however, considered the risk of bias of the individual primary studies. The conditional recommendation against is consistent with the use of hyaluronic acid injections, in the context of shared decision-making that recognizes the limited evidence of benefit of this treatment, when other alternatives have been exhausted or failed to provide satisfactory benefit.

The 2021 American Academy of Orthopaedic Surgeons (AAOS) Evidence-Based Clinical Practice Guideline for the Management of OA of the Knee (Non-Arthroplasty) does not recommend hyaluronic acid (HA) intra-articular injection(s) for routine use in the treatment of symptomatic osteoarthritis of the knee. Some studies demonstrated a statistical benefit with the use of HA but could not reach the significance for a minimally clinical meaningful difference, leading to the conclusion that

viscosupplementation can represent a viable option for some patients that failed other treatments when appropriately indicated. Analyses of these studies also demonstrated no significant differences among different viscosupplementation formulations.

References

1. Orthovisc [Package Insert]. Woburn, MA; Anika Therapeutics, Inc
2. Bannuru RR, Osani, MC, et al. OARSI guidelines for the non-surgical management of knee, hip, and polyarticular osteoarthritis. Osteoarth Cart 2019: 27: 1578-1589.
3. American Academy of Orthopaedic Surgeons Management of Osteoarthritis of the Knee (NonArthroplasty) Evidence-Based Clinical Practice Guideline. https://www.aaos.org/oak3cpg. Published 08/31/2021
4. Centers for Medicare & Medicaid Services Medicare Coverage Database. Local Coverage Determination (LCD) L39529: Intraarticular Knee Injections of Hyaluronan. https://www.cms.gov/medicare-coverage-database/view/lcd.aspx?lcdid=39529

Oxlumo *(lumasiran) injection*

Additional Gold Coast Health Plan Part B Criteria: Yes

Oxlumo is a HAO1-directed small interfering ribonucleic acid (siRNA) indicated for the treatment of primary hyperoxaluria type 1 (PH1) to lower urinary and plasma oxalate levels in pediatric and adult patients.

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

Additional Gold Coast Health Plan 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

Additional Gold Coast Health Plan Part B Criteria: Yes

Gold Coast Health Plan follows LCD L34771 for Immune Globulins.

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 (e.g., Gammagard S/D, Octagam). Patients with low tolerance for increased intravascular volume may want to avoid products high in sodium or albumin content (e.g., Bivigam).

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 https://www.cms.gov/medicare-coverage-database/view/lcd.aspx?lcdid=34771&ver=49&=

Phesgo *(pertuzumab, trastuzumab, and hyaluronidase-zzxf)*

Additional Gold Coast Health Plan Part B Criteria: Yes

Gold Coast Health Plan also follows LCD L37205: Chemotherapy Drugs and their Adjuncts.

Trastuzumab and pertuzumab are anti-HER2 monoclonal antibodies that bind to the HER2 receptor and inhibit proliferation of tumor cells that overexpress the receptor. Breast cancer is one type of tumor that can be positive for the HER2 receptor.

Phesgo is a combination product which includes the same active ingredients as Perjeta and Herceptin with the addition of hyaluronidase. The hyaluronidase component increases permeability of the subcutaneous tissue which increases the rate of absorption for the active ingredients. This product has the same breast cancer indications as the related products of trastuzumab and pertuzumab containing products. The indications include but may not be limited to use in combination with chemotherapy as neoadjuvant treatment of patients with HER2-positive, locally advanced, inflammatory, or early stage breast cancer (either greater than 2 cm in diameter or node positive); in combination with chemotherapy as adjuvant treatment of patients with HER2-positive early breast cancer at high risk of recurrence; and in combination with docetaxel for treatment of patients with HER2-positive metastatic breast cancer (MBC) who have not received prior anti-HER2 therapy or chemotherapy for metastatic disease.

The National Comprehensive Cancer Network (NCCN) Guidelines provide recommendations for the use of combination therapy with trastuzumab and pertuzumab.

References:

1. Phesgo [prescribing information]. South San Francisco, CA: Genentech, Inc.; June 2020.
2. Clinicaltrials.gov. A phase III, randomized, multicenter, open-label, two-arm study to evaluate the pharmacokinetics, efficacy, and safety of subcutaneous administration of the fixed-dose combination of pertuzumab and trastuzumab in combination with chemotherapy in patients with HER2-positive early breast cancer (NCT03493854). Available at: https://clinicaltrials.gov/ct2/show/NCT03493854?term=NCT03493854&draw=2&rank=1
3. National Comprehensive Cancer Network. Breast Cancer Version 1.2025 — January 31, 2025
4. Centers for Medicare & Medicaid Services. Local Coverage Determination (LCD) L37205: Chemotherapy Drugs and their Adjuncts. https://www.cms.gov/medicare-coverage-database/view/lcd.aspx?lcdId=37205&ver=15

PiaSky (crovalimab-akkz)

Additional Gold Coast Health Plan 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)*

Additional Gold Coast Health Plan 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

Prolia *(denosumab)*

Additional Gold Coast Health Plan Part B Criteria: Yes

Gold Coast Health Plan follows Must follow LCD L34648 Bisphosphonate Drug Therapy

Prolia (denosumab) is a RANK ligand (RANKL) inhibitor indicated for multiple skeletal related conditions including a) the treatment of postmenopausal women with osteoporosis at high risk for fracture, b) to increase bone mass in men with osteoporosis at high risk for fracture, c) the treatment of glucocorticoid-induced osteoporosis in men and women at high risk for fracture, d) to increase bone mass in men at high risk for fracture receiving androgen deprivation therapy for nonmetastatic prostate cancer, and e) to increase bone mass in women at high risk for fracture receiving adjuvant aromatase inhibitor therapy for breast cancer.

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.

Bisphosphonates have been a widely used treatment of osteoporosis for decades. Four bisphosphonates (alendronate, ibandronate, risedronate, and zoledronate) are available in the U.S. which are all available as generic preparations. Additionally, alendronate, risedronate, and zoledronate have evidence for broad-spectrum antifracture efficacy. The AACE Guidelines recommend (in the absence of contraindications) those who have “high fracture risk” can be started on oral agents.

The NCCN Guidelines for Prostate Cancer Version 1.2025 recommend antiresorptive medications to increase bone mineral density and reduce disease-related skeletal complications during androgen-deprivation therapy

(ADT) for prostate cancer, which can include denosumab, zoledronic acid, or alendronate.

The NCCN Guidelines for Breast Cancer Version 1.2025 recommends the use of a bisphosphonate or denosumab to maintain or improve bone mineral density and reduce risk of fractures in postmenopausal patients receiving adjuvant aromatase inhibitor therapy.

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.

AACE Guidelines suggest that a significant decrease in Bone Mineral Density (BMD) or recurrent fractures in a patient who is compliant to therapy may indicate a treatment failure. Rebound bone loss and fractures can occur following discontinuation of denosumab therapy. It is therefore recommended that patients be transitioned to an alternative antiresorptive therapy to prevent rebound bone loss and possible rebound fracture.

References

1. Camacho PM, Petak SM, Binkley N, et al. American Association of Clinical Endocrinologists/American College of Endocrinology Clinical Practice Guidelines for the Diagnosis and Treatment of Postmenopausal Osteoporosis – 2020 Update. Endocr Pract. 2020;26(Suppl 1):1-46. doi:10.4158/GL-2020-0524SUPPL
2. Chakhtoura M, El-Hajj Fuleihan G. Treatment of Hypercalcemia of Malignancy. Endocrinol Metab Clin North Am. 2021;50(4):781-792. doi:10.1016/j.ecl.2021.08.002
3. National Comprehensive Cancer Network. Breast Cancer (Version 1.2025)
4. National Comprehensive Cancer Network. Bone Cancer (Version 2.2025)
5. National Comprehensive Cancer Network. Multiple Myeloma (Version 1.2025)
6. National Comprehensive Cancer Network. Prostate Cancer (Version 1.2025)
7. Prolia [Package Insert]. Thousand Oaks, CA; Amgen, Inc.: 2010
8. Centers for Medicare & Medicaid Services. Local Coverage Determination (LCD) L34648: bisphosphonate Drug Therapy https://www.cms.gov/medicare-coverage-database/view/lcd.aspx?lcdid=34648&ver=29&keyword=Multiple+Myeloma&keywordType=starts&areaId=all&docType=F&contractOption=

all&sortBy=relevance&bc=1

Qalsody *(tofersen)*

Additional Gold Coast Health Plan 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

Reblozyl *(luspatercept-aamt)*

Additional Gold Coast Health Plan 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).

References

1. Reblozyl [Package Insert]. Summit, NJ: Celgene Corporation; 2023
2. Cappellini MD, Cohen A, Porter J, et al. Guidelines for the management of transfusion dependent thalassemia. 2021. Available at: https://issuu.com/internationalthalassaemiafederation/docs/final_guideline_4th
3. National Organization for Rare Disorders. Beta thalassemia. Accessed September 26, 2024. https://rarediseases.org/rarediseases/thalassemia-major/
4. National Comprehensive Cancer Network. Myelodysplastic syndromes (Version 2.2025). January 17, 2025, Available at: mds.pdf
5. Fenaux P, Haase D, Santini , et al. Myelodysplastic syndromes: ESMO Clinical Practice Guidelines for diagnosis, treatment and follow-up. Annals of Oncology. 2020 Jan 9; 32(2): 142- 156.

Rebyota *(fecal microbiota, live-jslm)*

Additional Gold Coast Health Plan 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.

References

1. Rebyota [Package Insert]. Roseville, MN; Reviotix, Inc.
2. Stuart Johnson, Valéry Lavergne, Andrew M Skinner, Anne J Gonzales-Luna, Kevin W Garey, Ciaran P Kelly, Mark H Wilcox, Clinical Practice Guideline by the Infectious Diseases Society of America (IDSA) and Society for Healthcare Epidemiology of America (SHEA): 2021 Focused Update Guidelines on Management of Clostridioides difficile Infection in Adults, Clinical Infectious Diseases, Volume 73, Issue 5, 1 September 2021, Pages e1029–e1044, https://doi.org/10.1093/cid/ciab549

Releuko *(filgrastim-ayow)*

Additional Gold Coast Health Plan Part B Criteria: Yes

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

1. Releuko [Package Insert]. Piscataway, NJ; Kashiv BioSciences, LLC: 2022
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 1.2025) October 11, 2024 Available at: https://www.nccn.org/professionals/physician_gls/pdf/growthfactors.pdf.

Remicade *(infliximab)*

Additional Gold Coast Health Plan 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.

References

1. Alikhan A, Sayed C, Alavi A, et al. North American clinical management guidelines for hidradenitis suppurativa: A publication from the United States and Canadian Hidradenitis Suppurativa Foundations: Part I: Diagnosis, evaluation, and the use of complementary and procedural management. J Am Acad Dermatol. 2019;81(1):76-90. doi:10.1016/j.jaad.2019.02.067
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
3. 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.
4. Remicade (infliximab) [Package Insert]. Horsham, PA; Janssen Biotech, Inc.: 1998
5. 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
6. 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.

7. Ward, MM, Deodhar, A, Akl, EA, et al. 2019 Update of the American College of Rheumatology/Spondylitis Association of America/Spondyloarthritis Research and Treatment Network Recommendations for the Treatment of Ankylosing Spondylitis and Nonradiographic Axial Spondyloarthritis. Arthritis Rheumatol. 2019 Oct;71(10):1599-1613

Revcovi *(elapegademase-lvlr)* injection

Additional Gold Coast Health Plan 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.

References

1. Revcovi [Package Insert]. Gaithersburg, MD; Leadiant Biosciences Inc.2018

Riabni *(rituximab-arrx)*

Additional Gold Coast Health Plan Part B Criteria: Yes

Gold Coast Health Plan also follows LCD L35026: Rituximab.

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.

References

1. Centers for Medicare & Medicaid Services. Local Coverage Determination (LCD) L35026: Rituximab. https://www.cms.gov/medicare-coverage-database/view/lcd.aspx?LCDId=35026
2. Riabni [Package Insert]. Thousand Oaks, CA; Amgen, Inc.: 2020
3. 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

Rituxan *(rituximab)*

Additional Gold Coast Health Plan Part B Criteria: Yes

Gold Coast Health Plan also follows LCD L35026: Rituximab.

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.

References

1. Centers for Medicare & Medicaid Services. Local Coverage Determination (LCD) L35026: Rituximab. https://www.cms.gov/medicare-coverage-database/view/lcd.aspx?LCDId=35026
2. Rituxan [Package Insert]. South San Francisco, CA; Genenteh, Inc.: 2010
3. 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

Rituxan Hycela *(rituximab/ hyaluronidase)*

Additional Gold Coast Health Plan Part B Criteria: Yes

Gold Coast Health Plan also follows LCD L35026: Rituximab.

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.

References

1. Centers for Medicare & Medicaid Services. Local Coverage Determination (LCD) L35026: Rituximab. https://www.cms.gov/medicare-coverage-

database/view/lcd.aspx?LCDId=35026

2. Rituxan Hycela [Package Insert]. South San Francisco, CA; Genentech, Inc.: 2017
3. 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

Rivfloza *(nedosiran)* injection solution

Additional Gold Coast Health Plan 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.

References

1. Rivfloza subcutaneous injection [prescribing information]. Plainsboro, NJ and Costa Mesa, CA: Novo Nordisk/Dicerna and Pyramid; 2023.
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. Baum MA, Langman C, Cochat P, et al. PHYOX2: a pivotal randomized study of nedosiran in primary hyperoxaluria type 1 or 2. Kidney International. 2023 Jan;103(1):207-217. DOI: 10.1016/j.kint.2022.07.025. PMID: 36007597.

Roctavian *(valoctocogene roxaparvovc-rvox)*

Additional Gold Coast Health Plan 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.

References:

1. Roctavian [package insert]. Novato, CA: BioMarin Pharmaceutical Inc.: Revised June 2023.
2. Clinicaltrials.gov. Study to evaluate the efficacy and safety of valoctocogene roxaparvovec, with prophylactic steroids in hemophilia A (GENEr8-3) (NCT04323098). Available at: https://classic.clinicaltrials.gov/ct2/show/NCT04323098.
3. Micromedex Healthcare Series: DRUGDEX. Thomson Micromedex, Greenwood Village, CO. Updated periodically.
4. World Federation of Hemophilia. Guidelines for the management of hemophilia. Haemophilia. 2020 August 3. Available at: https://onlinelibrary.wiley.com/doi/epdf/10.1111/hae.14046
5. National Organization for Rare Disorders. Hemophilia A. 2022 Aug 31. Available at: https://rarediseases.org/rarediseases/hemophilia-a/?filter=ovr-ds-resources.

Rolvedon *(eflapegrastim-xnst)*

Additional Gold Coast Health Plan Part B Criteria: Yes

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

1. Rolvedon [Package Insert]. Irvine, CA; Spectrum Pharmaceuticals, Inc.: 2022
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 1.2025) October 11, 2024. Available at: https://www.nccn.org/professionals/physician_gls/pdf/growthfactors.pdf.

Rybrevant (amivantamab-vmjw) injection, for IV use
Rybrevant Faspro (amivantamab and hyaluronidase-lpuj) subQ injection

Additional Gold Coast Health Plan Part B Criteria: NO

RYBREVANT is a bispecific EGF receptor-directed and MET receptor-directed antibody.
RYBREVANT FASPRO is a combination of amivantamab, a bispecific EGF receptor-directed and MET receptor-directed antibody, and hyaluronidase, an endoglycosidase.

RYBREVANT/RYBREVANT FASPRO are indicated (1) in combination with lazertinib for the first-line treatment of adult patients with locally advanced or metastatic non-small cell lung cancer (NSCLC) with epidermal growth factor receptor (EGFR) exon 19 deletions or exon 21 L858R substitution mutations, as detected by an FDA-approved test, (2) in combination with carboplatin and pemetrexed for the treatment of adult patients with locally advanced or metastatic NSCLC with EGFR exon 19 deletions or exon 21 L858R substitution mutations, whose disease has progressed on or after treatment with an EGFR tyrosine kinase inhibitor, (3) in combination with carboplatin and pemetrexed for the first-line treatment of adult patients with locally advanced or metastatic NSCLC with EGFR exon 20 insertion mutations, as detected by an FDA-approved test, AND (4) as a single agent for the treatment of adult patients with locally advanced or metastatic NSCLC with EGFR exon 20 insertion mutations, as detected by an FDA-approved test, whose disease has progressed on or after platinum-based chemotherapy.

RYBREVANT can cause infusion-related reactions (IRR) including anaphylaxis; signs and symptoms of IRR include dyspnea, flushing, fever, chills, nausea, chest discomfort, hypotension, and vomiting. The median time to IRR onset is approximately 1 hour.

RYBREVANT FASPRO can cause hypersensitivity and administration-related reactions (ARR); signs and symptoms of ARR include dyspnea, flushing, fever, chills, chest discomfort, hypotension, and vomiting. The median time to ARR onset is approximately 2 hours.

Premedicate with antihistamines, antipyretics, and glucocorticoids and infuse RYBREVANT or RYBREVANT FASPRO as recommended. Administer RYBREVANT via a peripheral line on Week 1 and Week 2 to reduce the risk of infusion-related reactions. Monitor patients for signs and symptoms of infusion reactions during RYBREVANT infusion in a setting where cardiopulmonary resuscitation medication and equipment are available. Interrupt infusion if IRR or ARR is suspected. Reduce the infusion rate or permanently discontinue RYBREVANT or RYBREVANT FASPRO based on severity. If an anaphylactic reaction occurs, permanently discontinue medication.

References**:**

1. Rybrevant. [Prescribing Information]. Horsham, PA; Janssen Biotech, Inc.: 2021. Available at: https://www.jnjlabels.com/package-insert/product-monograph/prescribing-information/RYBREVANT-pi.pdf.
2. Rybrevant Faspro. [Prescribing Information]. Horsham, PA; Janssen Biotech, Inc.: 2025. Available at: https://www.jnjlabels.com/package-insert/product-monograph/prescribing-information/RYBREVANT+Faspro-pi.pdf.

Ryplazim *(plasminogen, human-tvmh)*

Additional Gold Coast Health Plan 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

1. National organization for rare disease NORD. Rare disease database, congenital plasminogen deficiency. https://rarediseases.org/rare-diseases/congenital-plasminogen-deficiency/
2. Ryplazim [Package Insert]. Fort Lee, NJ; Prometic Biotherapeutics, Inc.: 2021.

Rystiggo *(rozanolixizumab-noli)*

Additional Gold Coast Health Plan 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.
Vyvgart (efgartigimod) is also a neonatal Fc receptor blocker approved for the treatment of gMG in adult patients who are AChR-Ab+. Guidelines do not

address Rystiggo or Vyvgart.

References

1. Howard JF Jr. Clinical Overview of MG. Myasthenia Gravis Foundation of America
(MGFA). Published June 2015. https://myasthenia.org/Professionals/Clinical-Overview-of-MG

2. 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

3. Rystiggo [Package Insert]. Smyrna, GA; UCB, Inc.: 2023

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. 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

Saphnelo *(anifrolumab-fnia)*

Additional Gold Coast Health Plan 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

1. Saphnelo [Package Insert]. Sodertalje, Sweden; AstraZeneca: 2021.
2. Benlysta [Package Insert]. Rockville, MD; Human Genome Sciences, Inc.: 2018
3. Fanouriakis A, Kostopoulou M, Alunno A, et al. Ann Rheum Dis. 2019;78:736–745. DOI: 10.1136/annrheumdis-2019-215089
4. Tunnicliffe DJ, Singh-Grewal D, Kim S, at al. Diagnosis, monitoring, and treatment of systemic lupus erythematosus: a systematic review of clinical practice guidelines. 2015 Oct; 67 (10): 1440 – 52.

Signifor LAR *(pasireotide)*

Additional Gold Coast Health Plan Part B Criteria: Yes

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

1. Signifor LAR [Package Insert]. East Hanover, NJ; Novartis Pharmaceuticals Corporation: 2014
2. Fleseriu M, Auchus R, Bancos I, et al. Consensus on diagnosis and management of Cushing's disease: a guideline update. *Lancet Diabetes Endocrinol*. 2021;9(12):847-875. doi:10.1016/S2213- 8587(21)00235-7
3. Fleseriu M, Biller BMK, Freda PU, et al. A Pituitary Society update to acromegaly management guidelines. *Pituitary*. 2021;24(1):1-13. doi:10.1007/s11102-020-01091-7

Simponi Aria *(golimumab)* IV

Additional Gold Coast Health Plan 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

1. Simponi Aria [Package Insert]. Horshman, PA; Janssen Biotech, Inc.: 2020
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
3. 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.
4. 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.

5. Ward, MM, Deodhar, A, Akl, EA, et al. 2019 Update of the American College of Rheumatology/Spondylitis Association of America/Spondyloarthritis Research and Treatment Network Recommendations for the Treatment of Ankylosing Spondylitis and Nonradiographic Axial Spondyloarthritis. Arthritis Rheumatol. 2019 Oct;71(10):1599-1613

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

Additional Gold Coast Health Plan 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

1. Skyrizi [Package Insert]. North Chicago, IL; AbbVie Inc.; 2024
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

Soliris *(eculizumab)*

Additional Gold Coast Health Plan 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.

References

1. 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.
2. Kaplan BS, Ruebner RL, Spinale JM, et al. Current treatment of atypical hemolytic uremic syndrome. Intractable Rare Dis Res. 2014 May; 3 (2): 34 – 45
3. Narayanaswami P, Sanders DB, Wolfe G, et al. International consensus guidance for management of myasthenia gravis: executive summary. Neurology. 2021 Jan 19; 96 (3): 114 – 22.
4. Sellner J, Boggild M, Clanet M, et al. EFNS guidelines on diagnosis and management of neuromyelitis optica. EJN. 2010; 17: 1019 – 32.
5. Soliris [Package Insert]. Cheshire, CT; Alexion Pharmaceuticals, Inc.: 2007
6. Howard JF Jr. Clinical Overview of MG. Myasthenia Gravis Foundation of America (MGFA). Published June 2015. https://myasthenia.org/Professionals/Clinical-Overview-of-MG
7. Vyvgart [Package Insert]. Zwijnaarde, Belgium; argenx BV: 2021
8. 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

9. 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
10. 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.
11. Chan, Koon-Ho, and Chi-Yan Lee. "Treatment of Neuromyelitis Optica Spectrum Disorders." International journal of molecular sciences vol. 22,16 8638. 11 Aug. 2021, doi:10.3390/ijms22168638.
12. Sellner J, Boggild M, Clanet M, et al. EFNS guidelines on diagnosis and management of neuromyelitis optica. EJN. 2010; 17: 1019 – 32. DOI: 10.1111/j.1468-1331.2010.03066.x
13. Wingerchuk DM, Banwell B, Bennett JL, et al. International consensus diagnostic criteria for neuromyelitis optica spectrum disorders. Neurology. 2015 Jul 14; 85(2):177-189. DOI: 10.1212/WNL.0000000000001729

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

Additional Gold Coast Health Plan Part B Criteria: Yes

Spevigo is an interleukin-36 receptor antagonist indicated for the treatment of generalized pustular psoriasis (GPP) in adults and pediatric patients 12 years of age and older and weighing at least 40 kg.

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

1. Spevigo [Package Insert]. Ridgefield, CT; Boehringer Ingelheim Pharmaceuticals, Inc.: 2022.
2. Fujita H, Terui T, et al. Japanese guidelines for the management and treatment of generalized pustular psoriasis: The new pathogenesis and treatment of GPP. Journal of Dermatology 2018; 45: 1235-1270.
3. Krueger J, Puig L, Thaci D. Treatment Options and goals for Patients with Generalized Pustular Psoriasis. Am J Clin Dermatol 23 (Suppl 1), 51–64 (2022). https://doi.org/10.1007/s40257-021-00658-9.
4. Robinson A, Van Voorhees, AS, et al. Treatment of pustular psoriasis: From the Medical Board of the National Psoriasis Foundation. J Am Acad Dermatol 2012;67:279-88.
5. Navarini AA, Burden AD, et al. European consensus statement on phenotypes of pustular psoriasis. J Eur Acad Dermatol Venereol. 2017 Nov;32(11):1792-1799. doi: 10.1111/jdv.14386

Spinraza *(nusinersen sodium)*

Additional Gold Coast Health Plan 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)*

Additional Gold Coast Health Plan 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) [e.g., sertraline, fluoxetine, paroxetine], serotonin-norepinephrine reuptake inhibitors (SNRIs) [e.g., 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

1. Spravato [Package Insert]. Lakewood, NJ; Renaissance Lakewood LLC: 2019
2. Voineskos, Daphne et al. "Management of Treatment-Resistant Depression: Challenges and Strategies." Neuropsychiatric disease and treatment vol. 16 221-234. 21 Jan. 2020, doi:10.2147/NDT.S198774.
3. Wisniewski SR, Fava M, Trivedi MH, et al. Acceptability of second-step treatments to depressed outpatients: a STAR*D report. Am J Psychiatry 2007; 164:753–760.
4. American Psychiatric Association. Arlington (VA): Practice Guideline for the Treatment of Patients with Major Depressive Disorder, 3rd edition. 2010.
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

Additional Gold Coast Health Plan 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.

References

1. Stelara [Package Insert]. Horsham, PA; Janssen Biotech, Inc.: 2016
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
3. 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
4. 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.

Stimufend (pegfilgrastim-fpgk)

Additional Gold Coast Health Plan Part B Criteria: Yes

Stimufend is indicated to decrease the incidence of infection, as manifested by febrile neutropenia, in patients with non-myeloid malignancies receiving myelosuppressive anti-cancer drugs associated with a clinically significant incidence of febrile neutropenia.

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

1. Stimufend [Package Insert]. Lake Zurich, IL; Fresenius Kabi USA, LLC: 2022
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 1.2025) October 11, 2024. Available at: https://www.nccn.org/professionals/physician_gls/pdf/growthfactors.pdf.

Susvimo *(ranibizumab)*

Additional Gold Coast Health Plan 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

1. Susvimo [Package Insert]. South San Francisco, CA; Genentech, Inc.: 2021
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

Additional Gold Coast Health Plan 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

1. Syfovre [Package Insert]. Waltham, MA; Apellis Pharmaceuticals, Inc.: 2023
2. Flaxel CJ, Adelman RA, Bailey ST, et al. Age-related macular degeneration preferred practice pattern. Ophthalmology. 2020 Jan (updated March 2022); 127 (1): 1 - 65. DOI: 10.1016/j.ophtha.2019.09.024
3. Clinicaltrials.gov. A study to compare the efficacy and safety of intravitreal APL-2 therapy with sham injections in patients with geographic atrophy secondary to age related macular degeneration (NCT03525613). Available at: https://classic.clinicaltrials.gov/ct2/show/NCT03525613
4. Clinicaltrials.gov. Study to compare the efficacy and safety of intravitreal APL-2 therapy with sham injections in patients with geographic atrophy secondary to age-related macular degeneration (NCT03525600). Available at: https://clinicaltrials.gov/ct2/show/NCT03525600.

Synojoynt *(hyaluronan or derivative)* for intra-articular injection

Additional Gold Coast Health Plan Part B Criteria: Yes

Gold Coast Health Plan follows LCD L39529 (Intraarticular Knee Injections of Hyaluronan).

Hyaluronic acid injections are indicated to treat osteoarthritis pain of the knee when conservative nonpharmacologic therapy and non-steroidal anti-inflammatory drugs (NSAIDs) or simple analgesics, such as acetaminophen, have failed.

The 2019 American College of Rheumatology (ACR)/Arthritis Foundation (AF) Guideline for the Management of Osteoarthritis of the Hand, Hip, and Knee recommends a comprehensive plan for the management of osteoarthritis (OA) in an individual patient that may include educational, behavioral, psychosocial, and physical interventions, as well as topical, oral, and intraarticular medications. The guidelines strongly recommend exercise, weight loss in patients with knee A who are overweight or obese, self-efficacy and self-management programs, tai chi, cane use, hand orthoses for first carpometacarpal (CMC) joint OA, tibiofemoral bracing for tibiofemoral knee OA, topical nonsteroidal anti-inflammatory drugs (NSAIDs) for knee OA, oral NSAIDs, and intraarticular glucocorticoid injections for knee OA.

Intraarticular hyaluronic acid injections are conditionally not recommended in patients with knee and/or first CMC joint OA and strongly not recommended

in patients with hip OA. In prior systematic reviews, apparent benefits of hyaluronic acid injections in OA have been reported. These reviews have not, however, considered the risk of bias of the individual primary studies. The conditional recommendation against is consistent with the use of hyaluronic acid injections, in the context of shared decision-making that recognizes the limited evidence of benefit of this treatment, when other alternatives have been exhausted or failed to provide satisfactory benefit.

The 2021 American Academy of Orthopedic Surgeons (AAOS) Evidence-Based Clinical Practice Guideline for the Management of OA of the Knee (Non-Arthroplasty) does not recommend hyaluronic acid (HA) intra-articular injection(s) for routine use in the treatment of symptomatic osteoarthritis of the knee. Some studies demonstrated a statistical benefit with the use of HA but could not reach the significance for a minimally clinical meaningful difference, leading to the conclusion that viscosupplementation can represent a viable option for some patients that failed other treatments when appropriately indicated. Analyses of these studies also demonstrated no significant differences among different viscosupplementation formulations.

References

1. Synojoynt [Package Insert]. Gyeonggi-do, Korea; Hanmi Pharm Co., Ltd
2. Bannuru RR, Osani, MC, et al. OARSI guidelines for the non-surgical management of knee, hip, and polyarticular osteoarthritis.Osteoarth Cart 2019: 27: 1578-1589.
3. American Academy of Orthopaedic Surgeons Management of Osteoarthritis of the Knee (NonArthroplasty) Evidence-Based Clinical Practice Guideline. https://www.aaos.org/oak3cpg. Published 08/31/2021
4. Centers for Medicare & Medicaid Services Medicare Coverage Database. Local Coverage Determination (LCD) L39529: Intraarticular Knee Injections of Hyaluronan. https://www.cms.gov/medicare-coverage-database/view/lcd.aspx?lcdid=39529

Synvisc/Synvisc One *(hyaluronan/ hyaluronic acid)* for intra-articular injection

Additional Gold Coast Health Plan Part B Criteria: Yes

Gold Coast Health Plan follows LCD L39529 (Intraarticular Knee Injections of Hyaluronan).

Hyaluronic acid injections are indicated to treat osteoarthritis pain of the knee when conservative nonpharmacologic therapy and non-steroidal anti-inflammatory drugs (NSAIDs) or simple analgesics, such as acetaminophen, have failed.

The 2019 American College of Rheumatology (ACR)/Arthritis Foundation (AF) Guideline for the Management of Osteoarthritis of the Hand, Hip, and Knee recommends a comprehensive plan for the management of osteoarthritis (OA) in an individual patient that may include educational, behavioral, psychosocial, and physical interventions, as well as topical, oral, and intraarticular medications. The guidelines strongly recommend exercise, weight loss in patients with knee A who are overweight or obese, self-efficacy and self-management programs, tai chi, cane use, hand orthoses for first carpometacarpal (CMC) joint OA, tibiofemoral bracing for tibiofemoral knee OA, topical nonsteroidal anti-inflammatory drugs (NSAIDs) for knee OA, oral NSAIDs, and intraarticular glucocorticoid injections for knee OA.

Intraarticular hyaluronic acid injections are conditionally recommended against in patients with knee and/or first CMC joint OA and strongly recommended against in patients with hip OA. In prior systematic reviews, apparent benefits of hyaluronic acid injections in OA have been reported. These reviews have not, however, considered the risk of bias of the individual primary studies. The conditional recommendation against is consistent with the use of hyaluronic acid injections, in the context of shared decision-making that recognizes the limited evidence of benefit of this treatment, when other alternatives have been exhausted or failed to provide satisfactory benefit.

The 2021 American Academy of Orthopaedic Surgeons (AAOS) Evidence-Based Clinical Practice Guideline for the Management of OA of the Knee (Non-Arthroplasty) does not recommend hyaluronic acid (HA) intra-articular injection(s) for routine use in the treatment of symptomatic osteoarthritis of the knee. Some studies demonstrated a statistical benefit with the use of HA but could not reach the significance for a minimally clinical meaningful difference, leading to the conclusion that viscosupplementation can represent a viable option for some patients that failed other treatments when appropriately indicated. Analyses of these studies also demonstrated no

significant differences among different viscosupplementation formulations.

References

1. Synvisc [Package Insert]. Ridgefiled, NJ; Biomatrix, Incorporated
2. Synvisc One [Package Insert]. Ridgefield, NJ: Biomatrix, Incoorporated
3. Bannuru RR, Osani, MC, et al. OARSI guidelines for the non-surgical management of knee, hip, and polyarticular osteoarthritis.Osteoarth Cart 2019: 27: 1578-1589.
4. American Academy of Orthopaedic Surgeons Management of Osteoarthritis of the Knee (NonArthroplasty) Evidence-Based Clinical Practice Guideline. https://www.aaos.org/oak3cpg. Published 08/31/2021
5. Centers for Medicare & Medicaid Services Medicare Coverage Database. Local Coverage Determination (LCD) L39529: Intraarticular Knee Injections of Hyaluronan. https://www.cms.gov/medicare-coverage-database/view/lcd.aspx?lcdid=39529

Tecartus *(brexucabtagene autoleucel)*

Additional Gold Coast Health Plan Part B Criteria: No

Gold Coast Health Plan follows NCD 110.24 for Chimeric Antigen Receptor (CAR) T-Cell Therapy.

Tecartus is a CD19-directed genetically modified autologous T cell immunotherapy indicated for the treatment of adult patients with relapsed or refractory B-cell precursor acute lymphoblastic leukemia (ALL).

References

1. Centers for Medicare & Medicaid Services. National Coverage Determination (NCD) 110.24 Chimeric Antigen Receptor (CAR) T-cell Therapy. https://www.cms.gov/medicare-coverage-database/view/ncd.aspx?ncdid=374
2. Tecartus [Package Insert]. Santa Monica, CA; Kite Pharma, Inc. 2024

Tepezza *(teprotumumab-trbw)*

Additional Gold Coast Health Plan Part B Criteria: Yes

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).

References

1. Tepezza [Package Insert]. Dublin, Ireland; Horizon Therapeutics Ireland DAC: 2020
2. Bartalena L, Kahaly GJ, Baldeschi L, et al. The 2021 European Group on Graves' orbitopathy (EUGOGO) clinical practice guidelines for the medical management of Graves' orbitopathy. Eur J Endocrinol. 2021 Aug 27;185(4):G43-G67. doi: 10.1530/EJE-21-0479.

Tezspire *(tezepelumab-ekko)*

Additional Gold Coast Health Plan 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, 2024.
3. Global Initiative for Asthma. Global Strategy for Asthma Management and Prevention, 2024

Tocilizumab Biosimilars (Actemra) injection, for IV use

Additional Gold Coast Health Plan Part B Criteria: NO

Tocilizumab and its biosimilars are indicated for the treatment of:

- Adult patients with moderately to severely active rheumatoid arthritis (RA) who have had an inadequate response to one or more disease-modifying anti-rheumatic drugs (DMARDs)
- Patients 2 years of age and older with active polyarticular juvenile idiopathic arthritis (PJIA)
- Patients 2 years of age and older with active systemic juvenile idiopathic arthritis (SJIA)
- Adult patients with giant cell arteritis (GCA)
- **Actemra ONLY**: slowing the rate of decline in pulmonary function in adult patients with systemic sclerosis-associated interstitial lung disease (SSc-ILD)
- **Actemra, Avtozma and Tyenne ONLY**: chimeric antigen receptor (CAR) T cell-induced severe or life-threatening cytokine release syndrome (CRS) in adults and pediatric patients 2 years of age and older

In clinical studies, most common adverse reactions (≥ 5% incidence) were upper respiratory tract infections, nasopharyngitis, headache, hypertension, increased ALT and injection site reactions. Cytochrome P450s in the liver are down-regulated by infection and inflammation stimuli including cytokines such as IL-6. Inhibition of IL-6 signaling in RA patients treated with tocilizumab may restore CYP450 activities to higher levels than those in the absence of tocilizumab leading to increased metabolism of drugs that are CYP450 substrates. In vitro studies showed that tocilizumab has the potential to affect expression of multiple CYP enzymes including CYP1A2, CYP2B6, CYP2C9, CYP2C19, CYP2D6 and CYP3A4.

Its effects on CYP2C8 or transporters is unknown. In vivo studies with omeprazole, metabolized by CYP2C19 and CYP3A4, and simvastatin, metabolized by CYP3A4, showed up to a 28% and 57% decrease in exposure one week following a single dose of Tocilizumab, respectively. The effect of tocilizumab on CYP enzymes may be clinically relevant for CYP450 substrates with narrow therapeutic index, where the dose is individually adjusted. Upon initiation or discontinuation of Tocilizumab, in patients being treated with these types of medicinal products, perform therapeutic monitoring of effect (e.g., warfarin) or drug concentration (e.g., cyclosporine or theophylline) and the individual dose of the medicinal product adjusted as needed. Exercise caution when coadministering Tocilizumab with CYP3A4 substrate drugs where decrease in effectiveness is undesirable, e.g., oral contraceptives, lovastatin, atorvastatin, etc. The effect of tocilizumab on CYP450 enzyme activity may persist for several weeks after stopping therapy.

References:

1. ACTEMRA [Package Insert]. South San Francisco, CA; Genentech, Inc.: 2013. Available at: https://www.accessdata.fda.gov/drugsatfda_docs/label/2013/125276s092lbl.pdf
2. AVTOZMA [Package Insert]. Jersey City, NJ; Celltrion, Inc.: 2025. Available at: https://www.accessdata.fda.gov/drugsatfda_docs/label/2025/761420s000lbl.pdf
3. TOFIDENCE [Package Insert]. Cambridge, MA; Biogen MA Inc,: 2023. Available at: https://www.accessdata.fda.gov/drugsatfda_docs/label/2024/761354s002lbl.pdf
4. TYENNE [Package Insert]. Lake Zurich, IL; Fresenius Kabi USA, LLC; 2024. Available at: https://www.accessdata.fda.gov/drugsatfda_docs/label/2025/761275s004,761449s001lbl.pdf

Tremfya *(guselkumab)* IV vial

Additional Gold Coast Health Plan 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.

References

1. Tremfya (guselkumab) [prescribing information]. Horsham, PA: Janssen Biotech Inc; September 2024.
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.
3. Rubin DT, Ananthakrishnan AN, Siegel CA, et al. ACG clinical guideline: ulcerative colitis in adults. Am J Gastroenterol. 2019; 114: 384–413.

Triluron *(hyaluronan/hyaluronic acid)* for intra-articular injection

Additional Gold Coast Health Plan Part B Criteria: Yes

Gold Coast Health Plan follows LCD L39529 (Intraarticular Knee Injections of Hyaluronan).

Hyaluronic acid injections are indicated to treat osteoarthritis pain of the knee when conservative nonpharmacologic therapy and non-steroidal anti-inflammatory drugs (NSAIDs) or simple analgesics, such as acetaminophen, have failed.

The 2019 American College of Rheumatology (ACR)/Arthritis Foundation (AF) Guideline for the Management of Osteoarthritis of the Hand, Hip, and Knee recommends a comprehensive plan for the management of osteoarthritis (OA) in an individual patient that may include educational, behavioral, psychosocial, and physical interventions, as well as topical, oral, and intraarticular medications. The guidelines strongly recommend exercise, weight loss in patients with knee A who are overweight or obese, self-efficacy and self-management programs, tai chi, cane use, hand orthoses for first carpometacarpal (CMC) joint OA, tibiofemoral bracing for tibiofemoral knee OA, topical nonsteroidal anti-inflammatory drugs (NSAIDs) for knee OA, oral NSAIDs, and intraarticular glucocorticoid injections for knee OA.

Intraarticular hyaluronic acid injections are conditionally not recommended in patients with knee and/or first CMC joint OA and strongly not recommended in patients with hip OA. In prior systematic reviews, apparent benefits of hyaluronic acid injections in OA have been reported. These reviews have not, however, considered the risk of bias of the individual primary studies. The conditional recommendation against is consistent with the use of hyaluronic acid injections, in the context of shared decision-making that recognizes the

limited evidence of benefit of this treatment, when other alternatives have been exhausted or failed to provide satisfactory benefit.

The 2021 American Academy of Orthopaedic Surgeons (AAOS) Evidence-Based Clinical Practice Guideline for the Management of OA of the Knee (Non-Arthroplasty) does not recommend hyaluronic acid (HA) intra-articular injection(s) for routine use in the treatment of symptomatic osteoarthritis of the knee. Some studies demonstrated a statistical benefit with the use of HA but could not reach the significance for a minimally clinical meaningful difference, leading to the conclusion that viscosupplementation can represent a viable option for some patients that failed other treatments when appropriately indicated. Analyses of these studies also demonstrated no significant differences among different viscosupplementation formulations.

References

1. Triluron [Package Insert]. Padua, Italy; Fidia Farmaceutici S.p.A.: 2019
2. Bannuru RR, Osani, MC, et al. OARSI guidelines for the non-surgical management of knee, hip, and polyarticular osteoarthritis. Osteoarth Cart 2019: 27: 1578-1589.
3. American Academy of Orthopaedic Surgeons Management of Osteoarthritis of the Knee (NonArthroplasty) Evidence-Based Clinical Practice Guideline. https://www.aaos.org/oak3cpg. Published 08/31/2021
4. Centers for Medicare & Medicaid Services Medicare Coverage Database. Local Coverage Determination (LCD) L39529: Intraarticular Knee Injections of Hyaluronan. https://www.cms.gov/medicare-coverage-database/view/lcd.aspx?lcdid=39529

Trivisc *(hyaluronan/hyaluronic acid)* for intra-articular injection

Additional Gold Coast Health Plan Part B Criteria: Yes

Gold Coast Health Plan follows LCD L39529 (Intraarticular Knee Injections of Hyaluronan).

Hyaluronic acid injections are indicated to treat osteoarthritis pain of the knee

when conservative nonpharmacologic therapy and non-steroidal anti-inflammatory drugs (NSAIDs) or simple analgesics, such as acetaminophen, have failed.

The 2019 American College of Rheumatology (ACR)/Arthritis Foundation (AF) Guideline for the Management of Osteoarthritis of the Hand, Hip, and Knee recommends a comprehensive plan for the management of osteoarthritis (OA) in an individual patient that may include educational, behavioral, psychosocial, and physical interventions, as well as topical, oral, and intraarticular medications. The guidelines strongly recommend exercise, weight loss in patients with knee A who are overweight or obese, self-efficacy and self-management programs, tai chi, cane use, hand orthoses for first carpometacarpal (CMC) joint OA, tibiofemoral bracing for tibiofemoral knee OA, topical nonsteroidal anti-inflammatory drugs (NSAIDs) for knee OA, oral NSAIDs, and intraarticular glucocorticoid injections for knee OA.

Intraarticular hyaluronic acid injections are conditionally not recommended in patients with knee and/or first CMC joint OA and strongly not recommended in patients with hip OA. In prior systematic reviews, apparent benefits of hyaluronic acid injections in OA have been reported. These reviews have not, however, considered the risk of bias of the individual primary studies. The conditional recommendation against is consistent with the use of hyaluronic acid injections, in the context of shared decision-making that recognizes the limited evidence of benefit of this treatment, when other alternatives have been exhausted or failed to provide satisfactory benefit.

The 2021 American Academy of Orthopaedic Surgeons (AAOS) Evidence-Based Clinical Practice Guideline for the Management of OA of the Knee (Non-Arthroplasty) does not recommend hyaluronic acid (HA) intra-articular injection(s) for routine use in the treatment of symptomatic osteoarthritis of the knee. Some studies demonstrated a statistical benefit with the use of HA but could not reach the significance for a minimally clinical meaningful difference, leading to the conclusion that viscosupplementation can represent a viable option for some patients that failed other treatments when appropriately indicated. Analyses of these studies also demonstrated no significant differences among different viscosupplementation formulations.

References

1. Trivisc [Package Insert]. Madrid, Spain; Tedec Meiji Farma
2. Bannuru RR, Osani, MC, et al. OARSI guidelines for the non-surgical management of knee, hip, and polyarticular osteoarthritis.Osteoarth

Cart 2019: 27: 1578-1589.

3. American Academy of Orthopaedic Surgeons Management of Osteoarthritis of the Knee (NonArthroplasty) Evidence-Based Clinical Practice Guideline. https://www.aaos.org/oak3cpg. Published 08/31/2021
4. Centers for Medicare & Medicaid Services Medicare Coverage Database. Local Coverage Determination (LCD) L39529: Intraarticular Knee Injections of Hyaluronan. https://www.cms.gov/medicare-coverage-database/view/lcd.aspx?lcdid=39529

TYSABRI (natalizumab) injection, for IV use
TYRUKO (natalizumab-sztn) injection, for IV use -- biosimilar

Additional Gold Coast Health Plan Part B Criteria: No

The safety and efficacy of natalizumab products in combination with antineoplastic, immunosuppressant, or immunomodulating agents have not been established. Patients receiving chronic immunosuppressant or immunomodulatory therapy or who have systemic medical conditions resulting in significantly compromised immune system function should not ordinarily be treated with natalizumab products. The risk of PML is also increased in patients who have been treated with an immunosuppressant prior to receiving natalizumab products.

In clinical trials, natalizumab was observed to induce increases in circulating lymphocytes, monocytes, eosinophils, basophils, and nucleated red blood cells. Observed changes persisted during natalizumab exposure, but were reversible, returning to baseline levels usually within 16 weeks after the last dose. Elevations of neutrophils were not observed. Natalizumab induces mild decreases in hemoglobin levels (mean decrease of 0.6 g/dL) that are frequently transient.

Cases of thrombocytopenia, including immune thrombocytopenic purpura (ITP), have been reported with the use of natalizumab products in the post-marketing setting. Symptoms of thrombocytopenia may include easy bruising, abnormal bleeding, and petechiae. Delay in the diagnosis and treatment of thrombocytopenia may lead to serious and life-threatening sequelae. If thrombocytopenia is suspected, natalizumab should be discontinued.

The most common adverse reactions (incidence ≥10%) were headache and fatigue in both the multiple sclerosis (MS) and Crohn's disease (CD) studies. Other common adverse reactions (incidence ≥10%) in the MS population were arthralgia, urinary tract infection, lower respiratory tract infection, gastroenteritis, vaginitis, depression, pain in extremity, abdominal discomfort, diarrhea NOS, and rash. Other common adverse reactions (incidence ≥10%) in the CD population were upper respiratory tract infections and nausea.

The most frequently reported adverse reactions resulting in clinical intervention (i.e., discontinuation of natalizumab) in the MS studies were urticaria (1%) and other hypersensitivity reactions (1%), and in the CD studies were the exacerbation of Crohn's disease (4.2%) and acute hypersensitivity reactions (1.5%).

References:
1. TYRUKO Prescribing Information. Princeton, NJ: Sandoz, Inc.; 2003. Available at: https://www.accessdata.fda.gov/drugsatfda_docs/label/2023/761322s000lbl.pdf. Accessed on 1/14/26.
2. TYSABRI Prescribing Information. Cambridge, MA: Biogen, Inc.; 2025. Available at: https://www.tysabri.com/content/dam/commercial/tysabri/pat/en_us/pdf/tysabri_prescribing_information.pdf. Accessed on 1/14/26.

Tyvaso *(treprostinil)* inhalation

Additional Gold Coast Health Plan 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.

References

1. Tyvaso [Package Insert]. Research Triangle Park, NC; United Therapeutics Corp.: 2022
2. 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

Tzield *(teplizumab-mzww)* vial

Additional Gold Coast Health Plan 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.

References

1. Tzield [Package Insert]. Red Bank, NJ; Provention Bio, Inc.: 2022
2. Diagnosis and Classification of Diabetes: Standards of Care in Diabetes - 2025. American Diabetes Association, 2025.
3. Clinicaltrials.gov. Teplizumab for Prevention of Type 1 Diabetes In Relatives "At-Risk". NCT01030861. Available at: https://clinicaltrials.gov/study/NCT01030861

Udenyca *(pegfilgrastim-cbqv)*

Additional Gold Coast Health Plan Part B Criteria: Yes

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

1. Udenyca [Package Insert]. Redwood City, CA; Coherus BioSciences, Inc.: 2019
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 1.2025) October 11, 2024. Available at: https://www.nccn.org/professionals/physician_gls/pdf/growthfactors.pdf.

Ultomiris (ravulizumab-cqvz)

Additional Gold Coast Health Plan 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

1. 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.
2. Kaplan BS, Ruebner RL, Spinale JM, et al. Current treatment of atypical hemolytic uremic syndrome. Intractable Rare Dis Res. 2014 May; 3 (2): 34 – 45
3. Narayanaswami P, Sanders DB, Wolfe G, et al. International consensus guidance for management of myasthenia gravis: executive summary. Neurology. 2021 Jan 19; 96 (3): 114 – 22.
4. Sellner J, Boggild M, Clanet M, et al. EFNS guidelines on diagnosis and management of neuromyelitis optica. EJN. 2010; 17: 1019 – 32. DOI: 10.1111/j.1468-1331.2010.03066.x
5. Ultomiris [Package Insert]. Boston, MA; Alexion Pharmaceuticals, Inc.: 2018
6. Howard JF Jr. Clinical Overview of MG. Myasthenia Gravis Foundation of America (MGFA). Published June 2015. https://myasthenia.org/Professionals/Clinical-Overview-ofMG.
7. Wingerchuk DM, Banwell B, Bennett JL, et al. International consensus diagnostic criteria for neuromyelitis optica spectrum disorders. Neurology. 2015 Jul 14; 85(2):177-189. DOI: 10.1212/WNL.0000000000001729

8. Friedemann P, Marignier R, Palace J, et al. International Delphi Consensus on the Management of AQP4-IgG+ NMOSD. Neurol Neuroimmunol Neuroinflamm 2023;10:e200124. doi:10.1212/NXI.0000000000200124
9. Sellner J, Boggild M, Clanet M, et al. EFNS guidelines on diagnosis and management of neuromyelitis optica. EJN. 2010; 17: 1019 – 32.

UNLOXCYT (cosibelimab-ipdl) injection, for IV use

Additional Gold Coast Health Plan Part B Criteria: YES – LCD L37205

The safety of UNLOXCYT was evaluated in Study CK-301-101 in 141 patients with metastatic or locally advanced disease CSCC. Patients received UNLOXCYT 800 mg every 2 weeks (n=115) or 1,200 mg every 3 weeks (n=26) as an intravenous infusion until disease progression or unacceptable toxicity. The median duration of exposure was 36 weeks (2 weeks to 3.7 years). Serious adverse reactions occurred in 31% of advanced patients with CSCC who received UNLOXCYT. The most frequent serious adverse reactions (> 2% of patients) were sepsis (2.8%), pneumonia (2.8%) and pyrexia (2.1%).

The most common (> 10%) adverse reactions were fatigue, musculoskeletal pain, rash, diarrhea, hypothyroidism, constipation, nausea, headache, pruritus, edema, localized infection, and urinary tract infection.

The efficacy of UNLOXCYT was evaluated in Study CK-301-101 (NCT03212404), a multicenter, multicohort, open-label study in patients with metastatic CSCC (mCSCC) or locally advanced CSCC (laCSCC) who were not candidates for curative surgery or curative radiation. Patients were excluded if they had the following: active or suspected autoimmune disease, allogeneic transplant within 6 months prior to treatment, prior treatment with anti–PD-1/PD-L1 blocking antibodies or other immune checkpoint inhibitor therapy, uncontrolled or significant cardiovascular disease, ECOG PS ≥ 2, or infection with HIV, hepatitis B or hepatitis C.

References:

1. Centers for Medicare & Medicaid Services. Local Coverage Determination (LCD) L37205: Chemotherapy Drugs and their Adjuncts. Available at: https://www.cms.gov/medicare-coverage-database/view/lcd.aspx?lcdid=37205&ver=15&keyword=chemotherapy&keywordType=starts&areaId=s6&docType=NCA,CAL,NCD,MEDCAC,TA,MCD,6,3,5,1,F,P&contractOption=all&sortBy=relevance&bc=1.
2. National Comprehensive Cancer Network. Squamous Cell Skin Cancer Version 1.2026. Available at: https://www.nccn.org/professionals/physician_gls/pdf/squamous.pdf. Accessed on 1/14/26.
3. UNLOXCYT Prescribing Information. Cranbury, NJ: Sun Pharmaceutical Industries, Inc.; 2025. Available at: https://doc-isolation-prod.prod.fire.glass/api/wopi/downloads/docisolation-viewer/v2/?fileAccessId=g_06b06c92-ca31-40ba-83f0-1b18dadc6ded&statusCode=1000&operationRestriction=3. Accessed on 1/14/26.

Uplizna *(inebilzumab-cdon)*

Additional Gold Coast Health Plan 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.

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.

References

1. Chan, Koon-Ho, and Chi-Yan Lee. "Treatment of Neuromyelitis Optica Spectrum Disorders." International journal of molecular sciences vol. 22,16 8638. 11 Aug. 2021, doi:10.3390/ijms22168638
2. Sellner J., Boggild M., Clanet M., et al. EFNS guidelines on diagnosis and management of neuromyelitis optica. Eur. J. Neurol. 17 (2010) 1019–1032, https://doi.org/10.1111/j.1468- 1331.2010.03066.x.
3. Sherman, Elena, and May H Han. "Acute and Chronic Management of Neuromyelitis Optica Spectrum Disorder." Current treatment options in neurology vol. 17,11 (2015): 48. doi:10.1007/s11940-015-0378-x
4. Uplinza [Package Insert]. Gaithersburg, MD; Viela Bio, Inc.: 2020
5. Friedemann P, Marignier R, Palace J, et al. International Delphi Consensus

on the Management of AQP4-IgG+ NMOSD. Neurol Neuroimmunol Neuroinflamm 2023;10:e200124. doi:10.1212/NXI.0000000000200124

Ustekinumab Biosimilars, injection for IV use

Brand: STELARA®

Ustekinumab is a human interleukin-12 and -23 antagonist indicated for the treatment of: Adult patients with: moderate to severe plaque psoriasis (PsO) who are candidates for phototherapy or systemic therapy; active psoriatic arthritis (PsA); moderately to severely active Crohn's disease (CD); moderately to severely active ulcerative colitis. It is also indicated for pediatric patients 6 years and older with: moderate to severe plaque psoriasis (PsO), who are candidates for phototherapy or systemic therapy, and active psoriatic arthritis (PsA).

In reference to Medicare Part B billing, the only indication that will apply is adults with moderate to severely active Crohn's disease or Ulcerative Colitis as these are the only indications that recommend IV dosing and must be administered by a provider. All other doses can be self-administered by a patient or caregiver.

Ustekinumab was evaluated in three randomized, double-blind, placebo-controlled clinical trials in adult subjects with moderately to severely active Crohn's disease (Crohn's Disease Activity Index [CDAI] score of 220 to 450). There were two 8-week intravenous induction trials (CD-1 and CD-2) followed by a 44-week subcutaneous randomized withdrawal maintenance trial (CD-3) representing 52 weeks of therapy. Subjects in CD- 1 had failed or were intolerant to treatment with one or more TNF blockers, while subjects in CD-2 had failed or were intolerant to treatment with immunomodulators or corticosteroids, but never failed treatment with a TNF blocker.

Ustekinumab was evaluated in two randomized, double-blind, placebo-controlled clinical trials [UC-1 and UC-2 (NCT02407236)] in adult subjects with moderately to severely active ulcerative colitis who had an inadequate response to or failed to tolerate a biologic (i.e., TNF blocker and/or vedolizumab), corticosteroids, and/or 6-MP or AZA therapy. The 8-week intravenous induction trial (UC-1) was followed by the 44-week subcutaneous randomized withdrawal maintenance trial (UC-2) for a total of 52 weeks of therapy.

Disease assessment was based on the Mayo score, which ranged from 0 to 12 and has four subscores that were each scored from 0 (normal) to 3 (most severe): stool frequency, rectal bleeding, findings on centrally-reviewed endoscopy, and physician global assessment. Moderately to severely active ulcerative colitis was defined at baseline (Week 0) as Mayo score of 6 to 12, including a Mayo endoscopy subscore of ≥2. An endoscopy score of 2 was defined by marked erythema, absent vascular pattern, friability, erosions; and a score of 3 was defined by spontaneous bleeding, ulceration. At baseline, subjects had a median Mayo score of 9, with 84% of subjects having moderate disease (Mayo score 6-10) and 15% having severe disease (Mayo score 11-12).

Subjects in these trials may have received other concomitant therapies including aminosalicylates, immunomodulatory agents (AZA, 6-MP, or MTX), and oral corticosteroids (prednisone).

The most common adverse reactions (≥3%) associated with ustekinumab in Crohn's disease were

vomiting, nasopharyngitis, injection site erythema, vulvovaginal candidiasis/mycotic infection, bronchitis pruritus, UTI and sinusitis. The most common adverse reactions seen in Ulcerative Colitis were nasopharyngitis, headache, abdominal pain, influenza, fever, diarrhea, sinusitis, fatigue and nausea.

References**:**

1. STELARA Prescribing Information. Horsham, PA: Janssen Biotech; 2020.
2. IMULDOSA Prescribing Information. Raleigh, NC: Accord BioPharma Inc; 2024.
3. PYZCHIVA Prescribing Information. Princeton, NJ: Sandoz, Inc; 2024.
4. SELARSDI Prescribing Information. Parsippany, NJ: Teva Pharmaceuticals; 2024.
5. STARJEMZA Prescribing Information. Berkeley Heights, NJ: Hikma Pharmaceuticals USA Inc; 2025.
6. STEQEYMA Prescribing Information. Jersey City, NJ: Celltrion USA Inc; 2024.
7. WEZLANA Prescribing Information. Thousand Oaks, CA: Amgen Inc; 2023.
8. YESINTEK Prescribing Information. Cambridge, MA: Biocon Biologics Inc.; 2024.

Vegzelma *(bevacizumab-abcd)*

Additional Gold Coast Health Plan Part B Criteria: Yes

Gold Coast Health Plan follows Centers for Medicare & Medicaid Services (CMS) Local Coverage Determination (LCD) L37205: Chemotherapy Drugs and their Adjuncts.

Vegzelma (bevacizumab-adcd) is a 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.

References

1. Centers for Medicare & Medicaid Services. Local Coverage Determination (LCD) L37205: Chemotherapy Drugs and their Adjuncts. https://www.cms.gov/medicare-coverage-database/view/lcd.aspx?lcdId=37205&ver=15
2. Vegzelma [Package Insert]. Incheon, Korea; Celltrion, Inc.: 2022
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 3.2025)
6. National Comprehensive Cancer Network. Colon Cancer (Version 2.2025)
7. National Comprehensive Cancer Network. Kidney Cancer (Version 3.2025)
8. National Comprehensive Cancer Network. Non-Small Cell Lung Cancer (Version 3.2025)

Veopoz *(pozelimab-bbfg)* 400 MG/2 ML vial

Additional Gold Coast Health Plan 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.

References

1. Clinicaltrials.gov. Open-Label Efficacy and Safety Study of Pozelimab in Patients With CD55- Deficient Protein-Losing Enteropathy (CHAPLE Disease) (NCT04209634).
2. Veopoz [Package Insert]. Tarrytown, NY: Regeneron Pharmaceuticals, Inc.; August 2023

Vivimusta *(Bendamustine)* IV

Additional Gold Coast Health Plan Part B Criteria: Yes

Gold Coast Health Plan also follows LCD L37205: Chemotherapy Drugs and their Adjuncts.

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.

References

1. Centers for Medicare & Medicaid Services. Local Coverage Determination (LCD) L37205: Chemotherapy Drugs and their Adjuncts. https://www.cms.gov/medicare-coverage-database/view/lcd.aspx?lcdId=37205&ver=15
2. Vivimusta [Package Insert]. Sermoneta, Italy; Corden Pharma Latina S.p.A.: 2022
3. National Comprehensive Cancer Network. Chronic lymphocytic leukemia/small lymphocytic lymphoma (Version 2.2025). February 7, 2025.
4. National Comprehensive Cancer Network. B-Cell lymphomas (Version 2.2025). February 10, 2025.

VORAXAZE® (glucarpidase) injection, for IV use

Additional Gold Coast Health Plan Part B Criteria: No

The efficacy of VORAXAZE was evaluated in a subset of 22 patients enrolled in Study 1 (NCT00001298), a single-arm, open-label study in patients who had markedly delayed methotrexate clearance (defined as more than 2 standard deviations greater than the mean excretion curve for methotrexate) due to impaired renal function. All patients received VORAXAZE 50 Units/kg as an intravenous injection over 5 minutes; those patients with pre-VORAXAZE methotrexate concentration >100 µmol/L were to receive a second dose of VORAXAZE 48 hours after the first dose. The protocol specified that patients continue receiving intravenous hydration, urinary alkalinization and leucovorin and that leucovorin administration be adjusted to ensure that it was not administered within 2 hours before or after VORAXAZE.

Because clinical trials are conducted under controlled but widely varying conditions, adverse reaction rates observed in clinical trials of VORAXAZE cannot be directly compared to rates in the clinical trials of other drugs and may not reflect the rates observed in practice. The evaluation of adverse reactions in patients who received VORAXAZE was confounded, because patients had toxic plasma methotrexate concentration due to prolonged methotrexate clearance, which is associated with myelosuppression, mucositis, acute hepatitis, and 3 renal dysfunction and failure.

The safety of VORAXAZE is based on data from 290 patients who were enrolled in Study 1 or Study 2, two single-arm, open-label, multicenter studies conducted in patients who had markedly delayed methotrexate clearance due to impaired renal function. Patients with osteosarcoma were eligible for these studies if the plasma methotrexate concentration was >50 µmol/L at 24 hours, >5 µmol/L at 48 hours, or >2 standard deviations above the mean methotrexate elimination curve at least 12 hours after methotrexate administration; and there was a ≥2-fold increase in serum creatinine above baseline. All other patients were eligible for these studies if the plasma methotrexate concentration was >10 µmol/L more than 42 hours after the start of the methotrexate or the plasma methotrexate concentration was >2 standard deviations above the mean methotrexate excretion curve at least 12 hours following methotrexate; and the serum creatinine was >1.5 times the upper limit of normal (ULN) or the creatinine clearance was <60 mL/min at least 12 hours following methotrexate administration.

The most common related adverse events (>1%) were paresthesia, flushing, nausea and/or vomiting, hypotension and headache.

References:

1. VORAXAZE Coding Guide. West Conshohocken, PA: BTG International Inc.; 2024. Available at: https://voraxaze.com/sites/voraxaze-library/files/2024-10/Voraxaze-Coding-Guide-2024.pdf. Accessed on 1/19/26.
2. VORAXAZE Prescribing Information. West Conshohocken, PA: BTG International Inc.; 2012. Available at: https://voraxaze.com/sites/voraxaze-library/files/2024-10/VORAXAZE-PI_August-2019_2-column-format.pdf. Accessed on 1/19/26.

Vyalev *(foscarbidopa and foslevodopa)*

Additional Gold Coast Health Plan 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).

Vyalev falls under the Local Coverage Determination (LCD) L33374 External Infusion Pumps.

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.

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.

3. National Institute for Health and Care Excellence. Foslevodopa-foscarbidopa for treating advanced Parkinson’s with motor symptoms. November 29, 2023. https://www.nice.org.uk/guidance/ta934/resources/foslevodopafoscarbidopa-for- treating-advanced-parkinsons-with-motor-symptoms-pdf-82615608069829.

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. LCD - External Infusion Pumps (L33794)

Vyepti *(eptinezumab-jjmr)*

Additional Gold Coast Health Plan 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

Vyvgart *(efgartigimod alfa-fcab)*

Additional Gold Coast Health Plan 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

Winrevair *(sotatercept)*

Additional Gold Coast Health Plan 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
4. Institute for Clinical and Economic Review. Sotatercept for pulmonary arterial hypertension. Final evidence report. January 8, 2024. https://icer.org/wp-content/uploads/2023/05/PAH_Final-Evidence-Report_For- Publication_01082024.pdf

Xenpozyme *(olipudase-alfa-rpcp)* 20 MG vial

Additional Gold Coast Health Plan 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

1. National Organization of Rare Disorders. Acid sphingomyelinase deficiency. 2019. Available at: https://rarediseases.org/rare-diseases/acid-sphingomyelinase-deficiency/
2. McGovern MM, Dionisi-Vici C, Giugliani R, at al. Consensus recommendation for a diagnostic guideline for acid sphingomyelinase deficiency. Genet Med. 2017 Sep; 19 (9): 967 - 74. DOI: 10.1038/gim.2017.7
3. Xenpozyme [Package Insert]. Cambridge, MA; Genzyme Corporation: 2022

Xgeva *(denosumab)*

Additional Gold Coast Health Plan Part B Criteria: Yes

Xgeva (denosumab) is a RANK ligand (RANKL) indicated for multiple skeletal related conditions including a) prevention of skeletal-related events in patients with multiple myeloma (MM) and in patients with bone metastases from solid tumors, b) treatment of adults and skeletally mature adolescents with giant cell tumor of bone that is unresectable or where surgical resection is likely to result in severe morbidity, and c) treatment of hypercalcemia of malignancy refractory to bisphosphonate therapy.

Zometa (zoledronic acid) is a bisphosphonate also indicated for the treatment of a) patients with MM and patients with documented bone metastases from solid tumors, in conjunction with standard antineoplastic therapy and b) hypercalcemia of malignancy.

The NCCN guidelines for Multiple Myeloma Version 1.2025 state that bony manifestations in the form of diffuse osteopenia and/or osteolytic lesions develop in 85% of patients with MM. The guidelines recommend all patients receiving primary myeloma therapy be given bone- targeting treatment with a category 1 recommendation for bisphosphonates (based upon high-level evidence, there is uniform NCCN consensus that the intervention is appropriate) and a category 2A recommendation for denosumab (based upon lower-level evidence, there is uniform NCCN consensus that the intervention is appropriate). Bisphosphonates (zoledronic acid preferred), denosumab, steroids, and/or calcitonin are also recommended for hypercalcemia.

The NCCN guidelines for Breast Cancer Version 1.2025 and Prostate Cancer Version 1.2025 recommend treatment with a bone modifying agent such as zoledronic acid (category 2A), pamidronate (category 2A), or denosumab (category 1) if bone metastasis is present.

References

1. Camacho PM, Petak SM, Binkley N, et al. American Association of Clinical Endocrinologists/American College of Endocrinology Clinical Practice Guidelines for the Diagnosis and Treatment of Postmenopausal Osteoporosis – 2020 Update. Endocr Pract. 2020;26(Suppl 1):1-46. DOI: 10.4158/GL-2020-0524SUPPL
2. Chakhtoura M, El-Hajj Fuleihan G. Treatment of Hypercalcemia of Malignancy. Endocrinol Metab Clin North Am. 2021;50(4):781-792. DOI:

10.1016/j.ecl.2021.08.002

3. National Comprehensive Cancer Network. Breast Cancer (Version 1.2025)
4. National Comprehensive Cancer Network. Bone Cancer (Version 2.2025)
5. National Comprehensive Cancer Network. Multiple Myeloma (Version 1.2025)
6. National Comprehensive Cancer Network. Prostate Cancer (Version 1.2025)
7. Xgeva [Package Insert]. Thousand Oaks, CA; Amgen Inc.: 2013
8. Zometa [Package Insert]. East Hanover, NJ; Novartis Pharmaceuticals Corporation: 2016

Xipere *(triamcinolone)*

Additional Gold Coast Health Plan Part B Criteria: Yes

Xipere (triamcinolone acetonide injectable suspension) is a corticosteroid indicated for the treatment of ophthalmic conditions which include temporal arteritis, uveitis, and sympathetic ophthalmia, and ocular inflammatory conditions unresponsive to topical corticosteroids.

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.

A Report by the American Academy of Ophthalmology reviewed 23 articles that provided level I or level II evidence from 18 studies on the use of periocular, suprachoroidal, and intravitreal triamcinolone acetonide injections and intravitreal dexamethasone and fluocinolone acetonide implants or inserts in noninfectious uveitic macular edema.

These reports consistently demonstrated that all investigated periocular and

intraocular corticosteroid therapies improved visual acuity, macular structure, or both. In the Periocular versus intravitreal corticosteroids for uveitic macular edema (POINT) randomized clinical trial, 3 forms of local corticosteroid therapy were compared: periocular triamcinolone acetonide injection (Kenalog; 40 mg), intravitreal triamcinolone acetonide injection (Triesence; 4 mg), and the 0.7-mg intravitreal dexamethasone implant. The periocular injection was by orbital floor or posterior sub-Tenon approach. The study provided level I evidence that all treatments were effective. The intravitreal approaches achieved superior effectiveness, offset by an increased risk of intraocular pressure (IOP) elevation. Nine articles reported 5 international, multicenter, randomized controlled studies involving treatment of noninfectious intermediate uveitis, posterior uveitis, and panuveitis with fluocinolone acetonide intravitreal implants or inserts. Across the studies, 3 devices contained different total amounts of fluocinolone acetonide and thus achieved different intravitreal concentrations of the drug. The studies focused on the effectiveness in uveitis more broadly, but also provided level I evidence and level II evidence that intravitreal fluocinolone acetonide could be an effective treatment for uveitic macular edema.

References

1. Xipere [Package Insert]. Alpharetta, GA; Clearside Biomedical, Inc.: 2021
2. Smith, JS, Thorne JE, Flaxel, CJ et al: Treatment of Noninfectious Uveitic Macular Edema with Periocular and Intraocular Corticosteroid Therapies: A Report by the American Academy of Ophthalmology. Ophthalmology. April 2024; doi: https://doi.org/10.1016/j.ophtha.2024.02.019

Xolair *(omalizumab)* vial/prefilled syringe

Additional Gold Coast Health Plan 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.

References

1. Global Initiative for Asthma. Difficult-To-Treat & Severe Asthma in adolescents and adult patients, 2024.
2. Global Initiative for Asthma. Global Strategy for Asthma Management and Prevention, 2024.
3. Xolair [Package Insert]. South San Francisco, CA: Genentech, Inc.: 2019
4. Zuberier T, Aberer W, Asero R, et al. The EAACI/GALEN/EDF/WAO guideline for the definition, classification, diagnosis, and management of urticaria. Allergy. 2018; 73: 1393 – 414.
5. Zuberbier T, Abdul Latiff AH, Abuzakouk M, et al. The international EAACI/GA²LEN/EuroGuiDerm/APAACI guideline for the definition, classification, diagnosis, and management of urticaria. Allergy. 2022; 77: 734–766. doi:10.1111/all.15090
6. Clinicaltrials.gov. Omalizumab as monotherapy and as adjunct therapy to multi-allergen oral immunotherapy (OIT) in food allergic children and adults (NCT03881696). Available at: https://classic.clinicaltrials.gov/ct2/show/NCT03881696.
7. Panel NI-SE, Boyce JA, Assa'ad A, et al. Guidelines for the diagnosis and management of food allergy in the United States: report of the NIAID-sponsored expert panel. J Allergy Clin Immunol. 2010; 126 (6 Suppl): S1 - 58.
8. Sampson HA, Aceves S, Bock SA, et al. Food allergy: a practice parameter update-2014. J Allergy Clin Immunol. 2014; 134 (5): 1016 - 25.
9. Santos AF, et al. EAACI guidelines on the diagnosis of IgE-mediated food allergy. Allergy. 2023;78(12):3057-3076. doi:10.1111/all.15902
10. Wood RA, Chinthrajah RS, Rudman Spergel AK, et al. Protocol design

and synopsis: Omalizumab as Monotherapy and as Adjunct Therapy to Multiallergen OIT in Children and Adults with Food Allergy (OUtMATCH). J Allergy Clin Immunol Glob. 2022;1(4):225-232. Published 2022 Jul 21. doi:10.1016/j.jacig.2022.05.006

11. Gevaert P, et al. Efficacy and safety of omalizumab in nasal polyposis: 2 randomized phase 3 trials. J Allergy Clin Immunol. 2020 Sept; 146 (3): 595-605.
12. Rank M, et al. The Joint Task Force on Practice Parameters GRADE guidelines for the medical management of chronic rhinosinusitis with nasal polyposis. J Allergy Clin Immunol. 2023 Feb; 151 (2): 386-398.

Yartemlea (narsoplimab-wuug) injection, for IV use

Additional Gold Coast Health Plan Part B Criteria: NO

YARTEMLEA is a MASP-2 inhibitor indicated for the treatment of adult and pediatric patients 2 years of age and older with hematopoietic stem cell transplant-associated thrombotic microangiopathy (TA-TMA).

The safety data described in this section reflect exposure to YARTEMLEA in the TA-TMA Study in which 28 adult patients received YARTEMLEA. In total, 24 patients received YARTEMLEA at a dose of 4 mg/kg intravenously once weekly for 4 or 8 weeks and 4 patients received 370 mg intravenously weekly for 8 weeks. The median duration of treatment with YARTEMLEA was 8 weeks (range: 2 to 16.4 weeks). Serious adverse reactions were reported in 61% of patients receiving YARTEMLEA. Serious adverse reactions in > 5% of patients who received YARTEMLEA included acute kidney injury, confusional state, acute respiratory failure, neutropenic sepsis, septic shock, pulmonary edema, and vomiting. Fatal adverse reactions occurred in 7% of patients, including neutropenic sepsis and septic shock. The most common adverse reactions (≥ 20%) were viral infections, sepsis, hemorrhage, diarrhea, vomiting, nausea, neutropenia, pyrexia, fatigue, and hypokalemia.

An additional 221 adult and pediatric patients with TA-TMA were treated with YARTEMLEA in a global expanded access program (EAP) that included patients for whom YARTEMLEA was their initial treatment following diagnosis of TA-TMA as well as patients who had previously failed or stopped other treatments. The median number of YARTEMLEA doses received by the 221 patients in the EAP was 8 and the median duration of therapy was 5.5 weeks. No new clinically significant safety signals were identified in patients treated in the EAP.

The efficacy of YARTEMLEA was assessed in (i) a single-arm, open-label study (TA-TMA Study) that enrolled 28 adult patients who developed TA-TMA following hematopoietic stem-cell transplantation (HCT) and (ii) 19 adult and pediatric patients with TA-TMA with evaluable patient-level response data enrolled in an expanded access program (EAP). In the TA-TMA Study, 24 patients received YARTEMLEA 4 mg/kg intravenously once weekly and 4 patients received YARTEMLEA 370 mg intravenously once weekly. The median number of YARTEMLEA administrations received by the 28 TA-TMA Study patients plus the 19 EAP patients was 8 (range: 2-34), and the median duration of therapy was 8 weeks (range: 2-

16 weeks).

References:

1. Yartemlea. [Prescribing Information]. Seattle, WA; Omeros Corporation: 2025. Available at: https://pi.omeros.com/us/yartemlea-uspi.pdf.

Yescarta *(axicabtagene ciloleucel)*

Additional Gold Coast Health Plan Part B Criteria: No

Yescarta is a CD19-directed genetically modified autologous T cell immunotherapy indicated for the treatment of:

- Adult patients with large B-cell lymphoma that is refractory to first-line chemoimmunotherapy or that relapses within 12 months of first-line chemoimmunotherapy.
- Adult patients with relapsed or refractory large B-cell lymphoma after two or more lines of systemic therapy, including diffuse large B-cell lymphoma (DLBCL) not otherwise specified, primary mediastinal large B-cell lymphoma, high grade B-cell lymphoma, and DLBCL arising from follicular lymphoma.

Gold Coast Health Plan follows NCD 110.24 for Chimeric Antigen Receptor (CAR) T-Cell Therapy.

References

1. Centers for Medicare & Medicaid Services. National Coverage Determination (NCD) 110.24 Chimeric Antigen Receptor (CAR) T-cell Therapy. https://www.cms.gov/medicare-coverage-database/view/ncd.aspx?ncdid=374
2. Yescarta [Package Insert]. Santa Monica, CA; Kite Pharma, Inc.: 2022

Yupelri *(revefenacin)*

Additional Gold Coast Health Plan Part B Criteria: Yes

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.

References

1. Global Strategy for the Diagnosis, Management, and Prevention of Chronic Obstructive Pulmonary Disease (2024 Report). Global Initiative for Chronic Obstructive Lung Disease, 2024.
2. Yupelri [Package Insert]. Morgantown, WV; Mylan Specialty L.P.: 2018

Yutiq *(fluocinolone)* implant

Additional Gold Coast Health Plan 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.

References

1. Yutiq [Package Insert]. Watertown, MA; EyePoint Pharmaceuticals US, Inc.: 2021
2. Flaxel CJ, Adelman RA, Bailey ST, et al. Age-Related Macular Degeneration Preferred Practice Pattern®. Ophthalmology. Jan 2020; 127(1): P1-P65. PMID 31757502
3. Reddy A, Liu S-H, Brady CJ, et al. Corticosteroid implants for chronic non-infectious uveitis. The Cochrane database of systematic reviews. 2023; 1(1), CD010469.

Ziextenzo *(pegfilgrastim-bmez)*

Additional Gold Coast Health Plan Part B Criteria: Yes

Ziextenzo is a leukocyte growth factor indicated to:

- Decrease the incidence of infection, as manifested by febrile neutropenia, in patients with non-myeloid malignancies receiving myelosuppressive anti-cancer drugs associated with a clinically significant incidence of febrile neutropenia.

- Increase survival in patients acutely exposed to myelosuppressive

doses of radiation (Hematopoietic Subsyndrome of Acute Radiation Syndrome)

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

1. Ziextenzo [Package Insert]. Princeton, NJ; Sandoz Inc.: 2019
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 1.2025) October 11, 2024. Available at: https://www.nccn.org/professionals/physician_gls/pdf/growthfactors.pdf.

ZIIHERA® (zanidatamab-hrii) injection, for IV use

Additional Gold Coast Health Plan Part B Criteria: No

ZIIHERA is indicated for the treatment of adults with previously treated, unresectable or metastatic HER2-positive (immunohistochemistry [IHC] 3+) biliary tract cancer (BTC), as detected by an FDA-approved test. This indication was FDA approved under accelerated approval based on overall response rate and duration of response. Continued approval for this indication may be contingent upon verification and description of clinical benefit in a confirmatory trial(s).
The efficacy of ZIIHERA was evaluated in 62 patients with HER2-positive (IHC 3+ by central assessment) BTC in Cohort 1 of HERIZON-BTC-01 (NCT04466891), an open-label, multicenter, single arm trial in patients with unresectable or metastatic disease. Patients were required to have received at least one prior gemcitabine-containing systemic chemotherapy regimen in the advanced disease setting and adequate cardiac function (defined as LVEF ≥ 50%).
Serious adverse reactions occurred in 53% of 80 patients with unresectable or metastatic HER2-positive BTC who received ZIIHERA. Serious adverse reactions in >2% of patients included biliary obstruction (15%), biliary tract infection (8%), sepsis (8%), pneumonia (5%), diarrhea (3.8%), gastric obstruction (3.8%), and fatigue (2.5%). A fatal adverse reaction of hepatic failure occurred in one patient who received ZIIHERA. Most common adverse reactions (≥ 20%) are diarrhea, infusion-related reaction, abdominal pain, and fatigue.

References:

1. National Comprehensive Cancer Network. Biliary Tract Cancers 2.2025. Available at: https://www.nccn.org/professionals/physician_gls/pdf/btc.pdf. Accessed September 22, 2025.
2. *Ziihera* Prescribing Information. Palo Alto, CA. Jazz Pharmaceuticals, Inc. Available at: https://pp.jazzpharma.com/pi/ziihera.en.USPI.pdf. Accessed on September 22, 2025.

Zilbrysq *(zilucoplan injection, solution)*

Additional Gold Coast Health Plan 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.

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.
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. Zilbrysq [Package Insert]. Smyrna, Georgia; UCB, Inc.: 2023
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-ofMG
6. Clinicaltrials.gov. Open-Label Extension of Zilucoplan in Subjects With Generalized Myasthenia Gravis (RAISE-XT). Available at: https://clinicaltrials.gov/study/NCT04225871.
7. Clinicaltrials.gov. Safety, Tolerability, and Efficacy of Zilucoplan in Subjects With Generalized Myasthenia Gravis (RAISE). Available at: https://clinicaltrials.gov/study/NCT04115293.
8. Vyvgart [Package Insert]. Zwijnaarde, Belgium; argenx BV: 2021
9. Rystiggo [Package Insert]. Smyrna, GA; UCB, Inc.: 2023
10. Ultomiris [Package Insert]. Boston, MA; Alexion Pharmaceuticals, Inc.: 2018

Zolgensma *(onasemnogene abeparvovec)*

Additional Gold Coast Health Plan Part B Criteria: No

Gold Coast Health Plan follows NCD 110.24 for Chimeric Antigen Receptor (CAR) T-Cell Therapy.

Zolgensma in indicated for the treatment of pediatric patients less than 2 years of age with spinal muscular atrophy (SMA) with bi-allelic mutations in the survival motor neuron 1 (SMN1) gene.

References

1. Centers for Medicare & Medicaid Services. National Coverage Determination (NCD) 110.24 Chimeric Antigen Receptor (CAR) T-cell Therapy. https://www.cms.gov/medicare-coverage-database/view/ncd.aspx?ncdid=374
2. Zolgensma [Package Insert]. Bannockburn, IL; Novartis Gene Therapies, Inc. 2023

Zymfentra *(infliximab-dyyb)*

Additional Gold Coast Health Plan 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.

References

1. Zymfentra [Package Insert]. Jersey City, New Jersey; Celltrion, Inc.: 2024
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
3. 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
4. Danese S, et al. Upadacitinib as induction and maintenance therapy for moderately to severely active ulcerative colitis: results from three phase 3, multicentre, double-blind, randomised trials. Lancet. 2022 Jun 4;399(10341):2113-2128.
5. Loftus EV Jr, et al. Upadacitinib Induction and Maintenance Therapy for Crohn's Disease. N Engl J Med. 2023 May 25;388(21):1966-1980.

Zynteglo *(onasemnogene abeparvovec)*

Additional Gold Coast Health Plan 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

1. Zynteglo [Package Insert]. Somerville, MA; bluebird bio, Inc.: 2022
2. Clinicaltrials.gov. A Study Evaluating the Efficacy and Safety of the LentiGlobin® BB305 Drug Product in Participants With Transfusion-

Dependent β-Thalassemia, Who do Not Have a β0/β0 Genotype. Available at: https://classic.clinicaltrials.gov/ct2/show/NCT02906202

3. Clinicaltrials.gov. A Study Evaluating the Efficacy and Safety of the LentiGlobin® BB305 Drug Product in Participants With Transfusion-Dependent β-Thalassemia. Available at: https://clinicaltrials.gov/study/NCT03207009.
4. Cappellini MD, Cohen A, Porter J, et al. Guidelines for the management of transfusion dependent thalassemia. 2021. Available at: https://issuu.com/internationalthalassaemiafederation/docs/final_guideline_4th
5. National Organization for Rare Disorders. Beta thalassemia. https://rarediseases.org/rarediseases/thalassemia-major/