P&T Committee Meeting Minutes
Commercial/Marketplace/CHIP
June 2024 e-Vote

DRUG REVIEWS

Zilbrysq (zilucoplan)

Review:
Zilbrysq is a complement inhibitor indicated for the treatment of generalized myasthenia gravis (gMG) in adult patients who are anti-acetylcholine receptor (AChR) antibody positive. Zilbrysq is the first self-administered complement inhibitor in gMG. Zilbrysq binds complement protein C5, inhibiting its cleavage to C5a and C5b and preventing the generation of C5b-9. The precise mechanism of Zilbrysq in gMG is unknown but is thought to involve reduction of C5b-9 deposition at the neuromuscular junction.

Prior to the initiation of Zilbrysq, patients should be vaccinated for meningococcal infection according the current ACIP recommendations at least 2 weeks before receiving the first dose of Zilbrysq. The recommended dosage of Zilbrysq is a once daily subcutaneous injection based on actual body weight (Table 6).

Table 6. Total Daily Dosing by Body Weight Range

Body Weight	Once Daily Dosage	Plunger Rod Color of Prefilled Syringe
Less than 56 kg	16.6 mg	RUBINE RED
56 kg to less than 77 kg	23 mg	ORANGE
77 kg and above	32.4 mg	DARK BLUE

Zilbrysq is intended for use under the guidance and supervision of a healthcare professional and patients may self-inject Zilbrysq after training in subcutaneous injection technique. It can be administered to the abdomen, thighs, or back of upper arms and the injection site should be rotated with each administration. Zilbrysq is supplied as single-dose prefilled syringes containing 16.6 mg/0.416 mL, 23 mg/0.574 mL, or 32.4 mg/0.81 mL of zilucoplan.

The efficacy and safety of Zilbrysq was evaluated in the RAISE trial, a 12-week randomized, double-blind, placebo-controlled trial in 174 adult patients with anti-AChR antibody positive generalized myasthenia gravis (gMG). Patients included in the trial had Myasthenia Gravis Foundation of America (MGFA) clinical classification class II to IV, positive serology for AChR binding autoantibodies, and MG-Activities of Daily Living (MG-ADL) total score of ≥6 (assessed the impact of gMG on daily functions of 8 signs or symptoms of gMG). Patients could be established on a stable dose of MG therapy at baseline, including acetylcholinesterase (AChE) inhibitors, steroids, or non-steroidal immunosuppressive therapies (NSISTs), either in combination or alone.

Patients were randomized to receive Zilbrysq 0.3 mg/kg (n=86) or placebo (n=88) once daily by subcutaneous injection. At baseline, approximately 85% of patients in each group received cholinesterase inhibitors, 63% received steroids, and 51% received NSISTs, at stable doses.

The primary efficacy endpoint was comparison of the change from baseline in MG-ADL scores after 12 weeks of treatment. Secondary endpoints included Quantitative Myasthenia Gravis (QMG) (13-item grading scale assessing muscle weakness), proportion of patients with improvements of at least 3 and 5 points in the MG_ADL score and QMG score at week 12 without rescue treatment.

At week 12, treatment with Zilbrysq demonstrated a statistically significant improvement from baseline compared to placebo for both MG_ADL total scores and QMG total scores (Table 7).

Table 7. Change from Baseline in MG-ADL and QMG Total Scores at Week 12 in Adult Patients with gMG who are Anti-AChR Antibody Positive (RAISE)

Efficacy Endpoints: LS Mean (95 % CI)	ZILBRYSQ (n = 86)	Placebo (n = 88)	ZILBRYSQ change LS mean difference vs. placebo (95% CI)	p-value*
MG-ADL Total Score	-4.39 (-5.28, -3.50)	-2.30 (-3.17, -1.43)	-2.09 (-3.24, -0.95)	< 0.001
QMG Total Score	-6.19 (-7.29, -5.08)	-3.25 (-4.32, -2.17)	-2.94 (-4.39, -1.49)	< 0.001

Abbreviations: CI = confidence interval; MG-ADL, myasthenia gravis activities of daily living scale; QMG, quantitative myasthenia gravis; LS = least square

The proportion of MG-ADL responders with a 3 point and 5 point improvement were 73.1% vs. 46.1% and 58% vs 33% for Zilbrysq vs. placebo, respectively. The proportion of clinical responders at higher response thresholds was consistently greater for Zilbrysq compared to placebo.

Zilbrysq carries a black box warning for the risk of serious meningococcal infections based on the risk of life-threatening and fatal meningococcal infections which have occurred in both vaccinated and unvaccinated patients treated with other complement inhibitors. Zilbrysq is available only through Zilbrysq REMS based on the meningococcal infection risk. Zilbrysq also presents an increased susceptibility to other infections, especially those caused by encapsulated bacteria, such as Neisseria meningitidis but also Streptococcus pneumoniae, Haemophilus influenzae, and to a lesser extent, Neisseria gonorrhoeae. It is recommended that patients treated with Zilbrysq receive vaccinations for the prevention of Streptococcus pneumoniae and Haemophilus influenzae type b (Hib) infections according to ACIP guidelines.

Other warnings for Zilbrysq include pancreatitis and pancreatic cysts which have been reported in patients treated with Zilbrysq. During clinical trials, 7 (3.3%) patients experienced pancreatic events including 4 patients with pancreatitis and 3 with pancreatic cysts. Increased lipase and amylase were reported in 6.9% and 4.7% of patients treated with Zilbrysq compared to 0% and 1.1% of patients treated with placebo. Lipase and Amylase levels should be evaluated prior to the initiation of Zilbrysq and treatment should be discontinued in patients with suspected pancreatitis until pancreatitis is ruled out or resolved.

The most common adverse reactions (≥10%) reported with Zilbrysq were injection site reactions, upper respiratory infections and diarrhea. Less common reactions (>5% to <10% included nausea and vomiting and increased amylase and lipase. Morphea has been observed in 5% of patients in open-label extension studies and in most cases occurred more than one year after treatment initiation. One patient discontinued Zilbrysq due to morphea.

The safety and efficacy of Zilbrysq has not been established in pediatric patients. Clinical studies did not include sufficient number of geriatric patients aged 65 years or older to determine if they respond differently from younger patients.

A Clinical Review including Clinical Information, Efficacy Evidence, Safety Evidence, Other Considerations and a Financial Review Based on Cost Analysis were presented.

Outcome: Zilbrysq is a pharmacy benefit and will not be added to the Commercial, Marketplace, and GHP Kids formulary. The following prior authorization criteria will apply:

- Medical record documentation of age 18 years or older **AND**
- Medical record documentation that Zilbrysq is prescribed by or in consultation with a neurologist **AND**
- Medical record documentation of a diagnosis of generalized myasthenia gravis (gMG) that is anti-acetylcholine receptor (AChR) positive **AND**
- Medical record documentation of Myasthenia Gravis Foundation of America Clinical Classification (MGFA) Class II to IV **AND**
- Medical record documentation of a baseline Myasthenia Gravis-Activities of Daily Living (MG-

ADL) score greater than or equal to 6 **AND**

- Medical record documentation of therapeutic failure on, intolerance to, or contraindication to corticosteroids **AND**
- Medical record documentation of therapeutic failure on intolerance to, or contraindication to at least two (2) non-steroidal immunosuppressive therapies OR has failed at least one (1) immunosuppressive therapy and required chronic plasmapheresis or plasma exchange (PE) **AND**
- Medical record documentation of failure on, intolerance to, or contraindication to intravenous immunoglobulin (IVIG)

AUTHORIZATION DURATION: 6 months. Subsequent approvals will be for 6 months and will require:

- Medical record documentation of continued disease improvement or lack of disease progression **AND**
- Medical record documentation that the member is responding positively to therapy as evidenced by an improvement of Myasthenia Gravis-Activities of Daily Living (MG-ADL) total score from baseline

GPI Level: GPI-12

QUANTITY LIMIT:

- **16.6 mg/0.416 mL prefilled syringe:** 0.416 mL per day, 28 day supply per fill
- **23.0 mg/0.574 mL prefilled syringe:** 0.574 mL per day, 28 day supply per fill
- **32.4 mg/0.81 mL prefilled syringe:** 0.81 mL per day, 28 day supply per fill

Additional evidence of the criteria used to make this decision can be found in the drug review presented to the committee.

FAST FACTS

ABECMA (idecabtagene vicleucel)

Clinical Summary: Abecma has an updated indication for 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. Previously Abecma was indicated following four prior lines of therapy.

An updated dosage range for Abecma recommends 300 to 510 x 10^6 CAR-positive T cells for a single dose infusion of chimeric antigen receptor (CAR)- positive T cells in one or more infusion bags (initial recommendations were 300 to 460 x 10^6 CAR-positive T cells).

Efficacy and safety findings from the KarMMa-3 trial support the change in indication for Abecma. KarMMa-3 is an open-label, randomized, controlled study in adult patients with r/r multiple myeloma who received two to four prior antimyeloma therapies including an immunomodulatory agent, a proteasome inhibitor and daratumumab, and were refractory to the most recent prior antimyeloma regimen.

In total, 386 patients were randomized 2:1 to receive either Abecma (n=254) or standard regimens (n=132). The standard regimens consisted of daratumumab, pomalidomide, dexamethasone [DPd], daratumumab, bortezomib, dexamethasone [DVd], ixazomib, lenalidomide, dexamethasone [IRd], carfilzomib, dexamethasone [Kd], or elotuzumab, pomalidomide, dexamethasone [EPd]), selected by Investigator prior to randomization contingent upon the patient's most recent antimyeloma treatment. Twenty-four patients did not receive Abecma due to death, adverse event, physician decision, failure to meet lymphodepleting chemotherapy treatment criteria, or inability to manufacture products. Three patients received CAR-positive T cells that did not meet product release specifications. The overall manufacturing failure was 2.4%.

The primary efficacy measure was progression free survival (PFS) as determined by Independent Review Committee (IRC) based on the International Myeloma Working Group (IMWG) Uniform Response Criteria for Multiple Myeloma. Overall response rate (ORR) and overall survival (OS) were also assessed (Table 1).

Table 1. Summary of Efficay results from KarMMa-3 (Intent-to-Treat Population)[1]

	ABECMA Arm (N=254)	Standard Regimens Arm (N=132)
Progression Free Survival (PFS)		
Number of events, n (%)	149 (59)	93 (70)
Median, months [95% CI][a]	13.3 [11.8, 16.1]	4.4 [3.4, 5.9]
Hazard Ratio [95% CI][b]	0.49 [0.38, 0.64]	
One-sided p-value[c]	< 0.0001	
Overall Response Rate (ORR), n (%)		
n (%)	181 (71)	55 (42)
95% CI (%)[d]	(66, 77)	(33, 50)
One-sided p-value[e]	< 0.0001	
CR or better (sCR+CR)	98 (39)	7 (5)
sCR	90 (35)	6 (4.5)
CR	8 (3.1)	1 (0.8)
VGPR	55 (22)	13 (10)
PR	28 (11)	35 (27)

New warnings for risk of early death are noted based on results from KarMMa-3 trial which demonstrated a higher proportion of patients experienced death within 9 months after randomization in the Abecma arm compared to standard regimens. Out of 20 deaths occurring prior to Abecma infusion, 15 occurred from disease progression, 3 occurred from adverse events and 2 occurred from unknown causes. Out of the 25 deaths that occurred after ABECMA infusion, 10 occurred from disease progression, 11 occurred from adverse events, and 4 occurred from unknown causes. Other warnings and reported adverse reactions are consistent with the known safety profile of Abecma.

Current Formulary Status: Medical benefit requiring prior authorization

Recommendation: No changes are recommended to the formulary placement or authorization duration of Abecma. The following changes are recommended to the prior authorization criteria to incorporate the updated indication.

Medical Benefit Policy 235.0 Abecma

- Medical record documentation that Abecma is prescribed by a hematologist/oncologist **AND**
- Medical record documentation of age greater than or equal to 18 years AND
- Medical record documentation of relapsed or refractory multiple myeloma AND
- Medical record documentation of at least ~~four~~ two prior lines of therapy, including an immunomodulatory agent, a proteasome inhibitor, and an anti-CD38 monoclonal antibody **AND**
- Medical record documentation that the member has not received prior treatment with CAR-T cell therapy or other genetically modified T cell therapy

Additional evidence of the criteria used to make this decision can be found in the drug review presented to the committee.

ALECENSA (alectinib)

Clinical Summary: Alecensa (alectinib) is now approved for the adjuvant treatment in adult patients following tumor resection of anaplastic lymphoma kinase (ALK)-positive non-small cell lung cancer (NSCLC) (tumors ≥ 4 cm or node positive) as detected by an FDA-approved test.

Alecensa was previously indicated for the treatment of patients with ALK-positive metastatic NSCLC as detected by an FDA-approved test. This indication has now been modified to specify adult patients only. The indication now reads as follows: treatment of adult patients with ALK-positive metastatic NSCLC as detected by an FDA-approved test.

Updated Dosing for New indication: No changes to dosing or current quantity limits. The recommended dosage of Alecensa is 600 mg orally twice daily.

Current Formulary Status: Alecensa is a pharmacy benefit on specialty tier or brand non-preferred tier for members with a three- tier benefit, requiring prior authorization with a quantity limit.

Recommendation: There are no changes recommended to formulary placement of Alecensa at this time. However, it is recommended to update the prior authorization criteria in the current policy to include the following:

- Medical record documentation that Alecensa is prescribed by a hematologist or oncologist **AND**
  - Medical record documentation of age greater than or equal to 18 years **AND**
  - **One** of the following:
    - Medical record documentation that Alecensa will be used for adjuvant treatment following tumor resection of anaplastic lymphoma kinase (ALK)-positive non-small cell lung cancer **OR**
    - Medical record documentation of a diagnosis of ALK-positive, metastatic non-small cell lung cancer

MEDISPAN AUTHORIZATION LEVEL: GPI-12, number of claims authorized = 1, enter for the remainder of the calendar year

QUANTITY LIMIT: No QLs need to be entered within the authorization unless the requested quantity exceeds the QL.

- QL FOR LETTER ONLY: 8 capsules per day, 30 day supply per fill

RE-AUTHORIZATION CRITERIA: Alecensa is configured as a prior authorization for new starts only. Alecensa will no longer be covered if it is identified that the member is not receiving appropriate follow-up care from the prescribing specialist or if the member has greater than or equal to a 90 day break in therapy.

Additional evidence of the criteria used to make this decision can be found in the drug review presented to the committee.

AVYCAZ (ceftazidime & Avibactam)

Clinical Summary:
Avycaz (cetfazidime/avibactam) is a combination cephalosporin/beta-lactamase inhibitor indicated for the treatment of susceptible Gram-negative microorganisms in Complicated Intra-abdominal Infections (cIAI), used in combination with metronidazole, Complicated Urinary Tract Infections (cUTI), including pyelonephritis and Hospital-acquired Bacterial Pneumonia and Ventilator-associated Bacterial Pneumonia (HABP/VABP) in patients 3 months or older.

The age has been updated now to include the pediatric population from birth (at least 31 weeks gestational age) to less than 3 months of age for the treatment of susceptible Gram-negative microorganisms in Complicated Intra-abdominal Infections (cIAI), used in combination with metronidazole, Complicated Urinary Tract Infections (cUTI), including pyelonephritis and Hospital-acquired Bacterial Pneumonia and Ventilator-associated Bacterial Pneumonia (HABP/VABP).

Current Formulary Status: Medical Benefit, Formulary, Prior Authorization required, QL.

Recommendation: It is recommended to update policy MBP 132.0 to include the new FDA approved age and to add to the description in the beginning of the medical benefit policy, the HABP/VABP indication to match the other two indications in the description.

Medical Benefit Policy for Avycaz: MBP 132.0

DESCRIPTION:
Avycaz (cetfazidime/avibactam) is a combination cephalosporin/beta-lactamase inhibitor indicated in combination with metronidazole, for the treatment of complicated intra-abdominal infections (cIAI) caused by the following susceptible microorganisms: Escherichia coli, Klebsiella pneumoniae, Proteus mirabilis, Enterobacter cloacae, Klebsiella oxytoca, Citrobacter freundii complex and Pseudomonas aeruginosa in ~~patients 3 months or older~~. adult and pediatric patients ≥31 weeks gestational age.
Avycaz is also indicated for the treatment of complicated urinary tract infections (cUTI) including pyelonephritis caused by the following susceptible microorganisms: Escherichia coli, Klebsiella pneumoniae, Enterobacter cloacae, Citrobacter freundii complex, Proteus mirabilis, and Pseudomonas aeruginosa in ~~patients 3 months or older~~. adult and pediatric patients ≥31 weeks gestational age.
Avycaz is also indicated for the treatment of hospital-acquired bacterial pneumonia and ventilator-associated bacterial pneumonia (HABP/VABP) caused by the following susceptible microorganisms: Enterobacter cloacae, Escherichia coli, Haemophilus influenzae, Klebsiella pneumoniae, Proteus mirabilis, Pseudomonas aeruginosa and, Serratia marcescens in adult and pediatric patients ≥31 weeks gestational age.

CRITERIA FOR USE: Requires Prior Authorization by Medical Director or Designee
Avycaz (cetfazidime/avibactam) will be considered medically necessary for the commercial, exchange, CHIP, and Medicaid lines of business when all of the following criteria are met:

- Prescribed by or in consultation with an infectious disease specialist AND
- Medical record documentation of one of the following:
    - o A diagnosis of complicated intra-abdominal infection caused by caused by the following susceptible microorganisms: Escherichia coli, Klebsiella pneumoniae, Proteus

mirabilis, Enterobacter cloacae, Klebsiella oxytoca, Citrobacter freundii complex and Pseudomonas aeruginosa OR
o A diagnosis of complicated urinary tract infections (cUTI) including pyelonephritis caused by the following susceptible microorganisms: Escherichia coli, Klebsiella pneumoniae, Enterobacter cloacae, Citrobacter freundii complex, Proteus mirabilis, and Pseudomonas aeruginosa OR
o A diagnosis of Hospital-acquired Bacterial Pneumonia and Ventilator-associated Bacterial Pneumonia (HABP/VABP) caused by the following susceptible microorganisms: Enterobacter cloacae, Escherichia coli, Haemophilus influenzae, Klebsiella pneumoniae, Proteus mirabilis, Pseudomonas aeruginosa and, Serratia marcescens.

AND

- Medical record documentation of culture and sensitivity showing the patient's infection is not susceptible to alternative antibiotic treatments OR a documented history of previous intolerance to or contraindication to other antibiotics shown to be susceptible on the culture and sensitivity.

AUTHORIZATION DURATION: Approval will be given for a duration of 14 days.
LIMITATIONS: A quantity limit of 3 vials per day should apply, with total duration of treatment not exceeding 14 days.
Additional evidence of the criteria used to make this decision can be found in the drug review presented to the committee.

BREYANZI (lisocabtagene maraleucel)

Clinical Summary: Breyanzi now has the following new indications:

- adult patients with relapsed or refractory chronic lymphocytic leukemia (CLL) or small lymphocytic lymphoma (SLL) who have received at least 2 prior lines of therapy, including a Bruton tyrosine kinase (BTK) inhibitor and a B-cell lymphoma 2 (BCL-2) inhibitor. This indication is approved under accelerated approval based on response rate and duration of response. Continued approval for this indication may be contingent upon verification and description of clinical benefit in confirmatory trial(s)
- adult patients with relapsed or refractory follicular lymphoma (FL) who have received 2 or more prior lines of systemic therapy. This indication is approved under accelerated approval based on response rate and duration of response. Continued approval for this indication may be contingent upon verification and description of clinical benefit in confirmatory trial(s)
- adult patients with relapsed or refractory mantle cell lymphoma (MCL) who have received at least 2 prior lines of systemic therapy, including a Bruton tyrosine kinase (BTK) inhibitor

Current Formulary Status: Medical benefit requiring prior authorization.

Recommendation: There are no changes recommended for the authorization duration or formulary placement of Breyanzi. It is recommended that the following prior authorization be added to MBP 228.0 to incorporate the new indications:

CLL/SLL

- Medical record documentation that Breyanzi is prescribed by a hematologist/oncologist **AND**
- Medical record documentation of age greater than or equal to 18 years **AND**
- Medical record documentation that the member has not received prior treatment with CAR-T cell therapy or other genetically modified T cell therapy **AND**
- Medical record documentation of a diagnosis of relapsed or refractory chronic lymphocytic leukemia (CLL) or small lymphocytic lymphoma (SLL) **AND**
- Medical record documentation of at least 2 prior lines of therapy, including a Bruton tyrosine kinase (BTK) inhibitor and a B-cell lymphoma 2 (BCL-2) inhibitor

FL

- Medical record documentation that Breyanzi is prescribed by a hematologist/oncologist **AND**
- Medical record documentation of age greater than or equal to 18 years **AND**

- Medical record documentation that the member has not received prior treatment with CAR-T cell therapy or other genetically modified T cell therapy **AND**
- Medical record documentation of a diagnosis of relapsed or refractory follicular lymphoma (FL) **AND**
- Medical record documentation of at least 2 prior lines of systemic therapy

MCL

- Medical record documentation that Breyanzi is prescribed by a hematologist/oncologist **AND**
- Medical record documentation of age greater than or equal to 18 years **AND**
- Medical record documentation that the member has not received prior treatment with CAR-T cell therapy or other genetically modified T cell therapy **AND**
- Medical record documentation of a diagnosis of relapsed or refractory mantle cell lymphoma (MCL) **AND**
- Medical record documentation of at least 2 prior lines of systemic therapy, including a Bruton tyrosine kinase (BTK) inhibitor.

Additional evidence of the criteria used to make this decision can be found in the drug review presented to the committee.

CARVYKTI (ciltacabtagene autoleucel)

Clinical Summary: Carvykti is now indicated for the treatment of adult patients with relapsed or refractory multiple myeloma who have received at least 1 prior line of therapy, including a proteasome inhibitor and an immunomodulatory agent, and are refractory to lenalidomide. Previously, this was indicated for the treatment of adult patients with relapsed or refractory multiple myeloma after four or more prior lines of therapy, including a proteasome inhibitor, an immunomodulatory agent, and an anti-CD38 monoclonal antibody.

The dosing of Carvykti for this indication is the same as the previous indication, with a target dose range of 0.5 to 1 x 10^6 chimeric antigen receptor (CAR)-positive viable T cells per kg of body weight given Intravenously, with a maximum dose of 1 x 10^8 CAR-positive viable T cells IV per single infusion.

Current Formulary Status: Medical Benefit that requires a prior authorization.

Recommendation: No changes are recommended to the formulary placement of Carvykti. It is recommended to update the medical benefit policy based on the new indication.

Medical Benefit Policy 256.0 Carvykti (ciltacabtagene autoleucel):

- Medical record documentation that Carvykti is prescribed by a hematologist/oncologist **AND**
- Medical record documentation of age greater than or equal to 18 years AND
- Medical record documentation of relapsed or refractory multiple myeloma AND
- Medical record documentation of at least ~~four~~ one prior line~~s~~ of therapy, including an immunomodulatory agent, a proteasome inhibitor, and ~~an anti-CD38 monoclonal antibody~~ are refractory to lenalidomide **AND**
- Medical record documentation that the member has not received prior treatment with CAR-T cell therapy or other genetically modified T cell therapy

Additional evidence of the criteria used to make this decision can be found in the drug review presented to the committee.

DOVATO (dolutegravir and lamivudine)

Clinical Summary:

- Dovato is indicated as a complete regimen for the treatment of HIV-1 infection in adults and adolescents 12 years of age and older and weighing at least 25 kg with no antiretroviral treatment history or to replace the current antiretroviral regimen in those who are virologically suppressed (HIV-1 RNA less than 50 copies/mL) on a stable antiretroviral regimen with no history of treatment failure and no known substitutions associated with resistance to the individual components of Dovato. It was previously indicated in patients 18 years of age and older.

- **Updated Dosing**: Dovato is a fixed-dose combination product containing 50 mg of dolutegravir and 300 mg of lamivudine. The recommended dosage regimen in adults and adolescents 12 years of age and older and weighing at least 25 kg is one tablet taken orally once daily with or without food

- **Summary of Updated Clinical Studies**:
    - The 48 week efficacy of Dovato was evaluated in an open-label multicenter trial (DANCE) in 30 evaluable treatment-naïve HIV-1–infected adolescents aged 12 to less than18 years and weighing at least 25 kg. Eighty-seven percent (26/30) of subjects achieved HIV-1 RNA <50 copies copies/mL at Week 48, and the mean increase from baseline in CD4+ cell count was 234 cells/mm3 at Week 48.

- **Summary of Updated Safety Considerations**:
    - Warnings and Precautions, Embryo-Fetal Toxicity was removed 4/2024
    - There are insufficient human data on the use of Dovato during pregnancy to definitively assess a drug-associated risk for birth defects and miscarriage. However, available human data from the APR with the individual components of Dovato do not indicate an increased risk of birth defects.

Current Formulary Status: Pharmacy Benefit; Brand Preferred, no Prior Authorization required; QL

Recommendation: No recommended changes.

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Additional evidence of the criteria used to make this decision can be found in the drug review presented to the committee.

DUPIXENT (dupilumab)

Clinical Summary: Dupixent is now indicated for the treatment of adult and pediatric patients aged 1 year and older, weighing at least 15 kg, with eosinophilic esophagitis (EoE).

Updated Dosing for New indication: The recommended dosage of DUPIXENT for adult and pediatric patients 1 year of age and older, weighing at least 15 kg:

Body Weight	Recommended Dosage in Adult and Pediatric Patients 1 Year and Older, Weighing At Least 15 kg
15 to less than 30 kg	200 mg every other week (Q2W)
30 to less than 40 kg	300 mg every other week (Q2W)
40 kg or more	300 mg every week (QW)

Summary of Updated Clinical Studies: Pediatric Subjects 1 to 11 Years of Age, Weighing at Least 15 kg, with EoE: The efficacy and safety of DUPIXENT was evaluated in pediatric subjects 1 to 11 years of age, weighing at least 15 kg, with EoE in a randomized, blinded, parallel-group, multicenter trial (Study EoE-2 Parts A and B; NCT04394351). Eligible subjects had ≥15 intraepithelial eosinophils per high-power field (eos/hpf) despite a treatment course of a proton pump inhibitor (PPI) either prior to or during the screening period and a history of EoE signs and symptoms. Part A evaluated weight-based dosing regimens of DUPIXENT, 200 mg Q2W (≥15 to <30 kg) and 300 mg Q2W (≥30 to <60 kg), or placebo in 61 subjects during the 16-week treatment period.

The recommended dosage of 300 mg QW for pediatric subjects 1 to 11 years of age weighing ≥40 kg is based on modeled pharmacokinetic data to provide comparable exposures to the 300 mg QW dosage in adult and pediatric subjects 12 years of age and older weighing ≥40 kg with EoE.

Current Formulary Status: Dupixent is currently on formulary as a specialty medication requiring prior authorization under commercial policy 457.0.

Recommendation: The following changes are recommended to the prior authorization criteria for the commercial Dupixent policy 457.0, reflecting the new age limit and minimum dosing weight for the indication of eosinophilic esophagitis.

- Medical record documentation that Dupixent is prescribed by or in consultation with an allergist, immunologist, or gastroenterologist **AND**
- Medical record documentation of age greater than or equal to 1 year **AND**
- Medical record documentation of weight greater than or equal to 15 kilograms **AND**
- Medical record documentation of a diagnosis of eosinophilic esophagitis **AND**
- Medical record documentation of greater than or equal to 15 intraepithelial eosinophils per high-power field (eos/hpf) **AND**
- Medical record documentation of contraindication to, intolerance to, or therapeutic failure on a proton pump inhibitor **AND**
- Medical record documentation that the member is experiencing chronic symptoms of esophageal dysfunction (for example, dysphagia, food impaction, food refusal, abdominal pain, heartburn, regurgitation, chest pain, odynophagia) **AND**
- Medical record documentation of contraindication to, intolerance to, or therapeutic failure on a swallowed inhaled respiratory glucocorticoid **AND**
  Medical record documentation that the member is receiving an appropriate dose# based on patient's age and weight

Additional evidence of the criteria used to make this decision can be found in the drug review presented to the committee.

ENHERTU (fam-trastuzumab deruxtecan-nxki)

Clinical Summary: Enhertu is now indicated for the:

- treatment of adult patients with unresectable or metastatic HER2-positive (IHC 3+) solid tumors who have received prior systemic treatment and have no satisfactory alternative treatment options.
  - This indication is approved under accelerated approval based on objective 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.
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The other indications of Enhertu include:

- treatment of adult patients with unresectable or metastatic HER2-positive (IHC 3+ or ISH positive) breast cancer who have received a prior anti-HER2-based regimen either in the metastatic setting or in the neoadjuvant or adjuvant setting and have developed disease recurrence during or within six months of completing therapy
  - Labeling further defines HER2-positive for this indication.
- treatment of adult patients with locally advanced or metastatic HER2-positive (IHC 3+ or IHC 2+/ISH positive) gastric or gastroesophageal junction adenocarcinoma who have received a prior trastuzumab-based regimen.
  - Labeling further defines HER2-positive for this indication.
- the treatment of adult patients with unresectable or metastatic HER2-low (IHC 1+ or IHC 2+/ISH-) breast cancer, as determined by an FDA-approved test, who have received a prior chemotherapy in the metastatic setting or developed disease recurrence during or within 6 months of completing adjuvant chemotherapy

- the treatment of adult patients with unresectable or metastatic non-small cell lung cancer (NSCLC) whose tumors have activating HER2 (ERBB2) mutations, as detected by an FDA-approved test, and who have received a prior systemic therapy.
    - This indication is also approved under accelerated approval based on objective 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.

Current Formulary Status: Enhertu is a medical benefit requiring a prior authorization. When processed at a specialty pharmacy, it is on the specialty tier or brand non preferred tier.

Recommendation: No changes recommended to the formulary placement or authorization duration of Enhertu at this time. However, it is recommended to update policy Medical Benefit Policy 208 to include the following highlighted changes.

Medical Benefit Policy 208 Enhertu:

Breast Cancer

- Prescription written by a hematologist or oncologist **AND**
- Medical record documentation of patient age greater than or equal to 18 years **AND**
- Medical record documentation of unresectable or metastatic HER2-positive (IHC 3+ or ISH positive) breast cancer **AND**
- Medical record documentation of one of the following:
    - Documentation of a prior anti-HER2 based therapy in the metastatic setting **OR**
    - Documentation of a prior anti-HER2 based therapy in the neoadjuvant or adjuvant setting **AND** documentation of disease recurrence during or within 6 months of completing therapy

OR

- Prescription written by a hematologist or oncologist **AND**
- Medical record documentation of patient age greater than or equal to 18 years **AND**
- Medical record documentation of unresectable or metastatic HER2-low (IHC 1+ or IHC 2+/ISH-) breast cancer, as detected by an Food and Drug Administration (FDA)-approved test **AND**
- Medical record documentation that Enhertu will be used as a single agent **AND**
- Medical record documentation of one of the following:
    - Documentation of a prior chemotherapy in the metastatic setting **OR**
    - Documentation of disease recurrence during or within 6 months of completing adjuvant chemotherapy

Gastric Cancer

- Medical record documentation that Enhertu is written by a hematologist/oncologist **AND**
- Medical record documentation of age greater than or equal to 18 years **AND**
- Medical record documentation of a diagnosis of locally advanced or metastatic HER2-positive (IHC 3+ or IHC 2+/ISH positive) gastric or gastroesophageal junction (GEJ) adenocarcinoma **AND**
- Medical record documentation of one or more prior trastuzumab-based therapies

Non-Small Cell Lung Cancer

- Medical record documentation that Enhertu is written by a hematologist/oncologist **AND**
- Medical record documentation of age greater than or equal to 18 years **AND**
- Medical record documentation of unresectable or metastatic non-small cell lung cancer (NSCLC) **AND**
- Medical record documentation of tumors that have activating HER2 (ERBB2) mutations, as detected by an FDA-approved test **AND**
- Medical record documentation that Enhertu will be used as a single agent **AND**
- Medical record documentation of a prior systemic therapy

HER2-Positive Solid Tumors

- Medical record documentation that Enhertu is written by a hematologist/oncologist **AND**
- Medical record documentation of age greater than or equal to 18 years **AND**

- Medical record documentation of unresectable or metastatic HER2-positive (IHC 3+) solid tumors **AND**
- Medical record documentation of prior systemic treatment and have no satisfactory alternative treatment options

Additional evidence of the criteria used to make this decision can be found in the drug review presented to the committee.

FANAPT (iloperidone)

Clinical Summary: Updated Indication: Fanapt is now indicated for the acute treatment of manic or mixed episodes associated with bipolar I disorder with adults. Previously, it was indicated for the treatment of schizophrenia in adults.

- Updated Dosing for New indication: The titration varies slightly depending on indication.

Indication and Population	Titration schedule							Recommended Dosage
	Day 1	*Day 2*	*Day 3*	*Day 4*	*Day 5*	*Day 6*	*Day 7*	
Schizophrenia	1mg twice daily	2 mg twice daily	4 mg twice daily	6 mg twice daily	Titration complete			3 mg to 6 mg twice daily
Bipolar I Disorder Manic or Mixed Episodes	1 mg twice daily	3 mg twice daily	6 mg twice daily	Titration complete				6 mg twice daily

- Summary of Updated Clinical Studies: The efficacy of Fanapt for the new indication was supported by a multicenter, randomized, double-blind, placebo-controlled study which enrolled patients who met DSM-5 criteria for bipolar disorder, manic or mixed type. Manic symptoms were assessed with the Young Mania Rating Scale (YMRS) which is an 11-item clinician rated scale to assess the degree of manic symptoms. The scores range from 0-60 with a higher score indicating greater severity.

  The primary endpoint of the 4-week trial was the change in YMRS total score from baseline to day 28. Fanapt was found to be superior to placebo on the primary endpoint.

Table 1: Primary Efficacy Results for Change from Baseline in YMRS Total Score in the Acute Treatment of Manic or Mixed Episodes Associated with Bipolar I Disorder in Adults

Study Number	Treatment Group (# ITT patients)	Primary Efficacy Endpoint: Change from Baseline to Day 28 in YMRS Total Score		
		Mean Baseline Score (SD)	LS Mean Change from Baseline (SE)	Placebo-subtracted Difference[a] (95% CI)
1	FANAPT (24 mg/day)* (n=198)	29.2 (5.27)	-14.0 (0.64)	-4.0 (-5.70, -2.25)
	Placebo (n=194)	28.8 (4.64)	-10.0 (0.63)	

ITT = intent-to-treat, YMRS = Young Mania Rating Scale, LS mean = least Squares mean, SD = standard deviation, SE = standard error
[a] Difference (drug minus placebo) in least-squares mean change from baseline
*Dose was superior to placebo

- Summary of Updated Safety Considerations: New warning/Precaution: Intraoperative Floppy Iris Syndrome has been observed during cataract surgery in some patients on or previously treated w/ alpha-1 adrenergic blockers. There does not appear to be a benefit of stopping alpha-1 blocker therapy prior to cataract surgery. The initiation of Fanapt in patients for whom cataract/glaucoma surgery is scheduled is not recommended.

Current Formulary Status: Fanapt is on the brand preferred tier with a prior authorization and a QL of 60 tablets per 30 days.

Recommendation: It is recommended to update the prior authorization criteria.

- Medical record documentation of a diagnosis of schizophrenia or manic or mixed episodes associated with bipolar I disorder **AND**
- Medical record documentation of a contraindication, intolerance or therapeutic failure to all formulary agents (risperidone, olanzapine, quetiapine, aripiprazole and ziprasidone)

Additional evidence of the criteria used to make this decision can be found in the drug review presented to the committee.

ONIVYDE (irinotecan liposome injection)

Clinical Summary: Onivyde is now indicated, in combination with oxaliplatin, fluorouracil and leucovorin for the first line treatment of adult patients with metastatic pancreatic adenocarcinoma. Previously, Onivyde was indicated in combination with fluorouracil and leucovorin, for the treatment of adult patients with metastatic pancreatic adenocarcinoma after disease progression following gemcitabine-based therapy.

The recommended dosage of Onivyde is 50 mg/m^2 (regardless of UGT1A1*28 allele genotype) administered by intravenous infusion over 90 minutes every 2 weeks. A corticosteroid and an anti-emetic should be administered 30 minutes prior to each Onivyde infusion. Dosage reductions due to adverse reactions are listed in Table 1.

Table 1. Recommended Dosage Modifications for ONIVYDE in combination with oxaliplatin, fluorouracil and leucovorin[1]

Toxicity[a]	Occurrence	ONIVYDE adjustment in patients receiving 50mg/m^2
Grade 3 or 4 Adverse reactions[b]	Withhold ONIVYDE Upon recovery to ≤ Grade 1[c,d,e], resume ONIVYDE at:	
	First	40 mg/m^2
	Second	32.5 mg/m^2
	Third	25 mg/m^2
	Fourth	Discontinue ONIVYDE
Grade 3 or 4 Hand foot syndrome	First	Discontinue ONIVYDE
Any grade neurocerebellar toxicity	First	Discontinue ONIVYDE
Grade ≥ 2 cardiac toxicity	First	Discontinue ONIVYDE
Interstitial lung disease	First	Discontinue ONIVYDE
Anaphylactic reaction	First	Discontinue ONIVYDE

a Toxicity grading per NCI CTCAE v5.0. bNo dosage modification is necessary for asthenia, alopecia and Grade 3 anorexia. c Do not resume until the absolute neutrophil count is ≥2000/mm3 (2x109/L) and the platelet count is ≥100,000/mm3 (100x109/L). d For Grade ≥3 nausea and vomiting, reduce dose only if occurs despite optimal anti-emetic therapy. e Refer to the Full Prescribing Information of fluorouracil and oxaliplatin. When ONIVYDE dose is reduced for adverse reactions, reduce fluorouracil (FU) and oxaliplatin doses: for first occurrence, reduce dose to 80% of original dose; for second occurrence, reduce dose to 65% of original dose; for third occurrence, reduce dose to 50% of original dose; discontinue therapy for fourth occurrence. Oxaliplatin may be discontinued if not well tolerated and treatment with ONIVYDE + FU/LV can continue. Maintain original dose level of leucovorin for first, second and third occurrence of toxicity.

The efficacy of Onivyde in combinations with oxiplatin, fluorouracil, and leucovorin (NALRIFOX) was evaluated in the NAPOLI 3 trial, a randomized, open-label, active controlled trial in 770 patients with metastatic pancreatic adenocarcinoma who had not previously received chemotherapy in the metastatic setting. Patients were randomized 1:1 to receive:

- NALIRIFOX: ONIVYDE 50 mg/m2 as an intravenous infusion over 90 minutes, followed by oxaliplatin 60 mg/m2 as an intravenous infusion over 120 minutes, followed by leucovorin 400 mg/m2 intravenously over 30 minutes, followed by fluorouracil 2400 mg/m2 intravenously over 46 hours, every 2 weeks.

- Gem+NabP: Nab-paclitaxel 125 mg/m2 as an intravenous infusion over 35 minutes, followed by gemcitabine 1000 mg/m2 intravenously over 30 minutes on days 1, 8 and 15 of each 28-day cycle.

Treatment continued until RECIST v1.1 defined disease progression or unacceptable toxicity. The main efficacy outcome measure was overall survival (OS). Investigator-assessed progression-free survival (PFS) and objective response rate (ORR) were also assessed. The NALIRIFOX arm demonstrated statistically significant improvement over the Gem+NabP arm in OS and PFS (Table 2).

Table 2. Efficacy Results of All Randomized Patients in NAPOLI 3[1]

	NALIRIFOX* (N=383)	**Gem+NabP** (N=387)
Overall Survival		
Number of Deaths, n (%)	259 (68)	285 (74)
Median Overall Survival (months)	11.1	9.2
(95% CI)	(10.0, 12.1)	(8.3, 10.6)
Hazard Ratio (95% CI) *	0.84 (0.71, 0.99)	
p-value †	0.0403	
Progression-Free Survival		
Death or Progression, n (%)	249 (65)	259 (67)
Median Progression-Free Survival (months)	7.4	5.6
(95% CI)	(6.0, 7.7)	(5.3, 5.8)
Hazard Ratio (95% CI) *	0.70 (0.59, 0.85)	
P-value †	0.0001	
Objective Response Rate #		
ORR (95% CI)	41.8 (36.8, 46.9)	36.2 (31.4, 41.2)
CR, n (%)	1 (0.3)	1 (0.3)
PR, n (%)	159 (41.5)	139 (35.9)

* NALIRIFOX= ONIVYDE+oxaliplatin/5-fluorouracil/leucovorin; Gem+NabP=gemcitabine+nab-paclitaxel; CI=confidence interval
** Based on the stratified Cox proportional hazard model; stratified by ECOG PS (0 vs. 1), region (North America vs. East Asia vs. Rest of the world), and liver metastases (yes vs. no) per interaction web response system
† Based on stratified log-rank test.
# ORR result was not statistically significant.

In the NAPOLI 3 trial, serious adverse reactions occurred in 54% of patients in the NALRIFOX treatment arm, including COVID-19, diarrhea, nausea, vomiting, fatigue, embolism, gastrointestinal tract stenosis or obstruction, hemorrhage, abdominal pain, cerebrovascular accident, dehydration, liver function test abnormalities, and pyrexia. Fatal adverse reactions occurred in 6% of patients, including cerebrovascular accident, hemorrhage, pneumonia, sepsis, and sudden death.

Warnings and Precautions were consistent with the known safety profile of Onivyde. Permanent discontinuation due to adverse reaction occurred in 17% of patients, most commonly neutropenia, thrombocytopenia, diarrhea, fatigue, infections, and cerebrovascular accident. Dose reduction and dose interruptions due to adverse reaction occurred in 52% and 1.9% of patients, respectively. The most common adverse reactions were diarrhea, fatigue, nausea, vomiting, decreased appetite, abdominal pain, mucosal inflammation, constipation and decreased weight. The most common lab abnormalities included decreased neutrophils, potassium, lymphocytes, and hemoglobin.

Current Formulary Status: Medical Benefit, When processed at Specialty pharmacy: Specialty tier or Brand NP tier for members with a three tier benefit, PA

Recommendation: No changes are recommended to the formulary placement of Onivyde. The following updates are recommended to Medical Benefit Policy 138.0 to incorporate the new indication for Onivyde.

Medical Benefit Policy 138.0 Onivyde

- Must be prescribed by an oncologist **AND**
- Medical record documentation of the patient being ≥18 years of age **AND**
- Medical record documentation of a diagnosis of metastatic adenocarcinoma of the pancreas **AND**

- Medical record documentation of one of the following:
  - Medical record documentation that Onivyde is being prescribed in combination with fluorouracil and leucovorin for disease progression following gemcitabine-based therapy **OR**
  - Medical record documentation that Onivyde is being prescribed in combination with oxaliplatin, fluorouracil and leucovorin for first line treatment

Additional evidence of the criteria used to make this decision can be found in the drug review presented to the committee.

XOLAIR (omalizumab)

Clinical Summary: Xolair is now FDA indicated for the treatment of IgE-mediated food allergy in adult and pediatric patients aged 1 year and older for the reduction of allergic reactions (Type I), including anaphylaxis, that may occur with accidental exposure to one or more foods. Xolair should be used in conjunction with food allergen avoidance.

The recommended dose for the treatment of IgE-mediated food allergy is Xolair 75mg to 600mg by subcutaneous injection every 2 to 4 weeks based on pretreatment serum total IgE level (IU/mL) and body weight. Table 4 below illustrates the recommended dose based on these parameters:

Table 4. Subcutaneous XOLAIR Doses Every 2 or 4 Weeks* for Adult and Pediatric Patients 1 Year of Age and Older with IgE-Mediated Food Allergy

Pretreatment Serum IgE (IU/mL)	Dosing Freq.	Body Weight (kg)												
		≥10-12	>12-15	>15-20	>20-25	>25-30	>30-40	>40-50	>50-60	>60-70	>70-80	>80-90	>90 - 125	>125 - 150
		Dose (mg)												
≥30 - 100	Every 4 Weeks	75	75	75	75	75	75	150	150	150	150	150	300	300
>100 - 200		75	75	75	150	150	150	300	300	300	300	300	450	600
>200 - 300		75	75	150	150	150	225	300	300	450	450	450	600	375
>300 - 400		150	150	150	225	225	300	450	450	450	600	600	450	525
>400 - 500		150	150	225	225	300	450	450	600	600	375	375	525	600
>500 - 600		150	150	225	300	300	450	600	600	375	450	450	600	
>600 - 700		150	150	225	300	225	450	600	375	450	450	525		
>700 - 800	Every 2 Weeks	150	150	150	225	225	300	375	450	450	525	600		
>800 - 900		150	150	150	225	225	300	375	450	525	600			
>900 - 1000		150	150	225	225	300	375	450	525	600				
>1000 - 1100		150	150	225	225	300	375	450	600					
>1100 - 1200		150	150	225	300	300	450	525	600					
>1200 - 1300		150	225	225	300	375	450	525						
>1300 - 1500		150	225	300	300	375	525	600						
>1500 - 1850			225	300	375	450	600							

Insufficient data to Recommend a Dose

*Dosing frequency:

Subcutaneous doses to be administered every 4 weeks

Subcutaneous doses to be administered every 2 weeks

The Omalizumab as Monotherapy in Food Allergic Children and Adults (OUtMATCH) is a multi center, randomized, double-blind, placebo-controlled trial that was designed as a phase 3 trial to more fully

evaluate the safety and efficacy of omalizumab as a treatment that blocks immune responses irrespective of antigen type for patients as young as 1 year of age who are allergic to multiple foods. The trial included 168 adult and pediatric persons from 1 to 55 years of age with a history of allergy to peanut and at least two other foods in the protocol-specified list. The FA trial enrolled patients who experienced dose-limiting symptoms (e.g., moderate to severe skin, respiratory or gastrointestinal symptoms) to a single dose of ≤100 mg of peanut protein and ≤300 mg protein for each of the other two foods (milk, egg, wheat, cashew, hazelnut, or walnut) during the screening double-blind placebo-controlled food challenge (DBPCFC). Patients with a history of severe anaphylaxis (defined as neurological compromise or requiring intubation) were excluded from the study. Patients were randomized 2:1 to receive a subcutaneous dosage of Xolair or placebo based on serum total IgE level (IU/mL), measured before the start of treatment, and by body weight for 16 to 20 weeks. The primary efficacy endpoint was the percentage of patients who were able to consume a single dose of ≥600 mg of peanut protein (equivalent to 2.5 peanuts) without dose-limiting symptoms (e.g., moderate to severe skin, respiratory or gastrointestinal symptoms) during DBPCFC (which occurred after 16 to 20 weeks of treatment). Table 16 shows Xolair treatment led to a statistically higher response rate (68%) than placebo (5%). Of note, 17% of subjects receiving Xolair had no significant change in the amount of peanut protein tolerated. Therefore, continuation of strict allergen avoidance is still necessary, despite treatment with Xolair. The secondary efficacy endpoints were the percentage of patients who were able to consume a single dose of ≥1000 mg of cashew, milk, or egg protein without dose-limiting symptoms during DBPCFC. The study met the secondary endpoints and demonstrated that XOLAIR treatment led to statistically higher response rates than placebo for all three foods. See Table 16 for details.

The safety of Xolair in patients with IgE mediated allergic reactions (Type 1) was also based on data from the OUtMATCH trial. Based on the primary analysis population in pediatric patients aged 1 year to 17 years, the most common adverse reactions were injection site reactions and pyrexia. During the primary analysis trial period, there were no discontinuations due to adverse reactions.
As a reminder, Xolair is associated with and has a boxed warning for anaphylaxis which can occur after the first dose but has also occurred beyond one year after beginning treatment. Therefore, Xolair must be initiated in the healthcare setting and the transition to self administration is deemed appropriate only after risk-benefit discussions between the provider and patient.

Table 16. DBPCFC Response Rates in Pediatric Patients for Single Dose of Peanut, Cashew, Milk or Egg Protein in FA Trial

Food, Challenge Dose	Response Rate[a] (%) (n/N)		Treatment Difference (%) (XOLAIR-Placebo) (95% CI)
	XOLAIR	Placebo	
Peanut, ≥600 mg	68% (75/110)	5% (3/55)	63% (50%, 73%)
Peanut, ≥1000 mg[b]	65% (72/110)	0% (0/55)	65% (56%, 74%)
Cashew, ≥1000 mg	42% (27/64)	3% (1/30)	39% (20%, 53%)
Milk, ≥1000 mg	66% (25/38)	11% (2/19)	55% (29%, 73%)
Egg, ≥1000 mg	67% (31/46)	0% (0/19)	67% (49%, 80%)

CI = Confidence interval; DBPCFC = Double-blind placebo-controlled food challenge; n = Number of responders; N = Total number of patients receiving food, challenge dose.
[a] Response defined as consumption of a single dose of the specified amount of food without dose-limiting symptoms.
[b] Consumption of a single dose of ≥1000 mg of peanut protein was an additional secondary endpoint. The key secondary efficacy endpoints were the percentage of patients who were able to consume a single dose of ≥1000 mg of cashew, milk, or egg protein.
Notes: Subjects without an exit DBPCFC or evaluable exit DBPCFC were counted as non-responders; P-values from two-sided Fisher's exact tests were <0.0001 for all the food challenge doses.

Current Formulary Status:
Pharmacy benefit: Requires a prior authorization and is placed at the non preferred or specialty tier
Medical benefit: Requires a prior authorization
Recommendation:
Pharmacy: Add the following to policy 661.0 – Xolair for Self-Administration
IgE Mediated Food Allergies

1. Medical record documentation of use for the maintenance reduction of IgE mediated food allergies (type 1) AND
2. Medical record documentation of a positive skin prick test response to one or more foods AND
3. Medical record documentation of a positive in vitro test for IGE to one or more foods AND
4. Prescriber attestation that reaction is significant enough for the member to require and receive a prescription for an epinephrine product AND
5. Medical record documentation that medication will be used in conjunction with a food allergen-avoidant diet AND
6. Medical record documentation of a dose consistent with FDA approved labeling AND
7. Medical record documentation of an IgE level of greater than 30 IU/mL AND
8. Medical record documentation that member is 1 year of age or older AND
9. Medical record documentation that Xolair is prescribed by an allergist or immunologist AND
10. Medical record documentation that Xolair is not being administered in combination with an additional monoclonal antibody used for the treatment of IgE mediated conditions.

Medispan Authorization Level: GPI-10
Authorization Duration: Initial approval will be for 12 months. Subsequent approvals will be for an additional 12 months and will require medical record documentation of improvement in signs and symptoms of disease.
Medical: Add the following to MBP 22.0 – Xolair
IgE Mediated Food Allergies

1. Medical record documentation of use for the maintenance reduction of IgE mediated food allergies (type 1) AND
2. Medical record documentation of a positive skin prick test response to one or more foods AND
3. Medical record documentation of a positive in vitro test for IGE to one or more foods AND
4. Prescriber attestation that reaction is significant enough for the member to require and receive a prescription for an epinephrine product AND
5. Medical record documentation that medication will be used in conjunction with a food allergen-avoidant diet AND
6. Medical record documentation of a dose consistent with FDA approved labeling AND
7. Medical record documentation of an IgE level of greater than 30 IU/mL AND
8. Medical record documentation that member is 1 year of age or older AND
9. Medical record documentation that Xolair is prescribed by an allergist or immunologist AND
10. Medical record documentation that Xolair is not being administered in combination with an additional monoclonal antibody used for the treatment of IgE mediated conditions.

Authorization Duration: Initial approval will be for 12 months or less if the reviewing provider feels it is medically appropriate. Subsequent approvals will be for an additional 12 months or less if the reviewing provider feels it is medically appropriate and will require medical record documentation of continued disease improvement or lack of disease progression. The medication will no longer be covered if patient experiences toxicity or worsening of disease.
Additional evidence of the criteria used to make this decision can be found in the drug review presented to the committee.

UPDATES

AGAMREE (vamorolone oral suspension)

Background: Agamree was reviewed at May 2024 P&T and a quantity limit of 225 mL/30 days was recommended. Agamree is supplied in 100 mL bottles and must be dispensed in the original bottles.

Recommendation: It is recommended that the QL for Agamree be updated as follows:
Quantity Limit: 300 mL per 30 days

Additional evidence of the criteria used to make this decision can be found in the drug review presented to the committee.

XDEMVY (lotilaner ophthalmic solution 0.25%) OXERVATE (cenegermin-bkbj ophth solution 0.002%)

Background: The following changes are recommended for Commercial Policy 794.0 for Xdemvy and Commercial Policy 623.0 for Oxervate

Recommendation: Update prescriber requirement in prior authorization:

Commercial Policy 794.0 for Xdemvy

- Medical record documentation that Xdemvy is prescribed by or in consultation with an ophthalmologist or optometrist **AND**

Commercial Policy 623.0 and Part D Policy 810.0D (for 2026) for Oxervate:

- Medical record documentation that Oxervate is prescribed by an ophthalmologist or optometrist **AND**

Additional evidence of the criteria used to make this decision can be found in the drug review presented to the committee.

REPATHA PUSHTRONEX (evolocumab)

Background: Amgen, the manufacturer of Repatha, has announced that they will discontinue the Pushtronex formulation effective 6/30/2024. Repatha Pushtronex is a 420 mg/3.5 mL single-dose on-body infusor with a prefilled cartridge.

Repatha is indicated for secondary prevention of atherosclerotic cardiovascular disease and heterozygous/homozygous familial hypercholesterolemia. Repatha is dosed as follows:

Indication	Dosage
Atherosclerotic cardiovascular disease, secondary prevention	• 140 mg SUBQ once every 2 weeks OR • 420 mg SUBQ once monthly
Familial hypercholesterolemia, heterozygous	• 140 mg SUBQ once every 2 weeks OR • 420 mg SUBQ once monthly
Familial hypercholesterolemia, homozygous	• 420 mg SUBQ once monthly • May increase to 420 mg SUBQ every 2 weeks if clinically meaningful response is not achieved in 12 weeks

Recommendation:
It is recommended that the following criterion be updated to account for the change in available formulations:

- ~~If requesting Repatha Syringe or Repatha Sureclick 420 mg dose (3 mL), medical record documentation of therapeutic failure on, intolerance to, or contraindication to Repatha Pushtronex **OR**~~
- If requesting Repatha Syringe or Repatha Sureclick 420 mg dose (3 mL), medical record documentation of one of the following:
    - Medical record documentation of a diagnosis of Clinical atherosclerotic cardiovascular disease (ASCVD), Primary hyperlipidemia, or Heterozygous familial hypercholesterolemia (HeFH) **AND** therapeutic failure on, intolerance to, or contraindication to Repatha 140 mg every 2 weeks **OR**
    - Medical record documentation of a diagnosis of Homozygous familial hypercholesterolemia (HoFH)

Additional evidence of the criteria used to make this decision can be found in the drug review presented to the committee.

SYFOVRE & IZERVAY UPDATE

Background: As part of Eye Disorder CarePath discussions, updates to the Syfovre and Izervay policy were recommended. Among the topics discussed were to delete the criteria point regarding CNV, change the authorization duration to allow for closer monitoring, and add criteria points regarding best corrected visual acuity and safety.

Recommendation: It is recommended to update the prior authorization criteria and update the authorization duration.
MBP 278.0 Syfovre (pegcetacoplan)

- Medical record documentation of the treatment of geographic atrophy (GA) secondary to age-related macular degeneration (AMD) **AND**
- Medical record documentation of a confirmed diagnosis of geographic atrophy (GA) using imagining modalities, including but not limited to fundus autofluorescence (FAF), fundus photography, or optical coherence tomography (OCT) **AND**
- Medical record documentation of a current (within 3 months) best corrected visual acuity (BCVA) of 20/320 or better (for example 20/200, 20/80, 20/70, etc) in the eye(s) to be treated with Syfovre
- ~~For new starts only: Medical record documentation of the absence of active, or history of, choroidal neovascularization* (CNV) in the eye(s) to be treated with Syfovre.~~

~~*Note: Age-related macular degeneration (AMD) with CNV is often referred to as exudative AMD (eAMD), neovascular AMD (nAMD), or wet AMD (wAMD).~~

AUTHORIZATION DURATION: ~~Approvals will be given for a lifetime duration.~~ Initial approval will be for **12 months** or less if the reviewing provider feels it is medically appropriate. Subsequent approvals will be for **12 months** or less if the reviewing provider feels it is medically appropriate and will require the following criteria:

- Medical record documentation of a current (within 3 months) best corrected visual acuity (BCVA) of better than 20/320 (for example 20/200, 20/80, 20/70, etc.) in the eye(s) being treated with Syfovre **AND**
- Medical record documentation of the absence, or resolution, of Retinal Vasculitis, Retinal Vascular Occlusion, and/or active Intraocular Inflammation (including but not limited to: vitritis, vitreal cells, iridocyclitis, uveitis, anterior chamber cells, iritis, and anterior chamber flare) **AND**
- One of the following:

- Medical record documentation of the absence of active choroidal neovascularization (CNV), or neovascular (wet) Age Related Macular Degeneration (nAMD) in the Syfovre-treated eye(s) **OR**
- Medical record documentation that the member's active CNV, or nAMD is NOT worsening **OR**
- Medical record documentation of rationale for continued use in the setting of worsening CNV, or nAMD (eg. The benefits of Syfovre outweigh the risks of Syfovre administration)

QUANTITY LIMIT: 0.2mL (30mg) per 25 days (15mg per eye per 25 days)

Additional evidence of the criteria used to make this decision can be found in the drug review presented to the committee.

VACCINATIONS FOLLOWING HEMATOPOIETIC STEM CELL TRANSPLANTATION

Background: Hematopoietic Stem Cell Transplantation (HSCT) involves ablation of the bone marrow followed by reimplantation of the person's own stem cells or stem cells from a donor. The ablation caused by the HSCT will also gradually remove immune memory from previous vaccination. Antibody titers to vaccine-preventable diseases (e.g., tetanus, poliovirus, measles, mumps, rubella, and encapsulated bacteria) decrease 1-4 years after autologous or allogeneic HSCT if the recipient is not revaccinated. HSCT recipients of all ages are at increased risk for certain vaccine-preventable diseases, including diseases caused by encapsulated bacteria (e.g., pneumococcal and Hib infections). As a result, HSCT recipients who received vaccines prior to their HSCT should receive repeat doses routinely after HSCT, regardless of the source of the transplanted stem cells.[1]

The recommended vaccination schedule after HSCT is[2]:

VACCINES			Months since transplant: 1	2	3	4	5	6	7	8	9	10	11	12	24 mo
Inactived influenza[1]	I	●				*					1 dose				
Pneumococcal conjugate[2]	I	●			3 doses									**	
Tetanus, diphtheria, pertussis[3]	I	●									3 doses				
Haemophilus influenzae B (Hib)	I	●									3 doses				
Inactivated Polio	I	●									3 doses				
Recombinant hepatitis B[4]	I	●									3 doses				
Mumps,measels, rubella[5]	L	●													2 doses
Varicella [6]	L	●													2 doses
Meningococcal[7] conjugate (MCV-4)	I	○									2 doses				
Human papilloma (HPV)[8]	I	○									3 doses				

I,inactivated; L,live

● *Recommended for all*

○ *Age/ risk based*

Currently, varicella, tetanus/diphtheria/pertussis, haemophilus influenzae B, inactivated polio, hepatitis B vaccines, meningococcal, and human papilloma virus vaccines are configured on the Commercial, Marketplace, and CHIP formularies with age limits restricting use to pediatric patients.

Influenza vaccine, pneumococcal vaccine, and mumps/measles/rubella vaccines are currently configured without age limits.

Recommendation: It is recommended to remove the age limits currently associated with varicella, tetanus/diphtheria/pertussis, haemophilus influenzae B, inactivated polio, hepatitis B

vaccines, and meningococcal vaccines in order to allow $0 coverage for those members who require additional vaccination post HSCT.
Coverage of human papilloma virus vaccine will be addressed in a later update.

Additional evidence of the criteria used to make this decision can be found in the drug review presented to the committee.

VICTOZA AND OZEMPIC FOR WEIGHT MANAGEMENT POLICY UPDATE (GHS EMPLOYEE)

Background: The following changes are recommended to the existing Victoza and Ozempic policies for weight management:

1. Out of state exemption of Geisinger Nutrition/Endocrinology requirement.
    a. Geisinger providers are unable to see patients out of state.
2. Quantity limit increased to allow off-label use of Victoza up to Saxenda dosing.
    a. Victoza dosed at 3mg (Saxenda max) is less expensive vs. Ozempic and more likely to get patients to >10% weight loss within first 6 months .
3. Clarification members can switch from Victoza to Ozempic after 6 months if weight loss <10% and don't need continued documentation of OSA/LFTs/A1c.
    a. Criteria was already met when Victoza was approved and comorbid conditions may have improved even though member hasn't lost 10% weight.
4. Correction of Victoza QL when used for diabetes.

Recommendation:

PROCEDURE:

An exception for coverage of Ozempic or Victoza may be made for members who meet the following criteria:

Ozempic or Victoza for Diabetes

- Medical record documentation of a diagnosis of type II diabetes mellitus

MEDISPAN APPROVAL LEVEL: GPI-12

QUANTITY LIMIT: *No QLs need to be entered within the authorization unless the requested quantity exceeds the QL.*

QL FOR LETTER ONLY:

- Victoza: 9 mL per ~~28~~30 days
- Ozempic: 3 mL per 28 days

Victoza for Weight Loss

- Medical record documentation of age greater than or equal to 18 years **AND**
- Medical record documentation of one of the following:
    - Victoza is managed by Geisinger Nutrition and Weight Management or Geisinger Endocrinology **OR**
    - Member resides outside of Pennsylvania **AND**
- Medical record documentation of body mass index (BMI) greater than or equal to 30 kg/m^2 **AND**
- Medical record documentation of at least one of the following specific weight related comorbid conditions:
    - Hemoglobin A1C (HgbA1c) between 6% - 6.4%
    - Elevated aspartate aminotransferase (AST) or alanine transaminase (ALT)
    - Obstructive sleep apnea requiring treatment with CPAP/BiPAP

MEDISPAN APPROVAL LEVEL: GPI-12

QUANTITY LIMIT: ~~*No*~~ *QLs need to be entered within the authorization* ~~*unless the requested quantity exceeds the QL*~~:

- Victoza: ~~9 mL per 28 days~~ 15 mL per 30 days

Ozempic for Weight Loss

- Medical record documentation of age greater than or equal to 18 years **AND**
- Medical record documentation of one of the following:
  - Ozempic is managed by Geisinger Nutrition and Weight Management or Geisinger Endocrinology **OR**
  - Member resides outside of Pennsylvania **AND**
- Medical record documentation of body mass index (BMI) greater than or equal to 30 kg/m^2 **AND**
- Medical record documentation of at least one of the following specific weight related comorbid conditions:
  - ~~Hemoglobin A1C (HgbA1c) between 6% - 6.4%~~
  - ~~Elevated aspartate aminotransferase (AST) or alanine transaminase (ALT)~~
  - ~~Obstructive sleep apnea requiring treatment with CPAP/BiPAP~~ **~~AND~~**
- Medical record documentation of therapeutic failure of Victoza defined as failure to achieve a 10% weight loss after 6 months of Victoza therapy

AUTHORIZATION DURATION: Initial approval will be for 6 months. Subsequent approvals will be indefinite. Reauthorization will require the following be met:

- Medical record documentation of 5% weight loss **AND**
- Medical record documentation of one of the following:
  - Ozempic is managed by Geisinger Nutrition and Weight Management or Geisinger Endocrinology **OR**
  - Member resides outside of Pennsylvania

MEDISPAN APPROVAL LEVEL: GPI-12

QUANTITY LIMIT: *No QLs need to be entered within the authorization unless the requested quantity exceeds the QL.*

QL FOR LETTER ONLY: Ozempic: 3 mL per 28 days

Additional evidence of the criteria used to make this decision can be found in the drug review presented to the committee.

VACCINATIONS FOLLOWING HEMATOPOIETIC STEM CELL TRANSPLANTATION

Background: Wegovy was previously reviewed through the April 2024 P&T e-vote for its new indication – to reduce the risk of major adverse cardiovascular events (cardiovascular death, non-fatal myocardial infarction, or non-fatal stroke) in adults with established cardiovascular disease and either obesity or overweight.

Recommendation: Some commercial plans do have weight loss coverage, and it is recommended that the prior authorization criteria in policy 686.0 Wegovy and Zepbound be updated as highlighted below.

Commercial Policy 686.0

- Medical record documentation that member has participated in comprehensive lifestyle modifications including reduced-calorie diet, physical activity, and behavioral health for at least 3 months prior to beginning Wegovy or Zepbound AND
- Medical record documentation of use as adjunct therapy to reduced calorie diet and increased physical activity for chronic weight management AND
- Medical record documentation of one of the following:
    - Medical record documentation of age greater than or equal to 18 years with one of the following:
        - Medical record documentation of body mass index (BMI) greater than or equal to 30 kg/m2 OR
        - Medical record documentation of body mass index (BMI) greater than or equal to 27 kg/m2 and at least one weight-related comorbid condition for the requested medication (e.g., Wegovy: hypertension, type 2 diabetes mellitus, dyslipidemia, or established cardiovascular disease*; Zepbound: hypertension, type 2 diabetes mellitus, or dyslipidemia)
    - For Wegovy only: Medical record documentation of age greater than or equal to 12 years and less than 18 years with an initial body mass index (BMI) in the 95th percentile or higher for age and sex

*Established cardiovascular disease defined as having one of the following:

- Acute coronary syndromes
- History of myocardial infarction
- Ongoing angina (stable or unstable)
- Prior coronary or other arterial revascularization
- Prior stroke or transient ischemic attack
- Peripheral arterial disease of atherosclerotic origin

Additional evidence of the criteria used to make this decision can be found in the drug review presented to the committee.

Voting responses were received from 26 of 50 members. The vote was unanimously approved.

The next bi-monthly scheduled meeting will be held on July 16th, 2024 at 1:00 p.m.

Meeting will be held virtually via phone/Microsoft Teams.