

Pharmacy Management Drug Policy

SUBJECT: Rare Diseases Clinical Review Prior Authorization (CRPA)

POLICY NUMBER: PHARMACY-98

EFFECTIVE DATE: 01/15/2021

LAST REVIEW DATE: 05/07/2026

If the member's subscriber contract excludes coverage for a specific service or prescription drug, it is not covered under that contract. In such cases, medical or drug policy criteria are not applied. This drug policy applies to the following line/s of business:

Policy Application

Category:	<input checked="" type="checkbox"/> Commercial Group (e.g., EPO, HMO, POS, PPO)	<input checked="" type="checkbox"/> Medicare Advantage
	<input checked="" type="checkbox"/> On Exchange Qualified Health Plans (QHP)	<input type="checkbox"/> Medicare Part D
	<input checked="" type="checkbox"/> Off Exchange Direct Pay	<input checked="" type="checkbox"/> Essential Plan (EP)
	<input checked="" type="checkbox"/> Medicaid & Health and Recovery Plans (MMC/HARP)	<input checked="" type="checkbox"/> Child Health Plus (CHP)
	<input type="checkbox"/> Federal Employee Program (FEP)	<input type="checkbox"/> Ancillary Services
	<input checked="" type="checkbox"/> Dual Eligible Special Needs Plan (D-SNP)	

DESCRIPTION:

A disease is considered rare if it affects less than 200,000 people in the United States. There are over 6,800 rare diseases and it is estimated that 25-30 million Americans live with a rare disease. The exact cause for many rare diseases remains unknown but it is believed that most are linked to a genetic mutation. Still, environmental factors may also play a role in some of these conditions. Considerable progress has been made in recent years to find ways to diagnose and treat rare diseases.

This policy is applicable to drugs that are included on a specific drug formulary. If a drug referenced in this policy is non-formulary, please reference the Non-Formulary Medication Exception Review Policy for review guidelines.

Approval time periods: Unless otherwise noted within individual drug criteria, approval time periods are defined under Policy Guidelines at the end of this policy

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DRUG SPECIFIC POLICIES/CRITERIA:

Actimmune – Interferon Gamma-1B (Medical & Rx)

1. For the treatment of Chronic Granulomatous Disease
 - a. The prescribing physician is an infectious disease specialist or a hematologist/oncologist
 - b. Diagnosis has been confirmed through neutrophil function tests
 - c. Combination therapy with antibiotics (i.e., trimethoprim/sulfamethoxazole) and/or antifungals (i.e., itraconazole) has been shown to reduce the risk of severe infections.
2. In the treatment of severe, malignant osteopetrosis
 - a. The prescribing physician is an orthopedic surgeon, hematologist, or an endocrinologist
 - b. The diagnosis is confirmed through radiological evidence.
3. Approved dosing for those with a body surface area greater than 0.5 m^2 is 50 mcg/m^2 (1 million units/ m^2) subcutaneously 3 times a week.
4. Doses above 50 mcg/m^2 will not be authorized.
5. Actimmune can be self-administered and therefore will be covered under the **pharmacy benefit**.
6. Actimmune will only be covered under the **medical benefit** if there is documentation that the patient has an inability to self-inject. For pediatric patients < 18 years of age, documentation must also include the inability of a caregiver to administer the medication. Self-injection criteria applies to:
 - a. New Starts and recertification requests for all lines of business except Medicare Advantage.
7. Quantity limit: 1 vial per 28 days. Upon each review and dose escalation request, the allowed quantity will be reviewed in accordance with FDA-approved BSA-based dosing and, as such, will be limited to the minimum number of vials to obtain the appropriate weekly dose. For pediatric patients, a higher quantity may be allowed based on the patient's predicted growth, on a case-by-case basis.

Adzynma (apadamtase alfa)-Medical

1. Must be prescribed by, or in consultation with, a hematologist **AND**
2. Must have a diagnosis of congenital thrombotic thrombocytopenic purpura (cTTP) confirmed by all of the following (a, b, and c):
 - a. ADAMTS13 activity <10% **AND**
 - b. The patient does not have anti-ADAMTS13 autoantibodies **AND**
 - c. Molecular genetic testing confirming a pathogenic variant or mutation of the *ADAMTS13* gene [characterized by homozygous or compound heterozygous mutations] **AND**
3. Requests for prophylactic use of Adzynma for individuals new to therapy will require:
 - a. The patient has a history of at least one documented TTP event **OR**
 - b. The patient is currently receiving prophylactic therapy with commercially available plasma-based therapies (e.g., fresh frozen plasma, solvent/detergent-treated plasma, factor VIII/VWF concentrations)
4. See prescribing information for full dosing and administration information
5. Adzynma will not be authorized for any other non-FDA approved indication including immune-mediated or acquired TTP
6. Initial approval will be for 6 months. Recertification will be for 12 months at a time and require documentation **OR** provider attestation that the following are met (a and b):
 - a. The patient is responding to therapy (e.g., improvement in acute TTP events, TTP manifestations, thrombocytopenia events, microangiopathic hemolytic anemia events) **AND**
 - b. Patient is not routinely using prophylactic plasma-based therapies **OR** routine use of prophylactic plasma-based therapies will be discontinued

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Aldurazyme- laronidase (Medical)

1. Must have a diagnosis of Hurler, Hurler-Scheie or Scheie form of MPS I confirmed by biochemical enzyme analysis for alpha-L-iduronidase enzyme deficiency in white blood cells or cultured skin fibroblasts
2. Patient must be followed by a physician experienced in metabolic disorders
3. Must have an affected 1st degree relative **OR** have clinical symptoms of the disease such as: Valvular heart disease, cardiomyopathy, obstructive sleep apnea, restrictive lung disease, reactive airway disease, joint stiffness, joint contractures, joint pain, spinal deformities, corneal clouding, glaucoma, developmental delay, mental retardation, communicating hydrocephalus, hearing loss, hepatomegaly, inguinal/umbilical hernia, and chronic infections
4. Must be ≥ 6 months of age
5. Current body weight and requested dose regimen must be submitted for initial review and each recertification request

Recommended Dosing:

- 0.58 mg/kg IV infusion once weekly

HCPCS: J1931

Aqvesme (mitapivat)-Rx

- I. **Aqvesme is considered medically necessary for the treatment of anemia in non-transfusion dependent alpha(α)-or beta(β)-thalassemia when the following criteria are met:**
 1. Must have a diagnosis of α - or β -thalassemia (β -thalassemia with or without α -globin gene mutations, hemoglobin E (HbE)/ β -thalassemia, or α -thalassemia (including hemoglobin H (HbH) disease)) based on Hb electrophoresis, Hb high-performance liquid chromatography (HPLC), and/or DNA analysis
 - a. Aqvesme will not be covered for any other diagnoses including homozygous or heterozygous sickle hemoglobin (HbS) or hemoglobin C (HbC)
 2. Must be at least 18 years of age
 3. Must be prescribed by or in consultation with a hematologist or physician knowledgeable in the treatment of thalassemia
 4. Must have documentation of hemoglobin (Hb) concentration ≤ 10.0 grams per deciliter (g/dL), based on an average of at least two Hb concentration measurements (separated by ≥ 7 days)
 5. Must be non-transfusion-dependent, defined as (a and b):
 - a. ≤ 5 red blood cell (RBC) units transfused in the previous 24 weeks **AND**
 - b. No RBC transfusion within the previous 8 weeks
 6. Initial approval will be granted for 6 months. Recertification will require documented achieved hemoglobin response, defined as an increase in Hb by 1 g/dL or greater from baseline, based on an average of at least two Hb concentration measurements (separated by ≥ 4 weeks). Recertification will be for 12 months at a time. **OR**
- II. **Aqvesme is considered medically necessary for the treatment of anemia in transfusion-dependent alpha(α)-or beta(β)-thalassemia when the following criteria are met:**
 1. Must have a diagnosis of α - or β -thalassemia (β -thalassemia with or without α -globin gene mutations, hemoglobin E (HbE)/ β -thalassemia, or α -thalassemia (including hemoglobin H (HbH) disease)) based on Hb electrophoresis, Hb high-performance liquid chromatography (HPLC), and/or DNA analysis
 - i. Aqvesme will not be covered for any other diagnoses including homozygous or heterozygous sickle hemoglobin (Hb S) or hemoglobin C (Hb C)
 2. Must be at least 18 years of age
 3. Must be prescribed by or in consultation with a hematologist or physician knowledgeable in the treatment of thalassemia
 4. Must be transfusion-dependent, defined as (a and b):

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- a. 6 to 20 red blood cells (RBC) units transfused in the previous 24 weeks **AND**
 - b. Transfusion-free period no longer than 6 weeks in the previous 24 weeks
 5. **For individuals with transfusion-dependent beta-thalassemia, must have serious side effects or drug failure with Reblozyl. This requirement does not apply to individuals with prior splenectomy.**
 - a. This applies to new starts only
 6. Initial approval will be granted for 6 months. Recertification will require documented reduction in RBC transfusion burden after receiving Aqvesme. Recertification will be for 12 months at a time.
- III. Quantity limit 56 tablets/28 days

Arcalyst - riloncept (Rx)

1. Must have a diagnosis of Cryopyrin-Associated Periodic Syndromes (CAPS) with one of the following conditions: Familial Cold Autoinflammatory Syndrome (FCAS) also known as Familial Cold Urticaria **OR** Muckle-Wells Syndrome (MWS) **AND**
 - a. Patient must be at least 12 years of age
 - b. Patient is not on concurrent therapy with any of the following – Ilaris, Kineret, Enbrel, Humira, infliximab or Simponi
 - c. The recommended dose for CAPS, FCAS, MWS
 - i. Adults: Loading dose: 320 mg, delivered as two 160 mg (2 mL) injections. Maintenance dose: 160 mg (2 mL) injection once weekly.
 - ii. Pediatric patients 12 years to 17 years: Loading dose: 4.4 mg/kg, up to a maximum of 320 mg, delivered as 1 or 2 injections (not to exceed 2 mL/injection). Maintenance dose: 2.2 mg/kg, up to a maximum of 160 mg (2 mL) injection, once weekly.
 - d. **Note** – it is not known whether Arcalyst is effective in patients with Neonatal-Onset Multisystem Inflammatory Disease (NOMID), also referred to as Chronic Infantile Neurologic Cutaneous Articular Syndrome (CINCA). **OR**
2. Must have a diagnosis of Deficiency of Interleukin-1 Receptor Antagonist (DIRA) confirmed by mutation in the *IL1RN* gene **AND**
 - a. Must be prescribed by or in consultation with a rheumatologist, geneticist, dermatologist, or a physician specializing in the treatment of autoinflammatory conditions **AND**
 - b. Patient must weigh at least 10 kg **AND**
 - c. According to the prescriber, the patient has demonstrated clinical benefit with Kineret (anakinra subcutaneous injection). Examples of clinical benefits include resolution of skin rash, bone pain, and fever, normal acute phase reactants (CRP<0.5 mg/dL), objective absence of skin rash, no radiological evidence of active bone disease, reduction in the use of corticosteroids **AND**
 - d. Patient is not on concurrent therapy with any of the following – Ilaris, Kineret, Enbrel, Humira, infliximab or Simponi
 - e. The recommended dose of Arcalyst for DIRA is as follows:
 - i. Adult and pediatric patients weighing at least 10 kg: 4.4 mg/kg up to a maximum of 320 mg delivered as 1 or 2 injections (2 mL/injection) once weekly **OR**
3. Must have diagnosis of recurrent pericarditis (RP) defined as a subsequent pericarditis episode after a symptom-free interval of at least 4-6 weeks
 - a. Must be prescribed by or in consultation with a cardiologist **AND**
 - b. Patient must be ≥ 12 years or older **AND**
 - c. Patient must be presenting with at least a second pericarditis recurrence (third pericarditis episode at minimum) despite treatment with NSAIDs, colchicine or corticosteroids, in any combination
 - i. The current episode is characterized by pericardial pain for ≥ 1 day with a numerical rating scale (NRS) pain score of ≥ 4 **AND** a C-reactive protein level of at least of at least 1 mg/dL **OR**
 - ii. The current episode must have met two or more of the following:

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- A. Pericarditis chest pain (typically sharp chest pain, improved with sitting up and leaning forward)
 - B. Pericardial rubs (superficial scratchy or squeaking sound heard with the diaphragm of a stethoscope over the left sternal border)
 - C. New widespread ST-elevation or PR depression on ECG
 - D. Pericardial effusion (new or worsening) **AND**
- d. Prescriber must attest that the patient will attempt to taper and discontinue NSAIDs, colchicine and/or corticosteroids while on Arcalyst **AND**
 - e. Arcalyst will not be approved for patients with pericarditis secondary to tuberculosis, post-thoracic blunt trauma, myocarditis, systemic autoimmune diseases (excluding Still's disease), or neoplastic, purulent, or radiation etiologies **AND**
 - f. Arcalyst will not be approved for patients with incessant or chronic pericarditis **AND**
 - g. Patient is not on concurrent therapy with any of the following – Ilaris, Kineret, Enbrel, Humira, infliximab or Simponi
 - h. The recommended dose for RP is as follows:
 - i. Adults: Loading dose: 320 mg, delivered as two 160 mg (2 mL) injections. Maintenance dose: 160 mg (2 mL) injection once weekly.
 - ii. Pediatric patients 12 years to 17 years: Loading dose: 4.4 mg/kg, up to a maximum of 320 mg, delivered as 1 or 2 injections (not to exceed 2 mL/injection). Maintenance dose: 2.2 mg/kg, up to a maximum of 160 mg (2 mL) injection, once weekly.
 - i. Initial approval of Arcalyst for recurrent pericarditis will be for 3 months. Recertification will require documentation that the patient has had no pericarditis recurrence while using Arcalyst **AND** documentation that NSAIDs, colchicine and/or corticosteroid doses have been reduced or discontinued.
4. Quantity limit of 4 vials/28 days
- a. The allowed quantity will be reviewed in accordance with FDA-approved weight and age-based dosing and, as such, will be limited to the minimum number of vials to obtain the appropriate weekly dose.
 - b. A one-time override of 5 vials per 28 days will be allowed for diagnosis of CAPs, FCAS, MWS and RP to accommodate for the loading dose. A quantity limit exception (8 vials/28 days) can be granted for diagnosis of DIRA requiring 2 injections administered once weekly.

Bylvay-odevixibat (Rx)

- 1. Must have a diagnosis of **progressive familial intrahepatic cholestasis (PFIC) types 1-6**, confirmed by molecular genetic testing **AND**
 - a. Must be ≥ 3 months of age **AND**
 - b. Must be prescribed by a hepatologist, gastroenterologist, or physician knowledgeable in the management of PFIC **AND**
 - c. Must have a serum bile acid concentration that exceeds the upper limit of normal **AND**
 - d. Prescriber attestation or documentation that the patient is experiencing significant pruritis **AND**
 - e. Bylvay will not be authorized in PFIC type 2 patients with ABCB11 variants resulting in non-functional or complete absence of bile salt export pump protein (BSEP-3).
 - f. For New Starts Only—must have serious side effects or drug failure with at least ONE conventional medication used for PFIC associated cholestasis/pruritis (e.g., ursodeoxycholic acid (ursodiol), cholestyramine, rifampin, naltrexone)
 - g. Initial approval for PFIC will be for 6 months. Recertification will require documentation that the patient is tolerating therapy and is experiencing a decrease in pruritis from baseline and/or decrease in serum bile acid concentration. Recertification will be required every 12 months.
- 2. Must have a diagnosis of **Alagille syndrome (ALGS)**, confirmed by molecular genetic testing (JAG1 or NOTCH2 mutation) **AND**

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- a. Must be 12 months of age or older **AND**
 - b. Must be prescribed by a hepatologist, gastroenterologist, or physician knowledgeable in the management of ALGS **AND**
 - c. Must have evidence of cholestasis defined as at least one of the following:
 - i. Total serum bile acid above the upper limit of normal (ULN) for age
 - ii. Conjugated bilirubin > 1 mg/dL
 - iii. Fat soluble vitamin deficiency otherwise unexplainable
 - iv. Gamma Glutamyl Transferase (GGT) > 3x ULN for age
 - v. Intractable pruritus explainable only by liver disease **AND**
 - d. Prescriber attestation or documentation that the patient is experiencing significant pruritis. **AND**
 - e. For New Starts Only—both of the following must be met:
 - i. Must have serious side effects or drug failure with at least ONE conventional medication used for ALGS associated cholestasis/pruritis (e.g., ursodeoxycholic acid (ursodiol), cholestyramine, rifampin, naltrexone) **AND**
 - ii. Must have serious side effects or drug failure to Livmarli
 - f. Initial approval for ALGS will be for 6 months. Recertification will require documentation that the patient is tolerating therapy and is experiencing a decrease in pruritis from baseline and/or decrease in serum bile acid concentration from baseline. Recertification will be required every 12 months.
3. For ALGS and PFIC, Bylvay will **not** be authorized if the patient has any of the following (a, b, or c):
- a. Cirrhosis
 - b. Portal hypertension
 - c. History of a hepatic decompensation event (i.e., variceal hemorrhage, ascites, hepatic encephalopathy)
4. Bylvay oral pellets are intended for patients weighing < 19.5 kg and Bylvay capsules are intended for patients weighing ≥ 19.5 kg
5. The recommended dosage:
- a. **For PFIC** is 40 mcg/kg once daily in the morning with a meal. If there is no improvement in pruritis after 3 months, the dosage may be increased in 40 mcg/kg increments up to 120 mcg/kg once daily, not to exceed a total daily dose of 6 mg.
 - b. **For ALGS** is 120 mcg/kg taken orally once daily in the morning with a meal.
6. Quantity limit of 30 /30 days for oral pellets and capsules

Upon each drug review and dose escalation request, the allowed quantity will be reviewed in accordance with the FDA-approved weight-based dosing for PFIC and ALGS (see prescribing information for details) and, as such, will be limited to the minimum number of oral pellets or capsules of each strength to obtain the appropriate daily dose.

Camzyos- mavacamten capsules (Rx)

1. Must be ≥ 18 years of age **AND**
2. Camzyos must be prescribed by, or in consultation, with, a cardiologist **AND**
3. Must have a diagnosis of symptomatic obstructive hypertrophic cardiomyopathy (oHCM) confirmed by echocardiogram **AND/OR** cardiac magnetic resonance showing one of the following (a or b):
 - a. Maximal end-diastolic left ventricular wall thickness of ≥15 mm
 - b. Maximal end-diastolic left ventricular wall thickness ≥13 mm **AND one** of the following (i or ii):
 - i. Family history of HCM **OR**
 - ii. A positive genetic test (e.g., *MYH7*, *TNNI3*, *TNNT2*, *TPM1*, *MYL2*, *MYL3*, *ACTC1*) **AND**
4. Diagnosis must not be due to a known infiltrative or storage disorder causing cardiac hypertrophy that mimicked obstructive HCM (i.e., Fabry disease, amyloidosis, or Noonan syndrome with left ventricular hypertrophy) **AND**
5. Must have New York Heart Association (NYHA) Class II or III functional status **AND**

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6. Left ventricular ejection fraction (LVEF) must be $\geq 55\%$ **AND**
7. Prescriber attestation must be received that REMS program requirements have been satisfied **AND**
8. Must have had serious side effects or drug failure to at least one non-vasodilating beta blocker (i.e., atenolol, bisoprolol, metoprolol) **AND** one non-dihydropyridine calcium channel blocker (must be separate trials), unless there is a documented medical reason why these agents cannot be used.
 - a. Please note failure of non-vasodilating beta blocker or non-dihydropyridine calcium channel blocker therapy does not preclude concomitant use of these therapies with Camzyos, **AND**
9. Initial and subsequent approvals will be granted for 6 months at a time.
10. Subsequent approvals will require submission of progress notes documenting that the patient has achieved/maintained a positive clinical response to therapy.
 - a. LVEF assessment by echocardiogram must be provided on each recertification request.
11. Camzyos will NOT be approved for continued therapy in patients with LVEF $<50\%$, symptomatic heart failure or worsening clinical status.
12. Camzyos will not be approved for any patients on strong or moderate CYP2C19 inhibitors or inducers, strong CYP3A4 inhibitors, or strong or moderate CYP3A4 inducers.
13. Quantity limit is 30 capsules/30 days.

Crenessity (crinecerfont)-Rx

1. Must be prescribed by or in consultation with an endocrinologist or pediatric endocrinologist **AND**
2. Must be 4 years of age and older **AND**
3. Must have a diagnosis of classic congenital adrenal hyperplasia (CAH) **AND**
 - a. Note: Crenessity will not be authorized in patients with non-classic CAH which typically has a later-onset and presents with milder symptoms or may be asymptomatic
4. Must have 21-hydroxylase deficiency as confirmed by **ONE** of the following (a, b, c, **OR** d):
 - a. Elevated 17-hydroxyprogesterone (17OHP) level
 - b. Confirmed pathogenic variant in the CYP21A2 gene
 - c. Positive newborn screening with confirmatory second-tier testing (e.g., liquid chromatography-tandem mass spectrometry)
 - d. Cosyntropin stimulation that shows a markedly elevated 17OHP level from baseline **AND**
5. Must currently be receiving supraphysiological doses of glucocorticoid treatment at baseline **AND**
6. Crenessity must be used in combination with glucocorticoid treatment **AND**
7. Must have documentation of the following (a **and** b) prior to initiation of Crenessity in order to assess clinical response:
 - a. Baseline glucocorticoid dose **AND**
 - b. Baseline serum androstenedione level
8. Initial approval will be for 6 months. Continued approval will be for 12 months at a time and require documentation of **ONE** of the following (a **or** b):
 - a. A reduction in glucocorticoid dose from baseline **OR**
 - b. A reduction in serum androstenedione from baseline
9. Quantity Limit:
 - a. Capsules: 60 capsules/30 days
 - i. For individuals concomitantly using a strong or moderate CYP3A4 inducers, a quantity limit exception will be authorized in accordance with FDA-approved labeling.
 - b. Oral solution: 30 mL (1 bottle)/30 days
 - i. Documentation that the patient is unable to swallow a capsule whole is required for the following scenarios (**A or B**)
 - A. For individuals weighing ≥ 55 kg **OR**
 - B. For individuals weighing ≥ 20 kg requiring a CYP3A4 dose adjustment
 - ii. Upon each review and dose escalation request for the oral solution the allowed quantity will be reviewed in accordance with FDA-approved labeling (including dose adjustments required

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for strong or moderate CYP3A4 inducers) and as such will be limited to the minimum number of full bottles necessary to obtain the appropriate daily dose.

Cuprimine (penicillamine capsules) and penicillamine tablets (Rx)

1. Must be used for an FDA approved indication: Wilson's Disease, Rheumatoid Arthritis or Cystinuria
2. For a diagnosis of Cystinuria:
 - a. Must be prescribed by a nephrologist, urologist, or physician knowledgeable in the treatment of cystinuria **AND**
 - b. Must have a diagnosis of cystinuria established by one of the following:
 - i. Stone analysis showing 100% cystine calculi **OR**
 - ii. Pathognomonic hexagonal cystine crystals on urine microscopy **OR**
 - iii. Genetic test confirming two defects in SLC7A9 and/or ALC3A1 gene **AND**
 - c. Prescriber must attest that the patient is unresponsive to high fluid intake, urine alkalization, and diet modification (i.e., sodium and protein restriction) **AND**
 - d. Prescriber must attest that the patient will continue high fluid intake, urine alkalization, and diet modification in combination with requested therapy
 - e. Initial authorization for cystinuria will be for 12 months. Recertification will be every 12 months and require evidence of clinical response defined as urinary cystine concentration < 250 mg/L **OR** decrease in cystine stone formation **AND**
3. **For new starts and recertification requests (for all indications):**
 - a. Brand Cuprimine will require documentation of serious side effects or drug failure with generic penicillamine capsules (generic Cuprimine) **AND** penicillamine tablets, unless there is adequate justification as to why both penicillamine capsules **AND** tablets are not clinically appropriate.
 - b. Penicillamine tablets will require documentation of serious side effects or drug failure with generic penicillamine capsules (generic Cuprimine), unless there is adequate justification as to why penicillamine capsules are not clinically appropriate.
4. Quantity limit: 180 capsules/30 days.
 - a. A quantity limit exception of 480 capsules/30 days can be granted for a diagnosis of Cystinuria
 - b. A quantity limit exception of 240 capsules /30 days can be granted for a diagnosis of Wilson's Disease

Daybue and Daybue Stix—trofinetide (Rx)

1. Must be prescribed by a neurologist or prescriber who specializes in the treatment of Rett Syndrome (RTT) **AND**
2. Must be 2 years of age or older **AND**
3. Must weigh \geq 9 kg **AND**
4. Must have a confirmed mutation of the *MECP2* gene **AND**
5. Must have a diagnosis of classic or typical RTT (see appendix) **AND**
6. Initial and recertification requests will be for 3 months at a time. Recertification will require documentation the patient is tolerating therapy, and the drug is providing ongoing benefit to in terms of disease improvement or stability (i.e., symptoms, quality of life measures, and/or functional measures).
7. Recommended dosage is twice daily, morning and evening, according to patient weight. See package insert for dosing.
8. Quantity limit:
 - a. Daybue oral solution: 450 mL (1 bottle) per 28 days.
 - i. Upon each review and dose escalation request, the allowed quantity will be reviewed in accordance with FDA-approved weight-based dosing, and as such, will be limited to the minimum number of bottles to obtain the appropriate daily dose. For pediatric patients, a higher quantity may be allowed based on the patients' predicted growth, on a case-by-case basis.

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- ii. Note: According to the package insert, Daybue oral solution must be discarded after 14 days of first opening the bottle. This will be taken into consideration when evaluating the appropriate quantity allowance.
- b. Daybue Stix: 60 packets for 30 days
 - i. A quantity limit exception will be authorized in accordance with the FDA weight-based dosing for the following:
 - 1. For individuals weighing 35 kg to less than 50 kg
 - A. 5000 mg strength packets: 120 packets/30 days
 - 2. For individuals weighing 50 kg or more
 - A. 6000 mg strength packets: 120 packets/30 days

Empaveli— pegcetacoplan (Rx)

- 2. Empaveli is considered medically necessary for the treatment of **paroxysmal nocturnal hemoglobinuria (PNH)** when the following criteria are met:
 - a. Must be 18 years of age or older **AND**
 - b. Must be prescribed by a hematologist or nephrologist **AND**
 - c. Must have a diagnosis of paroxysmal nocturnal hemoglobinuria (PNH) confirmed by a flow cytometry test
 - d. The recommended dose of Empaveli is 1,080 mg by subcutaneous infusion twice weekly via a commercially available infusion pump. For lactate dehydrogenase (LDH) levels greater than 2 × the upper limit of normal (ULN), adjust the dosing regimen to 1,080 mg every three days.
 - i. For patients switching from Soliris/Bkemv/Epysqli (eculizumab), initiate Empaveli while continuing Soliris/Bkemv/Epysqli (eculizumab) at its current dose. After 4 weeks, discontinue Soliris/Bkemv/ Epysqli (eculizumab) before continuing monotherapy with Empaveli.
 - ii. For patients switching from Ultomiris (ravulizumab), initiate Empaveli no more than 4 weeks after the last dose of Ultomiris (ravulizumab)
 - e. Initial approval for 6 months. Continued approval will be for 6 months and will require documentation that patient is tolerating therapy and is responding to treatment (i.e., decrease in number of transfusions, improvement in hemoglobin levels, normalization of LDH levels, symptom improvement)
- 3. Empaveli is considered medically necessary for the treatment of **complement 3 glomerulopathy (C3G) or immune-complex membranoproliferative glomerulonephritis (IC-MPGN)** when the following criteria are met:
 - a. Must be 12 years of age or older **AND**
 - b. Must be prescribed by or in consultation with a nephrologist **AND**
 - c. Must have a diagnosis of complement 3 glomerulopathy (C3G) or immune-complex membranoproliferative glomerulonephritis (IC-MPGN) confirmed on renal biopsy **AND**
 - d. Must be on a maximally recommended or tolerated dose of an angiotensin converting enzyme inhibitor (ACEI) or angiotensin receptor blocker (ARB) for at least 3 months prior to starting Empaveli, unless there is documentation that the patient is unable to tolerate or has a contraindication to an ACEi or ARB **AND**
 - e. Must meet one of the following:
 - i. Must have documentation of drug failure (i.e., worsening kidney function and/or inadequate reduction in proteinuria) with systemic oral glucocorticoids (e.g., prednisone, methylprednisolone), unless there is documentation of serious side effects or contraindications to systemic oral glucocorticoids **OR**
 - ii. Must have documentation of drug failure (i.e., worsening kidney function and/or inadequate reduction in proteinuria) trial with mycophenolate mofetil/mycophenolate sodium unless there is documentation of serious side effects or contraindications to mycophenolate mofetil/mycophenolate sodium **AND**
 - f. Must have baseline documentation of a urine protein: creatinine ratio (UPCR) ≥ 1.0 g/g **AND**

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- g. Must an estimated GFR ≥ 30 ml/min/1.73m²
- h. Initial approval will be for 6 month and recertification will be for 12 months at a time. Recertification will require documentation of the following:
 - i. Reduction in UPCR from baseline **AND**
 - ii. Must have an eGFR of ≥ 30 ml/min/1.73m²
3. Concomitant use of another complement inhibitor (i.e., Soliris/Bkemv/Epysqli (eculizumab), Ultomiris (ravulizumab), or Fabhalta (iptacopan)) will only be authorized for patients transitioning from either Soliris/Bkemv/Epysqli (eculizumab), Ultomiris (ravulizumab), or Fabhalta (iptacopan) to Empaveli. After the initial approval period, requests for concomitant use of Empaveli with Soliris/Bkemv/Epysqli (eculizumab), Ultomiris (ravulizumab), or Fabhalta (iptacopan) will be considered experimental/investigational and will not be approved.
4. Empaveli must be self-administered and therefore will be covered under the **pharmacy benefit**.
5. Quantity limit: 8 vials per 30 days. A quantity limit exception of 10 vials per 30 days may be granted for individuals requiring 1,080 mg dosed every three days.

Enjaymo— sutimlimab-jome (Medical)

1. Must be 18 years of age and older **AND**
2. Must be prescribed by a hematologist/oncologist or prescriber who specializes in the treatment of cold agglutinin disease (CAD) **AND**
3. Must be ≥ 39 kg **AND**
4. Must have a diagnosis of cold agglutinin disease confirmed by **all** the following:
 - a. Prescriber attestation that the patient has chronic hemolysis (i.e., not a result of a transient cause such as infection)
 - b. Polyspecific direct antiglobulin test (DAT) positive
 - c. Monospecific DAT positive for C3d
 - d. Cold agglutinin titer of 1:64 or higher measured at 4°C
 - e. Immunoglobulin G (IgG) DAT $\leq 1+$
 - f. Must not have overt malignant disease **AND**
5. Must have had serious side effects or drug failure with a rituximab-containing product (either as monotherapy or in combination with other agents). Use of a rituximab-containing product would not be required if the prescriber attests the patient has severe hemolysis or symptoms that require therapy with a more immediate response.
 - a. This applies to all lines of business including Medicare Part B
 - b. This applies to New Starts only **AND**
6. Must have hemoglobin level ≤ 10 g/dL. Note: consideration may be given to patients who are symptomatic with hemoglobin > 10 g/dL. **AND**
7. Must have bilirubin level above the normal reference range. Note: consideration may be given to patients with normal bilirubin level if the prescriber attests the patient is hemolyzing. **AND**
8. Must have one or more symptom(s) associated with CAD within the previous 3 months (i.e., symptomatic anemia, acrocyanosis, Raynaud's phenomenon, hemoglobinuria, disabling circulatory symptoms, or a major adverse vascular event). **AND**
9. Prescriber attests that they have counseled the patient on the importance of cold avoidance.
10. Enjaymo will not be approved for cold agglutinin syndrome secondary to infection, rheumatologic disease, or active hematologic malignancy.
11. Enjaymo will not be approved in combination with rituximab-containing products or rituximab combination therapies (i.e., with bendamustine, fludarabine, ibrutinib, or cytotoxic drugs) as Enjaymo has not been studied in combination with these therapies.
12. The recommended dose of Enjaymo in patients with CAD is based on body weight. For patients weighing 39 kg to less than 75 kg, the recommended dose is 6,500 mg and for patients weighing 75 kg or more, the recommended dose is 7,500 mg. Enjaymo is administered intravenously weekly for

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the first two weeks, with administration every two weeks thereafter. See prescribing information for full details.

- a. Note: In accordance with prescribing information, patients should be vaccinated against encapsulated bacteria at least 2 weeks prior to initiation of Enjaymo therapy according to the most current Advisory Committee on Immunization Practices (ACIP) recommendations for patients with persistent complement deficiencies. If urgent Enjaymo therapy is indicated in an unvaccinated patient, administer vaccine(s) as soon as possible.

13. Initial approval will be for 6 months. Recertification will be every 6 months and require documentation that includes the following:

- a. Normalization of hemoglobin level to ≥ 12 g/dL **OR**
- b. Increase in hemoglobin level of ≥ 2 g/dL. Note: consideration may be given on recertification if a patient has clinically benefited from therapy (i.e., transfusion avoidance, symptom benefit) despite a hemoglobin level rise of < 2 g/dL. **AND**
- c. RBC transfusion avoidance (no transfusion required) after the first 5 weeks of treatment.

HCPCS: J1302

Enspryng – satralizumab-mwge injection (Rx or Medical)

1. Must have a diagnosis of Neuromyelitis Optica Spectrum Disorder (NMOSD) confirmed by a positive anti-aquaporin-4 (AQP4) antibody test
2. Must be at least 18 years of age
3. Must be prescribed by an ophthalmologist or neurologist
4. Must have had at least 1 neuromyelitis optica relapse that required rescue therapy (such as corticosteroids or plasma exchange) in the last 12 months
5. Enspryng will be covered under the pharmacy benefit for self-injection unless there is documentation of an inability to self-inject and lack of a caregiver available to inject. With documentation of an inability to self-inject and lack of an available caregiver to inject, coverage under the medical benefit will be considered with the same clinical criteria above.
6. Quantity Limit of 1 syringe (1 mL) per 28 days
 - a. Coverage of an initial loading dose of 3 syringes (3 mL) per 28 days will be authorized for the first 4 weeks of treatment
 - b. Please see the package insert for recommendations regarding delayed or missed doses.

Evkeeza-evinacumab-dgnb (Medical)

1. Must be prescribed by or in consultation with a cardiologist, lipid specialist, or endocrinologist **AND**
2. Must be ≥ 1 year of age or older with a diagnosis of homozygous familial hypercholesterolemia (HoFH) **AND**
 - a. Genetic testing must demonstrate evidence of two mutant alleles at the low-density lipoprotein receptor (*LDLR*), apolipoprotein B (*APOB*), proprotein convertase subtilisin kexin type 9 (*PCSK9*) or low-density lipoprotein receptor adaptor protein 1 (*LDLRAP1*) gene **OR**
 - b. Patient has a history of untreated LDL-C > 400 mg/dL or treated LDL-C ≥ 300 mg/dL with either (i or ii)
 - i. Xanthoma before the age of 10 years **OR**
 - ii. Evidence of heterozygous FH in one parent **AND**
3. One of the following must be met (a or b):
 - a. **For individuals 10 years of age and older**, member must have failed to reach target LDL-C while receiving treatment with maximally tolerated high potency statin (goal is atorvastatin 40-80 mg daily or rosuvastatin 20-40 mg daily), in combination with ezetimibe, and a PCSK9 inhibitor (Repatha, Praluent) for at least 8 weeks. A trial with a PCSK9 inhibitor is not required if the member is known to have two LDL-receptor negative alleles (null homozygous). **OR**
 - b. **For individuals 1 to 9 years of age**, member must have failed to reach target LDL-C while

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- receiving treatment with at least one lipid lowering therapy (e.g., statins, ezetimibe, lipoprotein apheresis) for at least 8 weeks. **AND**
4. LDL-C must be ≥ 70 mg/dL for patients with clinical atherosclerotic cardiovascular disease (ASCVD) **OR** LDL-C must be ≥ 100 mg/dL for patients without documented clinical ASCVD
 - i. Clinical ASCVD defined as having a history of acute coronary syndrome, myocardial infarction (MI), stable or unstable angina, coronary/other arterial revascularization, stroke, TIA, peripheral arterial disease, or other documented atherosclerotic disease (such as coronary atherosclerosis, renal atherosclerosis, aortic aneurysm secondary to atherosclerosis, or Carotid plaque with $\geq 50\%$ stenosis) **AND**
 5. Evkeeza will not be approved in combination with Juxtapid unless the patient has demonstrated failure to achieve target LDL-C while on Juxtapid in combination with:
 - i. a high-intensity or maximally tolerated statin therapy **AND**
 - ii. ezetimibe **AND**
 - iii. a PCSK9 inhibitor (i.e., Praluent, Repatha) **AND**
 - iv. The patient has been on this drug combination for at least 8 weeks **AND**
 6. **If patient is unable to tolerate statin therapy**, documentation in progress notes must include:
 - i. A contraindication to statin therapy according to FDA labeling **OR**
 - ii. History of statin-related rhabdomyolysis
 1. Must have symptoms consistent with rhabdomyolysis (i.e., muscle pain, swelling, and weakness, dark urine) **AND**
 2. Must have creatine kinase (CK) level > 10 times upper limit of normal, myoglobinuria, or acute renal failure (increase in serum creatinine > 0.5 mg/dL) **AND**
 3. Patient was receiving a statin at the time of the event and symptoms resolved upon discontinuation of the statin **OR**
 - iii. History of statin intolerance. Documentation must include the following:
 1. Inability to tolerate at least 2 different statins
 - a. At least 1 statin must be hydrophilic (such as pravastatin, fluvastatin, or rosuvastatin) starting at the lowest starting average daily dose **AND**
 - b. Intolerance associated with confirmed, intolerable statin-related adverse effects (i.e., muscle related symptoms) or significant biomarker abnormalities (i.e., ALT/AST > 3 times the upper limit of normal accompanied by increase in total bilirubin > 2 times the upper limit of normal) **AND**
 - c. Non-statin causes of muscle symptoms or biomarker abnormalities have been ruled out (for example, hypothyroidism, reduced renal function, reduced hepatic function, rheumatologic disorders such as polymyalgia rheumatic, steroid myopathy, vitamin D deficiency, or primary muscle disease)
 7. Documentation of baseline LDL-C level must be provided-measurement must occur within 60 days prior to treatment **AND**
 8. Prescriber must attest that a discussion with the patient has taken place regarding a heart healthy diet, the importance of exercise, and smoking cessation (if applicable)
 9. The recommended dosage is 15 mg/kg administered by intravenous (IV) infusion every 4 weeks
 10. Evkeeza will not be approved for other causes of hypercholesterolemia, including those with heterozygous familial hypercholesterolemia (HeFH)
 11. Evkeeza will be covered under the medical benefit
 12. Initial approval will be for 6 months, further approval will require evidence of an adequate reduction in LDL-C level defined as reduction in LDL-C level as compared to baseline LDL-C. Recertification will be yearly after that.

HCPCS: J1305

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Fabhalta (iptacopan capsule)-Rx

1. Fabhalta is considered medically necessary for the **treatment of paroxysmal nocturnal hemoglobinuria (PNH)** when the following criteria are met:
 - a. Must be 18 years of age or older **AND**
 - b. Must be prescribed by a hematologist or nephrologist **AND**
 - c. Must have a diagnosis of paroxysmal nocturnal hemoglobinuria (PNH) confirmed by a flow cytometry test
 - d. Initial approval for 6 months. Continued approval will be for 6 months and will require documentation that patient is tolerating therapy and is responding to treatment (i.e., decrease in number of transfusions, improvement in hemoglobin levels, normalization of LDH levels, symptom improvement) **OR**
2. Fabhalta is considered medically necessary for the treatment of **primary immunoglobulin A nephropathy (IgAN)** when the following criteria are met:
 - a. Must be 18 years of age or older **AND**
 - b. Must be prescribed, or in consultation with, a nephrologist **AND**
 - c. Must have a diagnosis of primary immunoglobulin A nephropathy (IgAN), confirmed on biopsy **AND**
 - d. Must have an eGFR ≥ 30 mL/min/1.73 m² **AND**
 - e. Must provide baseline documentation that meets at least one of the following (note: documentation of the same laboratory parameter will be required upon recertification):
 - i. A total urine protein ≥ 1.0 g/day **OR**
 - ii. A urine protein-to-creatinine ratio (UPCR) ≥ 1.5 g/g **AND**
 - f. Must have received the maximum or maximally tolerated dose of an angiotensin-converting enzyme inhibitor (ACEi) or an angiotensin II receptor blocker (ARB) for a minimum of 3 months prior to starting Fabhalta, unless there is documentation that the patient is unable to tolerate or has a contraindication to an ACEi or ARB **AND**
 - g. Must meet one of the following:
 - i. Must have documentation of drug failure after a minimum 3-month trial with an SGLT2 inhibitor, unless the patient has documentation of serious side effects or contraindication to an SGLT2 inhibitor **OR**
 - ii. Must have documentation of drug failure after a minimum 6-week trial of systemic oral glucocorticoids (i.e., prednisone, methylprednisolone), unless the patient has documentation of serious side effects or contraindication to systemic oral glucocorticoids
 - h. Initial and recertification approvals will be for 9 months at a time. Continuation of therapy will require the following (documentation must be provided):
 - i. Evidence of one of the following:
 1. Reduction in total urine protein from baseline **OR**
 2. Reduction in UPCR from baseline **AND**
 - ii. Must have an eGFR ≥ 30 mL/min/1.73 m²
 - i. This indication is approved under accelerated approval based on reduction of proteinuria. It has not been established whether Fabhalta slows kidney function decline in patients with IgAN. Continued approval for this indication may be contingent upon verification and description of clinical benefit in a confirmatory clinical trial. **OR**
3. Fabhalta is considered medically necessary for the treatment of **complement 3 glomerulopathy (C3G)** when the following criteria are met:
 - a. Must be 18 years of age or older **AND**
 - b. Must be prescribed by or in consultation with a nephrologist **AND**
 - c. Must have a diagnosis of complement 3 glomerulopathy (C3G) confirmed on renal biopsy **AND**
 - d. Must be on a maximally recommended or tolerated dose of an angiotensin converting enzyme inhibitor (ACEI) or angiotensin receptor blocker (ARB) for at least 3 months prior to starting

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- Fabhalta, unless there is documentation that the patient is unable to tolerate or has a contraindication to an ACEi or ARB **AND**
- e. Must meet one of the following (1 or 2):
 - i. Must have documentation of drug failure (e.g., worsening kidney function and/or inadequate reduction in proteinuria) with systemic oral glucocorticoids (e.g., prednisone, methylprednisolone), unless there is documentation of serious side effects or contraindications to systemic oral glucocorticoids **OR**
 - ii. Must have documentation of drug failure (e.g., worsening kidney function and/or inadequate reduction in proteinuria) with mycophenolate mofetil/mycophenolate sodium unless there is documentation of serious side effects or contraindications to mycophenolate mofetil/mycophenolate sodium **AND**
 - f. Must have baseline documentation of a urine protein: creatinine ratio (UPCR) ≥ 1.0 g/g **AND**
 - g. Must an estimated GFR ≥ 30 ml/min/1.73m²
 - h. Initial approval will be for 6 month and recertification will be for 12 months at a time.
 - i. Recertification will require documentation of the following:
 1. Reduction in UPCR from baseline **AND**
 2. Must have an eGFR of ≥ 30 ml/min/1.73m²
4. Requests for non-FDA approved indications will not be covered.
 5. Fabhalta will not be approved in combination with Tarpeyo, Voyxact, Filspari, or Vanrafia.
 6. Concomitant use of another complement inhibitor (i.e., Soliris/Bkemv/Epysqli (eculizumab), Ultomiris (ravulizumab), Empaveli (pegcetacoplan)) will only be authorized for patients transitioning from Soliris/Bkemv/Epysqli (eculizumab), Ultomiris (ravulizumab), Empaveli (pegcetacoplan) to Fabhalta. After the initial approval period, requests for concomitant use of Fabhalta with Soliris/Bkemv/Epysqli (eculizumab), Ultomiris (ravulizumab), or Empaveli (pegcetacoplan) will be considered experimental/investigational and will not be approved.
 7. Quantity limit: 60 capsules/30 days

Filspari-sparsentan (Rx)

1. Filspari is considered medically necessary for the treatment of **primary immunoglobulin A nephropathy (IgAN)** when the following criteria are met:
 - a. Must be prescribed by, or in consultation with, a nephrologist **AND**
 - b. Must be 18 years of age or older **AND**
 - c. Must have a diagnosis of primary immunoglobulin A nephropathy (IgAN), confirmed on biopsy **AND**
 - d. Must have an eGFR ≥ 30 mL/min/1.73 m² **AND**
 - e. Must provide baseline documentation that meets at least one of the following (note: documentation of the same laboratory parameter will be required upon recertification):
 - i. A total urine protein ≥ 1.0 g/day **OR**
 - ii. A urine protein-to-creatinine ratio (UPCR) ≥ 1.5 g/g **AND**
 - f. Must have received the maximum or maximally tolerated dose of an angiotensin-converting enzyme inhibitor (ACEi) or an angiotensin II receptor blocker (ARB) for a minimum of 3 months prior to starting Filspari, unless there is documentation that the patient is unable to tolerate or has a contraindication to an ACEi or ARB **AND**
 - g. Prescriber must attest, or documentation must demonstrate, that Filspari will not be used in combination with any of the following: Renin- angiotensin-aldosterone system (RAAS) inhibitors, endothelin receptor antagonists (ERAs) or aliskiren. **AND**
 - h. Must meet one of the following:
 - i. Must have documentation of drug failure after a minimum 3-month trial with an SGLT2 inhibitor, unless the patient has documentation of serious side effects or contraindication to an SGLT2 inhibitor **OR**

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- ii. Must have documentation of drug failure after a minimum 6-week trial of systemic oral glucocorticoids (i.e., prednisone, methylprednisolone), unless the patient has documentation of serious side effects or contraindication to systemic oral glucocorticoids
 - i. Initial and recertification approvals will be for 9 months at a time. Continuation of therapy will require the following (documentation must be provided):
 - i. Evidence of **one** of the following:
 1. Reduction in total urine protein from baseline **OR**
 2. Reduction in UPCR from baseline **AND**
 - ii. Must have an eGFR ≥ 30 mL/min/1.73 m² **OR**
2. Filspari is considered medically necessary for the treatment of **focal segmental glomerulosclerosis (FSGS)** when the following criteria are met:
 - a. Must be prescribed by, or in consultation with, a nephrologist **AND**
 - b. Must be 8 years of age and older **AND**
 - c. Must have a documented diagnosis of focal segmental glomerulosclerosis (FSGS) confirmed either by biopsy or genetic mutation in podocyte protein associated with FSGS (see Appendix) for genetic mutations **AND**
 - d. Must have eGFR ≥ 30 mL /min/1.73 m² **AND**
 - e. Must have documented baseline urine protein to creatinine ratio (UPRC) of ≥ 1.5 g/g **AND**
 - f. Prescriber must attest, or documentation must demonstrate, that Filspari will not be used in combination with any of the following: Renin- angiotensin-aldosterone system (RAAS) inhibitors, endothelin receptor antagonists (ERAs) or aliskiren.
 - g. Filspari will **not** be authorized if the patient has nephrotic syndrome, where nephrotic syndrome is defined as the presence of all the following (i, ii, and iii):
 - i. Proteinuria > 3.5 g/24 hour (adults) or UPCR > 2.0 g/g (pediatric patients < 18 years of age)
 - ii. Serum albumin of < 3.0 g/L
 - iii. Edema
 - h. Initial and recertification will be for 9 months at a time. Recertification will require improvement in UPCR from baseline.
3. Requests for non-FDA approved indications will not be covered.
4. Filspari will not be approved in combination with Tarpeyo, Voyxact, Fabhalta, or Vanrafia
5. Quantity Limit: 30 tablets/30 days
 - a. A quantity limit exception of 60 tablets/30 days for the 400 mg strength tablet may be granted for a diagnosis of FSGS in patients weighing 50 kg or greater.

Filsuvez (birch triterpenes)-Rx

1. Must be prescribed by, or in consultation, with a dermatologist or pediatric dermatologist, or clinical expert in epidermolysis bullosa (EB) **AND**
2. Must be 6 months of age or older **AND**
3. Must have a diagnosis of dystrophic epidermolysis bullosa (DEB) or junctional epidermolysis bullosa (JEB), confirmed on genetic testing (e.g., mutations in *COL7A1* or *PLOD3* for DEB and *LAMA3*, *LAMB3*, *LAMC2*, *COL17A1*, *ITGA6*, *ITGB4*, or *ITGA3* for JEB) **AND**
4. Must have documentation within the previous month indicating which cutaneous wound(s) will be treated with Filsuvez **AND**
5. Prescriber must attest the following (**a and b**):
 - a. The wound(s) being treated is (are) 10 cm² to 50 cm² **AND**
 - b. The wound(s) being treated is (are) aged ≥ 21 days to < 9 months **AND**
6. Filsuvez will not be authorized in combination with Vyjuvek or Zevaskyn for the treatment of the same wound(s).

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7. Filzuvez will not be authorized for concomitant use with Vyjuvek or Zevaksyn for the treatment of different wounds located on different areas of the body, unless there is adequate documentation justifying the need for separate products on different wounds located on different areas of the body.
8. Use of Filsuvez on a wound(s) previously treated with Vyjuvek or Zevaskyn requires adequate documentation demonstrating inadequate response or treatment failure to previous treatment(s).
9. Initial and recertification approval will be for 3 months at a time. Recertification will require documentation of clinical improvement of the treated wound (s) **AND**
 - a. The treated wound(s) has not completed closed or has re-opened **OR**
 - b. New, previously untreated wound(s) require treatment.
10. Quantity Limit: 15 tubes/30 days
 - a. Requests for higher quantities will require the prescriber provide an estimate of how frequently the patient will require wound dressing changes (e.g., daily, every other day) **AND** number of wounds being treated.

Firdapse-amifampridine (Rx)

1. Must be prescribed by a neurologist or neuromuscular specialist
2. Must be 6 years of age or older
3. Must have a diagnosis of Lambert-Eaton Myasthenic Syndrome (LEMS) confirmed by electromyography **OR** calcium channel antibody testing
4. Quantity limit 300 tablets per 30 days

Galzin-zinc acetate capsule (Rx)

1. Must be 10 years of age or older **AND**
2. Must have a diagnosis of Wilson's Disease **AND**
3. Must have been previously treated with a chelating agent (e.g., penicillamine or trientine)
4. Quantity Limit: 90 capsules/30 days

Gamifant-emapalumab-lzsg (Medical)

1. Gamifant is considered medically necessary for the treatment of **primary hemophagocytic lymphohistiocytosis (HLH) with refractory, recurrent or progressive disease or intolerance with conventional HLH therapy** when the following criteria are met:
 - a. Prescribed by a physician who specializes in the treatment of HLH (such as a hematologist, oncologist, immunologist, or transplant specialist) **AND**
 - b. The patient has a diagnosis of Primary HLH confirmed by at least ONE of the following (either i., ii. or iii)
 - i. Genetic testing confirming biallelic pathogenic variants (e.g., PRF1, UNC13D/MUNC13-4, STX11 or STXBP2) **OR**
 - ii. Positive family history (affected siblings or parental consanguinity) consistent with primary HLH in a symptomatic individual **OR**
 - iii. Meet at least FIVE out of the following diagnostic criteria prior to treatment:
 - Low or absent NK-cell activity (according to local laboratory reference)
 - Fever $\geq 38.5^{\circ}\text{C}$ (or 101.3°F)
 - Splenomegaly
 - Elevated ferritin ≥ 500 micrograms/L
 - Elevated CD25 (i.e., soluble IL-2 receptor) $\geq 2,400$ U/mL
 - Hypertriglyceridemia (fasting triglycerides ≥ 265 mg/dL (3 mmol/L) and/or hypofibrinogenemia (fibrinogen $\leq 1.5\text{g/L}$)
 - Hemophagocytosis in bone marrow or spleen or lymph nodes
 - Cytopenias affecting at least 2 of 3 lineages in the peripheral blood:
 - Hemoglobin < 9 g/dL (or $< 10\text{g/dL}$ in infants < 4 weeks of age)

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- Platelets < 100 x 10⁹/L
 - Neutrophils < 1 x 10⁹/L, **AND**
 - c. Evidence of active disease that is refractory, recurrent, or progressive despite at least **ONE** conventional HLH therapy **OR** severe intolerance to at least **ONE** conventional therapy. Examples of conventional HLH treatments include etoposide and dexamethasone, cyclosporine A, anti-thymocyte globulin and intrathecal methotrexate following a standard of care treatment protocol **AND**
 - d. Administer dexamethasone concomitantly with Gamifant, **AND**
 - e. Administer Gamifant until hematopoietic stem cell transplantation (HSCT) is performed or unacceptable toxicity. Discontinue Gamifant when patient no longer requires therapy for the treatment of HLH.
 - f. Gamifant is dosed based on body weight. Therefore, current body weight and requested dose regimen must be submitted for initial review and each recertification request **AND**
 - g. Initial approval for primary HLH will be for 2-month duration. Continuation of therapy at 2-month intervals will require the following documentation of therapeutic benefit:
 - i. Complete response defined as normalization of all HLH abnormalities (i.e., no fever, no splenomegaly, neutrophils > 1x10⁹/L, platelets > 100x10⁹/L, ferritin < 2,000 ug/L, fibrinogen > 1.50 g/L, D-dimer < 500 ug/L, normal CNS symptoms, no worsening of sCD25 > 2-fold baseline); **OR**
 - ii. Partial response defined as normalization of ≥ 3 HLH abnormalities, **OR**
 - iii. HLH improvement defined as ≥ 3 HLH abnormalities improved by at least 50% from baseline **OR**
2. Gamifant is considered medically necessary for the treatment of **HLH/macrophage activation syndrome (MAS) in known or suspected Still's disease, including systemic Juvenile Idiopathic Arthritis (sJIA), with an inadequate response or intolerance to glucocorticoids, or with recurrent MAS** when the following criteria are met:
- a. Prescribed by a physician who specializes in the treatment of HLH (such as a hematologist, oncologist, immunologist, or transplant specialist) or physician who specializes in sJIA/Still's disease (such as a rheumatologist) **AND**
 - b. The patient has a diagnosis of HLH/macrophage activation syndrome (MAS) in known or suspected Still's disease, including systemic Juvenile Idiopathic Arthritis (sJIA) **AND**
 - c. Must have a diagnosis of active MAS defined as having met both of the following (i and ii):
 - i. Ferritin >684 ng/mL **AND**
 - ii. Must have at least TWO of the following:
 - 1. Platelet count ≤181×10⁹/L
 - 2. AST >48 U/L
 - 3. Triglycerides >156 mg/dL
 - 4. Fibrinogen levels ≤360 mg/dL **AND**
 - d. Must have ONE of the following (i or ii):
 - i. Inadequate response, intolerance, or contraindication to high-dose intravenous glucocorticoids **OR**
 - ii. Recurrent MAS (defined as two or more episodes of MAS) **AND**
 - e. Gamifant is dosed based on body weight. Therefore, current body weight and requested dose regimen must be submitted for initial review and each recertification request
 - f. For HLH/macrophage activation syndrome (MAS) in the setting of Still's disease (including sJIA), initial approval will be for a 2-month duration. Continuation of therapy will be at 2-month intervals and will require documentation of (i and ii):
 - i. Improvement in MAS signs/symptoms (i.e., fever, skin rash, hemorrhagic manifestations, CNS symptoms, respiratory function,) **AND**
 - ii. At least ONE of the following objective responses:

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1. White blood cell above lower limit of normal (LLN)
 2. Platelet count above LLN
 3. Lactate dehydrogenase (LDH) below 1.5×the upper limit of normal (ULN)
 4. ALT below 1.5× ULN
 5. AST below 1.5×ULN
 6. Fibrinogen >100 mg/dL,
 7. Ferritin levels decreased ≥80% from baseline or <2000 ng/mL
3. Prior authorization for Gamifant will apply regardless of the site of administration (applies to both the inpatient and outpatient setting). Gamifant must be administered by a healthcare professional and is covered under the medical benefit

Recommended Dosing:

- Primary HLH recommended starting dosage: 1 mg/kg as an intravenous infusion over 1 hour twice per week.
- HLH/MAS in Still's disease recommended starting dose: 6 mg/kg, followed by 3 mg/kg every 3 days for 5 doses, then 3 mg/kg twice per week. Given as an intravenous infusion over 1 hour.
- For both indications, the dose may be titrated up to a maximum of 10 mg/kg.

HCPCS: J9210

Hyftor 0.2% gel - sirolimus topical gel (Rx)

1. Must be prescribed by a dermatologist, neurologist, or prescriber who is knowledgeable in the treatment of tuberous sclerosis **AND**
2. The patient must be at least 6 years of age **AND**
3. Must be used for the treatment of facial angiofibroma associated with tuberous sclerosis **AND**
4. The patient must have 3 or more papules of angiofibroma (≥2 mm in diameter with redness in each) on the face at baseline
5. Initial approval will be for 3 months.
 - a. Initial Recertification will require documentation of improvement in size or redness of facial angiofibroma(s). Initial recertification will be approved for 6 months
 - b. Recertifications thereafter will require documentation that the patient has maintained a response to treatment of existing/currently treated papule(s) and will be approved for 6 months
6. Quantity Limit of 20 grams (2-tubes)/24 days

Ilaris - canakinumab (Medical)

1. Must meet the following prescriber requirement based on indication:
 - a. For treatment of active systemic juvenile idiopathic arthritis (SJIA) or Adult-Onset Still's Disease (AOSD), must be prescribed by a rheumatologist or immunologist
 - b. For treatment of Cryopyrin-Associated Periodic Syndromes (CAPS) or Periodic Fever Syndrome (PFS), must be prescribed by a geneticist, dermatologist, or prescriber who specializes in management of CAPS/PFS.
 - c. For treatment of acute gout flare, must be prescribed by a rheumatologist. **AND**
2. Must be at least 4 years of age and have a diagnosis of Cryopyrin-Associated Periodic Syndromes (CAPS) with one of the following conditions
 - a. Familial Cold Autoinflammatory Syndrome (FCAS) also known as Familial Cold Urticaria **OR**
 - b. Muckle-Wells Syndrome (MWS)
 - c. Dose is not to exceed 150mg every 8 weeks **OR**
3. Must be at least 2 years of age with a diagnosis of active systemic juvenile idiopathic arthritis (SJIA)
 - a. Must have failed to respond to and/or is intolerant to approved disease- modifying antirheumatic drugs (DMARDs) agents, such as methotrexate, NSAIDs, analgesics or corticosteroids either alone or in combination **AND**
 - b. For New Starts only, must have failed to respond to and/or is intolerant to the following:

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- i. For all non-Medicare Advantage lines of business: Enbrel or Humira/Simlandi/Hadlima
 - ii. For Medicare Advantage: Enbrel or Simlandi/Hadlima
- c. Dose is not to exceed 300mg every 4 weeks **OR**
4. Must be at least 18 years of age with a diagnosis of Adult-Onset Still's Disease (AOSD)
 - a. Must have failed to respond to and/or is intolerant to approved disease- modifying antirheumatic drugs (DMARDs) agents, such as methotrexate, NSAIDs, analgesics or corticosteroids either alone or in combination **AND**
 - b. Must have failed to respond to and/or is intolerant to a TNF inhibitor (i.e., infliximab, etanercept or adalimumab), or there is a medical reason why the patient cannot use a TNF inhibitor.
 - i. This applies to all lines of business including Medicare Advantage
 - ii. This applies to New Starts only
 - c. Dose is not to exceed 300mg every 4 weeks **OR**
5. Must be at least 2 years of age with a diagnosis of one of the following Periodic Fever Syndromes (Hereditary Periodic Fevers)
 - a. Tumor Necrosis Factor-Receptor Associated Periodic Syndrome (TRAPS)
 - b. Hyperimmunoglobulin D Syndrome (HIDS)/Mevalonate Kinase Deficiency (MKD)
 - c. Familial Mediterranean Fever (FMF)
 - d. Dose is not to exceed 300mg every 4 weeks.
6. Must be at least 18 years of age or older and used for treatment of an acute gout flare **AND**
 - a. Must be prescribed by a rheumatologist **AND**
 - b. Must have documentation that management of lifestyle factors have been implemented as appropriate (e.g., limiting alcohol intake, dietary modifications, weight loss) **AND**
 - c. Must have documentation of serious side effects or drug failure to the maximally tolerated dose, or contraindication, to all the following:
 - i. NSAIDs **AND**
 - ii. Colchicine **AND**
 - iii. Corticosteroids (oral and injectable) **AND**
 - d. The patient must currently be taking, or prescriber must attest that the patient will initiate a urate lowering medication for the prevention of recurrent gout (e.g., allopurinol, probenecid, febuxostat).
 - e. Approval will be for 3 months to allow for treatment of one acute gout flare (150 mg subcutaneously).
 - f. Treatment for subsequent acute gout flares will not be authorized unless the following are met:
 - i. Patient is optimized on urate lowering therapy for prevention (e.g., allopurinol, probenecid, febuxostat) **AND**
 - ii. There has been an interval of at least 12 weeks before a new dose of Ilaris will be administered
 - iii. For subsequent flare; approval will be for 3 months to allow for treatment of one acute gout flare (150 mg subcutaneously).
7. Patient does not have an infection and is not at high risk for infection
8. Patient is not on concurrent therapy with any of the following – Arcalyst, Kineret, Enbrel, Humira, infliximab or Simponi

Note – it is not known whether Ilaris is effective in patients with Neonatal-Onset Multisystem Inflammatory Disease (NOMID), also referred to as Chronic Infantile Neurologic Cutaneous Articular Syndrome (CINCA).

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Imaavy (nipocalimab)-Medical

1. Must be 12 years of age or older **AND**
2. Must be prescribed by or in consultation with a neurologist. If geographically available, it is also recommended for patients to have been evaluated by a neuromuscular specialist **AND**
3. Must have a diagnosis of generalized myasthenia gravis (gMG) **AND**
4. Must have Myasthenia Gravis Foundation of America (MGFA) clinical classification class II to IV **AND**
5. Must be antibody positive for either (a or b):
 - a. Anti-acetylcholine receptor (AChR) **OR**
 - b. Muscle-specific kinase (MuSK) **AND**
6. Must documentation of a baseline Myasthenia Gravis Activities of Daily Living (MG-ADL) score of at least 6 **AND**
7. Must meet one of the following (a or b):
 - a. Must have had serious side effects or drug failure to ONE of the following treatments for gMG (1 or 2).
 1. Corticosteroids for at least 3 months of treatment **OR**
 2. Non-steroidal immunosuppressive therapy (i.e., azathioprine, mycophenolate mofetil, cyclosporine) for at least 6 months of treatment **OR**
 - b. Despite treatment with at least ONE immunosuppressant agent (i.e., corticosteroid, non-steroidal immunosuppressive therapy), the member required at least ONE treatment with plasma exchange, plasmapheresis, or intravenous immunoglobulin within the previous 12 months **AND**
8. For individuals 18 years of age and older with AChR antibody positive gMG, must have serious side effects or drug failure to Vyvgart Hytrulo prefilled syringe (PFS). This applies to New Starts only for all lines of business.
9. Imaavy will not be approved in combination with Uplizna, Soliris/Bkemv/Epysqli, Ultomiris, Vyvgart, Vyvgart Hytrulo, Rystiggo, Zilbrysq, intravenous immunoglobulin (other than when used as rescue therapy), or rituximab-containing products as Imaavy has not been studied in combination with these therapies.
10. The recommended initial dosage of Imaavy is 30 mg/kg administered once via intravenous infusion over at least 30 minutes. Two weeks after the initial dosage administer a maintenance dosage of 15 mg/kg via intravenous infusion over at least 15 minutes. Continue the maintenance dosage every two weeks thereafter.
11. Initial approval will be for 6 months. Continued approval will require documentation of ≥ 2 -point improvement in the MG-ADL scale from baseline **OR** provider attests that patient is experiencing clinical benefit from treatment (i.e., reduction of myasthenia gravis exacerbations, improvement in symptoms such as swallowing, mobility, breathing). Recertification will be required every 12 months.

HCPCS: J9256

Imcivree—setmelanotide (Rx)

Based upon our review and assessment of peer-reviewed literature, Imcivree, has been medically proven to be effective and therefore **medically necessary** in the treatment of:

- A. **Acquired hypothalamic obesity (HO)** if **ALL** the following criteria are met:
 1. Must be prescribed by, or in consultation with, an endocrinologist, expert in rare genetic disorders of obesity, or a medical geneticist **AND**
 2. Must be ≥ 4 years of age or older **AND**
 3. Must have evidence of acquired HO with documentation of hypothalamic injury or dysfunction (e.g., hypothalamic lesion, hypothalamic tumor, hypothalamic damage) **AND**
 4. Must have weight gain associated with the hypothalamic injury, with weight gain occurring within 12 months post-hypothalamic injury/dysfunction **AND**
 5. Must have a BMI of ≥ 30 kg/m² for patients ≥ 18 years of age or BMI ≥ 95 th percentile for age and sex for patients 4 to <18 years of age **AND**

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6. Documentation of a recent (within the past month) height measurement, weight measurement, BMI, and growth chart (for pediatric patients) must be submitted for each review (initial and recertifications)
 7. Initial approval for acquired HO will be for 12 months.
 8. **Recertification for acquired HO** after the initial 12-month approval will require documentation of a $\geq 5\%$ decrease from baseline body weight, or a $\geq 5\%$ decrease from baseline body mass index (BMI) for patients with continued growth potential (pediatric patients). **OR**
- B. Obesity due to variants in the POMC, PCSK1, or LEPR genes** that are interpreted as 'pathogenic, likely pathogenic, or of uncertain significance (VUS),' or **Bardet-Biedl syndrome (BBS)** if **ALL** the following criteria are met:
1. Must be prescribed by, or in consultation with, an endocrinologist, expert in rare genetic disorders of obesity, or a medical geneticist **AND**
 2. Must be ≥ 2 years of age or older **AND**
 3. Must have one of the following diagnoses (**a or b**):
 - a. Must have a diagnosis of obesity due to POMC, PCSK1, and LEPR deficiencies that includes **ALL** the following (i-iv)
 - i. A diagnosis of Obesity is defined as:
 1. Adult patients with a BMI of ≥ 30 kg/m² **OR**
 2. Pediatric patients (6-17 years): For diagnosis of POMC, PCSK1, and LEPR deficiencies with body weight ≥ 95 th percentile for age using growth chart assessments **OR**
 3. Pediatric patients (2 to less than 6 years): For diagnosis of POMC, PCSK1, and LEPR deficiencies with baseline BMI ≥ 97 th percentile for age and sex and body weight ≥ 20 kg **AND**
 - ii. Documentation of a recent (within the past month) height measurement, weight measurement, BMI, and growth chart (for pediatric patients) must be submitted for each review (initial and recertifications) **AND**
 - iii. Obesity must be due to a homozygous or presumed compound heterozygous variant in at least one of the following genes, confirmed by genetic testing, **AND**:
 1. Proopiomelanocortin (POMC)
 2. Proprotein convertase subtilisin/kexin type 1 (PCSK1)
 3. Leptin receptor (LEPR)
 - iv. Documentation of genetic testing demonstrating that the variants in POMC, PCSK1, or LEPR genes are interpreted as '**pathogenic**', '**likely pathogenic**', **OR** '**of uncertain significance (VUS)**' must be submitted. **Coverage will not be provided for variants identified as 'benign' or 'likely benign.'** Note, direct to consumer (DTC) testing will not be accepted as these tests do not determine if the gene variant is disease-causing.
 - v. Initial approval will be for 4 months **OR**
 - b. Must have a diagnosis of monogenic or syndromic obesity due to Bardet-Biedl syndrome (BBS) that includes the following (i-iii):
 - i. A diagnosis of Obesity is defined as:
 1. Adult patients with a BMI of ≥ 30 kg/m² **OR**
 2. Pediatric patients (6-17 years): For diagnosis of BBS ≥ 97 th percentile using growth chart assessments **OR**
 3. Pediatric patients (2 to less than 6 years): For diagnosis of BBS with baseline BMI ≥ 97 th percentile for age and sex and body weight ≥ 20 kg **AND**
 - ii. Documentation of a recent (within the past month) height measurement, weight measurement, BMI, and growth chart (for pediatric patients) must be submitted for each review (initial and recertifications) **AND**
 - iii. Patient has either 4 primary features **OR** 3 primary and 2 secondary features of BBS:

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1. **Primary features:** Rod-cone dystrophy, Polydactyly, Obesity, Learning disabilities, Hypogonadism in males, Renal anomalies
2. **Secondary features:** Speech disorder/delay, Strabismus/cataracts/astigmatism, Brachydactyly/syndactyly, Developmental delay, Polyuria/polydipsia (nephrogenic diabetes insipidus), Ataxia/poor coordination/imbalance, Mild spasticity (especially lower limbs), Diabetes mellitus, Dental crowding/ hypodontia/small roots/high arched palate, left ventricular hypertrophy/congenital heart disease, Hepatic fibrosis **AND**
3. Initial approval will be for 12 months.

Recertification for obesity due to variants in the POMC, PCSK1, or LEPR genes:

After the initial approval of 4 months will require documentation of a $\geq 5\%$ decrease of baseline body weight, or a $\geq 5\%$ decrease of baseline body mass index (BMI) for patients with continued growth potential (pediatric patients). If the patient meets for recertification, approval will be for 8 months.

Recertification at the 1-year mark will require documentation that the patient achieved a $\geq 10\%$ decrease of baseline body weight or a $\geq 10\%$ decrease of BMI for patients with continued growth potential (pediatric patients). If the patient meets for recertification, approval will be for 1 year.

Recertifications thereafter will require documentation that the patient maintains a weight loss of $\geq 10\%$ decrease of baseline body weight or a $\geq 10\%$ decrease of BMI for patients with continued growth potential (pediatric patients). If the patient meets for recertification, approval will be for 1 year.

Recertification for obesity due to Bardet-Biedl syndrome (BBS) after the initial approval of 12 months will require documentation of a $\geq 5\%$ decrease of baseline body weight, or a $\geq 5\%$ decrease of baseline body mass index (BMI) for patients with continued growth potential (pediatric patients). If the patient meets for recertification, approval will be for 1 year.

Recertifications thereafter will require documentation that the patient maintains a weight loss of $\geq 5\%$ decrease of baseline body weight or a $\geq 5\%$ decrease of BMI for patients with continued growth potential (pediatric patients). If the patient meets for recertification, approval will be for 1 year.

C. Quantity Limit of 9 milliliters (9 vials) per 30 days.

a. See prescribing information for dosage and administration details.

D. Imcivree will not be covered in the following circumstances:

- a. Non-FDA approved genetic conditions that can cause obesity (such as: Alström syndrome, Prader-Willi syndrome [PWS], etc.)
- b. A lifetime history of suicide attempt or any suicidal behavior within the last month
- c. Imcivree will not be authorized if the member has prior gastric bypass surgery resulting in $>10\%$ weight loss durably maintained from the baseline pre-operative weight, with no evidence of weight regain

Increlex - mecasermin, Recombinant, rh-IGF-1 (Rx)

1. Must be prescribed by an endocrinologist or pediatric endocrinologist
2. Patient must be 2 years old or greater
3. Patient must have severe primary IGF-1 deficiency (Primary IGFD) defined as:
 - a. height standard deviation score ≤ -3.0
 - b. basal IGF-1 standard deviation score ≤ -3.0
 - c. normal or elevated GH **OR**
4. Patient must have growth hormone (GH) gene deletion with the development of neutralizing antibodies to GH
5. Normal dose of 40-120mcg/kg SQ twice daily given 20 minutes before or after a meal or snack to

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avoid hypoglycemia. Doses greater than 120mcg/kg will not be covered

6. Increlex will not be covered for growth promotion in patients with closed epiphyses or as a substitute for growth hormone replacement therapy.

Isturisa – osilodrostat tablets (Rx)

1. Must be 18 years of age or older
2. Must be prescribed by, or in consultation with, an endocrinologist
3. Must have a diagnosis of endogenous Cushing's Syndrome
4. Must have a mean urinary free cortisol (UFC) level that is at least 1.5x the upper limit of normal measured over three 24-hour measurements (ULN = 50 micrograms/24 hours or 145 nmol/24 hours)
5. Must have documentation of symptoms of Cushing's Syndrome (such as diabetes, central obesity, moon face, buffalo hump, osteoporosis, muscle wasting, hypertension, depression, and anxiety)
6. Must have documentation of a failed pituitary surgery or contraindication to Cushing's syndrome specific surgery
7. Must have had serious side effects or drug failure with oral ketoconazole **AND**
8. For Individuals with a diagnosis of Cushing's disease (Cushing's Syndrome that is caused by a pituitary adenoma), must have documentation of serious side effects or drug failure with at least 2 of the following (Note: if patient has had previous trial and failure of metopirone (metyrapone) then only 1 of the following is required):
 - a. Signifor (either LAR or SC formulation)
 - b. Lysodren (mitotane)
 - c. Cabergoline
9. Initial approval will be for 3 months. Recertification at 3 months and thereafter will require laboratory results to document a recent UFC level within normal limits **AND** improvement in the symptoms of Cushing's Syndrome.
10. For recertification, the prescriber must also make clear the maintenance dose they are planning to use. Approval will be allowed for this amount for 1 year.
11. Dose increases beyond the initial 3 months will require documentation to show UFC levels above the upper limit of normal and documentation that the patient is still experiencing Cushing's Syndrome symptoms. If approved, dosage increase authorizations will be for 1 year and will allow the amount requested only.
12. Dosing must be in accordance with FDA labeling, starting at 2 mg twice daily, and increased by 1 mg or 2 mg twice daily, no more frequently than every 2 weeks based on the rate of cortisol changes, individual tolerability, and improvement in signs and symptoms.

Please see the Isturisa Efficient Dosing chart at the bottom of this document (Figure 1A) for information on the number of tablets allowed per 30 days of each strength for a given dosing.

Joenja—leniolisib (Rx)

1. Must be prescribed by an immunologist, allergist, hematologist, or prescriber who specializes in the treatment of activated phosphoinositide 3-kinase delta (PI3K δ) syndrome (APDS)
 - a. Note: APDS is also known as PI3K δ -activating mutation causing senescent T cells, lymphadenopathy, and immunodeficiency (PASLI) **AND**
2. Must be \geq 12 years of age to 75 years old **AND**
3. Must be \geq 45 kg **AND**
4. Must have confirmed APDS-associated genetic PI3K δ mutation with a documented variant in either PIK3CD or PIK3R1 **AND**
5. Must meet at least one of the following(a-c):
 - a. Have nodal and/or extranodal lymphoproliferation **OR**
 - b. Have presence of \geq 1 measurable nodal lesion on CT or MRI **OR**

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- c. Have clinical findings and manifestations compatible with APDS (such as history of repeated oto-sino-pulmonary infections, organ dysfunction (i.e., lung, liver), bronchiectasis, cytopenias, gastrointestinal disease, immune dysregulation (i.e., decreased naive B cells, reversed CD4/CD8 ratio))
6. Initial approval will be for 3 months. Recertification will require documentation that the patient has responded to therapy (i.e., improvement in clinical findings and/or manifestations of APDS such lymphoproliferation, recurrent infections, cytopenia, immunophenotyping). Recertification will be for 6 months at a time.
7. Recommended dosage: 70 mg administered orally twice daily approximately 12 hours apart, with or without food, in adult and pediatric patients 12 years of age and older and weighing ≥ 45 kg. Note: Prior to treatment with Joenja, verify pregnancy status in individuals of reproductive potential prior to initiating treatment.
8. Quantity limit: 60 tablets/30 days

Juxtapid – lomitapide capsules (Rx)

1. Must be prescribed by or in consultation with a cardiologist, lipid specialist or endocrinologist **AND**
2. Must be ≥ 2 years of age with a diagnosis of homozygous familial hypercholesterolemia **AND**
 - a. Genetic testing must demonstrate evidence of two mutant alleles at the low-density lipoprotein receptor (*LDLR*), apolipoprotein B (*APOB*), proprotein convertase subtilisin kexin type 9 (*PCSK9*) or low-density lipoprotein receptor adaptor protein 1 (*LDLRAP1*) gene **OR**
 - b. Patient has a history of untreated LDL-C > 400 mg/dL or treated LDL-C ≥ 300 mg/dL with either (i or ii):
 - i. Xanthoma before the age of 10 years **OR**
 - ii. Evidence of heterozygous FH in one parent **AND**
3. One of the following must be met (a or b):
 - a. **For individuals 10 years of age and older**, member must have failed to reach target LDL-C while receiving treatment with maximally tolerated high potency statin (goal is atorvastatin 40-80 mg daily or rosuvastatin 20-40 mg daily), in combination with ezetimibe, and a PCSK9 inhibitor (Repatha, Praluent) for at least 8 weeks. A trial with a PCSK9 inhibitor is not required if the member is known to have two LDL-receptor negative alleles (null homozygous). **OR**
 - b. **For individuals 2 to 9 years of age**, member must have failed to reach target LDL-C while receiving treatment with at least one lipid lowering therapy (e.g., statins, ezetimibe, lipoprotein apheresis) for at least 8 weeks. **AND**
4. LDL-C must be ≥ 70 mg/dL for patients with clinical atherosclerotic cardiovascular disease (ASCVD) **OR** LDL-C must be ≥ 100 mg/dL for patients without documented clinical ASCVD
 - a. Clinical ASCVD defined as having a history of acute coronary syndrome, myocardial infarction (MI), stable or unstable angina, coronary/other arterial revascularization, stroke, TIA, peripheral arterial disease, or other documented atherosclerotic disease (such as coronary atherosclerosis, renal atherosclerosis, aortic aneurysm secondary to atherosclerosis, or Carotid plaque with $\geq 50\%$ stenosis)
5. If patient is unable to tolerate statin therapy, documentation in progress notes must include:
 - a. A contraindication to statin therapy according to FDA labeling **OR**
 - b. History of statin-related rhabdomyolysis
 - i. Must have symptoms consistent with rhabdomyolysis (i.e., muscle pain, swelling, and weakness, dark urine) **AND**
 - ii. Must have creatine kinase (CK) level > 10 times upper limit of normal, myoglobinuria, or acute renal failure (increase in serum creatinine > 0.5 mg/dL) **AND**
 - c. Patient was receiving a statin at the time of the event and symptoms resolved upon discontinuation of the statin **OR**
 - d. History of statin intolerance. Documentation must include the following:

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- e. Inability to tolerate at least 2 different statins
 - i. At least 1 statin must be hydrophilic (such as pravastatin, fluvastatin, or rosuvastatin) starting at the lowest starting average daily dose **AND**
 - ii. Intolerance associated with confirmed, intolerable statin-related adverse effects (i.e., muscle related symptoms) or significant biomarker abnormalities (i.e., ALT/AST > 3 times the upper limit of normal accompanied by increase in total bilirubin > 2 times the upper limit of normal) **AND**
 - iii. Non-statin causes of muscle symptoms or biomarker abnormalities have been ruled out (for example, hypothyroidism, reduced renal function, reduced hepatic function, rheumatologic disorders such as polymyalgia rheumatic, steroid myopathy, vitamin-D deficiency, or primary muscle disease)
6. Must have had trial and failure/intolerance to a PCSK9 inhibitor (i.e., Praluent, Repatha) when used in combination with a maximally tolerated statin plus ezetimibe
 - a. If patient is known to have two LDL-receptor negative alleles (null homozygous) then trial of PCSK9 inhibitor is not required
7. Documentation of baseline LDL-C level must be provided-measurement must occur within 60 days prior to treatment **AND**
8. Prescriber must attest that a discussion with the patient has taken place regarding a heart healthy diet, the importance of exercise, and smoking cessation (if applicable)
9. Initial approval will be for 8 weeks. Further approval will require evidence of an adequate reduction in LDL-C level defined as reduction in LDL-C level as compared to baseline LDL-C. Recertification will be required yearly thereafter.
10. Juxtapid will not be approved in combination with Evkeeza unless the patient has demonstrated failure to achieve target LDL-C while on Evkeeza in combination with:
 - a. high-intensity or maximally tolerated statin therapy **AND**
 - b. ezetimibe **AND**
 - c. a PCSK9 inhibitor (i.e., Praluent, Repatha) **AND**
 - d. the patient has been on this drug combination for at least 6 months.
11. Quantity limit of 28 capsules per 28 days for 2.5 mg, 5 mg and 10 mg and 56 capsules per 28 days for 20 mg and 30 mg strengths

Keveyis, generic dichlorphenamide and Ormalvi (dichlorphenamide) (Rx)

1. Diagnosis must be made by a neurologist or muscle disease specialist.
2. Member must have a diagnosis of primary hypokalemic periodic paralysis **AND**
 - a. The diagnosis must be confirmed by **BOTH** of the following:
 - i. A genetic test confirming a skeletal muscle calcium or sodium channel mutation **AND**
 - ii. Serum potassium concentration of less than 3.5 mEq/L during a paralytic attack
 - b. Must have had trial and failure with prescription potassium supplementation **AND**
 - c. The patient must have had a trial with oral acetazolamide therapy that did not result in improvement in severity or frequency of attacks **OR**
3. Member must have a diagnosis of primary hyperkalemic periodic paralysis **AND**
 - a. The diagnosis must be confirmed by **BOTH** of the following:
 - i. A genetic test confirming a skeletal muscle sodium channel mutation **AND**
 - ii. Serum potassium concentration of greater than 5.0 mEq/L during a paralytic attack **AND**
 - b. The patient must have had a trial with oral acetazolamide therapy that did not result in improvement in severity or frequency of attacks **AND**
4. **Requests for Keveyis and Ormalvi require documentation of serious side effects or drug failure with generic dichlorphenamide.**
5. For hypokalemic or hyperkalemic periodic paralysis, initial approval will be for 2 months. Recertification will require a documented improvement in the frequency or severity of attacks while

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- taking Keveyis or generic dichlorphenamide. Recertification will be approved for 1 year
6. Initial dosing is one 50 mg tablet twice daily and can be titrated up to a maximum of 200mg daily.
 7. Quantity limit of 120 tablets per 30 days

Korlym and generic mifepristone 300 mg tablets (Rx)

1. Must be 18 years of age or older
2. Member must have a diagnosis of endogenous Cushing's syndrome
3. Must also have a diagnosis of type 2 diabetes mellitus or glucose intolerance
4. Must have failed surgery or is not a candidate for surgery
5. Must be prescribed by, or in consultation with, an endocrinologist
6. Patients who meet the criteria for approval for treatment with Korlym will be approved for 12 months. Recertification will require patients to have stabilization/decrease in A1C or objective clinical response.
7. Requests for brand Korlym require documentation of serious side effects or drug failure with generic mifepristone 300 mg tablets (generic Korlym) will be required.
8. Recommended initial dosing is 300mg once daily with a meal.
9. Increase in 300mg increments to a maximum of 1200mg once daily based on clinical response and tolerability. Do not exceed 20mg/kg per day.
10. Quantity limit of 120 tablets per 30 days.

Livmarli—maralixibat (Rx)

1. Must have a diagnosis of **Alagille syndrome (ALGS)**, confirmed by molecular genetic testing (JAG1 or NOTCH2 mutation) **AND**
 - a. Must be ≥ 3 months of age **AND**
 - b. Must be prescribed by a hepatologist, gastroenterologist, or physician knowledgeable in the management of Alagille syndrome (ALGS) **AND**
 - c. Must have evidence of cholestasis defined as at least one of the following:
 - i. Total serum bile acid $> 3x$ upper limit of normal (ULN) for age
 - ii. Conjugated bilirubin > 1 mg/dL
 - iii. Fat soluble vitamin deficiency otherwise unexplainable
 - iv. Gamma Glutamyl Transferase (GGT) $> 3x$ ULN for age
 - v. Intractable pruritus explainable only by liver disease **AND**
 - d. Prescriber attestation or documentation that the patient is experiencing significant pruritis **AND**
 - e. For New Starts Only—must have serious side effects or drug failure with at least **ONE** conventional medication used for ALGS associated cholestasis/pruritis (e.g., ursodeoxycholic acid (ursodiol), cholestyramine, rifampin, naltrexone).
 - f. Initial approval will be for 6 months. Recertification will require documentation that the patient is tolerating therapy and is experiencing a decrease in pruritis from baseline and/or decrease in serum bile acid concentration from baseline. Recertification will be required every 12 months.
2. Must have a diagnosis of **progressive familial intrahepatic cholestasis (PFIC) types 1-6**, confirmed by molecular genetic testing **AND**
 - a. Must be ≥ 12 months of age **AND**
 - b. Must be prescribed by a hepatologist, gastroenterologist, or physician knowledgeable in the management of PFIC **AND**
 - c. Must have a serum bile acid concentration that exceeds the upper limit of normal **AND**
 - d. Prescriber attestation or documentation that the patient is experiencing significant pruritis. **AND**
 - e. Livmarli will not be authorized in PFIC type 2 patients with specific ABCB11 variants resulting in non-functional or complete absence of bile salt export pump **AND**
 - f. For New Starts Only—both of the following must be met:

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- i. Must have serious side effects or drug failure with at least **ONE** conventional medication used for ALGS associated cholestasis/pruritis (e.g., ursodeoxycholic acid (ursodiol), cholestyramine, rifampin, naltrexone) **AND**
 - ii. Must have serious side effects or drug failure to Bylvay
- g. Initial approval for PFIC will be for 6 months. Recertification will require documentation that the patient is tolerating therapy and is experiencing a decrease in pruritis from baseline and/or decrease in serum bile acid concentration. Recertification will be required every 12 months.
3. For ALGS and PFIC, Livmarli will **not** be authorized if the patient has any of the following (**a, b, or c**):
 - a. Decompensated cirrhosis (ALT >15 x ULN, INR >1.5 [unresponsive to vitamin K therapy], albumin <3.0 g/dL, history or presence of clinically significant ascites, variceal hemorrhage, and/or encephalopathy)
 - b. Portal hypertension
 - c. History of a hepatic decompensation event (i.e. variceal hemorrhage, ascites, hepatic encephalopathy)
4. Quantity limit:
 - a. For tablets: 30 tablet/30 days. A quantity limit exception of 60 tablets/30 days may be made for a diagnosis of PFIC.
 - b. For the oral solution: 30 mL/30 days. Upon each drug review and dose escalation request, the allowed quantity will be reviewed in accordance with the FDA-approved weight-based dosing for PFIC and ALGS (see prescribing information for dosing) and, as such, will be limited to the minimum number of whole bottles to obtain the appropriate daily dose/day supply.
 - i. Quantity approvals will be added to allow for dispensing of the whole bottle size needed (30mL)

Luxturna – voretigene neparvovec-rzyl (Medical)

1. Must be prescribed by an ophthalmic surgeon for administration at a certified treatment center **AND**
2. Must be ≥ 12 months of age based upon ongoing cell proliferation in those under 1 year of age **AND**
3. Must have a diagnosis of Biallelic RPE65 mutation-associated retinal dystrophy
 - a. Diagnosis must be confirmed by genetic testing **AND**
4. Patient must have viable retinal cells
 - a. Viable retinal cells must have been determined by retinal thickness on spectral domain optical coherence tomography (OCT >100 microns within the posterior pole) **AND**
5. Baseline full-field light sensitivity threshold (FST) test results for each eye must be submitted
6. A maximum of 1 dose of 1.5 x 10¹¹ vector genomes (vg) administered by subretinal injection in a total volume of 0.3 mL will be allowed per eye per lifetime. Authorization will be for 6 months to allow sufficient time for administration.

HCPCS: J3398

Myalept - metreleptin (Rx)

1. Diagnosis of either congenital or acquired generalized lipodystrophy **AND** at least one of the following co-morbidities: diabetes mellitus, hypertriglyceridemia, and/or increased fasting insulin
2. A1C > 7% despite adequate drug therapy (trial of combination diabetic drug therapy) **OR** triglycerides > 200 mg/dL despite adequate drug therapy (trial of a high dose statin and a fibrate agent).
3. Initial approval will be for 4 months. Initial recertification approval will require documentation of an improvement in A1C of at least 1 percentage point and/or an improvement in triglycerides of at least 20%. Subsequent approvals will require documentation of maintained triglyceride/ A1C improvement.
4. Treatment with metreleptin is contraindicated in patients with general obesity not associated with congenital leptin deficiency and will not be authorized
5. Treatment with metreleptin for HIV associated lipodystrophy will not be authorized
6. Quantity limit of 30 vials per 30 days.

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Mycapssa - octreotide acetate (Rx)

1. Must be prescribed by, or in consultation with, an endocrinologist **AND**
2. Must be 18 years of age or older **AND**
3. Must have a diagnosis of acromegaly **AND**
4. Must have failed pituitary surgery and/or radiation, or patient is not a candidate for surgery and/or radiation **AND**
5. Must be receiving treatment with either an injectable octreotide product (i.e., octreotide, Sandostatin, Sandostatin LAR) or injectable lanreotide products (i.e., lanreotide acetate injection) for at least 6 months, with a stable dose for at least the last 3 months of therapy **AND**
6. Must have documented clinical response (defined as improvement or normalization of growth hormone (GH) and/or insulin-like growth factor-1 (IGF-1)) with either an injectable octreotide product or lanreotide acetate **AND** patient is tolerating therapy.
7. Recommended dosing: Initiate Mycapssa at dosage of 40 mg daily, administered as 20 mg orally twice daily. Monitor insulin-like growth factor (IGF-1) levels and patient's signs and symptoms every two weeks during titration. Titrate dosage based on IGF-1 levels and patient's signs/symptoms. Increase dose in increments of 20 mg daily. The maximum recommended dosage of Mycapssa daily dosage is 80 mg daily. See prescribing information for full details on recommended dosage, titration, and monitoring.
8. Initial approval for acromegaly will be for 12 months. Recertification for any further approval will require documentation of stable or improved GH and/or IGF-1 while on Mycapssa therapy.
9. Quantity limit: 120 capsules/30 days

Palsonify (paltusotine)-Rx

1. Must be prescribed by, or in consultation with, an endocrinologist **AND**
2. Must be 18 years of age or older **AND**
3. Must have a diagnosis of acromegaly **AND**
4. Must have inadequate response despite pituitary surgery and/or radiation, or patient is not a candidate for surgery and/or radiation **AND**
5. Must have serious side effects or drug failure with maximally tolerated dose of lanreotide acetate (J1930 or J1932) **AND**
6. Documentation of baseline growth hormone (GH) and insulin-like growth factor-1 (IGF-1) will be required
7. Initial approval will be for 6 months. Recertification for further approval will require documentation of a decrease or normalization of GH and/or IGF-1 from baseline and will be for 12 months at a time.
8. Quantity limit: 60 tablets/30 days
 - a. A quantity limit exception of up to 120 tablets/30 days of the 30 mg strength may be authorized for individuals on moderate to strong CYP3A4 Inducers

Piasky-crovalimab-akkz (Medical)

1. Must be 13 years of age or older **AND**
2. Must be prescribed by a hematologist or nephrologist **AND**
3. Must have a diagnosis of paroxysmal nocturnal hemoglobinuria (PNH) confirmed by a flow cytometry test **AND**
4. Must have a body weight of 40 kg or greater **AND**
5. Concomitant use of another complement inhibitor (i.e., Soliris/Bkemv/Epysqli (eculizumab), Ultomiris (ravulizumab), Empaveli (pegcetacoplan), Fabhalta (iptacopan)) will only be authorized to allow for patients transitioning from one of these agents to Piasky. After the initial approval period, requests for concomitant use of Piasky with these complement inhibitors will be considered experimental/investigational and will not be approved.
6. Piasky will not be authorized for any other non-FDA approved indication.

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7. Initial approval for 6 months. Continued approval will be for 6 months and will require documentation that the patient is tolerating therapy and is responding to treatment (i.e., decrease in number of transfusions, improvement in hemoglobin levels, normalization of LDH levels, symptom improvement).
8. The recommended dosage regimen for Piasky consists of one loading dose administered by intravenous (IV) infusion (on Day 1), followed by four additional weekly loading doses administered by subcutaneous (SUBQ) injection (on Days 2, 8, 15, and 22). The maintenance dose starts on Day 29 and is then administered every 4 weeks by subcutaneous injection. Administer doses based on the patient's actual body weight, see full prescribing information for details. Of note, modification of the maintenance dose is required if the patient's body weight changes to become consistently greater than or lower than 100 kg during the course of therapy.

HCPCS: J1307

Procysbi - cysteamine capsules and packets (Rx)

1. Drug must be prescribed a nephrologist or genetic specialist. **AND**
2. Patient must have a diagnosis of nephropathic cystinosis **AND**
3. Procysbi will not be approved for patients with hypersensitivity to penicillamine **AND**
4. Member must have had documented intolerance to Cystagon (immediate release cysteamine). Intolerance is defined as severe nausea, vomiting, anorexia, fever, or lethargy that interferes with activity of daily living.
5. Based on comparable efficacy between the medications, Procysbi will not be authorized for those who fail to adhere to the standard Cystagon dosing regimen. The underlying cause of the non-adherence should be addressed and resolved.
6. Recommended maintenance dose is 1.3 gram/m²/day in 2 divided doses, every 12 hours, recommended initial dosing in cysteamine-naïve patients is 1/6-1/4 of the maintenance dose of Procysbi.
7. Procysbi should be taken at least 2 hours after and at least 30 minutes before eating.
8. Quantity Limit: 180/30 days for the 75mg capsules and 75 mg packets and 60/30 for the 25mg capsules and 300 mg packets. Upon each drug review and dose escalation request, the allowed quantity will be reviewed in accordance with the FDA-approved BSA-based dosing and, as such, will be limited to the minimum number of capsules or packets to obtain the appropriate daily dose.

Pyrukynd—mitapivat tablets (Rx)

1. Must be 18 years and older **AND**
2. Must be prescribed by a hematologist, geneticist, or prescriber who specializes in pyruvate kinase (PK) deficiency **AND**
3. Must have diagnosis of pyruvate kinase deficiency with documented presence of at least 2 mutant alleles in the pyruvate kinase liver and red blood cell (PKLR) gene, one of which is a missense mutation **AND**
4. Must have hemoglobin \leq 10 g/dL **OR**
5. Must have had more than 4 red blood cell (RBC) transfusions in the last year **AND**
6. Documentation of the following must be provided:
 - a. The number of RBC transfusions the patient has required in the past year (if applicable) **AND**
 - b. Baseline hemoglobin level **AND**
 - c. Baseline laboratory values for markers of hemolysis (i.e., indirect bilirubin, lactate dehydrogenase (LDH), haptoglobin) **AND**
7. Must be receiving at least 0.8 mg of folic acid daily
8. Pyrukynd will not be covered for patients who are homozygous for the c.1436G>A (p.R479H) variant or have 2 non-missense variants (without the presence of another missense variant) in the PKLR gene.
9. Recommended dosing: Starting dosage for Pyrukynd is 5 mg twice daily. Titrate from 5 mg twice daily to 20 mg twice daily, and then to the maximum recommended dose of 50 mg twice daily, with these

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dose increases occurring every 4 weeks (see Table 1). Discontinue Pyrukynd if no benefit has been observed by 24 weeks, based on the hemoglobin and hemolysis laboratory results and transfusion requirements. See package insert for full prescribing details including interruption or discontinuation taper schedule.

10. Initial and recertification requests will be approved for 6 months at a time and require documentation of the following:
 - a. Increase in hemoglobin \geq 1.5 g/dL from baseline **OR**
 - b. Reduction in the number of RBC transfusions while receiving Pyrukynd **OR**
 - c. Laboratory evidence demonstrating improvement in markers of hemolysis (i.e., indirect bilirubin, lactate dehydrogenase (LDH), haptoglobin)
11. For individuals who do not meet the above criteria for recertification, a one-time authorization of the appropriate dose taper pack will be granted to allow for gradual discontinuation of Pyrukynd.
12. Requests for non-FDA approved indications for Pyrukynd will not be covered.
13. Quantity Limit:
 - a. 5 mg, 20 mg, and 50 mg tablets: 56 tablets/28 days
 - b. For taper packs the quantity limits are listed below. Note: An additional taper pack may be authorized when clinically appropriate to allow for temporary interruption of therapy or permanent discontinuation of therapy.
 - i. 5 mg taper pack: 7 tablets (1 taper pack)/365 days
 - ii. 20 mg-5 mg taper pack: 14 tablets (1 taper pack)/365 days
 - iii. 50 mg-20 mg taper pack: 14 tablets (1 taper pack)/365 days

Table 1: Dose Titration Schedule

Duration	Dosage
Week 1 through Week 4	5 mg twice daily
Week 5 through Week 8	If Hb is below normal range or patient has required a transfusion within the last 8 weeks: <ul style="list-style-type: none"> • Increase to 20 mg twice daily and maintain for 4 weeks.
	If Hb is within normal range and patient has not required a transfusion within the last 8 weeks: <ul style="list-style-type: none"> • Maintain 5 mg twice daily.
Week 9 through Week 12	If Hb is below normal range or patient has required a transfusion within the last 8 weeks: <ul style="list-style-type: none"> • Increase to 50 mg twice daily and maintain thereafter.
	If Hb is within normal range and patient has not required a transfusion within the last 8 weeks: <ul style="list-style-type: none"> • Maintain current dose (5 mg twice daily or 20 mg twice daily).
Maintenance	If Hb decreases, consider up-titration to the maximum of 50 mg twice daily as per the above schedule.

Reblozyl-luspatercept-aamt (Medical)

1. Reblozyl is considered medically necessary for the treatment of **anemia in adults with beta thalassemia** when the following criteria are met:
 - a. Must have a diagnosis of beta thalassemia (including HbE/beta thalassemia and beta thalassemia combined with alpha-thalassemia) based on Hb electrophoresis, Hb high-performance liquid chromatography (HPLC), and/or DNA analysis.
 - i. Reblozyl will not be covered for any other diagnoses including alpha thalassemia and sickle cell beta thalassemia (also known as hemoglobin S/ β -thalassemia)
 - b. Must be at least 18 years of age

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- c. Must be followed by a hematologist or physician knowledgeable in the treatment of beta-thalassemia
 - d. Must require regular RBC transfusions defined as (i and ii):
 - i. A need for at least 6 RBC units in the previous 24 weeks
 - ii. Transfusion-free period no longer than 6 weeks in the previous 24 weeks
 - e. Reblozyl must be given by a healthcare professional and therefore, will only be covered under the medical benefit
 - f. Dosing for beta thalassemia should be initiated at 1 mg/kg every 3 weeks
 - i. If there is no reduction in RBC transfusion burden after 6 weeks of treatment (2 doses) at 1 mg/kg dosing, the dose should be increased to 1.25 mg/kg every 3 weeks
 - ii. If there is no reduction in RBC transfusion burden after 9 weeks of treatment (3 doses) at the maximum dose (1.25 mg/kg every 3 weeks), treatment should be discontinued and will not be approved for additional administration
 - g. The maximum recommended dose for this indication is 1.25 mg/kg every 3 weeks. Requests for higher doses will not be approved.
 - h. Current body weight and requested dosing regimen must be submitted for initial review and each recertification request
 - i. Initial approval will be granted for 6 months. Recertification will require documented reduction in RBC transfusion burden after receiving Reblozyl. Approval timeframes after the initial 6 months will be granted as outlined in the approval time frame table in the policy guideline section. **OR**
2. Reblozyl is considered medically necessary for the treatment of **anemia in adults with myelodysplastic syndromes (MDS)** when the following criteria are met:
- a. Must have a diagnosis of **very low-to intermediate-risk myelodysplastic syndrome AND**
 - i. Must be at least 18 years of age **AND**
 - ii. Must be followed by a hematologist, oncologist, or physician knowledgeable in the treatment of myelodysplastic syndromes **AND**
 - iii. Patient must have required two or more RBC units over an eight-week period in the preceding 16 weeks; **AND**
 1. Patient has no prior treatment with erythropoiesis stimulating agents (ESA); **OR**
 2. Patient must be refractory to an erythropoiesis stimulating agent, where refractory is defined as lack of 1.5 gm/dL rise in hemoglobin or lack of decrease in RBC transfusion requirement by 6 to 8 weeks of treatment **OR**
 3. Patient must have documented ineligibility to an ESA which is defined as a serum erythropoietin (EPO) level ≥ 500 mU/mL **OR**
 4. Patient must have documented intolerance, adverse event, or contraindication to an ESA **OR**
 - b. Must have a diagnosis of **very low-to intermediate-risk myelodysplastic/myeloproliferative neoplasm with ring sideroblasts and thrombocytosis (MDS/MPN-RS-T) AND**
 - i. Must be at least 18 years of age **AND**
 - ii. Must be followed by a hematologist, oncologist, or physician knowledgeable in the treatment of myelodysplastic syndromes **AND**
 - iii. Must have presence of ring sideroblasts is defined as $\geq 15\%$ ring sideroblasts or $\geq 5\%$ ring sideroblasts with an SF3B1 mutation **AND**
 - iv. Must have required two or more RBC units over an eight-week period in the preceding 16 weeks **AND**
 1. Patient must be refractory to an erythropoiesis stimulating agent, where refractory is defined as lack of 1.5 gm/dL rise in hemoglobin or lack of decrease in RBC transfusion requirement by 6 to 8 weeks of treatment **OR**
 2. Patient must have documented ineligibility to an ESA which is defined as a serum EPO level ≥ 500 mU/mL **OR**

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3. Patient must have documented intolerance, adverse event, or contraindication to an ESA
- c. Reblozyl must be given by a healthcare professional and therefore, will only be covered under the medical benefit
 - d. Dosing for MDS associated anemia should be initiated at 1 mg/kg every 3 weeks
 - i. If patient is not RBC transfusion-free after 6 weeks of treatment (2 doses) at 1 mg/kg dosing, the dose should be increased to 1.33 mg/kg every 3 weeks
 - ii. If patient is not RBC transfusion-free after 6 weeks of treatment (2 doses) at 1.33 mg/kg dosing, the dose should be increased to 1.75 mg/kg every 3 weeks
 - iii. If patient has not had any reduction in RBC transfusion burden after 9 weeks of treatment (3 doses) at 1.75 mg/kg dosing, treatment should be discontinued and will not be approved for additional administration
 - e. The maximum recommended dose for this indication is 1.75 mg/kg every 3 weeks. Requests for higher doses will not be approved
 - f. Current body weight and requested dosing regimen must be submitted for initial review and each recertification request
 - g. Initial approval will be granted for 6 months. Recertification will be for 6 months at a time and require documented reduction in RBC transfusion burden after receiving Reblozyl.

HCPCS: J0896

Recorlev-levoketoconazole (Rx)

1. Must be prescribed by, or in consultation with, an endocrinologist **AND**
2. Must be 18 years of age or older **AND**
3. Must have a diagnosis of endogenous Cushing's syndrome **AND**
4. Must have a mean urinary free cortisol (UFC) level that is at least 1.5x the upper limit of normal (ULN) measured over three 24-hour measurements (In clinical trials for Recorlev, ULN = 50 micrograms/24 hours or 138 nmol/24 hours) **AND**
5. Must have documentation of symptoms of Cushing's Syndrome (such as diabetes, central obesity, moon face, buffalo hump, osteoporosis, muscle wasting, hypertension, depression, and anxiety) **AND**
6. Must have documentation of failure of or contraindication to Cushing's syndrome specific surgery **AND**
7. Must have documentation of serious side effects or drug failure with oral ketoconazole **AND**
8. Individuals with a diagnosis of Cushing's Disease (Cushing's Syndrome that is caused by a pituitary adenoma) must have documentation of serious side effects or drug failure with at least 2 of the following. (Note: if patient has had previous trial and failure of metopirone (metyrapone) then only 1 of the following is required):
 - a. Signifor (either LAR or SC formulation)
 - b. Lysodren (mitotane)
 - c. Cabergoline
9. Recorlev will not be approved for individuals with pituitary or adrenal carcinoma
10. Recorlev will not be approved for the treatment of fungal infections
11. Initial approval will be for 6 months. Recertification at 6 months and thereafter will require laboratory results to document a recent UFC level within normal limits **AND** improvement in symptoms of Cushing's Syndrome. Recertification will be annually thereafter.
 - a. At the time of recertification, the prescriber must also make clear the maintenance dose they are planning to use. Approval will be allowed for this amount for 1 year.
12. Recommended dosing initially is 150 mg twice daily with or without food. Titrate the dosage by 150 mg daily not more frequently than every 2-3 weeks based on 24-hour urine free cortisol levels and patient tolerability. Monitor cortisol levels from at least two 24-hour urine free cortisol collections every 2-3 weeks until an adequate clinical response is achieved. The maximum recommended dosage is 1200 mg per day, administered as 600 mg twice daily. See full prescribing information for complete dosage and administration instructions.

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13. Quantity limit: 60 tablets/30 days. The maximum quantity allowed for any dose request is 240 tablets/30 days.
- Initial approval will be limited to 60 tablets/30 days
 - For dose escalation request during the initial titration period, the allowed quantity will be reviewed as follows:
 - Documentation of a recent, within the past 2-3 weeks, UFC level above the upper limit of normal must be submitted
 - Each dose escalation request will be limited to 1 additional 150 mg tablet per day
 - Approval will be granted until the end of the drug approval period or for 1 year
 - For dose escalation requests after the initial approval period, the allowed quantity will be reviewed as follows:
 - Documentation showing a recent UFC level above the upper limit of normal
 - Documentation that the patient is still experiencing Cushing's Syndrome symptoms
 - Approval will be granted until the end of the drug approval period or for 1 year

Redempro (plozasiran)-Rx

- Must be prescribed by or in consultation with a cardiologist, lipid specialist, endocrinologist, or gastroenterologist **AND**
- Must be 18 years of age and older **AND**
- Must have a diagnosis of Familial Chylomicronemia Syndrome (FCS) **AND**
- Must have fasting triglycerides (TGs) of ≥ 880 mg/dL (or 10 mmol/L) within the past 6 months **AND**
- Must have genetic testing performed and meet one of the following (a or b):
 - Genetic testing confirms biallelic pathogenic variants (i.e., homozygosity, compound heterozygosity or double heterozygosity) in FCS-causing genes.
 - Examples of FCS-causing genes include lipoprotein lipase (LPL), apolipoprotein C-II (APOC2), apolipoprotein C-VI (APOA5), glycosylphosphatidylinositol-anchored high-density lipoprotein binding protein 1 (GPIHBP1), lipase maturation factor 1 (LMF1) **OR**
 - Genetic testing is inconclusive (i.e., one or more variants of uncertain significance were identified) and one of the following are met (i, ii, or iii.):
 - Must have a familial chylomicronemia syndrome (FCS) score ≥ 10 [see Appendix] **OR**
 - Must have a North American familial chylomicronemia syndrome (NAFCS) score ≥ 45 [see Appendix]
 - NOTE: In patients ≥ 10 years of age, the NAFCS tool should only be used for patients who are not responsive to fibrates and high-dose omega-3 fatty acids even when the patient is compliant with therapy (i.e., TGs do not decrease by 20% or more and do not remain reduced). **OR**
- Must meet the following 1, 2, and 3):
 - Must be refractory to refractory to standard triglyceride therapies (e.g., statins, fibrates, high-dose omega-3 fatty acids) **AND**
 - Other causes of hypertriglyceridemia have been ruled out (e.g., alcohol excess, uncontrolled type 2 diabetes, medications and medical conditions known to raise triglycerides) **AND**
 - One of the following is met (A or B):
 - History of acute pancreatitis **OR**
 - History of recurrent abdominal pain without other known cause **AND**
- Must have documentation or prescriber attestation that the patient has implemented appropriate dietary fat restrictions (e.g., consuming ≤ 20 g of fat per day) to manage FCS.
- Redempro will not be covered for any other non-FDA approved indications
- Initial approval is for 6 months. Recertification will be every 12 months. Recertifications will require documentation of reduction in fasting TGs from baseline.

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9. Quantity Limit: 25 mg/0.5 mL (1 pre-filled syringe) per 90 days

Rethymic-allogeneic processed thymus tissue–agdc (Medical)

1. Must have surgical procedure performed by surgeon experienced with Rethymic **AND**
2. Must be < 18 years of age **AND**
3. Must have a diagnosis of congenital athymia that is confirmed by a pediatric immunologist or geneticist **AND**
4. Must have T-cell count lower than 50/mm³ or naïve T-cell (CD3⁺CD4⁺CD45RA⁺CD62L⁺ or CD3⁺CD8⁺CD45RA⁺ CD62L⁺ cells) count lower than 50/mm³ based on flow cytometry **AND**
5. Must have FOXP1 deficiency **OR**
6. Must have a diagnosis of Complete DiGeorge Syndrome plus **at least one** of the following:
 - a. Congenital heart defect
 - b. Hypoparathyroidism (or hypocalcemia requiring calcium replacement)
 - c. 22q11 hemizyosity
 - d. 10p13 hemizyosity
 - e. CHARGE syndrome (coloboma, heart defect, choanal atresia, growth and development retardation, genital hypoplasia, ear defects including deafness)
 - f. CHD7 mutation
 - g. Diabetic embryopathy **AND**
7. Prescriber must attest that the patient will be screened for anti-HLA antibodies prior to receiving Rethymic. Patients testing positive for anti-HLA antibodies should receive Rethymic from a donor who does not express those HLA alleles. **AND**
8. Prescriber must attest HLA matching will be performed in patients who have received a prior hematopoietic cell transplantation (HCT) or a solid organ transplant. To minimize risk of developing graft-versus-host-diseases (GVHD), HLA matching of Rethymic to recipient alleles that were not expressed in the HCT donor is recommended **AND**
9. For patients with pre-existing cytomegalovirus (CMV) infection, the prescriber must attest that the benefits and risks of Rethymic therapy have been discussed with the patient/caregiver **AND**
10. Dosage should not exceed 22,000 mm² of Rethymic/m² recipient body surface area (BSA) **AND**
11. Must not have received previous Rethymic treatment. Retreatment with Rethymic will be considered Experimental/Investigational **AND**
12. Rethymic will not be approved for treatment of patients with severe combined immunodeficiency (SCID) **AND**
13. Prescriber must attest that, in accordance with the FDA-approved prescribing information, the patient will receive intravenous immunoglobulin replacement and prophylactic antimicrobials prior to and after transplant until immune reconstitution (according to infection control protocols) occurs (Note: immune reconstitution sufficient to protect from infection is unlikely to develop prior to 6-12 months after treatment with Rethymic).
14. Authorization will be for 6 months to allow sufficient time for administration.

Revcovi-elapegamase-1v1r (Medical & Rx)

1. Prescribed by or in consultation with an immunologist, hematologist/oncologist or a physician that specializes in the treatment of ADA- SCID **AND**
2. The patient has a diagnosis of ADA-SCID confirmed by one of the following (a or b)
 - a. Absent or very low (< 1% of normal) adenosine deaminase (ADA) catalytic activity in plasma, urine, or dried blood spots prior to the initiation of enzyme replacement therapy **OR**
 - b. Molecular genetic testing confirming bi-allelic mutations in the ADA gene, **AND**
3. Must have elevated deoxyadenosine triphosphate (dATP) levels or total deoxyadenosine (dAdo) nucleotides in erythrocytes (red blood cells) compared to a laboratory standard, **AND**
4. Patient is not a suitable candidate for hematopoietic cell transplantation (HCT) at the time of the request **OR** patient has failed HCT, **AND**

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5. Must not have severe thrombocytopenia (considered to be a platelet count of < 50,000 cells/microliter)
6. Revcovi is dosed based on patient weight; therefore, current body weight and requested dose regimen must be submitted for initial review and each recertification request.
7. Revcovi will be reviewed under the **medical benefit** when administered by a health care professional. Revcovi may be self-administered after appropriate training from a healthcare professional and therefore would be considered under the **pharmacy benefit** if self-administered.
8. Initial approval will be for one year
9. Recertification every two years thereafter will require documentation of a positive response to treatment such as one or more of the following:
 - a. Improvement in immune status (total lymphocyte and B, T, and natural killer (NK) lymphocyte counts, quantitative immunoglobulin (Ig) concentration [IgG, IgA, IgM])
 - b. Improvement in clinical status (infection rate, incidence and duration of hospitalization, and performance status)
 - c. Normalization of plasma ADA activity, erythrocyte dATP or total dAdo nucleotide levels compared to a laboratory standard

Recommended Dosing:

- The starting dose of Revcovi depends on whether the patient was previously using Adagen. Please refer to the FDA approved prescribing literature for additional dosing and monitoring guidance.
 - a. Adagen-naïve patients: the starting weekly dose of Revcovi is 0.4 mg/kg IM based on ideal body weight, divided into two doses (0.2 mg/kg twice weekly), for a minimum of 12 to 24 weeks until immune reconstitution is achieved.
 - b. Transitioning from Adagen to Revcovi:
 - i. Previous Adagen weekly dose unknown or dose \leq 30 U/kg: Revcovi dose minimum of 0.2 mg/kg intramuscularly once weekly
 - ii. Previous Adagen weekly dose > 30 U/kg: Calculate Revcovi dose based on the following formula: Revcovi dose (mg/kg) = Adagen dose (U/kg) / 150

Ryplazim- plasminogen, human-tvm (Medical & Rx)

1. Must be prescribed by hematologist, geneticist, pulmonologist, ophthalmologist, or prescriber specializing in plasminogen deficiency type 1 **AND**
2. Must be 11 months of age or older **AND**
3. Must have diagnosis of plasminogen deficiency type 1 **AND**
4. Must have baseline plasminogen activity level \leq 45% (Note: if the patient is receiving plasminogen supplementation with fresh frozen plasma, allow for a 7-day washout period before obtaining baseline plasminogen activity level.) **AND**
5. Must have documented history of lesions consistent with a diagnosis of congenital plasminogen deficiency (i.e., ligneous conjunctivitis, ligneous gingivitis, growths in the mucous membrane of the middle ear, respiratory tract, gastrointestinal tract) **AND**
6. If requesting under the pharmacy benefit, prescriber must attest that the patient/caregiver has received detailed instructions and training and has shown the ability to safely and independently administer Ryplazim.
7. The recommended dosage for Ryplazim is 6.6 mg/kg body weight administered intravenously every 2 to 4 days. (See prescribing information for details on determination of dose and dosing frequency)
8. Quantity Limit: 1 vial/30 days.
 - a. Upon each drug review and dose escalation request, the allowed quantity will be reviewed in accordance with the FDA-approved weight-based dosing and, as such, will be limited to the minimum number of vials (rounded up to the nearest whole vial) to obtain the appropriate dose/day supply. See additional quantity limit information under approval section (below).
9. Initial approval will be for 12 weeks.

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- a. A quantity limit sufficient to allow for 6.6 mg/kg body weight administered every 2 days will be authorized for 12 weeks.
10. Recertification after the initial 12-week approval will be reviewed as follows:
 - a. Must provide documentation of the trough plasminogen activity level that was obtained approximately 72 hours after the initial dose of Ryplazim and prior to the second dose to confirm dosing frequency used in the initial 12-week approval period aligns with FDA-labeling.
 - b. Duration of continued approval will be dependent on the patient's initial 12-week response:
 - i. For patients who have documented resolution of lesions, approval will be authorized for 12 months. Quantity limit authorizations (dose and frequency) will be based on FDA-approved labeling
 - ii. For patients who do not have resolution of lesions or have new or recurrent lesions, continued approval will be authorized for an additional 12-weeks along with request for additional quantity to optimize dosing frequency. A quantity limit sufficient to allow for 6.6 mg/kg body weight administered every 2 days will be authorized for this additional 12-week period.
 1. If patient has a documented clinical efficacy after the additional 12 weeks (i.e., resolution of lesions, improvement in size/number of lesions, trough plasminogen activity level \geq 10% above baseline trough level), continued approval will be authorized for 12 months. Quantity limit authorizations (dose and frequency) will be based on FDA-approved labeling.
 2. Ryplazim will not be authorized beyond 24 weeks of therapy if confirmed (repeat) trough plasminogen activity level is $<$ 10% above baseline with no clinical efficacy.
11. Yearly recertification requests will require:
 - a. Documentation that the patient has maintained a clinical response to treatment.
 - b. Quantity limit authorizations (dose and frequency) will be based on FDA-approved labeling.

Rystiggo (rozanolixizumab-noli) - Medical

1. Must be 18 years of age or older **AND**
2. Must be prescribed by or in consultation with a neurologist. If geographically available, it is also recommended for patients to have been evaluated by a neuromuscular specialist **AND**
3. Must have a diagnosis of generalized myasthenia gravis (gMG) **AND**
4. Must have Myasthenia Gravis Foundation of America (MGFA) clinical classification class II to IVa **AND**
5. Must be antibody positive for either (a or b):
 - a. Anti-acetylcholine receptor (AChR) **OR**
 - b. Muscle-specific kinase (MuSK) **AND**
6. Must documentation of a baseline Myasthenia Gravis Activities of Daily Living (MG-ADL) score of at least 5 **AND**
7. Must meet one of the following (a or b)
 - a. Must have had serious side effects or drug failure to ONE of the following treatments for gMG (i or ii).
 - i. Corticosteroids for at least 3 months of treatment **OR**
 - ii. Non-steroidal immunosuppressive therapy (i.e., azathioprine, mycophenolate mofetil, cyclosporine) for at least 6 months of treatment **OR**
 - b. Despite treatment with at least ONE immunosuppressant agent (i.e., corticosteroid, non-steroidal immunosuppressive therapy), the member required at least ONE treatment with plasma exchange, plasmapheresis, or intravenous immunoglobulin within the previous 12 months. **AND**
8. For individuals with AChR positive gMG: Must have had serious side effects or drug failure with Vyvgart Hytrulo prefilled syringe (PFS). This applies to New Starts only for all lines of business.
9. Rystiggo will not be approved in combination with Uplizna, Soliris/Bkemv/Epysqli, Ultomiris, Vyvgart, Vyvgart Hytrulo, Imaavy, Zilbrysq, intravenous immunoglobulin (other than when used as rescue

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therapy), or rituximab-containing products as Rystiggo has not been studied in combination with these therapies.

10. The recommended dosage of Rystiggo is weight based (see Table 1) and is administered as a subcutaneous infusion once weekly for 6 weeks. Administer subsequent treatment cycles based on clinical evaluation. The safety of initiating subsequent cycles sooner than 63 days from the start of the previous treatment cycle has not been established.
11. Initial approval will be for 6 months. Continued approval will require documentation of ≥ 2 -point improvement in the MG-ADL scale from baseline **OR** provider attests that patient is experiencing clinical benefit from treatment (i.e., reduction of myasthenia gravis exacerbations, improvement in symptoms such as swallowing, mobility, breathing). Recertification will be required every 12 months.

Table 1: Recommended Dose Based on Body Weight

Body Weight of Patient	Dose	Volume to be Infused
Less than 50 kg	420 mg	3 mL
50 kg to less than 100 kg	560 mg	4 mL
100 kg and above	840 mg	6 mL

HCPCS: J9333

Sandostatin LAR and octreotide intramuscular injection (Rx and Medical)

1. Must be 18 years of age or older **AND**
2. Must have a diagnosis of **acromegaly AND**
 - a. Must be prescribed by, or in consultation with, an endocrinologist
 - b. Must have persistent disease despite pituitary surgery and/or radiation, or patient is not a candidate for surgery and/or radiation
 - c. **For New Starts Only for acromegaly diagnosis –must have serious side effects or drug failure with maximally tolerated dose of lanreotide acetate (J1930 or J1932)**
 - d. Documentation of baseline growth hormone (GH) and insulin-like growth factor-1 (IGF-1) will be required
 - e. Initial approval for acromegaly will be for 12 months. Recertification for any further approval will require documentation of a decrease or normalization of GH and/or IGF-1 from baseline **OR**
3. Must have a **cancer** diagnosis that meets the following:
 - a. Must be prescribed by, or in consultation with an Oncologist, Hematologist, or appropriate specialist [i.e., endocrinologist or gastroenterologist for neuroendocrine/adrenal tumor diagnosis] **AND**
 - b. The requested use (indication AND regimen) must meet **one** of the following:
 - i. Approved by the U.S. Food and Drug Administration (FDA) **OR**
 - ii. A National Comprehensive Cancer Network (NCCN) category level 1 or 2A recommendation **OR**
 - iii. Satisfied by the criteria required for the applicable line of business (LOB) for the treatment of cancer in the Off-Label Use of FDA Approved Drugs policy (Pharmacy-32) **AND**
 - c. Step therapy requirements must be met for select indications as outlined below:
 - i. **For all shared FDA label indications or compendia supported indications/regimens (defined as NCCN level of evidence 1 or 2A) related to neuroendocrine and/or adrenal tumor diagnosis**
 - ii. **For New Starts Only—must have serious side effects or drug failure with lanreotide acetate (J1930 or J1932)**
 - d. Initial certification for cancer diagnosis will be for 12 months. Recertification will require demonstration of stable or improved disease.
4. Recommended dosing (see package labeling for complete dosing recommendations):
 - a. **Patients Not Currently Receiving Sandostatin Injection Subcutaneously:**

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- i. Acromegaly: 50 mcg three times daily Sandostatin Injection subcutaneously for 2 weeks followed by Sandostatin LAR/ octreotide intramuscular injection 20 mg intragluteally every 4 weeks for 3 months
- ii. Carcinoid Tumors and VIPomas: Sandostatin Injection subcutaneously 100 to 600 mcg/day in 2-4 divided doses for 2 weeks followed by Sandostatin LAR/ octreotide intramuscular injection 20 mg every 4 weeks for 2 months
- b. Patients Currently Receiving Sandostatin Injection Subcutaneously:
 - i. Acromegaly: 20 mg every 4 weeks for 3 months
 - ii. Carcinoid Tumors and VIPomas: 20 mg every 4 weeks for 2 months
5. Quantity Limit: 1 kit/28 days. For the treatment of acromegaly, a quantity limit exception of 2 kits/28 days may be granted for the 20 mg strength to allow for a maximum daily dose of 40 mg.

HCPCS: J2353

Scenesse-afamelanotide (Medical)

Scenesse is indicated to increase pain free light exposure in adult patients with a history of phototoxic reactions from erythropoietic protoporphyria (EPP) and is considered medically necessary when the following criteria have been met **(1 - 9)**:

1. Must be 18 years of age or older, **AND**
2. Must be prescribed by a physician experienced in the treatment of cutaneous porphyrias such as a dermatologist, hepatologist or geneticist, **AND**
3. Must have a diagnosis of erythropoietic protoporphyria (EPP) confirmed by (a and/or b)
 - a. Biochemical analysis shows abnormally elevated (5-50 times) total erythrocyte protoporphyrin levels in peripheral red blood cells (erythrocytes) compared to the laboratory reference range (e.g., 300-5000 ug/dL; reference range < 80 ug/dL), **AND** Erythrocyte fractionation shows a predominance (85% - 100%) of metal-free vs. zinc-chelated protoporphyrin. Laboratory report should document total erythrocyte protoporphyrin/porphyrin; erythrocyte zinc protoporphyrin and erythrocyte metal-free (free) protoporphyrin, **OR**
 - b. Molecular genetic testing confirms biallelic pathologic variants in the ferrochelatase (FECH) gene, **AND**
4. Must have a history of documented characteristic symptoms of phototoxicity due to EPP such as burning, itching, swelling, pain and redness of the skin during or after exposure to sunlight or fluorescent light causing reduced quality of life, **AND**
5. Member does not have any of the following conditions:
 - Current Bowen's disease (squamous cell carcinoma in situ), basal cell carcinoma, or squamous cell carcinoma;
 - Personal history of melanoma or dysplastic nevus syndrome;
 - Non-erythropoietic protoporphyria (EPP) skin disorders such as xeroderma pigmentosum, epidermolysis bullosa, polymorphous light eruption (PLE), discoid light eruption (DLE), solar urticaria or due to other porphyrias such as porphyria cutanea tarda and congenital erythropoietic porphyria, **AND**
6. Standard dose is one 16mg implant inserted subcutaneously above the supra-iliac crest every 2 months.
Administration more frequently than every 2 months (shorter dose interval) will not be covered.
7. A quantity limit of 3 implants per year during periods of high sunlight exposure will apply.
Requests for more than 3 implants per year will be evaluated on a case-by-case basis with prescriber documentation of medical necessity.
8. Initial approval will be for 6 months.
9. Recertification will require the following:
 - Documentation of a positive response to treatment such as decreased frequency and severity of phototoxic reactions, increased duration of sun exposure, increased quality of life, **AND**

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- Patient has been examined to monitor preexisting and new skin pigmentary lesions
- Recertification timeframe after the initial approval will be for one year and will be limited to the total number of implants approved for that year. For example: recertification for one year with approval for a maximum of 3 implants to be administered every 2 months during the period of high sunlight exposure.

Additional drug information

Scenesse must be administered by a health care professional proficient in the subcutaneous implantation procedure; therefore, it is covered under the medical benefit.

HCPCS: J7352

Signifor LAR - pasireotide (Medical)

1. Must be prescribed by, or in consultation with, an endocrinologist **AND**
2. Must have a diagnosis of Cushing's disease
 - a. Must not be a candidate for surgery or have had treatment failure with previous surgery. A non-surgical candidate is defined as either having a medical contraindication to surgery or having a tumor which is surgically unapproachable.
 - b. A mean free cortisol (mUFC) level will be required at baseline and upon recertification.
 - c. Initial approval for Cushing's disease will be for 3 months. Continuation of therapy will require evidence of a reduction in mUFC from baseline. For individuals who achieve a reduction in mUFC after 3 months, recertification will be required every 12 months. **OR**
3. Must have a diagnosis of acromegaly
 - a. Must fail to achieve full biochemical control (Growth hormone <2.5 mcg/L and normal IGF1) on maximally tolerated treatment with lanreotide acetate (J1930 or J1932)
 - i. The required use of lanreotide acetate (J1930 or J1932) applies to all lines of business for new starts only.
 - b. Recommended dosing for acromegaly: The initial dose is 40 mg by intramuscular injection once every 4 weeks. The dose may be increased to a maximum of 60 mg for patients who have not normalized growth hormone (GH) and/or age and sex adjusted insulin-like growth factor-1 (IGF-1) levels after 3 months of treatment with Signifor LAR at 40 mg and who tolerate this dose.
 - c. Initial approval and recertification for acromegaly will be for 12 months at a time.

Recertification will require the following:

 - i. Recertification after the initial 12 months will require documentation of response to therapy, including:
 1. Reduction or stabilization in tumor volume from baseline assessed by MRI after initial 6 months of therapy **OR**
 2. Mean growth hormone (GH) less than 2.5 mcg/L and/or a normal insulin-like growth factor- 1 (IGF-1) level after at least 12 months of initial therapy
 - ii. Yearly recertification thereafter will require documentation that the patient has maintained a clinical response to treatment.
4. Quantity limit of 1 injection (maximum 60 mg) every 28 days.

HCPCS: J2502

Signifor SC – pasireotide solution (Rx)

1. Must be prescribed by, or in consultation with, an endocrinologist **AND**
2. Must have a diagnosis of Cushing's disease **AND**
3. Must not be a candidate for surgery or have had treatment failure with previous surgery. A non-surgical candidate is defined as either having a medical contraindication to surgery or having a tumor which is surgically unapproachable.
4. A mean free cortisol (mUFC) level will be required at baseline and upon recertification.

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5. Initial approval will be for 3 months. Continuation of therapy will require evidence of a reduction in mUFC from baseline. For individuals who achieve a reduction in mUFC after 3 months, recertification will be required every 12 months.
6. Usual dosage is 0.3 to 0.9mg SC twice a day
7. Quantity limit of 60 doses per 30 days

Skyclarys-omaveloxolone (Rx)

1. Must be prescribed by a neurologist or prescriber knowledgeable in the management of Friedreich's ataxia (FA) **AND**
2. Must be 16 age or older **AND**
3. Must have a diagnosis of FA confirmed by genetic testing [Note: 96% of affected individuals have homozygous GAA trinucleotide repeat expansions in the first intron of the FXN gene with the remaining individuals being compound heterozygous for a GAA expansion and a FXN point/insertion/deletion mutation]
4. Initial and recertification will be for 12 months at a time. Recertification requests will require documentation that the patient continues to benefit from therapy (i.e., medical assessment demonstrating disease progression has slowed). NOTE: Due to the heterogeneous nature of the disease, physician attestation of clinical benefit may be considered upon recertification.
5. Quantity limit: 90 capsules/30 days

Skysona-elivaldogene autotemcel (Medical)

1. Must be prescribed by an endocrinologist, neurologist, hematologist/oncologist, or prescriber who specializes in the management of cerebral adrenoleukodystrophy (CALD)
2. Must be designated male at birth **AND**
3. Must be 4-17 years of age **AND**
4. Must have a diagnosis of early, active cerebral adrenoleukodystrophy (CALD) defined as:
 - a. Neurologic function score, NFS ≤ 1 **AND**
 - b. Have gadolinium enhancement on brain magnetic resonance imaging (MRI) **AND**
 - c. Loes scores of 0.5-9. **AND**
5. Confirmed adenosine triphosphate binding cassette, sub family D, member 1 (*ABCD1*) gene mutation **AND**
6. Patient must **NOT** have a full *ABCD1*-gene deletion **AND**
7. Must have elevated very-long-chain fatty acid (VLCFA) values for all the following (see Appendix for VLCFA reference values in CALD):
 - a. Concentration of C26:0
 - b. Ratio of C24:0/C22:0
 - c. Ratio of C26:0/C22:0 **AND**
8. Patient must have negative serologic test for HIV infection (as per US FDA prescribing label, apheresis material from individuals with a positive test for HIV will not be accepted for Skysona manufacturing) **AND**
9. Patient has been screened for hepatitis B (HBV), hepatitis C (HCV), human immunodeficiency virus 1 & 2 (HIV-1/HIV-2) and human T-lymphotropic virus 1 & 2 (HTLV-1/HTLV-2) in accordance with clinical guidelines before collection of cells for manufacturing **AND**
10. Patient must **NOT** have active, uncontrolled HBV or HCV infection **AND**
11. Patient must **NOT** have any of the following indicators of hematological compromise:
 - a. Peripheral blood absolute neutrophil count (ANC) count < 1500 cells/mm³
 - b. Platelet count $< 100,000$ cells/mm³
 - c. Hemoglobin < 10 g/dL
 - d. Uncorrected bleeding disorder
12. Patient must **NOT** have any of the following indicators of hepatic compromise:

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- a. Aspartate transaminase (AST) value > 2.5×upper limit of normal (ULN)
 - b. Alanine transaminase (ALT) value > 2.5×ULN
 - c. Total bilirubin value > 3.0 mg/dL, except if there is a diagnosis of Gilbert's Syndrome and the participant is otherwise stable **AND**
13. Must **NOT** have renal compromise defined as estimated creatinine clearance (CrCl) < 50 mL/min **OR** estimated glomerular filtration rate (eGFR) < 70 mL/min/1.73 m² **AND**
14. **Prescriber must attest ALL the following:**
- a. Patient does **NOT** have a contraindication to the use of granulocyte colony stimulating factor (G-CSF), plerixafor, busulfan, cyclophosphamide, fludarabine, or any other medicinal products required during myeloablative and lymphodepleting conditioning including hypersensitivity to the active substances or to any of the excipients **AND**
 - b. Patient will avoid concomitant therapy with antiretroviral medications for at least one month prior to initiating medications for stem cell mobilization and for the expected duration for elimination of the medications, and until all cycles of apheresis are completed (Note: if a patient requires antiretroviral for HIV prophylaxis, confirm a negative test for HIV before beginning mobilization) **AND**
 - c. Patient will receive periodic lifelong monitoring for hematological malignancies (including myelodysplastic syndrome (MDS)) **AND**
 - d. Patient will **NOT** be administered vaccinations within the 6-weeks prior to the start of therapy and will **NOT** be administered concurrently while on therapy **AND**
 - e. Patient is up to date with all age-appropriate vaccinations, in accordance with current vaccination guidelines, prior to initiating therapy **AND**
 - f. Patient does not have a known and available human leukocyte antigen (HLA)-matched family donor **AND**
 - g. Patient is clinically stable and eligible for hematopoietic stem cell transplantation
 - h. Patient does **NOT** have isolated pyramidal tract disease
 - 1) NOTE: Patients with isolated pyramidal tract disease will be reviewed on a case-by-case basis
 - i. Patient does **NOT** have an active infection, including clinically important localized infections **AND**
 - j. Patient does **NOT** have an immediate family member with a known or suspected Familial Cancer Syndrome (including but not limited to hereditary breast and ovarian cancer syndrome, hereditary non-polyposis colorectal cancer syndrome, and familial adenomatous polyposis).
15. **Coverage will not be granted for any of the following:**
- a. Treatment of adrenal insufficiency due to adrenoleukodystrophy
 - b. Treatment of CALD secondary to head trauma
 - c. Prior history of HSCT
 - d. If the patient has previously received gene therapy
16. Skysona is indicated for one-time single-dose intravenous use only and therefore will not be authorized for retreatment. Authorization will be for 6 months to allow time for administration. Retreatment will be considered Experimental/Investigational when any FDA approved gene therapy, or any other gene therapy under investigation, has been previously administered.
17. The minimum recommended dose of Skysona is 5.0 × 10⁶ CD34+ cells/kg.
- a. Please refer to Skysona FDA-approved prescribing information for complete dosage and administration instructions
 - b. Skysona is for autologous use only
18. This indication is approved under accelerated approval based on 24-month Major Functional Disability (MFD)-free survival. Continued approval for this indication may be contingent upon verification and description of clinical benefit in a confirmatory trial(s).

HCPCS: J3387

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Sohonos (palovarotene)-Rx

1. Must be prescribed by or in consultation with an endocrinologist, geneticist, orthopedists, or prescriber specializing in fibrodysplasia ossificans progressiva (FOP) **AND**
2. Must have a diagnosis of FOP **AND**
3. Must have confirmed *ACVR1* R206H mutation **AND**
4. Must have radiographic evidence of heterotopic ossification (HO) (computed tomography (CT) scan, magnetic resonance imaging (MRI), x-ray, positron emission tomography (PET) scan, etc.) **AND**
5. Must meet at least one of the following (a or b):
 - a. Must be 8 years and older and designated female at birth **OR**
 - b. Must be 10 years and older and designated male at birth
6. Initial and recertification approvals will be for 6 months at a time. Recertification requests will require provider attestation that the patient is experiencing clinical benefit from treatment (reduction in annualized HO volume, reduction frequency/intensity of flare-ups, improvement in range of motion, etc.).
7. Quantity limit:
 - 1 mg: 112 tablets/28 days
 - 1.5 mg: 112 tablets/28 days
 - 2.5 mg: 140 tablets/28 days
 - 5 mg: 140 tablets/28 days
 - 10 mg: 56 tablets/28 days

Soliris(eculizumab), Bkembv (eculizumab-aeeb), Epysqli (eculizumab-aagh) (Medical)

Epysqli (eculizumab-aagh) is the preferred eculizumab formulation.

Requests for Soliris (eculizumab) and Bkembv (eculizumab-aeeb) require the use of Epysqli (eculizumab-aagh) OR medical justification as to why Epysqli (eculizumab-aagh) cannot be used.

- **This applies to new starts and existing users for all lines of business except Medicare Advantage.**
- **For Medicare Advantage this requirement only applies to new starts.**
- **All off-label uses of eculizumab will be evaluated based on the off-label policy criteria. If clinical criteria are met, then Epysqli (eculizumab-aagh) will be the required product.**

In addition to the above requirement, the Health Plan considers eculizumab, or eculizumab biosimilars, medically necessary for any of the following indications if the following criteria are met:

- a. Must have a diagnosis of **generalized myasthenia gravis AND**
 - i. Must be 6 years of age or older **AND**
 - ii. Must be followed by a neurologist. If geographically available, it is also recommended for patients to have been evaluated by a neuromuscular specialist. **AND**
 - iii. Must have Myasthenia Gravis Foundation of America (MGFA) clinical classification class II to IV
 - iv. Must be anti-acetylcholine receptor (AChR) antibody positive **AND**
 - v. Must meet one of the following (1 or 2):
 1. Must have had serious side effects or drug failure to ONE of the following treatments for gMG (A or B).
 - A. Corticosteroids for at least 3 months of treatment **OR**
 - B. Non-steroidal immunosuppressive therapy (i.e., azathioprine, mycophenolate mofetil, cyclosporine) for at least 6 months of treatment **OR**
 2. Despite treatment with at least ONE immunosuppressant agent (i.e., corticosteroid, non-steroidal immunosuppressive therapy), the member required at least ONE treatment with plasma exchange, plasmapheresis, or intravenous immunoglobulin within the previous 12 months. **AND**

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- vi. Must have a baseline score of 6 or greater on the Myasthenia Gravis-Activities of Daily Living (MG-ADL) scale **AND**
- vii. The following only applies to patients 18 years of age or older: Must have had serious side effects or drug failure with Vyvgart Hytrulo prefilled syringe (PFS). This applies to New Starts only for all lines of business.
- viii. Soliris/Bkemv/Epysqli will not be approved in combination with Uplizna, Vyvgart/Vyvgart Hytrulo, Rystiggo, Imaavy, Zilbrysq or Ultomiris as this combination has not been studied
- ix. Initial approval will be for 6 months. Recertification after this initial 6-month period will require documentation of at least a 2-point improvement in the MG-ADL baseline score. Recertification will be every 12 months. **AND**
- x. Patients who are currently intubated will be excluded from coverage **OR**
- b. Must have a diagnosis of **paroxysmal nocturnal hemoglobinuria (PNH)** confirmed by a flow cytometry **AND**
 - i. Must be prescribed by a hematologist or nephrologist **AND**
 - ii. For a diagnosis of PNH, must have had serious side effects or drug failure with Ultomiris. This applies to all lines of business including Medicare Part B. This applies to New Starts only.
 - iii. Concomitant use of another complement inhibitor (i.e., Ultomiris (ravulizumab), Empaveli (pegcetacoplan), or Fabhalta (iptacopan)) will only be authorized for patients transitioning from Ultomiris (ravulizumab), Empaveli (pegcetacoplan), Fabhalta (iptacopan) to Soliris/Bkemv/ Epysqli. After the initial approval period, requests for concomitant use of Soliris/Bkemv/Epysqli with Ultomiris (ravulizumab), Empaveli (pegcetacoplan), or Fabhalta (iptacopan) will be considered experimental/investigational and will not be approved.
 - iv. Initial and recertification authorizations for a diagnosis of PNH will be for 6 months at a time. Continued approval will require documentation that patient is tolerating therapy and is responding to treatment (i.e., decrease in number of transfusions, improvement in hemoglobin levels, normalization of LDH levels, symptom improvement) **OR**
- c. Must have a diagnosis of **atypical hemolytic uremic syndrome (aHUS)** confirmed by ADAMTS13 activity level above 5%.
 - i. Patients with Shiga toxin *E. coli* related hemolytic uremic syndrome (STEC-HUS) will be excluded **AND**
 - ii. Must be prescribed by a hematologist or nephrologist **AND**
 - iii. For a diagnosis of aHUS, must have had serious side effects or drug failure with Ultomiris
 - iv. Initial and recertification authorizations for a diagnosis of aHUS will be for 6 months at a time **OR**
- d. Must have a diagnosis of **Neuromyelitis Optica Spectrum Disorder (NMOSD)** confirmed by a positive Anti-AQP4 test
 - i. Must be at least 18 years of age
 - ii. Must be prescribed by an ophthalmologist or neurologist
 - iii. Must have had at least 1 neuromyelitis optica relapse that required rescue therapy (such as corticosteroids or plasma exchange) in the last 12 months
 - iv. For New Starts only—**For all lines of business including Medicare Part B**: Must have had serious side effects or drug failure of Ultomiris.

HCPCS:

J1300	Injection, eculizumab, 10 mg (effective until 3/31/2025)
J1299	Injection, eculizumab, 2 mg (effective 4/1/2025)
Q5151	Injection, eculizumab-aagh (epysqli), biosimilar, 2 mg (effective 4/1/2025)
Q5152	Injection, eculizumab-aeab (bkemv), biosimilar, 2 mg (effective 4/1/2025)

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Somavert – pegvisomant (Rx)

1. Must have a diagnosis of acromegaly
2. Must be prescribed by, or in consultation with, an endocrinologist
3. Patient must have had failure of surgery and/or radiation or is not a candidate for surgery and/or radiation **AND**
4. Patient has had an inadequate response or intolerance to other medical therapies (i.e., cabergoline, bromocriptine, octreotide).
5. IGF-1 levels and liver tests should be monitored and Somavert should be discontinued if LTs are greater than 3 times ULN
6. Quantity limit of 30 vials per 30 days.
 - A quantity limit exception will be granted for a one-time 40 mg loading dose of 2 x 20 mg vials.

Sylvant – siltuximab (Medical)

1. Must be prescribed by an oncologist or hematologist
2. Must have a diagnosis of Multicentric Castleman’s disease (MCD) with pathological confirmation on biopsy of involved tissue **AND**
3. Must be human immunodeficiency virus (HIV) negative and human herpesvirus-8 (HHV-8) negative
4. Approval will be for 1 year at a time. Further approval will require submission of documentation supporting the absence of disease progression (defined as increase in symptoms, radiologic progression, or deterioration in performance status)
5. Recommended dosage is 11mg/kg given over 1 hour by intravenous infusion every 3 weeks

HCPCS: J2860

Syprine, generic trientine capsules and Cuvrior (trientine tablets) (Rx)

1. Must have a diagnosis of Wilson’s Disease **AND**
2. The following age requirements must be met based on the product being requested:
 - a. Requests for Syprine or generic trientine capsules: 6 years and older
 - b. Requests for Cuvrior: 18 years and older **AND**
3. Must have had serious side effects or drug failure with penicillamine capsules (generic for Cuprimine) **AND**
4. Based on comparable indications, efficacy, safety profiles and dosing, ALL requests for trientine 500 mg capsules, Cuvrior, and Syprine will require use of generic trientine 250 mg capsules unless there is adequate justification by the prescriber as to why generic trientine 250 mg capsules are not clinically appropriate.
5. Quantity limit
 - a. Syprine and generic trientine 250 mg capsules: 240 capsules per 30 days
 - b. Cuvrior: 280 tablets per 28 days
 - c. Trientine 500 mg capsules: 120 capsules per 30 days

Tarpeyo-budesonide delayed release capsules (Rx)

1. Must be prescribed by, or in consultation with, a nephrologist **AND**
2. Must be 18 years of age or older **AND**
3. Must have a diagnosis of primary immunoglobulin A nephropathy (IgAN), confirmed on biopsy **AND**
4. Must have an eGFR ≥ 35 mL/min/1.73 m² **AND**
5. Must have proteinuria defined as ≥ 1 g/day **OR** urine protein creatinine ratio (UPCR) ≥ 0.8 g/g **AND**
6. Must be on an angiotensin-converting enzyme inhibitor (ACEi) or an angiotensin II receptor blocker (ARB) at the maximum or maximally tolerated dose for a minimum of 3 months, unless there is documentation that the patient is unable to tolerate or treatment with an ACEi or ARB is contraindicated **AND**
7. Must meet **ONE** of the following:

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- a. Must have documentation of drug failure after a minimum 3-month trial with an SGLT2 inhibitor, unless the patient has documentation of serious side effects or contraindication to an SGLT2 inhibitor **OR**
- b. Must have documentation of drug failure after a minimum 6-week trial of systemic oral glucocorticoids (i.e., prednisone, methylprednisolone), unless the patient has documentation of serious side effects or contraindication to systemic oral glucocorticoids **AND**
8. Requests for non-FDA approved indications will not be covered.
9. Tarpeyo will not be approved in combination with Filspari, Voyxact, Fabhalta, or Vanrafia
10. Approval will be granted for 10 months. Retreatment will not be covered as the safety and efficacy of treatment with subsequent courses of Tarpeyo have not been established.
11. Recommended dosage is 16 mg administered orally once daily in the morning at least 1 hour before a meal. When discontinuing, reduce dosage to 8 mg once daily for the last two weeks.
12. Quantity Limit: 120 capsules/30 days (maximum of 1,108 capsules/365 days). Quantity limit exceptions will not be authorized.

Tavneos- avacopan (Rx)

1. Must be 18 years of age or older **AND**
2. Must be prescribed by or in consultation with a rheumatologist, nephrologist, pulmonologist, or immunologist **AND**
3. Must have a diagnosis of anti-neutrophil cytoplasmic autoantibody (ANCA)-associated vasculitis (granulomatosis with polyangiitis [GPA] or microscopic polyangiitis [MPA]) **AND**
4. Prescriber must attest that the patient has active and severe disease
 - a. Active disease is defined as new, persistent, or worsening clinical signs and/or symptoms attributed to GPA or MPA and not related to prior damage
 - b. Severe disease is defined as vasculitis with life- or organ-threatening manifestations (i.e., alveolar hemorrhage, glomerulonephritis, central nervous system vasculitis, mononeuritis multiplex, cardiac involvement, mesenteric ischemia, limb/digit ischemia) **AND**
5. Must have a positive test for antibodies to either proteinase 3 (PR3) or myeloperoxidase (MPO)
 - a. If patient tests negative for PR3 or MPO antibodies, then histological evidence of GPA or MPA via biopsy will be acceptable **AND**
6. Tavneos must be used as adjunctive treatment in combination with standard of care therapy (i.e., cyclophosphamide, azathioprine, mycophenolate mofetil, rituximab, glucocorticoids) **AND**
7. Must have an estimated glomerular filtration rate (eGFR) ≥ 15 mL/min/1.73m² **AND**
8. Tavneos will not be approved for Eosinophilic Granulomatosis with Polyangiitis (EGPA)
9. Initial approval will be for 6 months. Recertification will require documentation of disease remission, defined as the absence of clinical signs or symptoms attributed to GPA or MPA while on Tavneos. Recertification requires that Tavneos will be used in combination with standard of care therapy. Recertifications will be approved for 2 years. Given the heterogenous nature of this disease that may have multi-organ involvement, consideration may be given on recertification from prescriber showing clear improvement in symptoms attributed to the use of Tavneos which warrants continued use (such as reduced rate of relapse, corticosteroid dose reduction, improvement in eGFR and albuminuria)
10. Quantity limit: 180 capsules/30 days.

Tepezza –teprotumumab-trbw (Medical)

Based on currently available published, peer-reviewed literature, Tepezza is considered **medical necessary** when the following are met:

1. Member must be at least 18 years old **AND**
2. Must be prescribed by an endocrinologist or ophthalmologist **AND**
3. Must have a diagnosis of Graves' disease with active thyroid eye disease (TED) **AND**
4. Must have a score of at least 4 on the Clinical Activity Score (CAS) **AND**
5. Documentation within the past 12 months must be provided to indicate one of the following:

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- a. Patient is euthyroid prior to starting treatment **OR**
 - b. Patient has mild hypo- or hyperthyroidism defined as a free thyroxine (T4) and free triiodothyronine (T3) levels less than 50% above or below the normal limits **AND** patient is currently receiving treatment to correct thyroid levels
6. FDA approved dosing is 10 mg/kg for the first infusion, followed by 20 mg/kg every 3 weeks for 7 additional infusions.
- a. If the prescriber agrees to dose rounding, then the approved dose may be rounded down to the nearest 500 mg vial if the resulting reduction is less than or equal to 10% of the calculated FDA-approved weight-based dose. This applies to all lines of business for new starts only.
7. Approval will be for 24 weeks to allow for 8 infusions total
8. Retreatment is considered not medically necessary and will not be covered based on currently available literature
9. The CAS Score includes the following elements (Note: a 7-point scale excluding the last three elements (h-j) is used when no previous assessment is available):
- a. Spontaneous retrobulbar pain
 - b. Pain on eye movements
 - c. Eyelid erythema
 - d. Conjunctival injection
 - e. Chemosis
 - f. Swelling of the caruncle
 - g. Eyelid edema or fullness
 - h. Increase in proptosis ≥ 2 mm
 - i. Decreased eye movements $\geq 5^\circ$ any direction
 - j. Decreased visual acuity ≥ 1 line of Snellen chart

HCPCS: J3241

Thiola, generic tiopronin, Thiola EC, Venxxiva, and generic tiopronin delayed release (Rx)

1. Must be prescribed by a nephrologist, urologist, or physician knowledgeable in the treatment of cystinuria **AND**
2. Must have a diagnosis of severe homozygous cystinuria established by **ONE** of the following:
 - a. Stone analysis showing 100% cystine calculi **OR**
 - b. Pathognomonic hexagonal cystine crystals on urine microscopy **OR**
 - c. Genetic test confirming two defects in *SLC7A9* and/or *ALC3A1* gene **AND**
3. Must weigh 20 kg or greater **AND**
4. Prescriber must attest that the patient is unresponsive to high fluid intake, urine alkalization, and diet modification (i.e., sodium and protein restriction) **AND**
5. Prescriber must attest that the patient will continue high fluid intake, urine alkalization, and diet modification in combination with requested therapy
6. Initial authorization will be for 12 months. Recertification will be every 12 months and require evidence of clinical response defined as urinary cystine concentration < 250 mg/L **OR** decrease in cystine stone formation.
7. Quantity Limit:
 - a. Thiola/tiopronin 100 mg: 300 tablets/30 days
 - b. Thiola EC/Venxxiva/tiopronin delayed-release
 - i. 100 mg: 300 tablets/30 days
 - ii. 300 mg: 90 tablets/30 days

Note: Initial dosing is 800 mg per day. A multi-clinic trial demonstrated an average dose of approximately 1,000 mg/day. Dosage can be adjusted depending on urinary cystine levels.

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Exceptions to the quantity limit can be made when there is documentation of conservative therapy in combination with standard dosing of Thiola/tiopronin. Conservative treatment includes Intake of at least 3 L of fluid (ten 10 oz. glassfuls), including 2 glasses with each meal and at bedtime. The patients should be expected to awake at night to urinate; they should drink 2 more glasses of fluids before returning to bed. Additional fluids should be consumed if there is excessive sweating or intestinal fluid loss. A minimum urine output of 2 L/day on a consistent basis should be sought. A modest amount of alkali should be provided in order to maintain urinary pH at a high normal range (6.5 to 7).

Tryngolza (olezarsen)- Rx

1. Must be prescribed by or in consultation with a cardiologist, lipid specialist, endocrinologist, or gastroenterologist **AND**
2. Must be 18 years of age and older **AND**
3. Must have a diagnosis of Familial Chylomicronemia Syndrome (FCS) **AND**
4. Must have fasting triglycerides (TGs) of ≥ 880 mg/dL (or 10 mmol/L) within the past 6 months **AND**
5. Must have genetic testing performed and meet one of the following (a or b):
 - a. Genetic testing confirms biallelic pathogenic variants (i.e., homozygosity, compound heterozygosity or double heterozygosity) in FCS-causing genes.
 - i. Examples of FCS-causing genes include lipoprotein lipase (LPL), apolipoprotein C-II (APOC2), apolipoprotein C-VI (APOA5), glycosylphosphatidylinositol-anchored high-density lipoprotein binding protein 1 (GPIHBP1), lipase maturation factor 1 (LMF1) **OR**
 - b. Genetic testing is inconclusive (i.e., one or more variants of uncertain significance were identified) and one of the following are met (i, ii, or iii):
 - i. Must have a familial chylomicronemia syndrome (FCS) score ≥ 10 [see Appendix] **OR**
 - ii. Must have a North American familial chylomicronemia syndrome (NAFCS) score ≥ 45 [see Appendix]
 - A. NOTE: In patients ≥ 10 years of age, the NAFCS tool should only be used for patients who are not responsive to fibrates and high-dose omega-3 fatty acids even when the patient is adherent to therapy **OR**
 - iii. Must meet the following (A, B, and C):
 - A. Must be refractory to refractory to standard triglyceride therapies (e.g., statins, fibrates, high-dose omega-3 fatty acids) **AND**
 - B. Other causes of hypertriglyceridemia have been ruled out (e.g., alcohol excess, uncontrolled type 2 diabetes, medications and medical conditions known to raise triglycerides) **AND**
 - C. One of the following is met (1 or 2):
 1. History of acute pancreatitis **OR**
 2. History of recurrent abdominal pain without other known cause **AND**
 6. Must have documentation or prescriber attestation that the patient has implemented appropriate dietary fat restrictions (e.g., consuming < 20 g of fat per day) to manage FCS.
 7. Tryngolza will not be covered for any other non-FDA approved indications
 8. Initial approval is for 6 months. Recertification will be every 12 months. Recertifications will require documentation of reduction in fasting TGs from baseline.
 9. Quantity Limit: 80 mg/0.8 mL (1 autoinjector) per 28 days

Tzield - teplizumab-mzww (Medical)

1. Must be prescribed by an endocrinologist **AND**
2. Must be 1 year of age or older **AND**
3. Must have a diagnosis of Stage 2 type 1 diabetes defined as (documentation must be submitted for criterion 3a and 3b):
 - a. At least two of the following pancreatic islet autoantibodies must be confirmed:

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- i. Glutamic acid decarboxylase 65 (GAD) autoantibodies
- ii. Insulin autoantibody (IAA)
- iii. Insulinoma-associated antigen 2 autoantibody (IA-2A)
- iv. Zinc transporter 8 autoantibody (ZnT8A)
- v. Islet cell autoantibody (ICA) **AND**
- b. Dysglycemia without overt hyperglycemia as determined by oral glucose tolerance testing (OGTT), confirmed on **two separate occasions** within the previous 7 weeks. Note: Individuals < 18 years of age only require **a single abnormal OGTT result** within the previous 7 weeks.
 - i. Dysglycemia is defined as:
 1. Fasting plasma glucose level > 110 mg/dL and < 126 mg/dL **OR**
 2. 2-hour plasma glucose \geq 140 mg/dL and < 200 mg/dL **OR**
 3. 30,60-, or 90-minute value on OGTT \geq 200 mg/dL **AND**
4. Prescriber must attest that the patient does not have clinical history that suggests type 2 diabetes **AND**
5. Tzield will not be covered for use in patients with Stage 3 Type 1 diabetes
6. Tzield will not be covered for any other non-FDA approved indication
7. Approval will be for 3 months to allow for 14-day treatment course.
8. Retreatment beyond a 14-day treatment course will be considered experimental/investigational and will not be authorized.
9. Tzield is administered by intravenous infusion (over a minimum of 30 minutes), using a body surface area-based dosing, once daily for 14 consecutive days. See package insert for complete dosing and administration.

HCPCS: J9381

Ultomiris – ravulizumab-cwvz injection (Medical)

1. Must be one month of age or older **AND**
2. Must have a diagnosis of **paroxysmal nocturnal hemoglobinuria (PNH)** confirmed by a flow cytometry **AND**
 - a. Must be prescribed by a hematologist or nephrologist
 - b. Concomitant use of another complement inhibitor (i.e., Soliris/Bkemv/Epysqli (eculizumab), Empaveli (pegcetacoplan), or Fabhalta (iptacopan)) will only be authorized for patients transitioning from Soliris/Bkemv/Epysqli (eculizumab), Empaveli (pegcetacoplan), or Fabhalta (iptacopan) to Ultomiris. After the initial approval period, requests for concomitant use of Ultomiris with Soliris/Bkemv/Epysqli (eculizumab), Empaveli (pegcetacoplan), or Fabhalta (iptacopan) will be considered experimental/investigational and will not be approved.
 - c. Initial and recertification authorizations for a diagnosis of PNH will be for 6 months at a time. Continued approval will require documentation that patient is tolerating therapy and is responding to treatment (i.e., decrease in number of transfusions, improvement in hemoglobin levels, normalization of LDH levels, symptom improvement) **OR**
3. Must have a diagnosis of **atypical hemolytic uremic syndrome (aHUS)** confirmed by ADAMTS13 activity level above 5%
 - a. Patients with Shiga toxin *E. coli* related hemolytic uremic syndrome (STEC-HUS) will be excluded **AND**
 - b. Must be prescribed by a hematologist or nephrologist
 - c. Initial and recertification authorizations for a diagnosis of aHUS will be for 6 months at a time **OR**
4. Must have a diagnosis of **generalized myasthenia gravis (gMG)** **AND**
 - a. Must be 18 years of age or older **AND**
 - b. Must be prescribed by or in consultation with a neurologist. If geographically available, it is also recommended for patients to have been evaluated by a neuromuscular specialist **AND**
 - c. Must have Myasthenia Gravis Foundation of America (MGFA) clinical classification class II to IV **AND**

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- d. Must be anti-acetylcholine receptor (AChR) antibody positive **AND**
 - e. Must have documentation of a baseline Myasthenia Gravis Activities of Daily Living (MG-ADL) score of at least 6 **AND**
 - f. Must meet one of the following (i or ii)
 - i. Must have had serious side effects or drug failure to ONE of the following treatments for gMG (1 or 2).
 - 1. Corticosteroids for at least 3 months of treatment **OR**
 - 2. Non-steroidal immunosuppressive therapy (i.e., azathioprine, mycophenolate mofetil, cyclosporine) for at least 6 months of treatment **OR**
 - ii. Despite treatment with at least ONE immunosuppressant agent (i.e., corticosteroid, non-steroidal immunosuppressive therapy), the member required at least ONE treatment with plasma exchange, plasmapheresis, or intravenous immunoglobulin within the previous 12 months. **AND**
 - g. Must have had serious side effects or drug failure with Vyvgart Hytrulo prefilled syringe (PFS). This applies to New Starts only for all lines of business.
 - h. Ultomiris will not be approved in combination with Uplizna, Vyvgart/Vyvgart Hytrulo, Rystiggo, Imaavy, Zilbrysq, or Soliris/Bkempv/Epysqli as this combination has not been studied
 - i. Initial approval will be for 6 months. Recertification after this initial 6-month period will require documentation of ≥ 2 -point reduction in MG-ADL. Recertification will be required every 12-month
5. Must have a diagnosis of **Neuromyelitis Optica Spectrum Disorder (NMOSD)** confirmed by a positive Anti-AQP4 test
- a. Must be at least 18 years of age
 - b. Must be prescribed by an ophthalmologist or neurologist
 - c. Must have had at least 1 neuromyelitis optica relapse that required rescue therapy (such as corticosteroids or plasma exchange) in the last 12 months
 - d. Must have had serious side effects or drug failure of Enspryng and Uplizna. This applies to all lines of business including Medicare Part B. This applies to New Starts only.
6. All other non-FDA approved indications will be excluded from coverage

HCPCS: J1303

Uplizna – inebilizumab-cdon (Medical)

- 1. Uplizna is considered medically necessary for the treatment of **Neuromyelitis Optica Spectrum Disorder (NMOSD)** when the following criteria are met:
 - a. Must be at least 18 years of age **AND**
 - b. Must be prescribed by an ophthalmologist or neurologist **AND**
 - c. Must have a diagnosis of NMOSD confirmed by a positive anti-aquaporin-4 (AQP4) antibody test **AND**
 - d. Must have had at least 1 neuromyelitis optica relapse that required rescue therapy (such as corticosteroids or plasma exchange) in the last 12 months **AND**
 - e. Must have had serious side effects or drug failure with Enspryng. This applies to all lines of business including Medicare Part B. This applies to New Starts only. **OR**
- 2. Uplizna is considered medically necessary for the treatment of **Immunoglobulin (Ig) G4-related disease (IgG4-RD)** when the following criteria are met:
 - a. Must be 18 years of age or older **AND**
 - b. Must be prescribed by or in consultation with a rheumatologist, immunologist, endocrinologist, nephrologist, or prescriber experienced treating IgG4-RD **AND**
 - c. Must have a diagnosis of IgG4-RD **AND**
 - d. Must meet all the following (1, 2, and 3) to confirm diagnosis:
 - i. Must have documentation of ≥ 2 organ system/sites involvement at any time during the disease course and at least ONE of the following organs are affected: pancreas, bile

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- ducts/biliary tree, orbits, lungs, kidneys, lacrimal glands, major salivary glands, retroperitoneum, aorta, pachymeninges, and/or thyroid gland **AND**
- ii. Must have documentation that other condition that mimic IgG4-RD have been ruled out (e.g., infection, malignancy, other autoimmune conditions) **AND**
 - iii. Must have a score of 20 points or greater as outlined in the step 3 inclusion criteria of the 2019 American College of Rheumatology (ACR)/European League Against Rheumatism (EULAR) Classification Criteria for IgG4-RD (see Appendix) **AND**
- e. Must be currently experiencing IgG4- related disease flare (or had a recent flare within the past 12 months) requiring glucocorticoid treatment **AND**
 - f. Must have evidence of steroid-refractory disease (e.g., symptoms do not sufficiently improve, inadequate decrease in serum IgG4 concentrations) or patient is glucocorticoid-dependent and cannot reduce dose sufficiently without experiencing a flare or worsening of symptoms (e.g., patient developing a flare upon the tapering of prednisone below 10 mg/day).
 - g. Initial and recertification authorizations will be for 12 months at a time. Recertification will require documentation that patient is experiencing clinical benefit from therapy (e.g., reduction in flares, reducing glucocorticoid use, symptom improvement). **OR**
3. **Uplizna** is considered medically necessary for the treatment of **generalized myasthenia gravis (gMG)** when the following criteria are met:
- a. Must be 18 years of age or older **AND**
 - b. Must be prescribed by or in consultation with a neurologist. If geographically available, it is also recommended for patients to have been evaluated by a neuromuscular specialist. **AND**
 - c. Must have a diagnosis of generalized myasthenia gravis (gMG) **AND**
 - d. Must have Myasthenia Gravis Foundation of America (MGFA) clinical classification class II to IV **AND**
 - e. Must be anti-acetylcholine receptor (AChR) antibody positive or Muscle-specific kinase (MuSK) positive **AND**
 - f. Must have documentation of a baseline Myasthenia Gravis Activities of Daily Living (MG-ADL) score of at least 6 **AND**
 - g. Must meet one of the following (i or ii)
 - i. Must have had serious side effects or drug failure to ONE of the following treatments for gMG (1 or 2).
 - 1. Corticosteroids for at least 3 months of treatment **OR**
 - 2. Non-steroidal immunosuppressive therapy (i.e., azathioprine, mycophenolate mofetil, cyclosporine) for at least 6 months of treatment **OR**
 - ii. Despite treatment with at least ONE immunosuppressant agent (i.e., corticosteroid, non-steroidal immunosuppressive therapy), the member required at least ONE treatment with plasma exchange, plasmapheresis, or intravenous immunoglobulin within the previous 12 months. **AND**
 - h. **For individuals with AChR positive gMG:** Must have had serious side effects or drug failure with Vyvgart Hytrulo prefilled syringe (PFS). This applies to New Starts only for all lines of business **except Medicare Part B**.
 - i. Uplizna will not be approved in combination with Soliris/Bkemv/ Epysqli, Ultomiris, Vyvgart/Vyvgart Hytrulo, Imaavy, Rystiggo or Zilbrysq, as Uplizna has not been studied in combination with these therapies.
 - j. Initial approvals will be for 6 months. Continued approval will require documentation of ≥ 2 -point improvement in the MG-ADL scale from baseline **OR** prescriber attests that patient is experiencing clinical benefit from treatment (i.e., reduction of myasthenia gravis exacerbations, improvement in symptoms such as swallowing, mobility, breathing). Recertification will be required every 12 months.

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Vanrafia (atrasentan)- Rx

1. Must be prescribed by, or in consultation with, a nephrologist **AND**
2. Must be 18 years of age or older **AND**
3. Must have a diagnosis of primary immunoglobulin A nephropathy (IgAN), confirmed on biopsy **AND**
4. Must have an eGFR ≥ 30 mL/min/1.73 m² **AND**
5. Must provide baseline documentation that meets at least one of the following (note: documentation of the same laboratory parameter will be required upon recertification):
 - a. A total urine protein ≥ 1.0 g/day **OR**
 - b. A urine protein-to-creatinine ratio (UPCR) ≥ 1.5 g/g **AND**
6. Must have received the maximum or maximally tolerated dose of an angiotensin-converting enzyme inhibitor (ACEi) or an angiotensin II receptor blocker (ARB) for a minimum of 3 months prior to starting Vanrafia, unless there is documentation that the patient is unable to tolerate or has a contraindication to an ACEi or ARB **AND**
7. Must meet one of the following:
 - a. Must have documentation of drug failure after a minimum 3-month trial with an SGLT2 inhibitor, unless the patient has documentation of serious side effects or contraindication to an SGLT2 inhibitor **OR**
 - b. Must have documentation of drug failure after a minimum 6-week trial of systemic oral glucocorticoids (i.e., prednisone, methylprednisolone), unless the patient has documentation of serious side effects or contraindication to systemic oral glucocorticoids
8. Initial and recertification approvals will be for 9 months at a time. Continuation of therapy will require the following (documentation must be provided):
 - a. Evidence of one of the following:
 - i. Reduction in total urine protein from baseline **OR**
 - ii. Reduction in UPCR from baseline **AND**
 - b. Must have an eGFR ≥ 30 mL/min/1.73 m²
9. Requests for non-FDA approved indications will not be covered.
10. Vanrafia will not be approved in combination with Filspari, Voyxact, Tarpeyo, or Fabhalta
11. Quantity Limit: 30 tablets/30 days
12. This indication is approved under accelerated approval based on a reduction of proteinuria. Continued approval for this indication may be contingent upon verification and description of clinical benefit in a confirmatory clinical trial.

Veopoz (pozelimab-bbfg)-Medical

1. Must be 1 year of age or older **AND**
2. Must have a diagnosis of CD55-deficient protein-losing enteropathy (PLE), also known as CHAPLE disease, confirmed by biallelic CD55 loss-of function mutation by genetic testing **AND**
3. Must be prescribed by or in consultation with a hematologist, gastroenterologist or prescriber who specializes in the treatment of PLE/CHAPLE disease **AND**
4. Must have active disease defined as:
 - a. Hypoalbuminemia ≤ 3.2 g/dL **AND**
 - b. One of the following signs or symptoms attributable to PLE/CHAPLE disease within the previous 6 months:
 - i. Diarrhea
 - ii. Vomiting
 - iii. Abdominal pain
 - iv. Peripheral or facial edema
 - v. Infection with concomitant hypogammaglobulinemia
 - vi. New thromboembolic event

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5. Veopoz will not be approved in combination with other complement inhibitors (e.g., Soliris/Bkemv/ Epsqli (eculizumab), Ultomiris (ravulizumab-cwvz))
6. See full prescribing information for recommended dosing
7. Initial approval will be for 6 months. Recertification will be for 12 months at a time and require documentation of clinical benefit (such as improvement in clinical symptoms [e.g., abdominal pain, bowel movement frequency, facial or peripheral edema severity], increase or stabilization of albumin and IgG concentrations, increase in growth percentiles).

Vijoice-alpelisib (Rx)

1. Must be 2 years of age or older **AND**
2. Must be prescribed by a prescriber who specializes in PIK3CA-Related Overgrowth Spectrum (PROS) **AND**
3. Must have a diagnosis of PROS, confirmed by a prescriber specializing in PROS **AND**
4. Must have documentation of a mutation in the PIK3CA gene **AND**
5. Prescriber must attest that the patient's condition is severe or life threatening **AND**
6. Must have at least one target lesion identified on imaging at baseline **AND**
7. Must provide a baseline sum of measurable target lesion volume
8. Vijoice will not be covered for any other diagnosis
9. Recommended dosing in adult patients is 250 mg orally, once daily, administered as recommended until disease progression or unacceptable toxicity. Recommended dosing in pediatric patients (2 to less than 18 years of age) is 50 mg orally, once daily, administered as recommended until disease progression or unacceptable toxicity. See full prescribing information for complete dosing and administration recommendations.
10. Initial approval will be for 6 months. Recertification will be for 12 months at a time and will require documentation of:
 - a. A decrease from baseline in sum of measurable target lesion volume, without debulking surgery, confirmed by at least one imaging assessment, in the absence of $\geq 20\%$ increase from baseline in any target lesion, progression of a non-target lesions, or appearance of any new lesions
11. Quantity limit:
 - a. 50 mg oral granules: 28 packets/28 days
 - b. 50 mg/day pack and 125 mg/day pack: 28 tablets/28 days
 - c. 250 mg/day pack: 56 tablets/28 days
12. **Note:** for applicable lines of businesses (Commercial, Exchange, Child Health Plus), a split-fill program will apply to new starts only for Vijoice 250 mg/day doses. An override to bypass the split-fill program will be provided for existing users that have been maintained on Vijoice.
13. 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 a confirmatory trial(s).

Voxzogo-vosoritide (Rx)

1. Must be prescribed by, or in consultation with, a geneticist, skeletal dysplasia specialist or pediatric endocrinologist **AND**
2. Must be less than 18 years of age **AND**
3. Must have a diagnosis of achondroplasia, confirmed by genetic testing (gain of function *FGFR3* gene mutation) **AND**
4. Must have documentation of a recent (within previous 6 months) annualized growth velocity (AGV) to establish baseline AGV **AND**
5. One of the following must be met (a or b):
 - a. Annualized growth velocity (AGV) ≥ 1.5 cm/year (based on documentation provided to satisfy criterion #4) **OR**

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- b. Radiographic evidence (within previous 6 months) demonstrating open epiphyses
AND
6. Must not have previous treatment with growth hormone, insulin-like growth factor 1, or anabolic steroids within the previous 6 months
7. Prescriber must attest that patient does not have planned or expected limb-lengthening surgery
 - a. If the patient had limb-lengthening surgery, it must have occurred at least 18 months prior to the Voxzogo request
8. Initial approval will be for 6 months. Recertification requests will be granted for 6 months and require recent (within 6 months) documentation of the following (a and b):
 - a. One of the following are met (i or ii)
 - i. A recent AGV \geq 1.5 cm/year **OR**
 - ii. Radiographic evidence demonstrating open epiphyses
AND
 - b. Evidence of an increase in AGV from baseline
9. Voxzogo will not be authorized if there is documented evidence of closed epiphyses
10. Voxzogo will not be authorized for use in combination with Yuviwel
11. The recommended dose of Voxzogo is based on the patient's body weight (see prescribing information)
12. Quantity limit: 30 vials (3 co-packs)/30 days
13. This indication is approved under accelerated approval based on an improvement in annualized growth velocity. Continued approval for this indication may be contingent upon verification and description of clinical benefit in confirmatory trial(s)

Voydeya-danicopan (Rx)

1. Must be 18 years of age or older **AND**
2. Must be prescribed by a hematologist or nephrologist **AND**
3. Must have a diagnosis of paroxysmal nocturnal hemoglobinuria (PNH) confirmed by a flow cytometry test **AND**
4. Must be receiving ravulizumab (e.g., Ultomiris) or eculizumab (e.g., Soliris, Bkemy, Epysqli) therapy for at least 6 months **AND**
5. Must have documented evidence of extravascular hemolysis (EVH) while receiving ravulizumab (e.g., Ultomiris) or eculizumab (e.g., Soliris, Bkemy, Epysqli). [examples of EVH: anemia, elevated absolute reticulocyte count, elevated LDH, elevated bilirubin, increase in transfusion requirements, etc.] **AND**
6. Prescriber must attest that Voydeya will be used in combination with ravulizumab (e.g., Ultomiris) or eculizumab (e.g., Soliris, Bkemy, Epysqli) **AND**
7. Voydeya will not be authorized in combination with any other complement inhibitor beyond those included in the FDA-labeled indication (e.g., Empaveli (pegcetacoplan), Fabhalta (iptacopan), Piasky (crovalimab)) as these combinations have not been studied and will be considered experimental/investigational.
8. Voydeya will not be authorized for any other non-FDA approved indication.
9. Initial approval for 6 months. Continued approval will be for 6 months and will require documentation that the patient is tolerating therapy and is responding to treatment (i.e., decrease in number of transfusions, improvement in hemoglobin levels, normalization of LDH levels, symptom improvement).
10. Quantity Limit: 180 tablets/30 days

Vyjuvek (beremagene geperpavec-svdt) (Medical or Rx)

1. Must be prescribed by, or in consultation with, a dermatologist or pediatric dermatologist, or clinical expert in epidermolysis bullosa (EB) **AND**
2. Must have a diagnosis of dystrophic epidermolysis bullosa (DEB) [either recessive DEB (RDEB) or dominant DEB (DDEB)] **AND**

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3. Must have confirmed mutation(s) in the collagen type VII alpha 1 chain (COL7A1) gene **AND**
4. Must have documentation within the previous month indicating which cutaneous wound(s) will be treated with Vyjuvek.
5. If Vyjuvek is being **administered by the patient or caregiver**, Vyjuvek will be considered for coverage on the **pharmacy benefit**. If Vyjuvek is being **administered by a healthcare professional**, Vyjuvek will be considered for coverage on the **medical benefit**.
6. Vyjuvek will not be authorized in combination with Filsuvez (birch triterpenes gel) or Zevaskyn for the treatment of the same wound (s)
7. Vyjuvek will not be authorized for concomitant use with Filsuvez or Zevaskyn for the treatment of different wounds located on different areas of the body, unless there is adequate documentation justifying the need for separate products on different wounds located on different areas of the body.
8. Use of Vyjuvek on a wound(s) previously treated with Filsuvez or Zevaskyn requires adequate documentation demonstrating inadequate response or treatment failure to previous treatment(s).
9. The recommended dosage of Vyjuvek gel is based on age (see prescribing information for dosing) and is applied topically to wound(s) once a week. Based on the prescribing information, no more than one vial per week of mixed Vyjuvek gel should be used (NOTE: mixed Vyjuvek gel includes Vyjuvek biological suspension combined with excipient gel).
10. Initial approval will be for 6 months. Recertification will be for 6 months at a time and require documentation of clinical improvement in the treated wound(s) **AND**
 - a. The treated wound(s) has not completely closed or has re-opened **OR**
 - b. New, previously untreated wound(s) require treatment
11. Quantity Limit: 10 mL allowed in a 28-day period.

Vykat XR (diazoxide choline)-Rx

1. Must be prescribed by or in consultation with an endocrinologist, medical geneticist, or prescriber who specializes in the treatment of Prader-Willi syndrome (PWS) **AND**
2. Must be 4 years of age or older **AND**
3. Must have a diagnosis PWS confirmed with genetic testing establishing abnormal DNA methylation of chromosome 15q11.2-q13 **AND**
4. Must have documentation of hyperphagia (e.g., intense/persistent hunger, extreme food-seeking behaviors) **AND**
5. Must have documentation of recent weight (within 30 days) to ensure appropriate dose **AND**
6. Provider must attest that caregiver or patient have implemented and will continue strategies to establish a food-secure environment **AND**
7. Vykat XR will not be authorized for treatment of hyperphagia in patients without Prader-Willi syndrome
8. Initial approval and recertification will be for 6 months at a time. Recertification will require:
 - a. Recent (within 30 days) documentation of weight to ensure appropriate dose **AND**
 - b. Documentation or provider attestation that Vykat XR is providing clinical benefit (e.g., decrease in food-related symptoms that interfere with activities of daily living)
9. Quantity limit: 30 tablets/30 days
 - a. Upon each drug review and dose escalation request, the allowed quantity will be reviewed in accordance with FDA-approved weight-based dosing and, as such, will be limited to the minimum number of tablets to obtain the appropriate daily dose.

Vyvgart - efgartigimod alfa-fcab (Medical) and Vyvgart Hytrulo efgartigimod alfa and hyaluronidase-qvfc vial (Medical) and prefilled syringe (Rx)

Vyvgart and Vyvgart Hytrulo are considered medically necessary for the treatment of **generalized myasthenia gravis (gMG)** when the following criteria are met:

1. Must be 18 years of age or older **AND**

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2. Must be prescribed by or in consultation with a neurologist. If geographically available, it is also recommended for patients to have been evaluated by a neuromuscular specialist. **AND**
3. Must have a diagnosis of generalized myasthenia gravis (gMG) **AND**
4. Must have Myasthenia Gravis Foundation of America (MGFA) clinical classification class II to IV **AND**
5. Must be anti-acetylcholine receptor (AChR) antibody positive **AND**
6. Must have documentation of a baseline Myasthenia Gravis Activities of Daily Living (MG-ADL) score of at least 5 **AND**
7. Must meet one of the following (a or b)
 - a. Must have had serious side effects or drug failure to ONE of the following treatments for gMG (1 or 2).
 - i. Corticosteroids for at least 3 months of treatment **OR**
 - ii. Non-steroidal immunosuppressive therapy (i.e., azathioprine, mycophenolate mofetil, cyclosporine) for at least 6 months of treatment **OR**
 - b. Despite treatment with at least ONE immunosuppressant agent (i.e., corticosteroid, non-steroidal immunosuppressive therapy), the member required at least ONE treatment with plasma exchange, plasmapheresis, or intravenous immunoglobulin within the previous 12 months **AND**
8. Requests for Vyvgart and Vyvgart Hytrulo vials: Must have an inability to self-inject with Vyvgart Hytrulo prefilled syringe (PFS).
 - i. **Applies to New Starts for all lines of business**
 - ii. **Applies to Existing Users for all non-Medicare Part B lines of business**
9. The recommended dosage for gMG is as follows:
 - a. Vyvgart is 10 mg/kg administered as an IV infusion over one hour once weekly for 4 weeks. In patients weighing 120 kg or more, the recommended dose of Vyvgart is 1200 mg (3 vials) per infusion. Administer subsequent treatment cycles based on clinical evaluation.
 - b. Vyvgart Hytrulo vial is 1,008 mg / 11,200 units administered subcutaneously over approximately 30 to 90 seconds in cycles of once weekly injections for 4 weeks. Administer subsequent treatment cycles based on clinical evaluation.
 - c. Vyvgart Hytrulo prefilled syringe is 1,000 mg / 10,000 units (1,000 mg efgartigimod alfa and 10,000 units hyaluronidase) administered subcutaneously over approximately 20 to 30 seconds in cycles of once weekly injections for 4 weeks. Administer subsequent treatment cycles based on clinical evaluation.
10. Initial approval for gMG will be for 6 months. Continued approval will require documentation of ≥ 2 -point improvement in the MG-ADL scale from baseline **OR** prescriber attests that patient is experiencing clinical benefit from treatment (i.e., reduction of myasthenia gravis exacerbations, improvement in symptoms such as swallowing, mobility, breathing). Recertification will be required every 12 months.

Vyvgart Hytrulo is considered medically necessary for the treatment of **chronic inflammatory demyelinating polyradiculoneuropathy (CIDP)** when the following criteria are met:

1. Must be 18 years of age or older **AND**
2. Must be prescribed by a neurologist or prescriber who specializes in the treatment of CIDP **AND**
3. Must have a confirmed diagnosis of CIDP with supporting documentation (e.g., electrodiagnostic testing, clinical assessment, nerve biopsy) **AND**
4. Must have documentation of baseline score on an objective scale to assess clinical response (e.g., Rankin, Modified Rankin, Medical Research Council (MRC), Inflammatory Rasch-built Overall Disability Scale (I-RODS), Inflammatory Neuropathy Cause and Treatment (INCAT) disability scale) **AND**
5. Must have documentation of serious side effects, contraindication, or drug failure to both of the following treatments:
 - a. Corticosteroid treatment **AND**

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- b. Intravenous or subcutaneous immune globulin (IVIG or SCIG) treatment in the past 24 months
AND
- 6. Requests for Vyvgart Hytrulo vials will require an inability to self-inject Vyvgart Hytrulo prefilled syringe (PFS).
 - i. Applies to New Starts for all lines of business
 - ii. Applies to Existing Users for all non-Medicare Part B lines of business
- 7. Vyvgart will not be authorized for CIDP as it is not FDA-approved for this indication.
- 8. The recommended dosage of Vyvgart Hytrulo for CIDP is 1,008 mg / 11,200 units (1,008 mg efgartigimod alfa and 11,200 units hyaluronidase) administered subcutaneously over approximately 30 to 90 seconds as once weekly injections. If a scheduled injection is missed, Vyvgart Hytrulo may be administered up to 3 days after the scheduled time point. Thereafter, resume the original dosing schedule.
- 9. Initial approval for CIDP will be for 6 months. Continued approval will be for 12 months at a time and require the following:
 - i. Documentation of clinical improvement from baseline on an objective scale (e.g., Rankin, Modified Rankin, Medical Research Council (MRC), Inflammatory Rasch-built Overall Disability Scale (I-RODS), Inflammatory Neuropathy Cause and Treatment (INCAT) disability scale) used for the initial request in criterion 2d.
 - a. Vyvgart/ Vyvgart Hytrulo will not be approved in combination with Uplizna, Soliris/Bkemv/ Epysqli, Ultomiris, Rystiggo, Imaavy, Zilbrysq, intravenous immunoglobulin (other than when used as rescue therapy), or rituximab-containing products as Vyvgart/ Vyvgart Hytrulo has not been studied in combination with these therapies.
 - b. Vyvgart and Vyvgart Hytrulo vials will be covered under the medical benefit as these are intended to be administered by a healthcare provider.
 - c. Vyvgart Hytrulo prefilled syringe (PFS) is intended for self-administration and will be covered under the pharmacy benefit.
 - d. Quantity limit for Vyvgart Hytrulo PFS: 4 syringes (20 mL) per 28 days

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Vyvgart - J9332

Vyvgart Hytrulo - J9334

Xolremdi-mavorixafor (Rx)

- 1. Must be prescribed by an immunologist, hematologist, or prescriber who specializes in the management of WHIM (warts, hypogammaglobulinemia, infections and myelokathexis) syndrome **AND**
- 2. Must be 12 years of age or older **AND**
- 3. Must have a diagnosis of WHIM syndrome confirmed by genotype variant of CXCR4 **AND**
- 4. Must have documentation of the following laboratory values at baseline, to assess clinical response to treatment:
 - a. Absolute lymphocyte count (ALC) **AND**
 - b. Absolute neutrophil count (ANC) **AND**
- 5. Must have ANC of ≤ 400 cells/ μ L prior to starting Xolremdi
- 6. Initial approval will be for 6 months. Recertification will be for 12 months at a time and requires documentation of improvement of ALC and/or ANC from baseline.
 - a. NOTE: If ALC and ANC values do not improve from baseline while on Xolremdi, then documentation must be submitted demonstrating objective clinical response to therapy that warrants continuation of Xolremdi (e.g., reduction or improvement in frequency, duration, or severity of infections; reduction in the need for antibiotics; fewer warts; improvement in white blood cell count (WBC) or absolute monocyte count (AMC)).
- 7. Quantity Limit: 120 capsules/30 days

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Yorvipath (palopegteriparatide)- Rx

1. Must be 18 years of age and older **AND**
2. Must be prescribed by or in consultation with an endocrinologist **AND**
3. Must have a diagnosis of chronic hypoparathyroidism of postsurgical, autoimmune, genetic, or idiopathic etiologies for at least 6 months **AND**
4. Must have documented history of hypocalcemia in the setting of inappropriately low serum parathyroid (PTH) levels **AND**
5. Patient must currently be receiving conventional therapy for hypoparathyroidism consisting of active vitamin D (calcitriol) and calcium supplementation **AND**
6. Prescriber must attest to the following (a and b):
 - a. The patient's hypoparathyroidism cannot be adequately controlled with conventional therapy alone **AND**
 - b. Prior to initiating Yorvipath, the following will be verified in accordance with the FDA-approved prescribing information (i and ii):
 - i. Serum 25(OH) vitamin D levels are within normal range **AND**
 - ii. Albumin-corrected serum calcium is ≥ 7.8 mg/dL (or ionized serum calcium is ≥ 4.40 mg/dL) **AND**
7. Yorvipath will not be authorized for *acute* postsurgical hypoparathyroidism (defined as postsurgical hypoparathyroidism for a duration of less than 6 months) **AND**
8. Yorvipath will not be authorized in combination with any other PTH analogs (e.g., teriparatide) **AND**
9. Yorvipath will not be authorized for non-FDA approved indications.
10. Initial and recertification approval will be for 12 months at a time. Recertification requests will require prescriber attestation the patient is demonstrating clinical benefit from therapy (e.g., reduction in dose or discontinuation of active vitamin D and/or therapeutic doses of elemental calcium; maintenance of albumin-adjusted serum calcium within normal range).
11. Quantity limit: 2 pens per 28 days

Zevaskyn (prademagene zamikeracel)-Medical

1. Must be prescribed by, or in consultation, with a dermatologist or pediatric dermatologist, or clinical expert in epidermolysis bullosa (EB) **AND**
2. Must be 6 years of age or older **AND**
3. Must have a diagnosis of **recessive** dystrophic epidermolysis bullosa (RDEB) confirmed by mutations in both *COL7A1 genes* **AND**
4. Must have documentation within the previous month indicating which cutaneous wound(s) will be treated with Zevaskyn **AND**
5. The wound(s) being treated must be a stage 2 wound, defined as an open skin wound with partial thickness loss of dermis that has not extended through the dermis into subcutaneous tissue **AND**
6. Zevaskyn will not be authorized in combination with Vyjuvek or Filsuvez for treatment of the same wound(s).
7. Zevaskyn will not be authorized for concomitant use with Vyjuvek or Filsuvez for the treatment of different wounds located on different areas of the body, unless there is adequate documentation justifying the need for separate products on different wounds located on different areas of the body.
8. Use of Zevaskyn on a wound(s) previously treated with Vyjuvek or Filsuvez requires adequate documentation demonstrating inadequate response or treatment failure of previous treatment(s).
9. A one-time approval will be authorized for the designated wound(s) to be treated that meet the above criteria. Approval will be authorized for 6 months to allow adequate time to schedule and perform surgical application.
 - a. Reauthorization will not be allowed for wound(s) previously treated with Zevaskyn.
 - b. A new request is required for subsequent wound(s) that have not previously been treated with Zevaskyn. Documentation of wound(s) previously treated with Zevaskyn will be required.

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Zilbrysq (zilucoplan)- Rx

1. Must be 18 years of age or older **AND**
2. Must be prescribed by or in consultation with a neurologist. If geographically available, it is also recommended for patients to have been evaluated by a neuromuscular specialist. **AND**
3. Must have a diagnosis of generalized myasthenia gravis (gMG) **AND**
4. Must have Myasthenia Gravis Foundation of America (MGFA) clinical classification class II to IV **AND**
5. Must be anti-acetylcholine receptor (AChR) antibody positive **AND**
6. Must have documentation of a baseline Myasthenia Gravis Activities of Daily Living (MG-ADL) score of at least 6 **AND**
7. Must meet one of the following (a or b)
 - a. Must have had serious side effects or drug failure to ONE of the following treatments for gMG (i or ii).
 - i. Corticosteroids for at least 3 months of treatment **OR**
 - ii. Non-steroidal immunosuppressive therapy (i.e., azathioprine, mycophenolate mofetil, cyclosporine) for at least 6 months of treatment **OR**
 - b. Despite treatment with at least ONE immunosuppressant agent (i.e., corticosteroid, non-steroidal immunosuppressive therapy), the member required at least ONE treatment with plasma exchange, plasmapheresis, or intravenous immunoglobulin within the previous 12 months. **AND**
8. Must have had serious side effects or drug failure with Vyvgart Hytrulo prefilled syringe (PFS). This applies to New Starts only.
9. Zilbrysq will not be approved in combination with Uplizna, Soliris/Bkemv/ Epysqli, Ultomiris, Vyvgart/Vyvgart Hytrulo, Imaavy, or Rystiggo as Zilbrysq has not been studied in combination with these therapies.
10. Initial approvals will be for 6 months. Continued approval will require documentation of ≥ 2 -point improvement in the MG-ADL scale from baseline **OR** prescriber attests that patient is experiencing clinical benefit from treatment (i.e., reduction of myasthenia gravis exacerbations, improvement in symptoms such as swallowing, mobility, breathing). Recertification will be required every 12 months.
11. Quantity Limit: 28 prefilled syringes/28 days

Zokinvy-lonafarnib (Rx)

1. Must be prescribed by or in consultation with a physician knowledgeable in the management of Hutchinson-Gilford Progeria Syndrome and processing-deficient Progeroid Laminopathies
2. Must have a diagnosis of one of the following:
 - a. Hutchinson-Gilford progeria syndrome (HGPS) (must meet both i and ii)
 - i. Presence of clinical features (e.g., growth deficiency, characteristic facial features, ectodermal, musculoskeletal) **AND**
 - ii. Heterozygous variant in LMNA gene confirmed by genetic testing
Note: Individuals with classic genotype HGPS (~90% individuals with HGPS) are heterozygous for pathogenic variant c.1824C>T. Individuals with nonclassic genotype HGPS (~10% individuals with HGPS) are heterozygous for another *LMNA* pathogenic variant in exon 11 splice junction or intron 11 that results in production of progerin. **OR**
 - b. Processing-deficient progeroid laminopathy with either:
 - i. Heterozygous *LMNA* mutation with progerin-like protein accumulation
 - ii. Homozygous or compound heterozygous *ZMPSTE24* mutations
3. Patient must be 12 months of age or older
4. Patient must have a BSA of 0.39 m² or greater
5. Requested dose is appropriate for patient's BSA (see table 1 and 2 for FDA-approved dosing)
6. Prescriber attestation indicating that the patient does not have overt renal, hepatic, or pulmonary disease or immune dysfunction

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7. Zokinvy will not be approved for other Progeroid Syndromes or processing proficient Progeroid Laminopathies
8. Quantity limit of 30 capsules per 30 days.
 - a. Upon each drug review and dose escalation request, the allowed quantity will be reviewed in accordance with FDA-approved BSA-based dosing (see table 1 and 2) and, as such, will be limited to minimum number of capsules of each strength to obtain the appropriate daily dose. For example, a patient with a BSA of 0.71 to 0.81 receiving a dose of 115mg/m² twice daily, will require a total daily dose of 175 mg. To obtain a daily dose of 175 mg, the patient would need 2-50 mg capsules/day (60 capsules/30 days) and 1-75 mg capsule/day (30 capsules/30 days).
9. Initial authorization period: 4 months. Subsequent recertifications after the initial 4-month approval will require documentation that patient is tolerating therapy, prescriber attestation that patient is responding to therapy, and is on appropriate dose for BSA.
10. **Note:** for applicable lines of businesses (Commercial, Exchange, Child Health Plus), a split-fill program will apply to new starts only. An override to bypass the split-fill program will be provided for existing users that have been maintained on Zokinvy.

Table 1 and Table 2: FDA-approved dosing for Zokinvy

Table 1 provides the BSA-based dosage recommendations for the starting dosage of 115 mg/m² twice daily.

Table 1: Recommended Dosage and Administration for 115 mg/m² Body Surface Area-Based Dosing

BSA (m ²)	Total Daily Dosage Rounded to Nearest 25 mg	Morning Dosing Number of Capsule(s)		Evening Dosing Number of Capsule(s)	
		ZOKINVY 50 mg	ZOKINVY 75 mg	ZOKINVY 50 mg	ZOKINVY 75 mg
0.39 - 0.48	100	1		1	
0.49 - 0.59	125		1	1	
0.6 - 0.7	150		1		1
0.71 - 0.81	175	2			1
0.82 - 0.92	200	2		2	
0.93 - 1	225	1	1	2	

Table 2 provides the BSA-based dosage recommendations for the dosage of 150 mg/m² twice daily.

Table 2: Recommended Dosage and Administration for 150 mg/m² Body Surface Area-Based Dosing

BSA (m ²)	Total Daily Dosage Rounded to Nearest 25 mg	Morning Dosing Number of Capsule(s)		Evening Dosing Number of Capsule(s)	
		ZOKINVY 50 mg	ZOKINVY 75 mg	ZOKINVY 50 mg	ZOKINVY 75 mg
0.39 - 0.45	125		1	1	
0.46 - 0.54	150		1		1
0.55 - 0.62	175	2			1
0.63 - 0.7	200	2		2	
0.71 - 0.79	225	1	1	2	
0.8 - 0.87	250	1	1	1	1
0.88 - 0.95	275	2	2	1	1
0.96 - 1	300		2		2

Ztalmy-ganaxolone (Rx)

1. Must be prescribed by or in consultation with a neurologist
2. Patient must be 2 years of age or older
3. Must have a diagnosis of seizures associated with cyclin-dependent kinase-like 5 deficiency disorder (CDD) confirmed by CDKL5 genetic testing
4. Documented trial and failure of at least two antiepileptic therapies
5. Initial approval will be for 6 months and require documentation of baseline monthly seizure frequency.
6. Recertification will require documentation of a sustained reduction in monthly seizure frequency compared to baseline.
7. Quantity limit: 1 bottle per 28 days. Upon each review and dose escalation request, the allowed quantity will be reviewed in accordance with FDA-approved weight-based dosing and, as such, will be limited to the minimum number of bottles to obtain the appropriate daily dose.

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Zynteglo-betibeglogene autotemcel (Medical)

Zynteglo (betibeglogene autotemcel) coverage varies by line of business as below:

For Managed Medicaid Care (MMC)/Health and Recovery Plan (HARP):

- Zynteglo (betibeglogene autotemcel) is reimbursed by Medicaid fee-for-service pharmacy program for Medicaid Managed Care Members

Please refer to the New York State Medicaid Fee-for-Service Practitioner Administered Drug Policies and Billing Guidance. Zynteglo clinical criteria can be found under the Clinical Criteria section at:

https://health.ny.gov/health_care/medicaid/program/practitioner_administered/ffs_practitioner_administer.htm

For All Lines of Business except MMC/HARP:

Zynteglo (betibeglogene autotemcel) is considered **medically necessary** for individuals with transfusion-dependent β -thalassemia if they meet criteria 1 through 8:

1. Documented diagnosis of β -thalassemia by globin gene testing confirming one of the following:
 - i. Non- β^0/β^0 genotype (i.e., β^0/β^+ , β^E/β^0 , and β^+/β^+) **OR**
 - ii. β^0/β^0 genotype (other examples include: $\beta^0/\beta^+(\text{IVS-I-110})$ and $\beta^+(\text{IVS-I-110})/\beta^+(\text{IVS-I-110})$)
2. Must be ≥ 4 years of age and ≤ 50 years of age
3. Must weigh ≥ 6 kg
4. Require regular peripheral blood transfusions to maintain target hemoglobin levels.
5. Documented history of receiving transfusions of ≥ 100 ml per kilogram of body weight of packed red cells per year or who had disease that had been managed under standard thalassemia guidelines with ≥ 8 transfusions per year in the previous 2 years at the time of treatment decision.
6. Karnofsky performance status of ≥ 80 for adults (≥ 16 years of age) or a Lansky performance status of ≥ 80 for adolescents (< 16 years of age).
7. Negative serologic test for HIV infection (as per US FDA prescribing label, apheresis material from individuals with a positive test for HIV will not be accepted for betibeglogene autotemcel manufacturing).
8. Individual does not have
 - a. Availability of a suitable, willing, and able human leukocyte antigen-identical or human leukocyte antigen-matched donor.
 - b. T2*-weighted magnetic resonance imaging measurement of myocardial iron of less than 10 msec or other evidence of severe iron overload in the opinion of treating physician.
 - c. Advanced liver disease (meets any one of the following):
 - i. Persistent aspartate transaminase, alanine transaminase, or direct bilirubin value greater than 3 times the upper limit of normal.
 - ii. Baseline prothrombin time or partial thromboplastin time greater than 1.5 times the upper limit of normal.
 - iii. Magnetic resonance imaging of the liver demonstrating clear evidence of cirrhosis.
 - iv. Liver biopsy demonstrating cirrhosis, any evidence of bridging fibrosis, or active hepatitis.
 - d. Baseline estimated glomerular filtration rate less than 70 mL/min/1.73 m².
 - e. History of receiving prior gene therapy or allogenic hematopoietic stem cell transplant.
 - f. Any prior or current malignancy (with the exception of adequately treated cone biopsied in situ carcinoma of the cervix uteri and basal or squamous cell carcinoma of the skin) or myeloproliferative or significant immunodeficiency disorder.
 - g. Any immediate family member (i.e., parent or siblings) with a known Familial Cancer Syndrome (including but not limited to hereditary breast and ovarian cancer syndrome, hereditary nonpolyposis colorectal cancer syndrome and familial adenomatous polyposis).
 - h. Active, uncontrolled HCV or HBV infection.

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- i. Contraindication to the use of granulocyte colony stimulating factor (G-CSF), plerixafor, busulfan, or any other medicinal products required during myeloablative conditioning, including hypersensitivity to the active substances or to any of the excipients.
- j. A white blood cell count less than $3 \times 10^9/L$, and/or platelet count less than $100 \times 10^9/L$ not related to hypersplenism.

Authorization will be for 6 months to allow sufficient time for administration.

Zynteglo (betibeglogene autotemcel) is considered **investigational** when the above criteria are not met.

Zynteglo (betibeglogene autotemcel) is considered **investigational** for all other indications.

Retreatment with Zynteglo (betibeglogene autotemcel) will be considered **investigational** when FDA approved gene therapy, or any other gene therapy under investigation, has been previously administered

HCPCS: J3393

Figure 1a-- Isturisa Efficient Dosing Chart

This chart reflects the number of tablets of each strength that will be covered to make any given dose of Isturisa within the FDA approved limit.

Dose	1 mg	5 mg
2 mg BID	120 tablets/30 days	
3 mg BID	180/30	
4 mg BID	240/30	
5 mg BID		60/30
6 mg BID	60/30	60/30
7 mg BID	120/30	60/30
8 mg BID	180/30	60/30
9 mg BID	240/30	60/30
10 mg BID		120/30
11 mg BID	60/30	120/30
12 mg BID	120/30	120/30
13 mg BID	180/30	120/30
14 mg BID	240/30	120/30
15 mg BID		180/30
16 mg BID	60/30	180/30
17 mg BID	120/30	180/30
18 mg BID	180/30	180/30
19 mg BID	240/30	180/30
20 mg BID		240/30
21 mg BID	60/30	240/30
22 mg BID	120/30	240/30
23 mg BID	180/30	240/30
24 mg BID	240/30	240/30
25 mg BID		300/30
26 mg BID	60/30	300/30

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27 mg BID	120/30	300/30
28 mg BID	180/30	300/30
29 mg BID	240/30	300/30
30 mg BID		360/30

Appendix

RTT Diagnostic criteria

<ul style="list-style-type: none"> Consider diagnosis when postnatal deceleration of head growth observed A period of regression followed by recovery or stabilization All main criteria and all exclusion criteria are required for typical or classic RTT 	
Inclusion criteria	<ul style="list-style-type: none"> Partial or complete loss of acquired purposeful hand skills Partial or complete loss of acquired spoken language Gait abnormalities: Impaired or absence of ability Stereotypic hand movements such as hand wringing/squeezing, clapping/tapping, mouthing, and washing/rubbing automatisms
Exclusion criteria	<ul style="list-style-type: none"> Brain injury secondary to trauma (peri- or postnatally), neurometabolic disease, or severe infection that causes neurological problems Grossly abnormal psychomotor development in first 6 months of life

Reference:

Neul JL, Kaufmann WE, Glaze DG, et al. Rett syndrome: revised diagnostic criteria and nomenclature. *Ann Neurol.* 2010;68(6):944-950. doi:10.1002/ana.22124

Genes included in the nephrotic syndrome/FSGS panel

Official gene symbol	OMIM ID	Official gene symbol	OMIM ID
ACTN4	604638	LAMA5	601033
ANKFY1	607927	LAMB2	150325
ANLN	616027	LMX1B	602575
APOL1	603743	MAFB	608968
ARHGAP24	610586	MAGI2	606382
ARHGDIA	601925	MYH9	160775
AVIL	613397	MYO1E	601479
CD2AP	604241	NEU1	608272
CDK20	610076	NFKB2	164012
COL4A3	120070	NPHS1	602716
COL4A4	120131	NPHS2	604766
COL4A5	303630	NUP107	607617
COL4A6	303631	NUP133	607613
COQ2	609825	NUP160	607614
COQ6	614647	NUP205	614352
COQ8B	615567	NUP93	614351
CRB2	609720	OSGEP	610107
CUBN	602997	PAX2	167409
DAAM2	606627	PDSS2	610564
DGKE	601440	PLCE1	608414
DLC1	604258	PODXL	602632

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EMP2	602334	PTPRO	600579
FAT1	600976	SCARB2	602257
GAPVD1	611714	SGPL1	603729
GON7	617436	SMARCAL1	606622
INF2	610982	TBC1D8B	301027
ITGA3	605025	TNS2	607717
ITGB4	147557	TP53RK	608679
ITSN1	602442	TPRKB	608680
ITSN2	604464	TRIM8	606125
KANK1	607704	TRPC6	603652
KANK2	614610	TTC21B	612014
KANK4	614612	WDR4	605924
KAT2B	602303	WDR73	616144
KIRREL1	607428	WT1	607102
LAGE3	300060	XPO5	607845
		YRDC	612276

OMIM=Online Mendelian Inheritance in Man

Reference: Rheault MN, Alpers CE, Barratt J, et al. Sparsentan versus Irbesartan in Focal Segmental Glomerulosclerosis. *N Engl J Med.* 2023;389(26):2436-2445. doi:10.1056/NEJMoa2308550. Supplementary Appendix.

Plasma Very Long Chain Fatty Acid (VLCFA) Values in X-Linked Adrenoleukodystrophy

VLCFA	Normal	Males with X-ALD
C26:0 $\mu\text{g/mL}^1$	0.23+0.09	1.30+0.45
C24:0/C22:0 ²	0.84+0.10	1.71+0.23
C26:0/C22:0 ²	0.01+0.004	0.07+0.03

The concentration of C26:0 is reported as $\mu\text{g/mL}$; some laboratories report this as $\mu\text{mol/L}$.

Lorenzo's oil, a mixture of erucic and oleic acids, is used therapeutically to normalize VLCFA levels. Thus erucic acid (C22:1) levels are routinely reported when measuring plasma VLCFA. Certain oils used in cooking, such as mustard seed oil, have naturally high levels of erucic acid and thus can lead to an elevation similar to that observed with Lorenzo's oil therapy.

References:

Raymond GV, Moser AB, Fatemi A. X-Linked Adrenoleukodystrophy. 1999 Mar 26 [Updated 2018 Feb 15]. GeneReviews® [Internet]. Seattle (WA): University of Washington, Seattle; 1993-2022. Available from: <https://www.ncbi.nlm.nih.gov/books/NBK1315/>. Accessed November 2022.

Steinberg S, Jones R, Tiffany C, Moser A. Investigational methods for peroxisomal disorders. *Curr Protoc Hum Genet.* 2008 Jul;Chapter 17:Unit 17.6. doi: 10.1002/0471142905.hg1706s58. PMID: 18633975.

Familial chylomicronemia syndrome (FCS) score

Item	Score
Fasting TGs level > 885 mg/dL for 3 consecutive blood analyses measured at least one month apart	+5
Fasting TG level >1,770 mg/dL at least once	+1
Previous TG level <177 mg/dL	-5
No secondary factor* (except pregnancy [‡] and ethinyl estradiol)	+2
History of pancreatitis	+1
Unexplained recurrent abdominal pain	+1
No history of familial combined hyperlipidemia	+1
No response to lipid lowering treatment (i.e., decrease in TGs by <20%)	+1
Age of symptom onset:	
<40 years	+1
<20 years	+2
<10 years	+3

TG=Triglycerides

*Secondary factors include alcohol, diabetes, metabolic syndrome, hypothyroidism, steroid therapy, and additional drugs

[‡] If diagnosis is made during pregnancy, then a second assessment is necessary to confirm diagnosis post-partum

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FCS score=sum of all items present. Scoring is as follows:

- ≥ 10: FCS very likely
- < 9 FCS unlikely
- ≤ 8 FCS very unlikely

Source: Moulin P, Dufour R, Avena M, et al. Identification and diagnosis of patients with familial chylomicronaemia syndrome (FCS): Expert panel recommendations and proposal of an "FCS score". *Atherosclerosis*. 2018;275:265-272.

North American FCS (NAFCS) score

This tool can facilitate a diagnosis of FCS and should only be used in patients > 1 year old with hypertriglyceridemia (≥ 440 mg/dL). For patients ≥ 10 years of age, the tool should only be used if the patient is treatment-resistant to fibrates and high-dose omega-3 fatty acids despite being adherent to therapy.

Category	Item	Score
Current age (years)	<1 year	Ineligible for NAFCS score
	≥1 to 9 years	+12
	≥ 10 years and age of HTG onset < 10 years	+12
	≥ 10 years and age of HTG onset ≥ 10 years	+0
BMI (percentile for children and adolescents)	< 25 kg/m ² or < 85 th percentile	+9
	≥ 25 kg/m ² or ≥ 85 th percentile	+0
History of pancreatitis	History of pancreatitis	+16
	Abdominal pain without history of pancreatitis	+9
	No history of abdominal pain or pancreatitis	+0
Secondary factors	≥ 1 secondary factor present (i.e., lifestyle factors, medications, clinical conditions) *	+0
	No secondary factors	+11
Laboratory values (any that apply)	All fasting TGs >880 mg/dL	+13
	Ratio TG/TC>8 mg/dL	+8
	ApoB < 1.0 g/L	+12
Additional factors (any that apply)	If patient is ≥1 to 9 years AND has no secondary factors	+7
	If ratio TG/TC >8 mg/dL AND APOB <1.0 g/L	+7
	If ratio TG/TC >8 mg/dL AND has no secondary factors	+5

HTG=Hypertriglyceridemia; TG=Triglycerides; TC=Total cholesterol; ApoB=Apolipoprotein B

* See source for complete list of secondary factors

NAFCS score is calculated based on sum of all items. NAFCS scoring is as follows:

- ≥ 60 indicates definite FCS
- ≥45 to 59 indicates probable or very likely FCS
- ≥30 to 44 indicates may have FCS but genetic testing should be considered

Source: Hegele RA, Ahmad Z, Ashraf A, et al. Development and validation of clinical criteria to identify familial chylomicronemia syndrome (FCS) in North America. *J Clin Lipidol*. 2024 Nov 12.

The 2019 American College of Rheumatology/European League Against Rheumatism classification criteria for IgG4-related disease Step 3 Inclusion criteria: domains and items**

Domain and Items	Score¶
<i>Histopathology</i>	
Uninformative biopsy	0
Dense lymphocytic infiltrate	+4
Dense lymphocytic infiltrate and obliterative phlebitis	+6
Dense lymphocytic infiltrate and storiform fibrosis with or without obliterative phlebitis	+13
<i>Immunostaining#</i>	
IgG4+:IgG+ ratio is 0 to 40% or indeterminate and the number of IgG4+ cells/HPF is 0 to 9.‡	0
IgG4+:IgG+ ratio is ≥41% and the number of IgG4+ cells/HPF is 0 to 9 or indeterminate; or the IgG4+:IgG+ ratio is 0 to 40% or indeterminate and the number of IgG4+ cells/HPF is ≥10 or indeterminate.	+7
IgG4+:IgG+ ratio is 41 to 70% and the number of IgG4+ cells/HPF is ≥10; or the IgG4+:IgG+ ratio is ≥71% and the number of IgG4+ cells/HPF is 10 to 50.	+14
IgG4+:IgG+ ratio is ≥71% and the number of IgG4+ cells/HPF is ≥51.	+16
<i>Serum IgG4 concentration</i>	
Normal or not checked	0

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>Normal but <2 times upper limit of normal	+4
2 to 5 times upper limit of normal	+6
>5 times upper limit of normal	+11
Bilateral lacrimal, parotid, sublingual, and submandibular glands	
No set of glands involved	0
1 set of glands involved	+6
2 or more sets of glands involved	+14
Chest	
Not checked or neither of the items listed is present	0
Peribronchovascular and septal thickening	+4
Paravertebral band-like soft tissue in the thorax	+10
Pancreas and biliary tree	
Not checked or none of the items listed is present	0
Diffuse pancreas enlargement (loss of lobulations)	+8
Diffuse pancreas enlargement and capsule-like rim with decreased enhancement	+11
Pancreas (either of above) and biliary tree involvement	+19
Kidney	
Not checked or none of the items listed is present	0
Hypocomplementemia	+6
Renal pelvis thickening/soft tissue	+8
Bilateral kidney cortex low-density areas	+10
Retroperitoneum	
Not checked or neither of the items listed is present	0
Diffuse thickening of the abdominal aortic wall	+4
Circumferential or anterolateral soft tissue around the infrarenal aorta or iliac arteries	+8
<p>¶ Only the highest-weighted item in each domain is scored. # Biopsies from lymph nodes, mucosal surfaces of the gastrointestinal tract, and skin are not acceptable for use in weighting the immunostaining domain. ** "Indeterminate" refers to a situation in which the pathologist is unable to clearly quantify the number of positively staining cells within an infiltrate yet can still ascertain that the number of cells is at least 10/high-power field (hpf). For a number of reasons, most often pertaining to the quality of the immunostain, pathologists are sometimes unable to count the number of IgG4+ plasma cells with precision yet even so, can be confident in grouping cases into the appropriate immunostaining result category.</p>	
<p>**Full classification criteria may be found at: https://acrjournals.onlinelibrary.wiley.com/doi/epdf/10.1002/art.41120</p>	
<p>Source: Wallace ZS, Naden RP, Chari S, et al. The 2019 ACR/EULAR Classification Criteria for IgG4-Related Disease. <i>Arthritis Rheumatol.</i> 2020;72(1):7-19. doi:10.1002/art.41120</p>	

CODES:

Eligibility for reimbursement is based upon the benefits set forth in the member's subscriber contract.

CODES MAY NOT BE COVERED UNDER ALL CIRCUMSTANCES. PLEASE READ THE POLICY AND GUIDELINES STATEMENTS CAREFULLY.

Codes may not be all inclusive as the AMA and CMS code updates may occur more frequently than policy updates.

APPROVAL TIME PERIODS – INITIAL AND RECERTIFICATION REVIEWS:

1. Unless otherwise stated within the individual drug criteria, approval time periods are listed in the table below
2. Continued approval at time of recertification will require documentation that the drug is providing ongoing benefit to the patient in terms of improvement or stability in disease state or condition. Such documentation may include progress notes, imaging or laboratory findings, and other objective or subjective measures of benefit which support that continued use of the requested product is medically necessary. Also, ongoing use of the requested product must continue to reflect the current policy's preferred formulary [Recertification reviews may result in the requirement to try more cost-effective treatment alternatives as they become available (i.e., generics or other

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guideline-supported treatment options)] and the requested dose must continue to meet FDA approved or off-label/guideline supported dosing

<u>Line of Business</u>	<u>Rx Initial approval</u>	<u>Rx Continued approval</u>	<u>Medical Initial approval</u>	<u>Medical Recert</u>
SafetyNet (Medicaid, HARP, CHP, Essential Plan)	1 year (or as stated within individual drug policy)	2 years (or as stated within individual drug policy)	All sites of service – 2 years	All sites of service – 2 years
Commercial / Exchange	1 year (or as stated within individual drug policy)	2 years (or as stated within individual drug policy)	All sites of service – 2 years	All sites of service – 2 years
Medicare	Defined in Medicare Drug Policy	Defined in Medicare Drug Policy	All sites of service – 2 years	All sites of service – 2 years

POLICY GUIDELINES:

1. Utilization Management are contract dependent and coverage criteria may be dependent on the contract renewal date. Additionally, coverage of drugs listed in this policy are contract dependent. Refer to specific contract/benefit language for exclusions.
2. This policy is applicable to drugs that are included on a specific drug formulary (Rx benefit only). If a drug referenced in this policy is non-formulary, please reference the Non-Formulary Medication Exception Review Policy for review guidelines.
3. Not all contracts cover all Medical Infusible drugs. Refer to specific contract/benefit plan language for exclusions of Injectable Medications.
4. This policy does not apply to Medicare Part D and D-SNP pharmacy benefits. The drugs in this policy may apply to all other lines of business including Medicare Advantage.
5. For members with Medicare Advantage, medications with a National Coverage Determination (NCD) and/or Local Coverage Determination (LCD) will be covered pursuant to the criteria outlined by the NCD and/or LCD. NCDs/LCDs for applicable medications can be found on the CMS website at <https://www.cms.gov/medicare-coverage-database/search.aspx>. Indications that have not been addressed by the applicable medication's LCD/NCD will be covered in accordance with criteria determined by the Health Plan (which may include review per the Health Plan's Off-Label Use of FDA Approved Drugs policy). Step therapy requirements may be imposed in addition to LCD/NCD requirements.
6. Supportive documentation of previous drug use must be submitted for any criterion that requires the trial of a preferred agent if the preferred drug is not found in claims history.
7. Dose and frequency should be in accordance with the FDA label or recognized compendia (for off-label uses). When services are performed in excess of established parameters, they may be subject to review for medical necessity.
 - a. On a case-by-case basis, for drugs that have FDA-approved weight and BSA-based dosing a higher quantity may be allowed for pediatric patients based on the patient's predicted growth.
8. For contracts where Insurance Law § 4903(c-1), and Public Health Law § 4903(3-a) are applicable, if trial of preferred drug(s) is the only criterion that is not met for a given condition, and one of the following circumstances can be substantiated by the requesting provider, then trial of the preferred drug(s) will not be required. The provider must make their intent to override a trial of the preferred drugs clear and must provide rationale and supporting documentation for one of the following:
 - The required prescription drug(s) is (are) contraindicated or will likely cause an adverse reaction or physical or mental harm to the member;
 - The required prescription drug is expected to be ineffective based on the known clinical history and conditions and concurrent drug regimen;

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- The required prescription drug(s) was (were) previously tried while under the current or a previous health plan, or another prescription drug or drugs in the same pharmacologic class or with the same mechanism of action was (were) previously tried and such prescription drug(s) was (were) discontinued due to lack of efficacy or effectiveness, diminished effect, or an adverse event;
 - The required prescription drug(s) is (are) not in the patient's best interest because it will likely cause a significant barrier to adherence to or compliance with the plan of care, will likely worsen a comorbid condition, or will likely decrease the ability to achieve or maintain reasonable functional ability in performing daily activities;
 - The individual is stable on the requested prescription drug. The medical profile of the individual (age, disease state, comorbidities), along with the rationale for deeming stability as it relates to standard medical practice and evidence-based practice protocols for the disease state will be taken into consideration.
 - The above criteria are not applicable to requests for brand name medications that have an AB rated generic. We can require a trial of an AB-rated generic equivalent prior to providing coverage for the equivalent brand name prescription drug.
9. This policy is subject to frequent revisions as new medications come onto the market. Some drugs will require prior authorization prior to criteria being added to the policy.
10. All requests will be reviewed to ensure they are being used for an appropriate indication and may be subject to an off-label review in accordance with our Off-Label Use of FDA Approved Drugs Policy (Pharmacy-32).
11. All utilization management requirements outlined in this policy are compliant with applicable New York State insurance laws and regulations. Policies will be reviewed and updated as necessary to ensure ongoing compliance with all state and federally mandated coverage requirements.
12. Manufacturers may either discontinue participation in, or may not participate in, the Medicaid Drug Rebate Program (MDRP). Under New York State Medicaid requirements, physician-administered drugs must be produced by manufacturers that participate in the MDRP. Products made by manufacturers that do not participate in the MDRP will not be covered under Medicaid Managed Care/HARP lines of business. Drug coverage will not be available for any product from a non-participating manufacturer. For a complete list of New/Reinstated & Terminated Labelers please visit: <https://www.medicaid.gov/medicaid/prescriptiondrugs/medicaid-drug-rebate-program/newreinstated-terminated-labeler-information/index.html>

UPDATES:

Date:	Revision:
05/07/2026	Revised
03/27/2026	Revised
03/26/2026	Revised
02/12/2026	Reviewed / Approved P&T Committee
01/23/2026	Revised
01/15/2026	Revised
01/06/2026	Revised
01/01/2026	Revised
11/19/2025	Revised
11/14/2025	Revised
11/01/2025	Revised & Reviewed / Approved P&T Committee
10/16/2025	Revised
09/24/2025	Revised
09/22/2025	Revised
09/01/2025	Revised

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08/14/2025	Reviewed / Approved P&T Committee
08/04/2025	Revised
06/18/2025	Revised
05/08/2025	Reviewed / Approved P&T Committee
04/11/2025	Revised
04/01/2025	Revised
03/13/2025	Revised
03/06/2025	Revised
02/19/2025	Revised
01/30/2025	Revised
01/13/2025	Revised
01/01/2025	Revised
11/26/2024	Revised
11/21/2024	Reviewed / Approved P&T Committee
11/01/2024	Revised
10/01/2024	Revised
09/25/2024	Revised
08/16/2024	Revised
07/01/2024	Revised
06/24/2024	Revised
05/09/2024	P&T Committee Approval
4/2024	Revised
3/2024	Revised
1/2024	Revised
12/2023	Revised
11/23	Revised
8/23	Revised
7/23	Revised
5/23	Revised
05/11/2023	P&T committee Approval
5/23	Revised
3/23	Revised
2/23	Revised
12/22	Revised
11/22	Revised
10/22	Revised
8/22	Revised
7/22	Revised
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5/22	P&T Committee Approval
4/22	Revised
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2/22	Revised
1/22	Revised
12/21	Revised
11/21	Revised
10/21	Revised
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7/21	Revised
6/21	Revised
5/21	Revised

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5/21	P&T Committee Approval
4/21	Revised
3/21	Revised
2/21	Revised
1/21	Created

REFERENCES:

In addition to the full FDA approved prescribing information for each individual drug, the following references have been utilized in creating this policy and specific drug criteria:

Aldurazyme-

1. Panel VPBMSHCatMA. Laronidase (Aldurazyme): National PBM Drug Monographs; 2004

Arcalyst-

1. Adler Y, Charron P, Imazio M, et al. 2015 ESC Guidelines for the diagnosis and management of pericardial diseases. *European Heart Journal*. 2015;36(42):2921-2964.

Bylvay-

1. Amirneni S, Haep N, Gad MA, et al. Molecular overview of progressive familial intrahepatic cholestasis. *World J Gastroenterol*. 2020 Dec 21;26(47):7470-7484.

Evkeeza-

1. Grundy SM, Stone NJ, Bailey AL, 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. *Circulation* 2019;139:e1082-e1143.

Filspari-

1. Wheeler DC, Toto RD, Stefánsson BV, et al. DAPA-CKD Trial Committees and Investigators. A pre-specified analysis of the DAPA-CKD trial demonstrates the effects of dapagliflozin on major adverse kidney events in patients with IgA nephropathy. *Kidney Int*. 2021 Jul;100(1):215-224.doi: 10.1016/j.kint.2021.03.033. Epub 2021 Apr 18. PMID: 33878338.

Increlex-

1. Guevara-Aguirre J, et al, "A randomized, double blind, placebo-controlled trial on safety and efficacy of recombinant human insulin-like growth factor-1 in children with growth hormone receptor deficiency", *Journal of Clinical Endocrinology & Metabolism*, 1995;80:1393-8
2. Backeljauw PF, et al, "Therapy for 6.5-7.5years with recombinant insulin-like growth factor 1 in children with growth hormone insensitivity syndrome: A clinical research center study.", *Journal of Clinical Endocrinology & Metabolism*, 2001;86:1504-10

Reblozyl-

1. Celgene Corporation Package Insert for Reblozyl. April 2020.

Redemplo/Tryngolza

1. https://pro.aace.com/sites/default/files/2019-02/FCS_082318_formatted.pdf
2. Moulin P, Dufour R, Aversa M, et al. Identification and diagnosis of patients with familial chylomicronaemia syndrome (FCS): Expert panel recommendations and proposal of an "FCS score". *Atherosclerosis*. 2018;275:265-272. doi:10.1016/j.atherosclerosis.2018.06.814
3. Hegele RA, Ahmad Z, Ashraf A, et al. Development and validation of clinical criteria to identify familial chylomicronemia syndrome (FCS) in North America. *J Clin Lipidol*. Published online November 12, 2024. doi:10.1016/j.jacl.2024.09.008

Somavert –

1. Ezzat S. Pharmacological approach to the treatment of acromegaly. *Neurosurgery Focus*. 2004; 14(4): E3.

Skysona

1. Raymond GV, Moser AB, Fatemi A. X-Linked Adrenoleukodystrophy. 1999 Mar 26 [Updated 2018 Feb 15]. *GeneReviews*® [Internet]. Seattle (WA): University of Washington, Seattle; 1993-2022. Available from: <https://www.ncbi.nlm.nih.gov/books/NBK1315/>. Accessed November 2022.
2. Steinberg S, Jones R, Tiffany C, Moser A. Investigational methods for peroxisomal disorders. *Curr Protoc Hum Genet*. 2008 Jul;Chapter 17:Unit 17.6. doi: 10.1002/0471142905.hg1706s58. PMID: 18633975.

Tavneos-

1. Bossuyt, X., Cohen Tervaert, JW., Arimura, Y. *et al*. Revised 2017 international consensus on testing of ANCA in granulomatosis with polyangiitis and microscopic polyangiitis. *Nat Rev Rheumatol* **13**, 683–692 (2017). <https://doi.org/10.1038/nrrheum.2017.140>

Pharmacy Management Drug Policy

Rare Diseases CRPA

2. Chung SA, Langford CA, Maz M, et al. 2021 American College of Rheumatology/Vasculitis Foundation guideline for the management of antineutrophil cytoplasmic antibody-associated vasculitis. *Arthritis Rheumatol*. 2021 Aug;73(8):1366- 1383.

Tarpeyo-

1. Wheeler DC, Toto RD, Stefánsson BV, et al. DAPA-CKD Trial Committees and Investigators. A pre-specified analysis of the DAPA-CKD trial demonstrates the effects of dapagliflozin on major adverse kidney events in patients with IgA nephropathy. *Kidney Int*. 2021 Jul;100(1):215-224.doi: 10.1016/j.kint.2021.03.033. Epub 2021 Apr 18. PMID: 33878338.

Tepezza

1. Douglas RS, Kahaly GJ, Ugradar S, et al. Teprotumumab Efficacy, Safety, and Durability in Longer-Duration Thyroid Eye Disease and Re-treatment: OPTIC-X Study. *Ophthalmology*. 2022;129(4):438-449. doi:10.1016/j.ophtha.2021.10.017
2. Douglas RS, Couch S, Wester ST, et al. Efficacy and Safety of Teprotumumab in Patients With Thyroid Eye Disease of Long Duration and Low Disease Activity. *J Clin Endocrinol Metab*. 2023;109(1):25-35. doi:10.1210/clinem/dgad637
3. Fahrenbruch R, Kintzel P, et al. Dose Rounding of Biologic and Cytotoxic Anticancer Agents: A Position Statement of the Hematology/Oncology Pharmacy Association. *American Society of Clinical Oncology*. March 2018. Volume 14, Issue 3. Jop.ascopubs.org

Vyvgart/Vyvgart Hytrulo

1. G.I. Wolfe, L. Herbelin, S.P. Nations, B. Foster, W.W. Bryan, R.J. Barohn *Neurology* Apr 1999, 52 (7) 1487; DOI: 10.1212/WNL.52.7.1487
2. Van den Bergh PY, van Doorn PA, Hadden RD, et al. European Academy of Neurology/Peripheral Nerve Society guideline on diagnosis and treatment of chronic inflammatory demyelinating polyradiculoneuropathy: report of a joint task force – second revision. *J Peripher Nerv Syst*. 2021;26(3):242-368.

Zokinvy-

1. Rare Diseases FAQ. Available at: <https://www.genome.gov/FAQ/Rare-Diseases>. Accessed January 15, 2021
2. Zokinvy™. Package insert. Eiger Biopharmaceuticals;2020.
3. Gordon LB, Brown WT, Collins FS. Hutchinson-Gilford Progeria Syndrome. 2003 Dec 12 [Updated 2019 Jan 17]. In: Adam MP, Ardinger HH, Pagon RA, et al., editors. *GeneReviews*® [Internet]. Seattle (WA): University of Washington, Seattle; 1993-2020. Available at <https://www.ncbi.nlm.nih.gov/books/NBK1121/>. Accessed on January 15, 2020.
4. Gordon LB, Shappell H, Massaro J, et al. Association of lonafarnib treatment vs. no treatment with mortality rate in patients with Hutchinson-Gilford Progeria Syndrome. *JAMA*. 2018;319(16):1687-1695.
5. Gordon LB, Kleinman ME, Miller DT, et al. Clinical trial of a farnesyltransferase inhibitor in children with Hutchinson-Gilford Progeria Syndrome. *Proc Natl Acad Sci USA*. 2012;109(41):16666-16671.
6. Gordon LB, Kleinman ME, Massaro J, et al. Clinical trial of the protein farnesylation inhibitors lonafarnib, pravastatin, and zoledronic acid in children with Hutchinson-Gilford Progeria Syndrome. *Circulation*. 2016;134(2):114-125.