Policy and Procedure	
PHARMACY PRIOR AUTHORIZATION POLICY AND CRITERIA ORPTCOTH022.0226	**MISCELLANEOUS PRODUCTS** **MEDICATIONS FOR RARE INDICATIONS** See Table 2 for Applicable Medications
Effective Date: 4/1/2026	**Review/Revised Date**: 07/18, 09/18, 03/19, 08/19, 08/20, 04/21, 06/21, 09/21, 08/22, 11/22, 04/23, 06/23, 08/23, 11/23, 04/24, 05/24, 08/24, 08/24, 09/24, 10/24, 12/24, 02/25, 04/25, 06/25, 08/25, 10/25, 12/25, 02/26 (snm/kn)
Original Effective Date: 10/18	**P&T Committee Meeting Date**: 08/18, 0918(cv), 04/19, 10/19, 10/20, 04/21, 06/21, 10/21, 10/22, 12/22, 04/23, 06/23, 08/23, 12/23, 04/24, 06/24, 08/24, 10/24, 12/24, 02/25, 04/25, 0625, 08/25, 10/25, 12/25, 2/26
Approved by: Oregon Region Pharmacy and Therapeutics Committee	

SCOPE:
Providence Health Plan and Providence Health Assurance as applicable (referred to individually as “Company” and collectively as “Companies”).

APPLIES TO:
Commercial
Medicaid

POLICY CRITERIA:

COVERED USES:
All Food and Drug Administration (FDA) approved indications not otherwise excluded from the benefit.

REQUIRED MEDICAL INFORMATION:
For Initial Authorization, both of the following must be met:
1. Confirmation of FDA-labeled indication and drug-specific criteria (See Table 2)
2. Dosing is within FDA-labeled guidelines OR documentation has been submitted in support of therapy with a higher dose for the intended diagnosis such as high-quality peer reviewed literature, guidelines, other clinical information

For Reauthorization, all the following must be met:
1. Documentation of benefit of therapy as evidence by improvement in symptoms, disease stabilization or lack of decline compared to the natural disease progression
2. Dosing is within FDA-labeled guidelines OR documentation has been submitted in support of therapy with a higher dose for the intended diagnosis such as high-quality peer reviewed literature, guidelines, other clinical information
3. Confirmation of drug-specific criteria, if applicable (See Table 2)

EXCLUSION CRITERIA:
For Aqneursa only - concurrent therapy with arimoclomol citrate (Miplyffa)

For Filsuvez and Vyjuvek only:
1. Skin graft within the past three months
2. Current evidence or a history of squamous cell carcinoma in the area(s) that will undergo treatment
3. Combination therapy with Vyjuvek and Filsuvez

For Galafold only – combination therapy with enzyme replacement therapy [such as agalsidase beta (Fabrazyme)] for the treatment of Fabry disease

For Miplyffa only – concurrent therapy with levacetylleucine (Aqneursa)

For Zevaskyn only – concurrent therapy with Vyjuvek or Filsuvez

AGE RESTRICTIONS:
Age must be appropriate based on FDA-approved indication

PRESCRIBER RESTRICTIONS:
Must be prescribed by, or in consultation with a specialist in the respective disease state.

COVERAGE DURATION:

Drug	Initial Authorization Coverage Duration	Reauthorization Coverage Duration
Aqneursa	12 months	12 months
Cholbam	6 months	12 months
Crenessity	6 months	12 months
Ctexli	6 months	12 months
Daybue	6 months	12 months
Enjaymo	6 months	12 months
Filsuvez	3 months	12 months
Forzinity	6 months	12 months
Kebilidi	12 weeks (one treatment course per lifetime)	
Miplyffa	12 months	12 months
Nulibry	3 months	12 months
Pyrukynd	6 months	12 months
Qalsody	6 months	12 months
Ryplazim	6 months	6 months
Skysona	12 weeks (one treatment course per lifetime)	
Sohonos	12 months	12 months
Spevigo IV	2 weeks (limited to one 900 mg [two vials] infusion)	
Vykat™ XR	6 months	12 months
Vyjuvek	6 months	12 months

Xolremdi	6 months	12 months
Zevaskyn	12 weeks (one treatment course per lifetime)	
Ztalmy	12 months	12 months

For all other medications: Initial authorization will be approved for one year and reauthorization will be approved until no longer eligible with the plan, subject to formulary or benefit changes.

QUANTITY LIMIT:

Drug	Quantity Limit
Aqneursa	Four packets per day
Crenessity	50 mg and 100 mg capsules: two capsules per day 50 mg/mL oral solution: 2 mL per day
Filsuvez	23.5 gram/day (1 single-use tube per day)
Forzinity	Four 280 mg/3.5 mL vials every 28 days
Galafold	14 capsules per 28 days (0.5 capsules per day)*
Joenja	Two tablets per day
Miplyffa	Three capsules per day
Olpruva	One kit (therapy pack) per 30 days
Pyrukynd	Two tablets per day
Spevigo SQ	4 mL/28 days
Vyjuvek	Four vials (10 mL) per 28 days
Xolremdi	120 capsules per 30 days (4 capsules per day)
Ztalmy	1110 mL (10 bottles of 110 mL each) per 30 days

*Galafold is dosed every other day

Requests for indications that were approved by the FDA within the previous six (6) months may not have been reviewed by the health plan for safety and effectiveness and inclusion on this policy document. These requests will be reviewed using the New Drug and or Indication Awaiting P&T Review; Prior Authorization Request ORPTCOPS047.

Requests for a non-FDA approved (off-label) indication requires the proposed indication be listed in either the American Hospital Formulary System (AHFS), Drugdex, or the National Comprehensive Cancer Network (NCCN) and is considered subject to evaluation of the prescriber's medical rationale, formulary alternatives, the available published evidence-based research and whether the proposed use is determined to be experimental/investigational.

Coverage for Medicaid is limited to a condition that has been designated a covered line item number by the Oregon Health Services Commission listed on the Prioritized List of Health Care Services.

Coverage decisions are made on the basis of individualized determinations of medical necessity and the experimental or investigational character of the treatment in the individual case.

INTRODUCTION:
In the United States, Congress defines a rare disease as one that affects fewer than 200,000 people[5]. Congress recognized that people with rare diseases often did not have many treatment options, so it created the Orphan Drug Act (ODA) of 1983 to incentivize drug developers to create medications for these populations[4]. Since then, a significant number of drugs have emerged on the market for use in rare indication with more to come. On June 29, 2017, The Food and Drug Administration (FDA) unveiled a strategic plan to reduce its backlog of orphan drug requests to expedite the process.[6]

FDA APPROVED INDICATIONS: See Table 2

POSITION STATEMENT:
The purpose of this policy is to ensure safe and effective therapy for patients with rare diseases. A list of rare diseases can be found at National Institute of Health (NIH) website[2] and a list of orphan drugs can be found at the FDA website[3].

Sodium phenylbutyrate is available in multiple different dosage forms including a generically available tablet and powder. Pheburane pellets and Olpruva pellet packet for suspension are both alternative formulations that offer better palatability. Pheburane and Olpruva were FDA approved based on bioequivalence studies and have not been shown to be safer or more effective formulations.

REFERENCE/RESOURCES:
1. Current package insert for each listed drug
2. National Institute of Health. Genetic and Rare Diseased Information Center (GARD). Accessed August 22, 2025. Available from https://rarediseases.info.nih.gov/
3. Food and Drug Administration. Search Orphan Drug Designations and Approvals. https://www.accessdata.fda.gov/scripts/opdlisting/oopd/index.cfm (accessed August 22, 2025).
4. Orphan Drugs, 21 C.F.R § 316 (1992)
5. U.S. Food and Drug Administration. Center for Drug Evaluation and Research. Rare Disease at FDA (2020). Accessed August 22, 2025. Available from https://www.fda.gov/patients/rare-diseases-fda
6. U.S. Food and Drug Administration. Center for Drug Evaluation and Research. Orphan Drug Modernization Plan (2018). Accessed August 22,

2025. Available from https://www.fda.gov/industry/designating-orphan-product-drugs-and-biological-products/orphan-drug-modernization-plan
7. Stone WL, Basit H, Master SR. Gaucher Disease. StatPearls. November 12, 2023. Accessed August 22, 2025. Available at: Gaucher Disease - StatPearls - NCBI Bookshelf (nih.gov).
8. Rosee PL, Horne A, Hines M, et al. Recommendations for the management of hemophagocytic lymphohistiocytosis in adults. *Blood*. 2019: 133(23):2465-2477. Available at: Recommendations for the management of hemophagocytic lymphohistiocytosis in adults | Blood | American Society of Hematology (ashpublications.org).
9. Rett Syndrome Diagnosis. International Rett Syndrome Foundation. Accessed August 22, 2025. Available at: Rett Syndrome Diagnosis - International Rett Syndrome Foundation.
10. Beales PL, Elcioglu N, Woolf AS, Parker D, Flinter FA. New criteria for improved diagnosis of Bardet-Biedl syndrome: results of a population survey. J Med Genet. 1999;36(6):437-446.
11. ACT sheets and algorithms. American College of Medical and Generics and Genomics. Accessed August 22, 2025. Available at: ACT Sheets and Algorithms (acmg.net).
12. Jäger U, Barcellini W, Broome CM, et al. Diagnosis and treatment of autoimmune hemolytic anemia in adults: Recommendations from the First International Consensus Meeting. Blood Rev. 2020 May;41:100648

Table 1: BILLING GUIDELINES AND CODING

Pharmacy Benefit		
Brand Name	**Generic Name**	
Aqneursa	Levacetylleucine	Pharmacy benefit
Buphenyl	sodium phenylbutyrate tablet	Pharmacy benefit
Carbaglu	carglumic acid tablet for suspension	Pharmacy benefit
Cerdelga	eliglustat tartrate capsule	Pharmacy benefit
Cholbam	cholic acid capsule	Pharmacy benefit
Crenessity	crinecerfont capsules/oral solution	Pharmacy benefit
Ctexli	chenodiol tablet	Pharmacy benefit
Daybue	trofinetide oral solution	Pharmacy benefit
Dojolvi	triheptanoin liquid	Pharmacy benefit
Forzinity	elamipretide vial	Pharmacy benefit
Galafold	migalastat capsule	Pharmacy benefit
Imcivree	setmelanotide vial	Pharmacy benefit
Joenja	leniolisib phosphate tablet	Pharmacy benefit
Keveyis	dichlorphenamide tablet	Pharmacy benefit
Miplyffa	Arimoclomol citrate capsule	Pharmacy benefit

Myalept	metreleptin vial	Pharmacy benefit
Olpruva	sodium phenylbutyrate pellet pack kit	Pharmacy benefit
Pheburane	sodium phenylbutyrate oral pellet	Pharmacy benefit
Procysbi	cysteamine delayed release capsules and cysteamine granules	Pharmacy benefit
Pyrukynd	mitapivat sulfate tablet	Pharmacy benefit
Ravicti	glycerol phenylbutyrate liquid	Pharmacy benefit
Skyclarys	omaveloxolone capsule	Pharmacy benefit
Sohonos	palovarotene capsule	Pharmacy benefit
Xolremdi	mavorixafor capsules	Pharmacy benefit
Xuriden	uridine triacetate granules	Pharmacy benefit
Zavesca	miglustat capsule (100 mg)	Pharmacy benefit
Zokinvy	lonafarnib capsule	Pharmacy benefit
Ztalmy	ganaxolone suspension	Pharmacy benefit

Medical Benefit		
HCPCS	**Coding Description**	**Brand Name**
J1302	Injection, sutimlimab-jome, 10 mg	Enjaymo
J1304	Injection, tofersen, 1 mg	Qalsody
J1747†	Injection, spesolimab-sbzo, 1 mg	Spevigo IV
J1809	Injection, fosdenopterin, 0.1 mg	Nulibry
J3590, C9399	Unclassified drugs or biologics	Kebilidi
J3590, C9399	Unclassified drugs or biologics	Skysona
J9210	Injection, emapalumab-lzsg, 1 mg	Gamifant
J2998, C9090	Injection, plasminogen, human-tvmh, 1 mg	Ryplazim
J9376	Injection, pozelimab-bbfg, 1 mg	Veopoz
J3401	Beremagene geperpavec-svdt for topical administration, containing nominal 5 x 10^9 pfu/ml vector genomes, per 0.1 ml	Vyjuvek
J3590, C9399	Unclassified drugs or biologics	Zevaskyn
ADMINISTRATION CODES		
96365	Ther/proph/diag iv inf init	
96366	Ther/proph/diag iv inf addon	
96372	Ther/proph/diag inj sc/im	
96374	Ther/proph/diag inj iv push	
96401	Chemo anti-neopl sq/im	
96409	Chemo iv push sngl drug	
96413	Chemo iv infusion 1 hr	
93415	Chemo iv infusion addl hr	
62322	Njx interlaminar lmbr/sac	(Qalsody)
62323	Njx interlaminar lmbr/sac	(Qalsody)
15040	Harvest cultured skin graft	(Zevaskyn)
MODIFIER CODES†		

-JA	Administered Intravenously	
-JB	Administered Subcutaneously	
-JW	Drug Amount Discarded/Not Administered to Any Patient	
-JZ	Zero drug amount discarded/Not administered to Any Patient	

*Coding Notes:
• The above code list is provided as a courtesy and may not be all-inclusive. Inclusion or omission of a code from this policy neither implies nor guarantees reimbursement or coverage. Some codes may not require routine review for medical necessity, but they are subject to provider contracts, as well as member benefits, eligibility and potential utilization audit.
• HCPCS/CPT code(s) may be subject to National Correct Coding Initiative (NCCI) procedure-to-procedure (PTP) bundling edits and daily maximum edits known as "medically unlikely edits" (MUEs) published by the Centers for Medicare and Medicaid Services (CMS). This policy does not take precedence over NCCI edits or MUEs. Please refer to the CMS website for coding guidelines and applicable code combinations.

†Must be billed with the JA modifier for the intravenous infusion of the drug or billed with the JB modifier for the subcutaneous injection form of administration

Appendix 1*:* Beales' modified diagnostic criteria for Bardet-Biedl syndrome[10]

Four features required	
Primary features	Rod-cone dystrophy
	Polydactyly
	Obesity
	Learning disabilities
	Hypogonadism in males
	Renal anomalies
Three primary and two secondary features required	
Secondary features	Speech disorder/delay
	Strabismus/cataracts/astigmatism
	Brachydactyly/syndactyly
	Developmental delay
	Polyuria/polydipsia (nephrogenic diabetes insipidus)
	Ataxia/poor coordination/imblanace
	Mild spasticity (especially lower limbs)
	Diabetes mellitus
	Dental crowding/hypodontia/small roots/high arched palate
	Left ventricular hypertrophy/congenital heart disease
	Hepatic fibrosis

PHARMACY PRIOR AUTHORIZATION POLICY AND CRITERIA ORPTCOTH022	MISCELLANEOUS PRODUCTS MEDICATIONS FOR RARE INDICATIONS See Table 2 for Applicable Medications

Table 2: FDA Indication(s) and Criteria for Authorization

Drug	FDA Indication(s)	Initial Authorization Criteria	Reauthorization Criteria
Aqneursa (levacetylleucine)	Treatment of neurological manifestations of Niemann-Pick disease type C (NPC) in adults and pediatric patients weighing equal or greater than 15 kg.	• Diagnosis of Niemann-Pick disease type C (NPC) confirmed by mutations in both alleles of NPC1 or NPC2, or mutation in only one allele of NPC1 or NPC2 plus either positive filipin staining or elevated cholestane triol/oxysterols (over two times the upper limit of normal) • Documentation of at least one neurological sign of disease • Documentation of baseline score for one of following disease severity tests: Scale for the Assessment and Rating of Ataxia (SARA, or modified SARA) or 5-domain NPC Clinical Severity Scale (NPCCSS)	Documentation of benefit of therapy as evidence by improvement from baseline in the 5-domain NPC Clinical Severity Scale (NPCCSS) score, or SARA/mSARA score
Buphenyl (sodium phenylbutyrate tablet)	Adjunctive therapy in the chronic management of patients with urea cycle disorders involving deficiencies of carbamoyl phosphate synthetase (CPS), ornithine transcarbamylase (OTC), or argininosuccinic acid synthetase (AS). All patients with neonatal-onset deficiency (complete enzymatic deficiency, presenting within the first 28 days of life. Patients with late-onset disease (partial enzymatic deficiency, presenting after the first month of life) who have a history of hyperammonemic encephalopathy.	N/A	N/A

PHARMACY PRIOR AUTHORIZATION POLICY AND CRITERIA ORPTCOTH022	MISCELLANEOUS PRODUCTS MEDICATIONS FOR RARE INDICATIONS See Table 2 for Applicable Medications

Drug	FDA Indication(s)	Initial Authorization Criteria	Reauthorization Criteria
Carbaglu (Carglumic acid tablet for suspension)	• Adjunctive therapy to standard of care for the treatment of acute hyperammonemia due to N-acetylglutamate Synthase (NAGS) deficiency. • Maintenance therapy for the treatment of chronic hyperammonemia due to NAGS deficiency. • Pediatric and adult patients as adjunctive therapy to standard of care for the treatment of acute hyperammonemia due to propionic acidemia (PA) or methylmalonic acidemia (MMA).	For NAGS deficiency: confirmed mutation in the NAGS gene	N/A
Cerdelga (Eliglustat tartrate capsule)	Long-term treatment of adult patients with Gaucher disease type 1 (GD1) who are CYP2D6 extensive metabolizers (Ems), intermediate metabolizers (Ims), or poor metabolizers (PMs) as detected by an FDA-cleared test. Limitations of Use: • Patients who are CYP2D6 ultra-rapid metabolizers (URMs) may not achieve adequate concentrations of CERDELGA to achieve a therapeutic effect. • A specific dosage cannot be recommended for those patients whose CYP2D6 genotype cannot be determined (indeterminate metabolizers).	1. Diagnosis confirmed by one of the following[7]: a. Mutation in the glucocerebrosidase beta-1 (GBA1) gene b. Enzyme assay demonstrating less than 15% of mean normal glucocerebrosidase enzyme activity 2. Member is a CYP2D6 extensive metabolizer, intermediate metabolizer, or poor metabolizer as detected by an FDA-cleared test	N/A

PHARMACY PRIOR AUTHORIZATION POLICY AND CRITERIA ORPTCOTH022	MISCELLANEOUS PRODUCTS MEDICATIONS FOR RARE INDICATIONS See Table 2 for Applicable Medications

Drug	FDA Indication(s)	Initial Authorization Criteria	Reauthorization Criteria
Cholbam (Cholic acid capsule)	• Bile acid synthesis defect, due to single enzyme defects • Adjunctive treatment of peroxisomal disorders, including Zellweger spectrum disorders, in patients who exhibit manifestations of liver disease, steatorrhea, or complications due to decreased absorption of fat-soluble vitamins Limitations of Use: • Safety and efficacy on extrahepatic manifestations of the above diagnoses have not been established	1. Documentation of baseline liver function tests (LFTs) AND 2. For bile acid synthesis disorder: documentation of a single enzyme defect 3. For peroxisomal disorder, including Zellweger spectrum disorders, both of the following criteria must be met: a. Documentation of manifestations of at least one of the following: i. Liver disease (e.g., jaundice, elevated serum transaminases) ii. Steatorrhea iii. Complications from decreased fat-soluble vitamin absorption (such as poor growth) AND b. The medication will be used as adjunctive therapy	N/A
Crenessity (crinecerfont capsules/oral solution)	Adjunctive treatment to glucocorticoid replacement to control androgens in adults and pediatric patients 4 years of age and older with classic congenital adrenal hyperplasia (CAH)	1. Diagnosis of classic CAH due to 21-hydroxylase deficiency (21-OHD) 2. Documentation that medication will be used concomitantly with glucocorticoid replacement therapy 3. Stable glucocorticoid dose (for at least 4 weeks) of greater than 13 mg/m2/day hydrocortisone equivalents for adults and greater than 12 mg/m2/day hydrocortisone equivalents for pediatric patients	N/A

Drug	FDA Indication(s)	Initial Authorization Criteria	Reauthorization Criteria
		4. For pediatric patients weighing at least 55 kg or patients weighing at least 20 kg if CYP3A4 dose adjustment is required: capsule formulation is requested or documentation is provided that patient is unable to swallow capsule whole.	
Ctexli (chenodiol tablet)	Treatment of cerebrotendinous xanthomatosis (CTX) in adults	N/A	N/A
Daybue (Trofinetide oral solution)	Treatment of Rett syndrome in adults and pediatric patients 2 years of age and older.	Confirmed mutation in the MCEP2 gene[9]	N/A
Dojolvi (Triheptanoin liquid)	As a source of calories and fatty acids for the treatment of pediatric and adult patients with molecularly confirmed long-chain fatty acid oxidation disorders (LC-FAOD).	See the American College of Medical Genetics and Genomics ACT sheet under Newborn Screening and accompanying algorithm for Fatty Acid Oxidation Disorders diagnostic criteria.[11]	N/A
Enjaymo (sutimlimab-jome injection)	Treatment of hemolysis in adults with cold agglutinin disease (CAD)	Diagnosis of primary cold agglutinin disease (CAD) by all the following: 1. Chronic hemolysis, confirmed by low levels of haptoglobin, and high levels of unconjugated bilirubin and lactate dehydrogenase 2. Positive direct antiglobulin (Coombs) test for C3d. (Note: a positive is graded as a 1+, 2+, or 3+) 3. Cold agglutinin titer of 1:64 or higher at 4 degrees Celsius 4. Presence of one or more symptom associated with CAD such as	N/A

Drug	FDA Indication(s)	Initial Authorization Criteria	Reauthorization Criteria
		symptomatic anemia, acrocyanosis, Raynaud's phenomenon, hemoglobinuria	
Filsuvez (birch triterpenes)	Treatment of wounds associated with dystrophic and junctional epidermolysis bullosa (EB) in adult and pediatric patients 6 months of age and older	1. Confirmed diagnosis by genetic testing of mutation in the collagen type VII alpha 1 chain (COL7A1) gene. For junctional EB, autosomal recessive mutations in the laminin-332 genes (LAMA3, LAMB3, LAMC2). Note: other genes that can be involved include COL17A1, LAMA3A, ITGA6, ITGB4, ITGA313 2. Treatment will be used on a cutaneous wound (or wounds) that are clean in appearance with adequate granulation tissue, excellent vascularization, and do not appear infected	1. Documentation of successful response to therapy as indicated by complete wound healing or decrease in wound size 2. Patient continues to have incomplete wound closures that are clean in appearance with adequate granulation tissue, excellent vascularization, and do not appear infected
Forzinity (elamipretide vial)	To improve muscle strength in adult and pediatric patients with Barth syndrome weighing at least 30 kg	1. Confirmed diagnosis of Barth syndrome by either genetic testing for TAZ gene deficiency or MLCL/CL ratio assay 2. Patient weight is greater than or equal to 30 kg	N/A
Galafold (Migalastat capsule)	Treatment of adults with a confirmed diagnosis of Fabry disease and an amenable galactosidase alpha gene (GLA) variant based on in vitro assay data	Confirmation of an amenable galactosidase alpha (GLA) gene variant (see package insert)	N/A
Gamifant (emapalumab-lzsg vial)	Treatment of adult and pediatric (newborn and older) patients with primary hemophagocytic lymphohistiocytosis (HLH) with refractory, recurrent or	For HLH: Diagnosis of primary HLH based on a molecular diagnosis OR family history consistent with primary HLH OR 5 out of the following 8 criteria fulfilled[8]:	N/A

Drug	FDA Indication(s)	Initial Authorization Criteria	Reauthorization Criteria
	progressive disease or intolerance with conventional HLH therapy. Treatment of adult and pediatric (newborn and older) patients with 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.	1. Fever 2. Splenomegaly 3. Cytopenias affecting 2 of 3 lineages in the peripheral blood: hemoglobin less than 9 g/dL, platelets less than 100 x 109/L, neutrophils less than 1 x 109/L 4. Hypertriglyceridemia (fasting triglycerides greater than 3 mmol/L or equal or greater than 265 mg/dL) and/or hypofibrinogenemia (equal or less than 1.5 g/L) 5. Hemophagocytosis in bone marrow, spleen, or lymph nodes with no evidence of malignancy 6. Low or absent NK-cell activity 7. Ferritin equal or greater than 500 mcg/L 8. Soluble CD 25 equal or greater than 2400 U/mL	
Imcivree (Setmelanotide)	Chronic weight management in adult and pediatric patients two years and older with obesity due to • POMC, PCSK1, or LEPR deficiency confirmed by genetic testing demonstrating variants in POMC, PCSK1, or LEPR genes that are interpreted as pathogenic, likely pathogenic, or of uncertain significance (VUS) • Bardet-Biedl syndrome (BBS)	One of the following: 1. Confirmed pathogenic mutation in the POMC, PCSK1, or LEPR gene 2. Bardet-Biedl Syndrome (as diagnosed by four primary features or three primary and two secondary features [see Appendix 1][10])	N/A

Drug	FDA Indication(s)	Initial Authorization Criteria	Reauthorization Criteria
	Limitations of Use: • Setmelanotide is not indicated for the treatment of patients with the following conditions as setmelanotide would not be expected to be effective: ○ Obesity due to suspected POMC, PCSK1, or LEPR deficiency with POMC, PCSK1, or LEPR variants classified as benign or likely benign. • Other types of obesity not related to POMC, PCSK1 or LEPR deficiency, or BBS, including obesity associated with other genetic syndromes and general (polygenic) obesity		
Joenja (leniolisib phosphate tablet)	• Treatment of activated phosphoinositide 3-kinase delta (PI3Kδ) syndrome (APDS) in adult and pediatric patients 12 years of age and older.	1. Confirmed mutation in the PIK3CD gene (APDS1) or the PIK3R1 gene (APDS2) 2. Patient must weigh at least 45 kg 3. Must have at least one measurable lymph node on computed tomography (CT) or magnetic resonance imaging (MRI) scan	Patient must weigh at least 45 kg
Kebilidi (eladocagene exuparvovec-tneq suspension)	Treatment of adult and pediatric patients with aromatic L-amino acid decarboxylase (AADC) deficiency	Genetic confirmation of biallelic mutations in the DDC gene	N/A
Keveyis (dichlorphenamide tablet)	Treatment of primary hyperkalemic periodic paralysis, primary hypokalemic periodic paralysis, and related variants.	N/A	N/A

Drug	FDA Indication(s)	Initial Authorization Criteria	Reauthorization Criteria
Miplyffa (arimoclomol citrate capsule)	Indicated for use in combination with miglustat for the treatment of neurological manifestations of Niemann-Pick disease type C (NPC) in adult and pediatric patients 2 years of age and older	1. Diagnosis of Niemann-Pick disease type C (NPC) confirmed by mutations in both alleles of NPC1 or NPC2, or mutation in only one allele of NPC1 or NPC2 plus either positive filipin staining or elevated cholestane triol/oxysterols (over two times the upper limit of normal) 2. Documentation of at least one neurological sign of disease 3. Documentation of baseline score for one of following disease severity tests: Scale for the Assessment and Rating of Ataxia (SARA, or modified SARA) or 5-domain NPC Clinical Severity Scale (NPCCSS)	Documentation of benefit of therapy as evidence by improvement from baseline in the 5-domain NPC Clinical Severity Scale (NPCCSS) score or SARA/mSARA score
Myalept (Metreleptin vial)	Adjunct to diet as replacement therapy to treat the complications of leptin deficiency in patients with congenital or acquired generalized lipodystrophy. Limitations of Use: • The safety and effectiveness of metreleptin for the treatment of complications of partial lipodystrophy have not been established. • The safety and effectiveness of metreleptin for the treatment of liver disease, including nonalcoholic steatohepatitis (NASH), have not been established.	N/A	N/A

Drug	FDA Indication(s)	Initial Authorization Criteria	Reauthorization Criteria
	• Metreleptin is not indicated for use in patients with HIV-related lipodystrophy. • Metreleptin is not indicated for use in patients with metabolic disease, including diabetes mellitus and hypertriglyceridemia, without concurrent evidence of congenital or acquired generalized lipodystrophy.		
Nulibry (fosdenopterin vial)	To reduce the risk of mortality in patients with molybdenum cofactor deficiency (MoCD) Type A.	Confirmed mutation in the MOCS1 gene OR suspected MoCD Type A	Genetic testing to confirm mutation in the MOCS1 gene (Nulibry should be discontinued if the MoCD Type A diagnosis is not confirmed by genetic testing)
Olpruva (sodium phenylbutyrate pellet pack kit)	As adjunctive therapy to standard of care, which includes dietary management, for the chronic management of adult and pediatric patients 1 year of age and older weighing 7 kg or greater, with urea cycle disorders (UCDs) involving deficiencies of carbamylphosphate synthetase (CPS), ornithine transcarbamylase (OTC), or argininosuccinic acid synthetase (AS) Limitations of Use: • Not indicated for the treatment of acute hyperammonemia • Not recommended for patients younger than 1 year of age due to the volume of free water required for daily administration	Patient had a therapeutic failure to Pheburane (sodium phenylbutyrate pellets), defined as elevated ammonia or plasma amino acid levels after the patient has been taking the medication (at an adequate dose) for at least two months OR Patient has documented contraindication to sodium phenylbutyrate	N/A
Opfolda (Miglustat capsule)	• Adult patients with late-onset Pompe disease (lysosomal acid alpha-glucosidase [GAA] deficiency)	Confirmed mutation in the GAA/LYAG gene	N/A

Drug	FDA Indication(s)	Initial Authorization Criteria	Reauthorization Criteria
	weighing ≥40 kg and who are not improving on their current enzyme replacement therapy (ERT). • Given in combination with Pombiliti, a hydrolytic lysosomal glycogen-specific enzyme.		
Pheburane (sodium phenylbutyrate oral pellet)	Indicated as adjunctive therapy to standard of care, which includes dietary management, for the chronic management of adult and pediatric patients with urea cycle disorders (UCDs), involving deficiencies of carbamylphosphate synthetase (CPS), ornithine transcarbamylase (OTC) or argininosuccinic acid synthetase (AS). Limitations of Use: Episodes of acute hyperammonemia may occur in patients while on Pheburane. Pheburane is not indicated for the treatment of acute hyperammonemia, which can be a life-threatening medical emergency that requires rapid acting interventions to reduce plasma ammonia levels.	N/A	N/A
Procysbi (cysteamine delayed-release capsules & granules)	Treatment of nephropathic cystinosis in adults and pediatric patients 1 year of age and older.	1. Confirmed diagnosis of nephropathic cystinosis as evidenced by measuring leukocyte cystine levels (LCL) or genetic analysis of the CTNS gene (gene that encodes cystinosin) 2. Documentation of trial and failure, contraindication or intolerance to	N/A

Drug	FDA Indication(s)	Initial Authorization Criteria	Reauthorization Criteria
		immediate release cysteamine capsules (Cystagon).	
Pyrukynd (mitapivat sulfate tablet)	Treatment of hemolytic anemia in adults with pyruvate kinase deficiency	1. Diagnosis of pyruvate kinase deficiency (PKD). Must include documentation supporting diagnosis (such as chart notes and labs), such as: A. Markers of chronic hemolytic anemia (such as low hemoglobin, low haptoglobin, elevated bilirubin, and elevated reticulocytes) and evidence of family history of PKD B. Pyruvate kinase enzyme activity below the lower limit of normal per the laboratory standard (actual laboratory results must be included) C. At least two mutant alleles in the PKLR gene 2. Documentation of one of the following: A. Hemoglobin less than or equal to 10 mg/dL taken within the previous three months B. Patient has had as six or more red blood cell transfusions in the last twelve months	1. One of the following: A. Sustained increase in hemoglobin (Hb) of at least 1.5 mg/dL from pre-treatment level. Note: initial hemoglobin level prior to treatment plus a recent level (within the last three months) must be provided B. Documentation of a reduction in transfusion burden in the previous 6 months, compared with prior to treatment
Qalsody (Tofersen)	Treatment of Amyotrophic lateral sclerosis (ALS) in adults who have a mutation in the superoxide dismutase 1 (SOD1) gene	1. Confirmed mutation in the superoxide dismutase 1 (SOD1) gene	Stabilization or slowing of disease progression from pre-treatment baseline ALSFRS-R scores

Drug	FDA Indication(s)	Initial Authorization Criteria	Reauthorization Criteria
	This indication is approved under accelerated approval based on reduction in plasma neurofilament light chain (NfL) observed in patients treated with Qalsody. Continued approval for this indication may be contingent upon verification of clinical benefit in confirmatory trial(s).	2. Documentation of baseline ALS Functional Rating Scale-Revised (ALSFRS-R) 3. Forced vital capacity (FVC) greater than or equal to 50% of predicted (taken within the past three months) 4. Documentation of weakness attributable to ALS	
Ravicti (glycerol phenylbutyrate liquid)	Use as a nitrogen-binding agent for chronic management of patients with urea cycle disorders (UCDs) who cannot be managed by dietary protein restriction and/or amino acid supplementation alone. RAVICTI must be used with dietary protein restriction and, in some cases, dietary supplements (e.g., essential amino acids, arginine, citrulline, protein-free calorie supplements). Limitations of Use: • Ravicti is not indicated for the treatment of acute hyperammonemia in patients with UCDs because more rapidly acting interventions are essential to reduce plasma ammonia levels. • The safety and efficacy of Ravicti for the treatment of N-acetylglutamate synthase (NAGS) deficiency has not been established.	1. Patient has had a therapeutic failure to Pheburane (sodium phenylbutyrate pellets), defined as elevated ammonia or plasma amino acid levels after the patient has been taking the medication (at an adequate dose) for at least two months OR Patient has documented contraindication to sodium phenylbutyrate	N/A
Ryplazim	Treatment of patients with plasminogen deficiency type 1 (hypoplasminogenemia)	1. Diagnosis of plasminogen deficiency type 1 confirmed by one of the following:	For initial reauthorization: 1. Documented positive response to therapy, defined

Drug	FDA Indication(s)	Initial Authorization Criteria	Reauthorization Criteria
(plasminogen, human-tvmh vial)		A. Genetic testing (biallelic pathogenic variants in PLG gene) B. Confirmed hypoplasminogenemia (reduced plasminogen protein levels and functional activity) 2. Documentation of plasminogen activity level of 45% or lower of laboratory standard within the previous six months 3. Documentation of clinical signs and symptoms of the disease (such as ligneous conjunctivitis, gingivitis, tonsillitis, abnormal wound healing)	as improvement in lesion number/size or improved function from baseline For subsequent reauthorization: 1. Documentation of no new or recurring lesions 2. Documentation that trough plasminogen activity levels are maintained at least 10% above baseline trough levels (indicating absence of anti-plasminogen antibodies)
Skyclarys (omaveloxolone capsule)	Treatment of Friedreich's ataxia in adults and adolescents aged 16 years and older.	1. Confirmed mutation in the Frataxin (FXN) gene	
Skysona (Elivaldogene)	To slow the progression of neurologic dysfunction in boys 4-17 years of age with early, active cerebral adrenoleukodystrophy (CALD). Early, active cerebral adrenoleukodystrophy refers to asymptomatic or mildly symptomatic (neurologic function score, NFS ≤ 1) boys who have gadolinium enhancement on brain magnetic resonance imaging (MRI) and Loes scores of 0.5-9. • This indication is approved under accelerated approval based on 24-month Major Functional Disability	1. Confirmed mutation in the Adenosine Triphosphate (ATP)-binding cassette, subfamily D, member 1 (ABCD1) gene on the x chromosome 2. Patient has early active cerebral adrenoleukodystrophy (CALD) defined by ALL of the following: a. Elevated very-long-chain fatty acid (VLCFA) values b. Active central nervous system (CNS) disease established by central radiographic review of	N/A

Drug	FDA Indication(s)	Initial Authorization Criteria	Reauthorization Criteria
	(MFD)-free survival. Continued approval for this indication may be contingent upon verification and description of clinical benefit in a confirmatory trial(s). Limitations of Use • SKYSONA does not prevent the development of or treat adrenal insufficiency due to adrenoleukodystrophy. • An immune response to SKYSONA may limit the persistence of descendent cells of SKYSONA, causing rapid loss of efficacy of SKYSONA in patients with full deletions of the human adenosine triphosphate binding cassette, sub family D, member 1 (*ABCD1)* gene. • SKYSONA has not been studied in patients with CALD secondary to head trauma. • Given the risk of hematologic malignancy with SKYSONA, and unclear long-term durability of SKYSONA and human adrenoleukodystrophy protein (ALDP) expression, careful consideration should be given to the appropriateness and timing of treatment for each boy, especially for boys with isolated pyramidal tract disease based on available treatment	brain magnetic resonance imaging (MRI) demonstrating: i. Loes score between 0.5 and 9 (inclusive) on the 34-point scale ii. Gadolinium enhancement on MRI of demyelinating lesions c. Neurologic Function Score (NFS) of 1 or less 3. Documentation is provided indicating that patient has NONE of the following: a. History of hematopoietic stem cell transplant (HSCT) b. History of elivaldogene autotemcel treatment c. HLA-matched willing sibling donor	

Drug	FDA Indication(s)	Initial Authorization Criteria	Reauthorization Criteria
	options since their clinical symptoms do not usually occur until adulthood.		
Sohonos (Palovarotene)	Fibrodysplasia ossificans progressiva (FOP) – for the reduction in the volume of new heterotopic ossification. Approved for adults and children aged 8 years and older for females and 10 years and older for males	1. Confirmed R206H mutation in the activin A type 1 receptor (ACVR 1) gene 2. Documentation of one of the following scores: Cumulative Analogue Joint Involvement Scale (CAJIS), fibrodysplasia ossificans progressiva (FOP) – Physical Function Questionnaire (FOP-PFQ)	Documentation of one of the following must be met: 1. Reduction in the volume of new heterotopic ossification as confirmed by radiographic assessment such as X-ray, computed tomography (CT), magnetic resonance imaging (MRI) 2. Reduction in the rate of flare-ups 3. Stabilization or improvement in one of the following: Cumulative Analogue Joint Involvement Scale (CAJIS), fibrodysplasia ossificans progressiva (FOP) – Physical Function Questionnaire (FOP-PFQ)
Spevigo (Spesolimab)	Treatment of generalized pustular psoriasis (GPP) in adults and pediatric patients 12 years of age and older and weighing at least 40 kg	FOR IV ONLY: 1. Diagnosis of generalized pustular psoriasis (GPP), confirmed by both of the following: a. Primary, sterile, macroscopically visible pustules on non-acral skin AND b. Pustulation is not restricted to psoriatic plaques 2. Presence of an acute flare of generalized pustular psoriasis of	FOR IV ONLY: 1. All criteria for initial authorization must be met 2. Documentation of a clinical response to prior treatment with spesolimab, defined as achieving a Generalized Pustular Psoriasis Physician Global Assessment (GPPGA) score of 0 or 1

Drug	FDA Indication(s)	Initial Authorization Criteria	Reauthorization Criteria
		moderate to severe intensity, as defined by: a. Generalized Pustular Psoriasis Physician Global Assessment (GPPGA) total score of 3 or greater AND b. The presence of new or worsening pustules AND c. Generalized Pustular Psoriasis Physician Global Assessment (GPPGA) pustulation sub score of 2 or greater AND d. At least 5% of body surface area (BSA) with erythema and the presence of pustules 3. Requests for one additional dose may be approved one week after initial dose for treatment of the same flare if the following criteria are met: a. Generalized Pustular Psoriasis Physician Global Assessment (GPPGA) total score of 2 or higher AND b. Generalized Pustular Psoriasis Physician Global Assessment (GPPGA) pustulation sub score of 2 or higher	
Veopoz (Pozelimab-bbfg)	Adult and pediatric patients one year of age and older with CD55-deficient protein-losing enteropathy (PLE), also known as CHAPLE disease.	Confirmed CD55 loss-of-function mutation	N/A

PHARMACY PRIOR AUTHORIZATION POLICY AND CRITERIA ORPTCOTH022	MISCELLANEOUS PRODUCTS MEDICATIONS FOR RARE INDICATIONS See Table 2 for Applicable Medications

Drug	FDA Indication(s)	Initial Authorization Criteria	Reauthorization Criteria
Vyjuvek (beremagene geperpavec)	Treatment of wounds in adult and pediatric patients with dystrophic epidermolysis bullosa (DEB) with mutations in the *collagen type VII alpha 1 chain (COL7A1)* gene	1. Confirmed mutation in the collagen type VII alpha 1 chain (COL7A1) gene 2. Treatment will be used on a cutaneous wound (or wounds) that are clean in appearance with adequate granulation tissue, excellent vascularization, and do not appear infected	1. Documentation of successful response to therapy as indicated by complete wound healing or decrease in wound size 2. Patient continues to have incomplete wound closures that are clean in appearance with adequate granulation tissue, excellent vascularization, and do not appear infected
Vykat™ XR tablet (diazoxide choline)	Treatment of hyperphagia in adults and pediatric patients 4 years of age and older with Prader-Willi syndrome (PWS)	1. Diagnosis of Prader-Willi syndrome (PWS) confirmed by genetic testing 2. Documentation that patient experiences moderate to severe symptoms of hyperphagia related to PWS and provides documentation of associated symptoms (e.g. food-seeking behaviors) 3. Dose is appropriate based on recent body weight	1. Documentation of improvement in hyperphagic symptoms, such as a decrease in food-related aggression or manipulation, or lessened food preoccupation that interferes with normal daily activities. 2. Dose is appropriate based on recent body weight
Xolremdi (mavorixafor)	Patients 12 years of age and older with WHIM syndrome (warts, hypogammaglobulinemia, infections and myelokathexis) to increase the number of circulating mature neutrophils and lymphocytes	1. Confirmed variant in the CXCR4 gene 2. Documentation of baseline absolute neutrophil count (ANC) and absolute lymphocyte count (ALC)	Documentation of sustained improvement in absolute neutrophil count (ANC) and absolute lymphocyte count (ALC)
Xuriden (uridine triacetate granules)	Adult and pediatric patients for the treatment of hereditary orotic aciduria.	Confirmed mutation in the UMPS gene	N/A

PHARMACY PRIOR AUTHORIZATION POLICY AND CRITERIA ORPTCOTH022	MISCELLANEOUS PRODUCTS MEDICATIONS FOR RARE INDICATIONS See Table 2 for Applicable Medications

Drug	FDA Indication(s)	Initial Authorization Criteria	Reauthorization Criteria
Zavesca (miglustat capsule)	Monotherapy for the treatment of adult patients with mild to moderate type 1 Gaucher disease for whom enzyme replacement therapy is not a therapeutic option (e.g., due to allergy, hypersensitivity, or poor venous access).	1. Confirmed mutation in the GBA1 gene 2. For Niemann-Pick disease type C (NPC): Documentation that miglustat will be used in combination with Miplyffa for NPC.	N/A
Zevaskyn (prademagene zamikeracel cellular sheet)	Treatment of wounds in adults and pediatric patients with recessive dystrophic epidermolysis bullosa (RDEB)	Confirmed mutations in both COL7A1 genes Treatment will be used on partial-thickness RDEB wounds open chronically for at least six months	N/A
Zokinvy (lonafarnib capsule)	Patients 12 months of age and older with a body surface area (BSA) of 0.39 m2 and above: • To reduce the risk of mortality in Hutchinson-Gilford Progeria Syndrome (HGPS) • For the treatment of processing-deficient Progeroid Laminopathies with either: • Heterozygous LMNA mutation with progerin-like protein accumulation • Homozygous or compound heterozygous ZMPSTE24 mutations Limitations of Use: • Zokinvy is not indicated for other Progeroid Syndromes or processing-proficient Progeroid Laminopathies. Based upon its mechanism of action, Zokinvy would not be expected to be effective in these populations.	• For HGPS: Confirmed mutation in the LMNA gene • For PPL: Heterozygous LMNA mutation with progerin-like protein accumulation, homozygous or compound heterozygous ZMPSTE24 mutation	N/A

PHARMACY PRIOR AUTHORIZATION POLICY AND CRITERIA ORPTCOTH022	MISCELLANEOUS PRODUCTS MEDICATIONS FOR RARE INDICATIONS See Table 2 for Applicable Medications

Drug	FDA Indication(s)	Initial Authorization Criteria	Reauthorization Criteria
Ztalmy (ganaxolone suspension)	Treatment of seizures associated with cyclin-dependent kinase-like 5 (CDKL5) deficiency disorder (CDD) in patients 2 years of age and older	Detection of pathogenic or likely pathogenic variants in CDKL5	N/A