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Prior Authorization Criteria Update: Orphan Drugs

Plain Language Summary:

- Since 2020, the Medicaid fee-for-service (FFS) program has added 24 medicines to the orphan drug policy. Medicines are designated as "orphan" when they are approved by the Food and Drug Administration (FDA) for very rare conditions. This policy requires that providers follow prescribing recommendations from the Food and Drug Administration before the Oregon Health Plan will pay for the medicine.
- Because these conditions are so rare, this policy has only been used once for the Medicaid fee-for-service (FFS) population. Thus, this policy continues to improve bandwidth for topics at the Pharmacy and Therapeutics (P&T) meetings.
- We recommend minor updates to simplify this policy.

Purpose of Update:

The purpose of this update is evaluate utilization of the orphan drug policy. Orphan drugs are defined by the FDA as drugs and biologics intended for the safe and effective treatment, diagnosis or prevention of rare diseases that affect fewer than 200,000 people in the United States or that affect more than 200,000 people but are not expected to recover the costs of developing and marketing a treatment. Due to the rare incidence of these conditions, there are few FFS patients prescribed these medications, and estimated savings as a result of orphan drug policies is limited. In 2020, the Pharmacy and Therapeutics (P&T) Committee, approved implementation of prior authorization criteria for select orphan drugs to improve bandwidth for topics at P&T meetings and support medically appropriate use of these therapies based on information in the FDA label (**Appendix 1**). Since 2020, 24 orphan drugs have been added to this policy (**Table 1**). However, despite the increasing number of additions to this policy, a review of FFS claims and prior authorization requests identified only one circumstance in which this criteria was utilized reflecting the rare prevalence of these conditions. Because this criteria is utilized infrequently, we recommend simplifying criteria to reference FDA labeling instead of including information from the FDA label in the criteria. FDA labeling related to dosing, monitoring, and indication is occasionally updated after the initial approval, and including links to the FDA label will allow alignment between the policy and FDA label when changes are made.

Table 1. Unique molecular entities included in the policy by year

Year	Cumulative Number of Drugs Included on the Policy
2020	5
2021	13
2022	17
2023	24

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Table 2. Recommended new orphan drugs to add to the policy

Generic Name	Brand Name
ADAMTS13, recombinant-krhn	ADZYNMA
Allogeneic processed thymus tissue-agdc	RETHYMIC
Beremagene geperpavec-svdt	VYJUVEK
Birch triterpenes	FILSUVEZ
Elivaldogene autotemcel	SKYSONA
Levoketoconazole	RECORLEV

Recommendation:

- Simplify PA criteria by linking to FDA labeling instead of including details of the labeling in the PA.
- Include new, recently approved orphan drugs in the policy.

Appendix 1. Proposed Prior Authorization Criteria

Orphan Drugs

Goal(s):

- To support medically appropriate use of orphan drugs (as designated by the FDA) which are indicated for rare conditions
- To limit off-label use of orphan drugs

Length of Authorization:

- Up to 6 months

Requires PA:

- See Table 1 (pharmacy and physician administered claims)

Covered Alternatives:

- Current PMPDP preferred drug list per OAR 410-121-0030 at www.orpdl.org
- Searchable site for Oregon FFS Drug Class listed at www.orpdl.org/drugs/

Table 1. Included orphan drugs

ADAMTS13, recombinant-krhn (ADZYNMA)
Allogeneic processed thymus tissue-agdc (RETHYMIC)
Alpelisib (VIJOICE)
Avacopan (TAVNEOS)

Belumosudil (REZUROCK)
Beremagene geperpavec-svdt (VYJUVEK)
Birch triterpenes (FILSUVEZ)
Burosumab-twza (CRYSVITA)
Cerliponase alfa (BRINEURA)
Elapegademase-lvlr (REVCOVI)
Elivaldogene autotemcel (SKYSONA)
Fosdenopterin (NULIBRY)
Givosiran (GIVLAARI)
Leniolisib (JOENJA)
Levoketoconazole (RECORLEV)
Lonafarnib (ZOKINVY)
Lumasiran (OXLUMO)
Luspatercept (REBLOZYL)
Maralixibat (LIVMARLI)
Mitapivat (PYRUKYND)
Nedosiran (RIVFLOZA)
Odevixibat (BYLVAY)
Olipudase alfa-rpcp (XENPOZYME)
Palovarotene (SOHONOS)
Plasminogen, human-tvmh (RYPLAZIM)
pozelimab-bbfg (VEOPOZ)
Sodium thiosulfate (PEDMARK)
Sutimlimab-jome (ENJAYMO)
Trientine tetrahydrochloride (CUVRIOR)
Velmanase alfa-tycv (LAMZEDE)

~~Table 1. Indications for orphan drugs based on FDA labeling~~

~~Drug~~	~~Indication~~	~~Age~~	~~Dose~~	~~Recommended Monitoring~~
~~Alpelisib (VIJOICE)~~	~~PIK3CA-Related Overgrowth Spectrum (PROS) in those who require systemic therapy~~	~~≥ 2 yrs~~	~~Pediatric 2 to <18 yrs:~~ ~~• 50 mg once daily~~ ~~• May consider increase to 125 mg once daily if ≥6 years after 24 weeks of treatment~~ ~~• May gradually increase to 250 mg once daily once patient turns 18~~ ~~Adult:~~ ~~• 250 mg once daily~~	~~Baseline Monitoring~~ ~~• Fasting BG, HbA1c~~ ~~Ongoing Monitoring~~ ~~• Fasting BG weekly x 2 weeks, then at least once every 4 weeks, then as clinically indicated~~ ~~• HbA1c every 3 months and as clinically indicated~~
~~Avacopan (TAVNEOS)~~	~~Severe active anti-neutrophil cytoplasmic autoantibody~~	~~≥18 yrs~~	~~30 mg (three 10 mg capsules) twice daily, with food~~	~~Baseline Monitoring~~

	(ANCA)-associated vasculitis (granulomatosis with polyangiitis [GPA] and microscopic polyangiitis [MPA]) in combination with glucocorticoids.			• Liver function tests ALT, AST, ALP, and total bilirubin • Hepatitis B (HBsAg and anti-HBc) Ongoing Monitoring • Liver function tests every 4 wks for 6 months, then as clinically indicated
Burosumab-twza (CRYSVITA)	X-linked hypophosphatemia (XLH) FGF23-related hypophosphatemia in tumor-induced osteomalacia (TIO)	XLH ≥ 6 mo TIO ≥ 2 yrs	Pediatric <18 yrs: Initial (administered SC every 2 wks): XLH • <10 kg: 1mg/kg • ≥10 mg: 0.8 mg/kg TIO • 0.4 mg/kg Max dose of 2 mg/kg (not to exceed 90 mg for XLH or 180 mg for TIO) Adult: XLH 1 mg/kg monthly (rounded to nearest 10 mg; max 90 mg) TIO: 0.5 mg/kg monthly initially (Max dose 2 mg/kg or 180mg every 2 wks)	Baseline and Ongoing Monitoring • Use of active vitamin D **analogues** or oral phosphate within prior week; concurrent use is contraindicated • Fasting serum phosphorous: do not administer if serum phosphorous is within or above normal range • Renal function: use is contraindicated in ESRD or with severe renal impairment (CrCl <30 mL/min for adults or eGFR <30 mL/min/1.73m^2 for pediatric patients) • 25-hydroxy vitamin D levels: supplementation with vitamin D (cholecalciferol or ergocalciferol) is recommended as needed. Additional baseline monitoring for TIO only: • Documentation that tumor cannot be located or is unresectable • Elevated FGF-23 levels • Documentation indicating concurrent treatment for the underlying tumor is not planned (i.e., surgical or radiation)
Belumosudil (REZUROCK)	Treatment of chronic graft-versus-host disease after failure of at least two prior lines of systemic therapy	≥ 12 yrs	200 mg orally once daily with food 200 mg twice daily when coadministered with strong CYP3A inducers or proton pump inhibitors	Baseline & Ongoing Monitoring • Total bilirubin, AST, ALT at least monthly • Pregnancy test (if childbearing potential)
Cerliponase alfa (BRINEURA)	To slow the loss of ambulation in symptomatic Batten Disease (late infantile neuronal ceroid lipofuscinosis type 2 or TPP1 deficiency)	3-17 yrs	300 mg every other week via intraventricular route	Baseline Monitoring • Enzymatic or genetic testing to confirm tripeptidyl peptidase 1 deficiency or CLN2 gene mutation • Baseline motor symptoms (e.g., ataxia, motor function, etc) • ECG in patients with a history of bradycardia, conduction disorders or structural heart disease Ongoing Monitoring • Disease stabilization or lack of decline in motor symptoms compared to natural history

Elapegademase-lvlr (REVCOVI)	adenosine deaminase severe combined immune deficiency (ADA-SCID)	N/A	Initial: 0.2 mg/kg twice weekly; No max dose	Baseline Monitoring • CBC or platelet count Ongoing Monitoring • trough plasma ADA activity • trough erythrocyte dAXP levels (twice yearly) • total lymphocyte counts
Fosdenopterin (NULIBRY)	To reduce risk of mortality in patients with molybdenum cofactor deficiency (MoCD) Type A	N/A	Dosed once daily; Preterm Neonate (Gestational Age <37 wks) Initial: 0.4mg/kg Month 1: 0.7 mg/kg Month 3: 0.9 mg/kg Term Neonate (Gestational Age ≥ 37 wks) Initial: 0.55 mg/kg Month 1: 0.75 mg/kg Month 3: 0.9 mg/kg Age ≥1 yr: 0.9 mg/kg	Initiation of therapy is recommended with known or presumed MoCD Type A. Discontinue therapy if diagnosis is not confirmed with genetic testing.
Givosiran (GIVLAARI)	acute hepatic porphyria	≥ 18 yrs	2.5 mg/kg monthly	Baseline and ongoing monitoring • Liver function tests • Blood homocysteine levels-If homocysteine elevated, assess folate, vitamin B12, and vitamin B6
Leniolisib (JOENJA)	Activated phosphoinositide 3-kinase delta (PI3Kδ) syndrome (APDS)	≥ 12 years AND ≥ 45kg	70 mg administered orally twice daily approximately 12 hours apart	Baseline and ongoing monitoring • Pregnancy test (if childbearing potential)
Lonafarnib (ZOKINVY)	To reduce risk of mortality in Hutchinson-Gilford Progeria Syndrome For treatment of processing-deficient Progeroid Laminopathies with either: ○ Heterozygous LMNA mutation with progerin-like protein accumulation ○ Homozygous or compound heterozygous ZMPSTE24 mutations	≥12 mo AND ≥0.39 m^2 BSA	• Initial 115 mg/m^2 twice daily • Increase to 150 mg/m^2 twice daily after 4 months Round all doses to nearest 25 mg	Baseline and ongoing monitoring • Contraindicated with strong or moderate CYP3A inducers, midazolam, lovastatin, simvastatin, or atorvastatin • Comprehensive metabolic panel • CBC • Ophthalmological evaluation • Blood pressure • Pregnancy test (if childbearing potential)
Lumasiran (OXLUMO)	Treatment of primary hyperoxaluria type 1 to lower	N/A	**<10 kg**	N/A

	urinary and plasma oxalate levels		Loading: 6 mg/kg once/month for 3 doses Maintenance: 3 mg/kg once/month **10 kg to <20 kg** Loading: 6 mg/kg once/month for 3 doses Maintenance: 6 mg/kg once every 3 months **≥ 20 kg** Loading: 3 mg/kg once/month for 3 doses Maintenance: 3 mg/kg once every 3 months All maintenance dosing begins 1 month after last loading dose.	
Luspatercept (REBLOZYL)	Anemia (Hgb <11 g/dL) due to beta thalassemia in patients requiring regular red blood cell transfusions Anemia (Hgb <11 g/dL) due to myelodysplastic syndromes with ring sideroblasts or myelodysplastic/ myeloproliferative neoplasm with ring sideroblasts and thrombocytosis	≥ 18 yr	Initial: 1 mg/kg SC Max dose of 1.25 mg/kg every 3 wks for beta thalassemia Max dose of 1.75 mg/kg every 3 wks for myelodysplastic syndromes	Baseline Monitoring/Documentation • Number of red blood cell transfusions in the prior 2 months; minimum of 2 RBC units over the prior 8 wks in patients with myelodysplastic syndromes • Trial and failure of an erythropoiesis stimulating agent in patients with myelodysplastic syndromes • Hemoglobin level • Blood pressure Ongoing Monitoring • Discontinue if there is not a decrease in transfusion burden after 3 maximal doses (about 9-15 wks) • Hemoglobin level • Blood pressure
Maralixibat (LIVMARLI)	Cholestatic pruritis in patients with Alagille syndrome	≥ 3 mo	Initial: 190 mcg/kg once daily, 30 min before first meal of day Goal: 380 mcg/kg once daily after 1 week on initial dose, as tolerated	Baseline/Ongoing Monitoring • Liver function tests (ALT, AST, total bilirubin and direct bilirubin) • Fat soluble vitamins (A, D, E, K); INR used as surrogate for Vitamin K
Mitapivat (PYRUKYND)	Hemolytic anemia in adults with pyruvate kinase (PK) deficiency.	≥ 18 yr	Initial: 5 mg twice daily Titration: If Hb less than normal range or patient required	Baseline/Ongoing Monitoring • Hgb, transfusion requirement

			transfusion in previous 8 weeks, then after 4 weeks increase to 20 mg twice daily, and after another 4 weeks increase to 50 mg twice daily. Max dose: 50 mg twice daily Discontinuation should include down-titration.	
Nedosiran RIVFLOZA	Lower urinary oxalate levels in those with primary hyperoxaluria type 1 (PH1) and relatively preserved renal function, e.g., eGFR ≥ 30 mL/min/1.73 m^2	≥ 9 yr	Weight ≥ 50 kg: 160 mg once monthly Weight <50 kg and age ≥12 yr: 128 mg once monthly Weight <50 kg and age 9 to 11 yr: 3.3 mg/kg once monthly; max 128 mg.	Baseline/Ongoing Monitoring • eGFR
Odevixibat (BYLVAY)	Pruritus in patients with progressive familial intrahepatic cholestasis (PFIC) Limitation of Use: may not be effective in PFIC type 2 in patients with ABCB11 variants resulting in non-functional or complete absence of bile salt export pump protein (BSEP 3)	≥ 3 mo	Initial: 40 mcg/kg once daily with morning meal Titration: After 3 months of initial dose, 40 mcg/kg increments Max dose: 120 mcg/kg once daily; not to exceed 6 mg	Baseline/Ongoing Monitoring • Liver function tests (ALT, AST, total bilirubin and direct bilirubin) • Fat soluble vitamins (A, D, E, K); INR used as surrogate for Vitamin K
Olipudase alfa-rpcp (XENPOZYME)	Non-central nervous system manifestations of acid sphingomyelinase deficiency (ASMD)	N/A	Initial: Age based dose escalation table per Package insert Maintenance: 3 mg/kg via IV infusion every 2 weeks Weight: • If BMI ≤ 30, use actual body weight • If BMI > 30, use adjusted body weight Adjusted body weight (kg) = (actual height in M)^2 x 30	Baseline Monitoring • Liver function tests (ALT, AST) within 1 month • Pregnancy test (if childbearing potential) Ongoing Monitoring • Liver function tests (ALT, AST) within 72 hours of infusions during dose escalation, then during routine clinical management once at maintenance dose
Palovarotene, (SOHONOS)	Fibrodysplasia ossificans progressive (FOP)	≥ 8 yr females	≥ 14 years: Daily: 5 mg	Baseline Monitoring • Pregnancy test (if childbearing potential)

		≥ 10 yr males	Flare wk 1-4: 20 mg once daily Flare wk 5-12: 10 mg once daily <14 years weight based: Daily 10-19.9 kg: 2.5 mg 20-39.9 kg: 3 mg 40-59.9 kg: 4 mg ≥ 60 kg: 5 mg Flare week 1-4 (daily dose) 10-19.9 kg: 10 mg 20-39.9 kg: 12.5 mg 40-59.9 kg: 15 mg ≥ 60 kg: 20 mg Flare week 5-12 (daily dose) 10-19.9 kg: 5 mg 20-39.9 kg: 6 mg 40-59.9 kg: 7.5 mg ≥ 60 kg: 10 mg Week 5-12 flare dosing may be extended in 4-week intervals and continued until symptoms resolve. If marked worsening of original symptoms or another flare occurs during flare-up treatment, may restart 12 week flare-up dosing. (all ages)	• Assessment of skeletal maturity in growing pediatric patients: hand/wrist & knee x-ray, standard growth curves, pubertal staging. • Psychiatric symptoms or signs of depression Ongoing Monitoring • Pregnancy test (if childbearing potential) • Assessment of skeletal maturity in growing pediatric patients every 6-12 months until skeletal maturity or final adult height. • Spine assessment for bone density • New or worsening psychiatric symptoms or signs of depression
Plasminogen, human-tvmh (RYPLAZIM)	Treatment of patients with plasminogen deficiency type 1 (hypoplasmino-genemia)	N/A	6.6 mg/kg body weight given IV every 2 to 4 days	Baseline Monitoring • Plasminogen activity level (allow 7 day washout if receiving with fresh frozen plasma) • CBC (bleeding) Ongoing Monitoring • Trough Plasminogen activity level 72 hours after initial dose and every 12 wks with ongoing therapy • CBC (bleeding)
pozelimab-bbfg (VEOPOZ)	CD55-deficient protein-losing enteropathy (PLE or CHAPLE disease)	≥ 1 yr	Day 1 loading dose: 30 mg/kg single IV infusion Day 8 and after maintenance dose): 10 mg/kg SC weekly	Baseline Monitoring • Meningococcal vaccination at least 2 wk prior to first drug dose unless risks of delayed therapy outweigh risk of meningococcal infection. Ongoing Monitoring • Signs of meningococcal infection

			May increase to 12 mg/kg if inadequate response after at least 3 weekly doses Max maintenance dose: 800 mg once weekly	
Sodium thiosulfate (PEDMARK)	Decrease ototoxicity associated with cisplatin infusions lasting ≤ 6 hours. Not approved for use with longer infusions.	≥ 1 mo to ≤18 yr	< 5 kg: 10 g/m^2 5-10 kg: 15 g/m^2 >10 kg: 20 g/m^2	Baseline Monitoring • Serum potassium and sodium
Sutimlimab-jome (ENJAYMO)	Decrease need for RBC transfusion due to hemolysis in cold agglutinin disease (CAD)	≥ 18 yr	Dosed IV infusion weekly for two weeks, then every two weeks thereafter. **39 to <75 kg:** 6500 mg **≥75 kg:** 7500 mg	Baseline Monitoring • Vaccination against encapsulated bacteria (*Neisseria meningititides* (any serogroup), *Streptococcus pneumonia*, and *Haemophilus influenza*) at least prior to treatment or as soon as possible if urgent therapy needed
Trientine tetrahydrochloride (CUVRIOR)	Stable Wilson's disease who are de-coppered and tolerant to penicillamine	≥ 18 yr	Total daily dose in transition from penicillamine per table in package insert.	Baseline/Ongoing Monitoring • Serum NCC levels at baseline, 3 months, then roughly every 6 months serum levels or 6 to 12 months with urinary copper excretion
Velmanase alfa-tycv (LAMZEDE)	Treatment of non-central nervous system manifestations of alpha-mannosidosis	N/A	1 mg/kg (actual body weight) once weekly by IV infusion	Baseline and ongoing monitoring • Pregnancy test (if childbearing potential)
Abbreviations: ALP = alkaline phosphatase; ALT = alanine aminotransferase, AST = aspartate aminotransferase; BG = blood glucose; BSA = body surface area; CBC = complete blood count; CrCL = creatinine clearance; ECG = electrocardiogram; eGFR = estimated glomerular filtration rate; ESRD = end stage renal disease; HbA1c = glycalated hemoglobin; Hgb = hemoglobin; INR = international normalized ratio; IV = intravenous; mo = months; NCC = non-ceruloplasmin copper; RBC = red blood cells; SC = subcutaneously; wks = weeks; yrs = years				

Approval Criteria		
1. What diagnosis is being treated?	Record ICD10 code.	
2. Is the diagnosis funded by OHP?	**Yes:** Go to #4	**No:** For current age ≥ 21 years: Pass to RPh. Deny; not funded by the OHP For current age < 21 years: Go to #3

Approval Criteria		
3. Is there documentation that the condition is of sufficient severity that it impacts the patient's health (e.g., quality of life, function, growth, development, ability to participate in school, perform activities of daily living, etc)?	**Yes:** Go to #4	**No:** Pass to RPh. Deny; medical necessity.
4. Is the request for a drug FDA-approved for the indication, age, and dose as defined in ~~**Table 1**~~the FDA label (see links in **Table 1)**? Note: This includes all information required in the FDA-approved indication, including but not limited to, the following as applicable: diagnosis, disease severity, biomarkers, place in therapy, and use as monotherapy or combination therapy.	**Yes**: Go to #5	**No:** Pass to RPh. Deny; medical appropriateness.
5. Is the request for continuation of therapy in a patient previously approved by FFS?	**Yes:** Go to **Renewal Criteria**	**No:** Go to #6
6. Is baseline monitoring recommended for efficacy or safety (e.g., labs, baseline symptoms, etc) AND has the provider submitted documentation of recommended baseline and ongoing monitoring parameters described in the FDA label?* *FDA pages for drugs and biologics: https://www.accessdata.fda.gov/scripts/cder/daf/index.cfm https://www.fda.gov/vaccines-blood-biologics/cellular-gene-therapy-products/approved-cellular-and-gene-therapy-products	**Yes:** Go to #7	**No:** Pass to RPh. Deny; medical appropriateness.
7. Is this medication therapy being prescribed by, or in consultation with, an appropriate medical specialist?	**Yes:** Go to #8	**No:** Pass to RPh. Deny; medical appropriateness.

Approval Criteria		
8. Have other therapies been tried and failed?	**Yes:** Approve for up to 3 months (or length of treatment) whichever is less Document therapies which have been previously tried	**No:** Approve for up to 3 months (or length of treatment) whichever is less Document provider rationale for use as a first-line therapy

Renewal Criteria		
1. Is there documentation based on chart notes that the patient experienced a significant adverse reaction related to treatment?	**Yes:** Go to #2	**No:** Go to #3
2. Has the adverse event been reported to the FDA Adverse Event Reporting System?	**Yes:** Go to #3 Document provider attestation	**No:** Pass to RPh. Deny; medical appropriateness
3. Is baseline efficacy monitoring available?	**Yes:** Go to #4	**No:** Go to #5
4. Is there objective documentation of improvement from baseline OR for chronic, progressive conditions, is there documentation of disease stabilization or lack of decline compared to the natural disease progression?	**Yes:** Approve for up to 6 months Document benefit	**No:** Pass to RPh. Deny; medical appropriateness
5. Is there documentation of benefit from the therapy as assessed by the prescribing provider (e.g., improvement in symptoms or quality of life, or for progressive conditions, a lack of decline compared to the natural disease progression)?	**Yes**: Approve for up to 6 months Document benefit and provider attestation	**No:** Pass to RPh. Deny; medical appropriateness

P&T/DUR Review: 12/23; 10/23; 6/23; 2/23; 12/22; 6/22; 4/22; 12/21; 10/21; 6/21; 2/21; 8/20; 6/20; 2/20
Implementation: 1/1/24; 11/1/23; 7/1/23; 4/1/23; 1/1/23; 7/1/22; 5/1/22; 1/1/2022; 7/1/2021; 3/1/21; 11/1/20; 9/1/20; 7/1/20