

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. 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	<p><u>Pediatric 2 to <18 yrs:</u></p> <ul style="list-style-type: none"> • 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 <p><u>Adult:</u></p> <ul style="list-style-type: none"> • 250 mg once daily 	<p><u>Baseline Monitoring</u></p> <ul style="list-style-type: none"> • Fasting BG, HbA1c <p><u>Ongoing Monitoring</u></p> <ul style="list-style-type: none"> • 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 (ANCA)-associated vasculitis (granulomatosis with polyangiitis [GPA] and microscopic polyangiitis [MPA]) in combination with glucocorticoids.	≥18 yrs	30 mg (three 10 mg capsules) twice daily, with food	<p><u>Baseline Monitoring</u></p> <ul style="list-style-type: none"> • Liver function tests ALT, AST, ALP, and total bilirubin • Hepatitis B (HBsAg and anti-HBc) <p><u>Ongoing Monitoring</u></p> <ul style="list-style-type: none"> • Liver function tests every 4 wks for 6 months, then as clinically indicated
Burosumabtwza (CRYSVITA)	<p>X-linked hypophosphatemia (XLH)</p> <p>FGF23-related hypophosphatemia in tumor-induced osteomalacia (TIO)</p>	<p><u>XLH</u></p> <p>≥ 6 mo</p> <p><u>TIO</u></p> <p>≥ 2 yrs</p>	<p><u>Pediatric <18 yrs:</u></p> <p>Initial (administered SC every 2 wks):</p> <p><u>XLH</u></p> <ul style="list-style-type: none"> • <10 kg: 1mg/kg • ≥10 mg: 0.8 mg/kg <p><u>TIO</u></p> <ul style="list-style-type: none"> • 0.4 mg/kg 	<p><u>Baseline and Ongoing Monitoring</u></p> <ul style="list-style-type: none"> • 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

			<p>Max dose of 2 mg/kg (not to exceed 90 mg for XLH or 180 mg for TIO)</p> <p><u>Adult:</u> <u>XLH</u> 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)</p>	<ul style="list-style-type: none"> Renal function: use is contraindicated in ESRD or with severe renal impairment (CrCl <30 mL/min for adults or eGFR <30 mL/min/1.73m² for pediatric patients) 25-hydroxy vitamin D levels: supplementation with vitamin D (cholecalciferol or ergocalciferol) is recommended as needed. <p><u>Additional baseline monitoring for TIO only:</u></p> <ul style="list-style-type: none"> 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	<p>200 mg orally once daily with food</p> <p>200 mg twice daily when coadministered with strong CYP3A inducers or proton pump inhibitors</p>	<p><u>Baseline & Ongoing Monitoring</u></p> <ul style="list-style-type: none"> 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	<p><u>Baseline Monitoring</u></p> <ul style="list-style-type: none"> 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 <p><u>Ongoing Monitoring</u></p> <ul style="list-style-type: none"> Disease stabilization or lack of decline in motor symptoms compared to natural history
Elapegademas e-ivlr (REVCOVI)	adenosine deaminase severe combined immune deficiency (ADA-SCID)	N/A	Initial: 0.2mg/kg twice weekly; No max dose	<p><u>Baseline Monitoring</u></p> <ul style="list-style-type: none"> CBC or platelet count <p><u>Ongoing Monitoring</u></p> <ul style="list-style-type: none"> 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	<p>Dosed once daily;</p> <p>Preterm Neonate (Gestational Age <37 wks) Initial: 0.4mg/kg Month 1: 0.7 mg/kg Month 3: 0.9 mg/kg</p> <p>Term Neonate (Gestational Age ≥ 37 wks)</p>	Initiation of therapy is recommended with known or presumed MoCD Type A. Discontinue therapy if diagnosis is not confirmed with genetic testing.

			Initial: 0.55 mg/kg Month 1: 0.75 mg/kg Month 3: 0.9 mg/kg Age ≥1 yr: 0.9 mg/kg	
Givosiran (GIVLAARI)	acute hepatic porphyria	≥ 18 yrs	2.5 mg/kg monthly	<u>Baseline and ongoing monitoring</u> <ul style="list-style-type: none"> Liver function tests Blood homocysteine levels-If homocysteine elevated, assess folate, vitamin B12, and vitamin B6
Lonafarnib (ZOKINVY)	To reduce risk of mortality in Hutchinson-Gilford Progeria Syndrome For treatment of processing-deficient Progeroid Laminopathies with either: <ul style="list-style-type: none"> Heterozygous LMNA mutation with progerin-like protein accumulation Homozygous or compound heterozygous ZMPSTE24 mutations 	≥12 mo AND ≥0.39 m ² BSA	<ul style="list-style-type: none"> Initial 115 mg/m² twice daily Increase to 150 mg/m² twice daily after 4 months Round all doses to nearest 25 mg	<u>Baseline and ongoing monitoring</u> <ul style="list-style-type: none"> 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 urinary oxalate levels	N/A	<10 kg <u>Loading:</u> 6 mg/kg once/month for 3 doses <u>Maintenance:</u> 3 mg/kg once/month 10 kg to <20 kg <u>Loading:</u> 6 mg/kg once/month for 3 doses <u>Maintenance:</u> 6 mg/kg once every 3 months ≥ 20 kg <u>Loading:</u> 3 mg/kg once/month for 3 doses <u>Maintenance:</u> 3 mg/kg once every 3 months All maintenance dosing begins 1 month after last loading dose.	N/A
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	≥ 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	<u>Baseline Monitoring/Documentation</u> <ul style="list-style-type: none"> 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

	sideroblasts or myelodysplastic/myeloproliferative neoplasm with ring sideroblasts and thrombocytosis		myelodysplastic syndromes	<p>in patients with myelodysplastic syndromes</p> <ul style="list-style-type: none"> Hemoglobin level Blood pressure <p><u>Ongoing Monitoring</u></p> <ul style="list-style-type: none"> 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	≥ 1 yr	<p>Initial: 190 mcg/kg once daily, 30 min before first meal of day</p> <p>Goal: 390 mcg/kg once daily after 1 week on initial dose, as tolerated</p>	<p><u>Baseline/Ongoing Monitoring</u></p> <ul style="list-style-type: none"> 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	<p>Initial: 5 mg twice daily</p> <p>Titration: If Hb less than normal range or patient required 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.</p> <p>Max dose: 50 mg twice daily</p> <p>Discontinuation should include down-titration.</p>	<p><u>Baseline/Ongoing Monitoring</u></p> <ul style="list-style-type: none"> <u>Hgb. transfusion requirement</u>
Odevixibat (BYLVAY)	<p>Pruritus in patients with progressive familial intrahepatic cholestasis (PFIC)</p> <p>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)</p>	≥ 3 mo	<p>Initial: 40 mcg/kg once daily with morning meal</p> <p>Titration: After 3 months of initial dose, 40 mcg/kg increments</p> <p>Max dose: 120 mcg/kg once daily; not to exceed 6 mg</p>	<p><u>Baseline/Ongoing Monitoring</u></p> <ul style="list-style-type: none"> Liver function tests (ALT, AST, total bilirubin and direct bilirubin) Fat soluble vitamins (A, D, E, K); INR used as surrogate for Vitamin K
Plasminogen, human-tvmh (RYPLAZIM)	Treatment of patients with plasminogen deficiency type 1 (hypoplasminogenemia)	N/A	6.6 mg/kg body weight given IV every 2 to 4 days	<p><u>Baseline Monitoring</u></p> <ul style="list-style-type: none"> Plasminogen activity level (allow 7 day washout if receiving with fresh frozen plasma) CBC (bleeding) <p><u>Ongoing Monitoring</u></p> <ul style="list-style-type: none"> Trough Plasminogen activity level 72 hours after initial dose

				and every 12 wks with ongoing therapy
				<ul style="list-style-type: none"> CBC (bleeding)
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	<u>Baseline Monitoring</u> <ul style="list-style-type: none"> Vaccination against encapsulated bacteria (<i>Neisseria meningitidis</i> (any serogroup), <i>Streptococcus pneumoniae</i>, and <i>Haemophilus influenzae</i>) at least prior to treatment or as soon as possible if urgent therapy needed

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 = intravenously; mo = months; 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 #3	No: Pass to RPh. Deny; not funded by the OHP.
3. Is the request for a drug FDA-approved for the indication, age, and dose as defined in Table 1 ?	Yes: Go to #4	No: Pass to RPh. Deny; medical appropriateness.
4. Is the request for continuation of therapy in a patient previously approved by FFS?	Yes: Go to Renewal Criteria	No: Go to #5
5. Is baseline monitoring recommended for efficacy or safety (e.g., labs, baseline symptoms, etc) AND has the provider submitted documentation of recommended monitoring parameters?	Yes: Go to #6	No: Pass to RPh. Deny; medical appropriateness.
6. Is this medication therapy being prescribed by, or in consultation with, an appropriate medical specialist?	Yes: Go to #7	No: Pass to RPh. Deny; medical appropriateness.
7. 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: 6/22(SF); 4/22; 12/21; 10/21; 6/21; 2/21; 8/20; 6/20; 2/20

Implementation: 7/1/22; 5/1/22; 1/1/2022; 7/1/2021; 3/1/21; 11/1/20; 9/1/20; 7/1/20