**Prior Authorization Criteria Update: Orphan Drug**

**Purpose of the Update:**
This update identifies orphan drugs recently approved by the FDA to add to the orphan drug policy (Table 1).

**Table 1. New orphan drugs**

<table>
<thead>
<tr>
<th>Generic Name</th>
<th>Brand Name</th>
</tr>
</thead>
<tbody>
<tr>
<td>sodium thiosulfate</td>
<td>PEDMARK</td>
</tr>
</tbody>
</table>

**Recommendation:**
- PA was modified to include new, recently approved orphan drugs.
## 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](http://www.orpdl.org)
- Searchable site for Oregon FFS Drug Class listed at [www.orpdl.org/drugs/](http://www.orpdl.org/drugs/)

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

<table>
<thead>
<tr>
<th>Drug</th>
<th>Indication</th>
<th>Age</th>
<th>Dose</th>
<th>Recommended Monitoring</th>
</tr>
</thead>
</table>
| 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 (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 | Baseline Monitoring  
  - 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) | XLH ≥ 6 mo TIO | Pediatric <18 yrs:  
  Initial (administered SC every 2 wks): XLH | Baseline and Ongoing Monitoring  
  - Use of active vitamin D analogues or oral phosphate within prior week; concurrent use is contraindicated |
<table>
<thead>
<tr>
<th>Drug Name (Brand)</th>
<th>Indication</th>
<th>Age</th>
<th>Dosage</th>
<th>Monitoring Details</th>
</tr>
</thead>
<tbody>
<tr>
<td>Belumosudil (REZUROCK)</td>
<td>Treatment of chronic graft-versus-host disease after failure of at least two prior lines of systemic therapy</td>
<td>≥ 12 yrs</td>
<td>200 mg orally once daily with food</td>
<td>Baseline &amp; Ongoing Monitoring, Total bilirubin, AST, ALT at least monthly, Pregnancy test (if childbearing potential)</td>
</tr>
<tr>
<td>Cerliponase alfa (BRINEURA)</td>
<td>To slow the loss of ambulation in symptomatic Batten Disease (late infantile neuronal ceroid lipofuscinosis type 2 or TPP1 deficiency)</td>
<td>3-17 yrs</td>
<td>300 mg every other week via intraventricular route</td>
<td>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</td>
</tr>
<tr>
<td>Elapegademase-lvr (REVCOVI)</td>
<td>Adenosine deaminase severe combined immune deficiency (ADA-SCID)</td>
<td>N/A</td>
<td>Initial: 0.2mg/kg twice weekly; No max dose</td>
<td>Baseline Monitoring, CBC or platelet count, Ongoing Monitoring, trough plasma ADA activity, trough erythrocyte dAXP levels (twice yearly), total lymphocyte counts</td>
</tr>
</tbody>
</table>

FGF23-related hypophosphatemia in tumor-induced osteomalacia (TIO) ≥ 2 yrs
- <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)

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/1.73m² 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)
<table>
<thead>
<tr>
<th>Medicine</th>
<th>Indication</th>
<th>Dosing Schedule</th>
<th>Monitoring</th>
<th>Notes</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Fosdenopterin</strong></td>
<td>To reduce risk of mortality in patients with molybdenum cofactor deficiency (MoCD) Type A</td>
<td>N/A</td>
<td>Dosed once daily; Preterm Neonate (Gestational Age &lt;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</td>
<td>Initiation of therapy is recommended with known or presumed MoCD Type A. Discontinue therapy if diagnosis is not confirmed with genetic testing.</td>
</tr>
<tr>
<td><strong>Givosiran</strong></td>
<td>acute hepatic porphyria</td>
<td>≥ 18 yrs</td>
<td>2.5 mg/kg monthly</td>
<td>Baseline and ongoing monitoring - Liver function tests - Blood homocysteine levels: If homocysteine elevated, assess folate, vitamin B12, and vitamin B6</td>
</tr>
<tr>
<td><strong>Lonafarnib</strong></td>
<td>To reduce risk of mortality in Hutchinson-Gilford Progeria Syndrome For treatment of processing-deficient Progeroid Laminopathies with either: o Heterozygous LMNA mutation with progerin-like protein accumulation o Homozygous or compound heterozygous ZMPSTE24 mutations</td>
<td>≥12 mo AND ≥0.39 m² BSA</td>
<td>Initial 115 mg/m² twice daily Increase to 150 mg/m² twice daily after 4 months Round all doses to nearest 25 mg</td>
<td>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)</td>
</tr>
<tr>
<td><strong>Lumasiran</strong></td>
<td>Treatment of primary hyperoxaluria type 1 to lower urinary oxalate levels</td>
<td>N/A</td>
<td>&lt;10 kg Loading: 6 mg/kg once/month for 3 doses Maintenance: 3 mg/kg once/month 10 kg to &lt;20 kg Loading: 6 mg/kg once/month for 3 doses Maintenance: 6 mg/kg once every 3 months ≥ 20 kg</td>
<td>N/A</td>
</tr>
<tr>
<td>Drug</td>
<td>Condition</td>
<td>Age</td>
<td>Initial Dose</td>
<td>Max Dose</td>
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<tr>
<td>Luspatercept</td>
<td>Anemia (Hgb &lt;11 g/dL) due to beta thalassemia in patients requiring regular red blood cell transfusions</td>
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</tbody>
</table>
|              | 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

| Maralixibat   | Cholestatic pruritis in patients with Alagille syndrome                   | ≥ 1 yr | Initial: 190 mcg/kg once daily, 30 min before first meal of day Goal: 390 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     | 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 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 | Baseline/Ongoing Monitoring: 
  - Hgb, transfusion requirement
| **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  
| **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)  
| **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/m²  
5-10 kg: 15 g/m²  
>10 kg: 20 g/m² | 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 meningitides* (any serogroup), *Streptococcus pneumonia*, and *Haemophilus influenza*) 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 = glycated 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.
### Approval Criteria

<table>
<thead>
<tr>
<th>Step</th>
<th>Question</th>
<th>Yes: Go to</th>
<th>No: Pass to RPh. Deny; medical appropriateness.</th>
</tr>
</thead>
<tbody>
<tr>
<td>3.</td>
<td>Is the request for a drug FDA-approved for the indication, age, and dose as defined in <strong>Table 1</strong>?</td>
<td>Go to #4</td>
<td></td>
</tr>
<tr>
<td>4.</td>
<td>Is the request for continuation of therapy in a patient previously approved by FFS?</td>
<td>Go to Renewal Criteria</td>
<td>Go to #5</td>
</tr>
<tr>
<td>5.</td>
<td>Is baseline monitoring recommended for efficacy or safety (e.g., labs, baseline symptoms, etc) AND has the provider submitted documentation of recommended monitoring parameters?</td>
<td>Go to #6</td>
<td>Pass to RPh. Deny; medical appropriateness.</td>
</tr>
<tr>
<td>6.</td>
<td>Is this medication therapy being prescribed by, or in consultation with, an appropriate medical specialist?</td>
<td>Go to #7</td>
<td></td>
</tr>
<tr>
<td>7.</td>
<td>Have other therapies been tried and failed?</td>
<td>Approve for up to 3 months (or length of treatment) whichever is less Document therapies which have been previously tried</td>
<td>Approve for up to 3 months (or length of treatment) whichever is less Document provider rationale for use as a first-line therapy</td>
</tr>
</tbody>
</table>

### Renewal Criteria

<table>
<thead>
<tr>
<th>Step</th>
<th>Question</th>
<th>Yes: Go to</th>
<th>No: Pass to RPh. Deny; medical appropriateness</th>
</tr>
</thead>
<tbody>
<tr>
<td>1.</td>
<td>Is there documentation based on chart notes that the patient experienced a significant adverse reaction related to treatment?</td>
<td>Go to #2</td>
<td></td>
</tr>
<tr>
<td>2.</td>
<td>Has the adverse event been reported to the FDA Adverse Event Reporting System?</td>
<td>Go to #3</td>
<td>Pass to RPh. Deny; medical appropriateness</td>
</tr>
<tr>
<td>3.</td>
<td>Is baseline efficacy monitoring available?</td>
<td>Go to #4</td>
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<tr>
<td>Renewal Criteria</td>
<td>Yes: Approve for up to 6 months</td>
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<tr>
<td><strong>4.</strong> 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?</td>
<td>Document benefit</td>
<td></td>
<td></td>
</tr>
<tr>
<td><strong>5.</strong> 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)?</td>
<td>Document benefit and provider attestation</td>
<td></td>
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<tr>
<td></td>
<td><strong>No:</strong> Pass to RPh. Deny; medical appropriateness</td>
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</tr>
</tbody>
</table>

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