Orphan Drug Policy: Prior Authorization Update

Purpose of the Update:
This update identifies 2 candidates for addition to the orphan drug policy due to lack of utilization in FFS since FDA approval (Table 1). See Appendix 1 for Highlights of Prescribing Information from the manufacturer, including indications, dosage and administration, formulations, contraindications, warnings and precautions, adverse reactions, drug interactions and use in specific populations.

Table 1. Candidates for Addition to the Orphan Drug Policy

<table>
<thead>
<tr>
<th>Generic Name (Brand)</th>
<th>Diagnosis</th>
<th>Year of Approval</th>
<th>FFS Utilization Since Approval</th>
<th>Relevant ICD-10 codes</th>
<th>FFS patients with claims for relevant ICD-10 codes*</th>
</tr>
</thead>
<tbody>
<tr>
<td>givosiran (Givlaari™)</td>
<td>adults with acute hepatic porphyria</td>
<td>2019</td>
<td>0</td>
<td>E80.21</td>
<td>5</td>
</tr>
<tr>
<td>REVC0VI (elapegademase-lvlr)</td>
<td>pediatric and adult patients with adenosine deaminase severe combined immune deficiency (ADA-SCID)</td>
<td>2018</td>
<td>0</td>
<td>D81.31</td>
<td>0</td>
</tr>
</tbody>
</table>

* Estimated based on number of patients with FFS medical claims with the indicated diagnosis over a 1 year period (1/01/2019 to 12/31/2019). Diagnoses are based on ICD-10 codes associated with medical claims data, may not exactly match the FDA-approved indication, and may not reflect members currently enrolled in FFS.

Recommendation:
- Implement PA to support medically appropriate use of givosiran and elapegademase-lvlr based on FDA labeling.
Appendix 1. Prescribing Information Highlights

HIGHLIGHTS OF PRESCRIBING INFORMATION
These highlights do not include all the information needed to use GIVLAARI™ safely and effectively. See full prescribing information for GIVLAARI.

GIVLAARI (givosiran) injection, for subcutaneous use
Initial U.S. Approval: 2019

-------------------INDICATIONS AND USAGE-------------------
GIVLAARI is an aminolevulinate synthase 1-directed small interfering RNA indicated for the treatment of adults with acute hepatic porphyria (AHP). (1)

-------------------DOSAGE AND ADMINISTRATION-------------------
The recommended dose of GIVLAARI is 2.5 mg/kg once monthly by subcutaneous injection. (2.1)

-------------------DOSE FORMS AND STRENGTHS-------------------
Injection: 189 mg/mL in a single-dose vial. (3)

-------------------CONTRAINDICATIONS-------------------
Severe hypersensitivity to givosiran. (4)

-------------------WARNINGS AND PRECAUTIONS-------------------
• Anaphylactic Reaction: Ensure that medical support is available to appropriately manage anaphylactic reactions when administering GIVLAARI. Monitor for signs and symptoms. If anaphylaxis occurs, discontinue GIVLAARI and administer appropriate medical treatment. (5.1)
• Hepatic Toxicity: Measure liver function at baseline and periodically during treatment with GIVLAARI. Interrupt or discontinue treatment with GIVLAARI for severe or clinically significant transaminase elevations. (2.1, 5.2)
• Renal Toxicity: Monitor renal function during treatment with GIVLAARI as clinically indicated. (5.3)
• Injection Site Reactions: May occur, including recall reactions. Monitor for reactions and manage clinically as needed. (5.4)

-------------------ADVERSE REACTIONS-------------------
The most common adverse reactions (≥20% of patients) included nausea and injection site reactions. (6.1)

To report SUSPECTED ADVERSE REACTIONS, contact Anylam Pharmaceuticals at 1-877-256-9526 or FDA at 1-800-FDA-1088 or www.fda.gov/medwatch.

-------------------DRUG INTERACTIONS-------------------
Sensitive CYP1A2 and CYP2D6 Substrates: Avoid concomitant use with CYP1A2 and CYP2D6 substrates for which minimal concentration changes may lead to serious or life-threatening toxicities. (7.1)

See 17 for PATIENT COUNSELING INFORMATION.

Revised: 11/2019
HIGHLIGHTS OF PRESCRIBING INFORMATION
These highlights do not include all the information needed to use REVCOWI™ safely and effectively. See full prescribing Information for REVCOWI.

REVCOWI (elapegademase-lvrl) injection, for intramuscular use
Initial U.S. Approval: 2018

-----------------------------------------INDICATIONS AND USAGE-----------------------------------------
REVCOWI is a recombinant adenosine deaminase indicated for the treatment of adenosine deaminase severe combined immune deficiency (ADA-SCID) in pediatric and adult patients.

-----------------------------------------DOSAGE AND ADMINISTRATION-----------------------------------------
• Patients transitioning from Adagen to REVCOWI: The starting dose of REVCOWI is 0.2 mg/kg weekly, intramuscularly. See Full Prescribing Information (FPI) for conversion formula from Adagen to REVCOWI. (2.1)
• Adagen-naïve patients: The starting dose of REVCOWI is 0.4 mg/kg weekly based on ideal body weight, divided into two doses (0.2 mg/kg twice a week), intramuscularly. (2.1)
• For complete information, maintenance dosing and therapeutic monitoring, see FPI. (2.1, 2.3)
• REVCOWI is for intramuscular injection only. See FPI for administration instructions. (2.2)

-----------------------------------------DOSAGE FORMS AND STRENGTHS-----------------------------------------
Injection: 2.4 mg/1.5 mL (1.6 mg/mL) in a single-dose vial. (3)

-----------------------------------------CONTRAINDICATIONS-----------------------------------------
None (4)

-----------------------------------------WARNINGS AND PRECAUTIONS-----------------------------------------
• Injection Site Bleeding in Patients with Thrombocytopenia:
  Increased risk of local bleeding in patients with thrombocytopenia; should not be used if thrombocytopenia is severe. (5.1)
• Delay in Improvement of Immune Function: Protect immune deficient patients from infections until improvement in immune function. (5.2)

-----------------------------------------ADVERSE REACTIONS-----------------------------------------
The most common adverse reactions reported were cough (50%) and vomiting (33%). (6.1)

To report SUSPECTED ADVERSE REACTIONS, contact Lendynt at toll-free phone 1-888-393-4584 or FDA at 1-800-FDA-1088 or www.fda.gov/medwatch.

Revised: 10/2018
### Appendix 2. 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](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>
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<tbody>
<tr>
<td>Burosumab-twza (CRYSVITA)</td>
<td>X-linked hypophosphatemia (XLH)</td>
<td>XLH ≥ 6 months</td>
<td>Pediatric &lt;18 years: Initial (administered SC every 2 weeks): XLH</td>
<td>Baseline and Ongoing Monitoring: Use of active vitamin D analogues or oral phosphate within prior week; concurrent use is contraindicated</td>
</tr>
<tr>
<td></td>
<td>FGF23-related hypophosphatemia in tumor-induced osteomalacia (TIO)</td>
<td>TIO ≥ 2 years</td>
<td>&lt;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 for TIO)</td>
<td>Fasting serum phosphorous: do not administer if serum phosphorous is within or above normal range</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>Adult: XLH 1 mg/kg monthly (rounded to nearest 10 mg; max 90 mg)</td>
<td>Renal function: use is contraindicated in ESRD or with severe renal impairment (CrCl &lt;30 mL/min for adults or eGFR &lt;30 mL/min/1.73m² for pediatric patients)</td>
</tr>
<tr>
<td></td>
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<td></td>
<td></td>
<td>25-hydroxy vitamin D levels: supplementation with vitamin D (cholecalciferol or ergocalciferol) is recommended as needed. Additional baseline monitoring for TIO only:</td>
</tr>
</tbody>
</table>

Author: Servid

October 2020
<table>
<thead>
<tr>
<th>Drug</th>
<th>Indication</th>
<th>Age Range</th>
<th>Dosage/Route</th>
<th>Monitoring/Documentation</th>
</tr>
</thead>
<tbody>
<tr>
<td>Cerliponase alfa (BRINEURA)</td>
<td>To slow the loss of ambulation in symptomatic Batten Disease</td>
<td>3-17 years</td>
<td>300 mg every other week via intraventricular route</td>
<td>- Baseline Monitoring&lt;br&gt;  - Enzymatic or genetic testing to confirm tripeptidyl peptidase 1 deficiency or CLN2 gene mutation&lt;br&gt;  - Baseline motor symptoms (e.g., ataxia, motor function, etc)&lt;br&gt;  - ECG in patients with a history of bradycardia, conduction disorders or structural heart disease&lt;br&gt;  - Disease stabilization or lack of decline in motor symptoms compared to natural history</td>
</tr>
<tr>
<td>elapegademase-lvrl (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&lt;br&gt;  - CBC or platelet count&lt;br&gt;  - trough plasma ADA activity&lt;br&gt;  - trough erythrocyte dAXP levels (twice yearly)&lt;br&gt;  - total lymphocyte counts</td>
</tr>
<tr>
<td>Givosiran (GIVLAARI)</td>
<td>Acute hepatic porphyria</td>
<td>≥ 18 years</td>
<td>2.5 mg/kg monthly</td>
<td>- Baseline and ongoing monitoring&lt;br&gt;  - Liver function tests</td>
</tr>
<tr>
<td>Luspatercept (REBLOZYL)</td>
<td>Anemia (Hg &lt;11 g/dL) due to beta thalassemia in patients requiring regular red blood cell transfusions&lt;br&gt; Anemia (Hg &lt;11 g/dL) due to myelodysplastic</td>
<td>≥ 18 years</td>
<td>Initial: 1 mg/kg subcutaneously&lt;br&gt; Max dose of 1.25 mg/kg every 3 weeks for beta thalassemia</td>
<td>- Baseline Monitoring/Documentation&lt;br&gt;  - Number of red blood cell transfusions in the prior 2 months; minimum of 2 RBC units over the prior 8 weeks in patients with myelodysplastic syndromes&lt;br&gt;  - Trial and failure of an erythropoiesis stimulating agent in patients with myelodysplastic syndromes</td>
</tr>
</tbody>
</table>
syndromes with ring sideroblasts or myelodysplastic/myeloproliferative neoplasm with ring sideroblasts and thrombocytosis

Max dose of 1.75 mg/kg every 3 weeks for 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 weeks)
- Hemoglobin level
- Blood pressure

### Approval Criteria

<table>
<thead>
<tr>
<th>Step</th>
<th>Question</th>
<th>Yes: Go to</th>
<th>No: Go to</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>What diagnosis is being treated?</td>
<td>Record ICD10 code.</td>
<td></td>
</tr>
<tr>
<td>2</td>
<td>Is the diagnosis funded by OHP?</td>
<td>Yes: Go to #3</td>
<td>No: Pass to RPh. Deny; not funded by the OHP.</td>
</tr>
<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>Yes: Go to #4</td>
<td>No: Pass to RPh. Deny; medical appropriateness.</td>
</tr>
<tr>
<td>4</td>
<td>Is the request for continuation of therapy in a patient previously approved by FFS?</td>
<td>Yes: Go to <strong>Renewal Criteria</strong></td>
<td>No: 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>Yes: Go to #6</td>
<td>No: 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>Yes: Go to #7</td>
<td>No: Pass to RPh. Deny; medical appropriateness.</td>
</tr>
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## Approval Criteria

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| 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

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| 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 |