Givlaari® (givosiran)

Definitions

Givlaari is a double-stranded small interfering RNA that causes degradation of aminolevulinate synthase 1 (ALAS1) mRNA in hepatocytes through RNA interference, reducing the elevated levels of liver ALAS1 mRNA. This leads to reduced circulating levels of neurotoxic intermediates aminolevulinic acid (ALA) and porphobilinogen (PBG), factors associated with attacks and other disease manifestations of AHP. GIVLAARI is indicated for the treatment of adults with acute hepatic porphyria (AHP).

Length of authorization
Coverage is provided for 12 months and may be renewed.

Dosing
Max Units (per dose and over time) 2.5 mg/kg administered by subcutaneous injection once monthly by a healthcare professional only.

Guideline

- Member has been diagnosed with acute hepatic porphyria (including acute intermittent porphyria, hereditary coproporphyria, variegate porphyria, ALA dehydratase deficient porphyria); AND
- Member is at least 18 years of age; AND
- Medication is prescribed by or in consultation with, a porphyria specialist (e.g. hepatologist, gastroenterologist, etc.); AND
- Member has had elevated urinary or plasma PBG (porphobilinogen) or ALA (aminolevulinic acid) values within the past year; AND
Clinical presentation of disease has been documented (e.g. abdominal pain, constipation, nausea/vomiting, symptoms of ileus, tachycardia, hypertension, dark urine, skin photosensitivity or other cutaneous symptoms, disease-specific common laboratory abnormalities [hyponatremia, hypomagnesemia], seizures, CKD, etc.); AND

- Active disease has been documented with at least 2 porphyria attacks requiring hospitalization, urgent healthcare visit, or intravenous hemin administration at home, within the past 6 months; AND
- Individuals currently receiving prophylactic intravenous hemin therapy will discontinue hemin within 3 to 6 months of initiation with givosiran

Renewal Criteria
- Individual continues to meet initial approval criteria
- Absence of unacceptable toxicity from the drug (e.g. anaphylactic reactions, severe hepatic toxicity, severe renal toxicity, etc.)
- Disease response as evidenced by a decrease in the frequency of acute porphyria attacks, and/or hospitalizations/urgent care visits, and/or a decrease requirement of hemin intravenous infusions

Limitations/Exclusions
- Member has not had a liver transplant

Applicable Procedure Codes

<table>
<thead>
<tr>
<th>Code</th>
<th>Description</th>
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</thead>
<tbody>
<tr>
<td>J3490</td>
<td>Givlaari (givosiran sodium), 189mg/mL soln (unclassified drugs)</td>
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Applicable NDCs

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<th>Description</th>
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<tbody>
<tr>
<td>71336-1001-01</td>
<td>Givlaari (givosiran sodium), 189mg/ml single use vial</td>
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Applicable Diagnosis Codes

<table>
<thead>
<tr>
<th>Code</th>
<th>Description</th>
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<tbody>
<tr>
<td>E80.21</td>
<td>Unspecified porphyria</td>
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<tr>
<td>E80.20</td>
<td>Acute intermittent (hepatic) porphyria</td>
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<tr>
<td>E80.29</td>
<td>Other porphyria</td>
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</table>

References

1. ENVISION: A study to evaluate the efficacy and safety of GIVOSIRAN (ALN-AS1) in patients with acute hepatic porphyrinas (AHP).