Medical Policy:

Givlaari® (givosiran) injection for subcutaneous use

POLICY NUMBER	LAST REVIEW	ORIGIN DATE
MG.MM.PH.203	April 4, 2025	

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 will be provided for 12 months and may be renewed.

Dosing Limits [Medical Benefit]

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

Max Units (per dose and over time) [HCPS Unit]:

576 billable units every month

Guideline

I. Initial Approval Criteria

1. <u>Acute Hepatic Porphyria</u>

A. Member has been diagnosed with **acute hepatic porphyria** (including acute intermittent porphyria, hereditary coproporhyria, variegate porphyria, ALA dehydratase deficient porphyria); as evidenced by one of the following:
   i. Patient has had elevated urinary or plasma PBG (porphobilinogen) and ALA (delta-aminolevulinic acid) levels within the previous year; **OR**
   ii. Patient has a mutation in an affected gene as identified on molecular genetic testing; **AND**

B. Member is at least 18 years of age; **AND**

C. Medication is prescribed by or in consultation with, a porphyria specialist (e.g. hepatologist, gastroenterologist, etc.); **AND**

D. Patient will avoid known triggers of porphyria attacks (i.e., alcohol, smoking, exogenous hormones, hypocaloric diet/fasting, certain medications such as barbiturates, hydantoins, sulfa-antibiotics, anti-epileptics, etc.); **AND**

E. Patient meets one of the following:
   i. Patient has history of at least 2 porphyria attacks requiring hospitalization, urgent healthcare visit, or intravenous hemin administration at home, within the past 6 months; **OR**
   ii. Patient has a history of 1 severe attack with CNS, ANS or PNS involvement within the past 6 months(e.g. hallucinations, seizure, paralysis, respiratory failure, etc.); **AND**

F. Individuals currently receiving prophylactic intravenous hemin therapy will discontinue hemin within 3 to 6 months of initiation with givosiran

II. Renewal Criteria

1. Individual continues to meet initial approval criteria; **AND**
2. Absence of unacceptable toxicity from the drug (e.g. anaphylactic reactions, severe hepatic toxicity, severe renal toxicity, etc.) ; **AND**
3. 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; **AND**
4. Patient has a reduction/normalization of biochemical markers (i.e., ALA, PBG) compared to baseline; **AND**
5. Patient will not use in combination with prophylactic intravenous hemin therapy

Limitations/Exclusions

1. Member has not or is not anticipating a liver transplant

Applicable Procedure Codes

Code	Description
J0223	Givlaari (givosiran sodium), 189mg/mL soln

Applicable NDCs

Code	Description
71336-1001-01	Givlaari (givosiran sodium), 189mg/ml single use vial

ICD-10 Diagnoses

Code	Description
E80.20	Unspecified porphyria
E80.21	Acute intermittent (hepatic) porphyria
E80.29	Other porphyria

Revision History

Company(ies)	DATE	REVISION
EmblemHealth & ConnectiCare	04/04/2025	Annual Review: Updated ICD-10 codes. Initial criteria: Acute Hepatic Porphyria Updated order the following to make it an "OR" statement: "Member has been diagnosed with acute hepatic porphyria (including acute intermittent porphyria, hereditary coproporhyria, variegate porphyria, ALA dehydratase deficient porphyria) as evidenced by one of the following: Patient has had elevated urinary or plasma PBG (porphobilinogen) and ALA (delta-aminolevulinic acid) levels within the previous year; OR Patient has a mutation in an affected gene as identified on molecular genetic testing; AND" Removed: "Active disease has been documented with", replaced with: "Patient has history of" at the start of the following: "at least 2 porphyria attacks requiring hospitalization, urgent healthcare visit, or intravenous hemin administration at home, within the past 6 months; OR"
EmblemHealth & ConnectiCare	2/29/2024	Annual Review: Updated dosing limits Initial Criteria: Acute Hepatic Porphyria: Added: Patient will avoid known triggers of porphyria attacks (i.e., alcohol, smoking, exogenous hormones, hypocaloric diet/fasting, certain medications such as barbiturates, hydantoins, sulfa-antibiotics, anti-epileptics, etc.); AND Patient has a mutation in an affected gene as identified on molecular genetic testing; AND" Removed: "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 Patient is currently receiving off-label hemin treatment for attack prophylaxis; OR" Updated timeframe from the past year to the past 6 months in the following statement: :Patient has a history of 1 severe attack with CNS, ANS or PNS involvement within the 6 months(e.g. hallucinations, seizure, paralysis, respiratory failure, etc.)" Renewal Criteria: Added: Patient has a reduction/normalization of biochemical markers (i.e., ALA, PBG) compared to baseline; AND Patient will not use in combination with prophylactic intravenous hemin therapy
EmblemHealth & ConnectiCare	6/5/2023	Annual Revision: 1. Updated exclusion criteria to include "or is not anticipating" a liver transplant 2. Updated the definition of patients with active, symptomatic disease by adding additional criteria: "Patient is currently receiving off-label hemin treatment for attack prophylaxis; **OR** Patient has a history of 1 severe attack with CNS, ANS or PNS involvement within the past year (e.g. hallucinations, seizure, paralysis, respiratory failure, etc.)"
EmblemHealth & ConnectiCare	6/17/2022	Transferred policy to new template

EmblemHealth & ConnectiCare	7/15/2019	Annual review

References

1. Gazyva prescribing information. Genentech, Inc. South San Francisco, CA 2016.
2. Clinical Pharmacology Elsevier Gold Standard. 2017.
3. Micromedex® Healthcare Series: Thomson Micromedex, Greenwood Village, Co. 2017.
4. National Comprehensive Cancer Network. Cancer Guidelines and Drugs and Biologics Compendium. 2017.
5. AHFS Drug Information. American Society of Health-Systems Pharmacist or Wolters Kluwer Lexi-Drugs. Bethesda, MD. 2017.