Givlaari® (Givosiran)

Policy Number: CS2026D0087L
Effective Date: April 1, 2026

➲ Instructions for Use

Table of Contents **Page**

Commercial Policy
• Givlaari® (Givosiran)

Application

This Medical Benefit Drug Policy does not apply to the states listed below; refer to the state-specific policy/guideline, if noted:

State	Policy/Guideline
Florida	Refer to the state's Medicaid clinical policy
Kansas	Refer to the state's Medicaid clinical policy
North Carolina	None
Ohio	Givlaari® (Givosiran) (for Ohio Only)
Pennsylvania	Givlaari® (Givosiran) (for Pennsylvania Only)
Texas	Refer to drug specific criteria found within the Texas Medicaid Provider Procedures Manual

Coverage Rationale

Givlaari is proven and/or medically necessary for the treatment of acute hepatic porphyrias:

Initial Therapy

- Diagnosis of an acute hepatic porphyria (AHP) (i.e., acute intermittent porphyria, hereditary coproporphyria, variegate porphyria, ALA dehydratase deficient porphyria); **and**
- **One** of the following:
  - Patient has active disease as defined in the clinical trial by having at least 2 documented porphyria attacks within the past 6 months; **or**
  - Patient is currently receiving treatment with prophylactic hemin to prevent porphyria attacks

  and
- Provider attestation that the patient's baseline (before givosiran is initiated) hemin administration requirements (prophylactic or treatment) and rate and/or number of porphyria attacks has been documented; **and**
- Patient has not had a liver transplant; **and**
- Patient will not receive concomitant prophylactic hemin treatment while on Givlaari; **and**
- Prescribed by, or in consultation with, a hematologist, or a specialist with expertise in the diagnosis and management of AHPs; **and**
- Givlaari dosing is in accordance with the United States Food and Drug Administration approved labeling; **and**
- Initial authorization will be for no more than 12 months

Continuation Therapy

- Patient has previously received Givlaari for the treatment of AHP; **and**
- Documentation that the patient has experienced a positive clinical response while on Givlaari; **and**
- Patient has not had a liver transplant; **and**
- Patient will not receive concomitant prophylactic hemin treatment while on Givlaari; **and**
- Prescribed by, or in consultation with, a hematologist, or a specialist with expertise in the diagnosis and management of AHPs; **and**
- Givlaari dosing is in accordance with the United States Food and Drug Administration approved labeling; **and**
- Reauthorization will be for no more than 12 months

Applicable Codes

The following list(s) of procedure and/or diagnosis codes is provided for reference purposes only and may not be all inclusive. Listing of a code in this policy does not imply that the service described by the code is a covered or non-covered health service. Benefit coverage for health services is determined by federal, state, or contractual requirements and applicable laws that may require coverage for a specific service. The inclusion of a code does not imply any right to reimbursement or guarantee claim payment. Other Policies and Guidelines may apply.

HCPCS Code	Description
J0223	Injection, givosiran, 0.5 mg

Diagnosis Code	Description
E80.0	Hereditary erythropoietic porphyria
E80.1	Porphyria cutanea tarda
E80.20	Unspecified porphyria
E80.21	Acute intermittent (hepatic) porphyria
E80.29	Other porphyria

Background

Acute hepatic porphyria refers to a family of ultra-rare genetic diseases that lead to deficiency in one of the enzymes of the heme biosynthesis pathway in the liver. Severe, unexplained abdominal pain is the most common symptom, which can be accompanied by limb, back, or chest pain, nausea, vomiting, confusion, anxiety, seizures, weak limbs, constipation, diarrhea, or dark or reddish urine. Long-term complications and comorbidities of AHP can include hypertension, chronic kidney disease, or liver disease including hepatocellular carcinoma. Currently, the population of AHP patients with diagnosed, active disease in the U.S. and Europe is estimated to be approximately 3,000.

Givosiran 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.

Clinical Evidence

The efficacy of Givlaari was established in the Phase 3 ENVISION trial, a randomized, double-blind, placebo-controlled multicenter study in 94 patients with AHP [89 patients with acute intermittent porphyria (AIP), 2 patients with variegate porphyria (VP), 1 patient with hereditary coproporphyria (HCP), and 2 patients with no identified mutation]. Inclusion criteria specified a minimum of 2 porphyria attacks requiring hospitalization, urgent healthcare visit, or intravenous hemin administration at home in the 6 months prior to study entry. Hemin use during the study was permitted for the treatment of acute porphyria attacks. Patients were randomized to receive Givlaari or placebo during the 6-month double-blind period. Efficacy in the 6-month double-blind period was measured by the rate of porphyria attacks that required hospitalizations, urgent healthcare visit, or intravenous hemin administration at home. The mean rate of porphyria attacks was 1.9 and 6.5 for Givlaari and placebo, respectively. This represented a 70% (95% CI: 60, 80) reduction in porphyria attacks for patients receiving Givlaari vs. placebo. The mean number of days of hemin use was 4.7 (95% CI: 2.8, 7.9) with Givlaari vs. 12.8 (95% CI: 7.6, 21.4) with placebo.

Professional Societies

In 2023, the American Gastroenterological Association (AGA) published a clinical practice update on the diagnosis and management of acute hepatic porphyrias. In regard to givosiran, a best practice advice statement in the expert review states that prophylactic heme therapy or givosiran, administered in an outpatient setting, should be considered in patients with recurrent attacks (4 or more per year).

U.S. Food and Drug Administration (FDA)

This section is to be used for informational purposes only. FDA approval alone is not a basis for coverage.

Givlaari (givosiran) is an aminolevulinate synthase 1-directed small interfering RNA indicated for the treatment of adults with acute hepatic porphyria (AHP). The recommended dose of Givlaari is 2.5 mg/kg administered via subcutaneous injection once monthly. Dosing is based on actual body weight.

References

1. Givlaari [package insert]. Cambridge, MA: Alnylam Pharmaceuticals, Inc., September 2025.
2. ENVISION: A Study to Evaluate the Efficacy and Safety of Givosiran (ALN-AS1) in Patients With Acute Hepatic Porphyrias (AHP). Clinicaltrials.gov website https://clinicaltrials.gov/ct2/show/NCT03338816?term=givosiran&cond=porphyria&draw=1&rank=5. Accessed February 2, 2026.
3. Sardh E, Harper P, Balwani M, et al. Phase 1 Trial of an RNA Interference Therapy for Acute Intermittent Porphyria. n Engl J Med. 2019 Feb 7;380(6):549-558.
4. Balwani M, Wang B, Anderson KE, et al. Acute hepatic porphyrias: Recommendations for evaluation and long-term management. Hepatology. 2017 Oct;66(4):1314-1322.
5. Stölzel U, Doss MO, Schuppan D. Clinical Guide and Update on Porphyrias. Gastroenterology. 2019 Aug;157(2):365-381.
6. Wang B, Bonkovsky HL, Lim JK, Balwani M. AGA Clinical Practice Update on Diagnosis and Management of Acute Hepatic Porphyrias: Expert Review. *Gastroenterology*. 2023;164(3):484-491. doi:10.1053/j.gastro.2022.11.034.

Policy History/Revision Information

Date	Summary of Changes
04/01/2026	**Application** ***Indiana*** • Removed language indicating this Medical Benefit Drug Policy does not apply to the state of **Indiana** ***Louisiana*** • Removed content/language pertaining to the state of **Louisiana** **Supporting Information** • Updated *References* section to reflect the most current information • Archived previous policy versions CS2025D0087K and CSIND0087.06

Instructions for Use

This Medical Benefit Drug Policy provides assistance in interpreting UnitedHealthcare standard benefit plans. When deciding coverage, the federal, state or contractual requirements for benefit plan coverage must be referenced as the terms of the federal, state or contractual requirements for benefit plan coverage may differ from the standard benefit plan. In the event of a conflict, the federal, state or contractual requirements for benefit plan coverage govern. Before using this policy, check the federal, state or contractual requirements for benefit plan coverage. UnitedHealthcare reserves the right to modify its Policies and Guidelines as necessary. This Medical Benefit Drug Policy is provided for informational purposes. It does not constitute medical advice.

UnitedHealthcare may also use tools developed by third parties, such as the InterQual® criteria, to assist us in administering health benefits. The UnitedHealthcare Medical Benefit Drug Policies are intended to be used in connection

with the independent professional medical judgment of a qualified health care provider and do not constitute the practice of medicine or medical advice.