



Drug Coverage Policy

Effective Date 12/15/2025

Coverage Policy NumberIP0118

Policy Title.....Givlaari

Hepatology – Givlaari

- Givlaari™ (givosiran subcutaneous injection – Alnylam)

INSTRUCTIONS FOR USE

The following Coverage Policy applies to health benefit plans administered by Cigna Companies. Certain Cigna Companies and/or lines of business only provide utilization review services to clients and do not make coverage determinations. References to standard benefit plan language and coverage determinations do not apply to those clients. Coverage Policies are intended to provide guidance in interpreting certain standard benefit plans administered by Cigna Companies. Please note, the terms of a customer's particular benefit plan document [Group Service Agreement, Evidence of Coverage, Certificate of Coverage, Summary Plan Description (SPD) or similar plan document] may differ significantly from the standard benefit plans upon which these Coverage Policies are based. For example, a customer's benefit plan document may contain a specific exclusion related to a topic addressed in a Coverage Policy. In the event of a conflict, a customer's benefit plan document always supersedes the information in the Coverage Policies. In the absence of a controlling federal or state coverage mandate, benefits are ultimately determined by the terms of the applicable benefit plan document. Coverage determinations in each specific instance require consideration of 1) the terms of the applicable benefit plan document in effect on the date of service; 2) any applicable laws/regulations; 3) any relevant collateral source materials including Coverage Policies and; 4) the specific facts of the particular situation. Each coverage request should be reviewed on its own merits. Medical directors are expected to exercise clinical judgment where appropriate and have discretion in making individual coverage determinations. Where coverage for care or services does not depend on specific circumstances, reimbursement will only be provided if a requested service(s) is submitted in accordance with the relevant criteria outlined in the applicable Coverage Policy, including covered diagnosis and/or procedure code(s). Reimbursement is not allowed for services when billed for conditions or diagnoses that are not covered under this Coverage Policy (see "Coding Information" below). When billing, providers must use the most appropriate codes as of the effective date of the submission. Claims submitted for services that are not accompanied by covered code(s) under the applicable Coverage Policy will be denied as not covered. Coverage Policies relate exclusively to the administration of health benefit plans. Coverage Policies are not recommendations for treatment and should never be used as treatment guidelines. In certain markets, delegated vendor guidelines may be used to support medical necessity and other coverage determinations.

OVERVIEW

Givlaari, an aminolevulinic acid synthase 1-directed small interfering RNA, is indicated for the treatment of **acute hepatic porphyria** (AHP) in patients ≥ 18 years of age.¹

Givlaari is a double-stranded small interfering RNA that causes degradation of aminolevulinic acid synthase 1 (ALAS1) mRNA in hepatocytes through RNA interference, reducing the elevated levels of liver ALAS1 mRNA.¹ This leads to reduced circulating levels of neurotoxic intermediates aminolevulinic acid and porphobilinogen, factors associated with attacks and other disease manifestations of AHP. In the pivotal trial, inclusion criteria specified a minimum of two 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.

Disease Overview

Porphyria is a group of metabolic disorders caused by abnormalities in the chemical steps that lead to the production of heme.² AHPs are a subgroup of porphyrias in which the enzyme deficiency occurs within the liver.³ AHPs include acute intermittent porphyria (AIP), variegate porphyria (VP), 5-aminolevulinic acid dehydratase deficiency porphyria (ALAD), and hereditary coproporphyria (HCP) and are characterized by acute neurovisceral symptoms with or without cutaneous manifestations.^{3,4} Symptoms and treatments for AIP, VP, ALAD, and HCP are similar; however, VP and HCP patients often develop photosensitivity. Signs and symptoms of AHP usually occur intermittently and include abdominal pain, constipation, muscle weakness, pain in the arms and legs, insomnia, emotional complications, rapid pulse, and high blood pressure. Although most symptomatic patients with AHP have complete resolution of their symptoms between attacks, those with numerous recurrences may develop chronic pain.

Dosing Information

The recommended dose is 2.5 mg/kg administered by subcutaneous injection once monthly by a healthcare professional only.

Guidelines

The Porphyrias Consortium of the National Institutes of Health's Rare Diseases Clinical Research Network has developed recommendations for evaluation and long-term management of AHPs (2017).⁵ Initial assessments should include diagnostic confirmation by biochemical testing, subsequent genetic testing to determine the specific AHP, and a complete medical history and physical examination. Preventative measures should be taken to prevent attacks. Hemin therapy (e.g., Panhematin[®] [hemin injection for intravenous infusion]) is recommended for preventative management in AHP and treatment during acute attacks. Patients with \geq four attacks per year are candidates for either prophylactic or "on demand" infusions. The need for ongoing prophylaxis should be assessed every 6 to 12 months. Repeated long-term treatment with hemin therapy can lead to iron overload and contribute to hepatic damage and fibrosis. Carbohydrate loading (glucose tablets or dextrose solutions) has been used in early stages of an acute attack, but there are no clear data showing a benefit. Women with AHP can develop cyclic attacks correlated with the menstrual cycle. Options to prevent these attacks include recognizing and removing exacerbating factors, a gonadotropin releasing-hormone analog, switching to a low dose hormonal contraceptive, or prophylactic hemin therapy infusions.

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POLICY STATEMENT

Prior Authorization is required for benefit coverage of Givlaari. Approval is recommended for those who meet the **Criteria** and **Dosing** for the listed indication. Extended approvals are allowed if the patient continues to meet the Criteria and Dosing. Requests for doses outside of the established dosing documented in this policy will be considered on a case-by-case basis by a clinician (i.e., Medical Director or Pharmacist). All approvals are provided for the duration noted below. Because

of the specialized skills required for evaluation and diagnosis of patients treated with Givlaari as well as the monitoring required for adverse events and long-term efficacy, approval requires Givlaari to be prescribed by or in consultation with a physician who specializes in the condition being treated.

Documentation: Documentation is required where noted in the criteria as **[documentation required]**. Documentation may include, but is not limited to, chart notes, laboratory tests, claims records, and/or other information. All documentation must include patient-specific identifying information.

Givlaari is considered medically necessary when the following are met:

FDA-Approved Indication

- 1. Acute Hepatic Porphyria.** Approve for 1 year if the patient meets ALL of the following (A, B, C, and D):
 - A.** Patient is ≥ 18 years of age; AND
 - B.** Diagnosis of acute hepatic porphyria was confirmed by BOTH of the following (i and ii):
 - i.** Patient demonstrated clinical features associated with acute hepatic porphyria **[documentation required]**; AND
Note: Examples of clinical features associated with acute intermittent porphyria include neurovisceral symptoms, blistering lesions, hepatic involvement, peripheral neuropathy, abdominal pain, constipation, muscle weakness, and pain in the arms and legs.
 - ii.** Patient meets ONE of the following (a or b):
 - a.** Elevated urinary aminolevulinic acid (ALA) greater than the upper limit of normal **[documentation required]**; OR
 - b.** Elevated urinary porphobilinogen (PBG) greater than the upper limit of normal **[documentation required]**; AND
 - C.** Prior to starting treatment with Givlaari, the patient has a history of one porphyria attack in the last 6 months that required a hospitalization, urgent healthcare visit, or intravenous hemin administration at home; AND
 - D.** The medication is prescribed by or in consultation with a gastroenterologist, hepatologist, or a physician who specializes in acute hepatic porphyria.

Dosing. Approve 2.5 mg/kg administered by subcutaneous injection given no more frequently than once every 30 days.

Conditions Not Covered

Givlaari for any other use is considered not medically necessary. Criteria will be updated as new published data are available.

Coding Information

Note: 1) This list of codes may not be all-inclusive.
2) Deleted codes and codes which are not effective at the time the service is rendered may not be eligible for reimbursement.

Considered Medically Necessary when criteria in the applicable policy statements listed above are met:

HCPCS Codes	Description
J0223	Injection, givosiran, 0.5 mg

References

1. Givlaari™ intravenous infusion [prescribing information]. Cambridge, MA: Alnylam; April 2024.
2. Porphyria. U.S. National Library of Medicine; National Institutes of Health; Department of Health and Human Services. Available at: <https://ghr.nlm.nih.gov/condition/porphyria>. Accessed on October 06, 2025.
3. Wang B, Rudnick S, Cengia B, et al. Acute hepatic porphyrias: review and recent progress. *Hepatol Commun*. 2018;3(2):193-206.
4. Bissell DM, Wang B. Acute hepatic porphyria. *J Clin Transl Hepat*. 2015;3(1):17-26.
5. Balwani M, Wang B, Anderson K, et al. Acute hepatic porphyrias: recommendations for evaluation and long term management. *Hepatology*. 2017;66(4):1314-1322.

Revision Details

Type of Revision	Summary of Changes	Date
Selected Revision	No criteria changes	12/15/2024
Annual Revision	<p>Policy Title Updated from "Givosiran" to "Hepatology – Givlaari"</p> <p>Added documentation statement and documentation requirements throughout the policy.</p> <p>Acute Hepatic Porphyria Updated initial approval duration from 6 months to 1 year</p> <p>Updated from "(for example neurovisceral symptoms, blistering lesions, hepatic involvement, peripheral neuropathy, abdominal pain, constipation, muscle weakness, pain in the arms and legs) to "Note: examples of clinical features associated with acute intermittent porphyria include neurovisceral symptoms, blistering lesions, hepatic involvement, peripheral neuropathy, abdominal pain, constipation, muscle weakness, and pain in the arms and legs."</p> <p>Updated from "Elevated urinary or plasma porphobilinogen (PBG) greater than the upper limit of normal" to "Elevated urinary porphobilinogen (PBG) greater than the upper limit of normal"</p> <p>Updated from "Prior to starting treatment with givosiran (Givlaari), the individual has a history of one porphyria attack in the last 6 months that</p>	12/15/2025

	<p>required a hospitalization, urgent healthcare visit, or intravenous hemin administration " to "Prior to starting treatment with Givlaari, the patient has a history of one porphyria attack in the last 6 months that required a hospitalization, urgent healthcare visit, or intravenous hemin administration at home"</p> <p>Removed medical geneticist from specialty requirement.</p> <p>Removed reauthorization criteria.</p>	
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The policy effective date is in force until updated or retired.

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