

POLICY: Hepatology – Givlaari™ (givosiran injection solution, for subcutaneous use – Alnylam Pharmaceuticals)

DATE REVIEWED: 12/18/2019; selected revision 05/20/2020

OVERVIEW

Givlaari™, an aminolevulinate synthase 1-directed small interfering RNA, is indicated for the treatment of patients ≥ 18 years of age with acute hepatic porphyria (AHP).¹ 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 and porphobilinogen, factors associated with attacks and other disease manifestations of AHP. In the pivotal trial, 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. The recommended dose is 2.5 mg/kg administered by subcutaneous injection once monthly by a healthcare professional only.

Disease Overview

Porphyria is a group of metabolic disorders caused by abnormalities in the chemical steps that lead to the production of heme.² Heme is necessary for the transport of oxygen to cells in the body. If synthesis of heme is hindered, an accumulation of porphyrins or porphyrin precursors (intermediate chemicals) accumulates in the cell, resulting in oxygen depletion. AHPs are a subgroup of porphyrias in which the enzyme deficiency occurs within the liver. 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 Symptoms and treatments for AIP, VP, ALAD, and HCP are similar. Unlike AIP and ADP patients, 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. Hospitalization is often required for acute attacks. Although most symptomatic patients with AHP have complete resolution of their symptoms between attacks, those with numerous recurrent occurrences may develop chronic pain. Due to the high prevalence of chronic kidney disease, serum creatinine and estimated glomerular filtration rate should be monitored annually for all symptomatic patients.

POLICY STATEMENT

Prior authorization is recommended for medical benefit coverage of Givlaari. Approval is recommended for those who meet the Criteria and Dosing for the listed indication(s). 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. In cases where the approval is authorized in months, 1 month is equal to 30 days. 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.

RECOMMENDED AUTHORIZATION CRITERIA

Coverage of Givlaari is recommended in those who meet the following criteria:

FDA-Approved Indications

1. Acute Hepatic Porphyria. Approve for 1 year if the patient meets the following criteria (A and B):

- A) The patient is ≥ 18 years of age; AND
- B) 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
- C) Givlaari is prescribed by, or in consultation with, with a gastroenterologist, hepatologist, or a physician who specializes in acute hepatic porphyria.

Dosing. Approve the following dosing regimen (A and B):

- A) The dose is 2.5 mg/kg administered by subcutaneous injection; AND
- B) The dose is given no more frequently than once every 30 days.

CONDITIONS NOT RECOMMENDED FOR APPROVAL

Givlaari has not been shown to be effective, or there are limited or preliminary data or potential safety concerns that are not supportive of general approval for the following conditions.

1. Coverage is not recommended for circumstances not listed in the Recommended Authorization Criteria. Criteria will be updated as new published data are available.

REFERENCES

1. Givlaari™ injection solution [prescribing information]. Cambridge, MA: Alnylam Pharmaceuticals; November 2019.
2. Porphyria. U.S. National Library of Medicine; National Institutes of Health; Department of Health and Human Services. <https://ghr.nlm.nih.gov/condition/porphyria>. Last accessed: December 3, 2019.
3. Balwani M, Wang B, Anderson K, et al. Acute hepatic porphyrias: Recommendations for evaluation and long term management. *Hepatology*; 2017;66(4): 1314-1322.

HISTORY

Type of Revision	Summary of Changes	Date Reviewed
New Policy	--	12/18/2019
Selected revision	Acute Hepatic Porphyria. The requirement for a history of one porphyria attack in the last 6 months that required hospitalizations, urgent healthcare visit, or intravenous hemin administration at home was added to the criteria.	05/20/2020