Generic Name: Givosiran

Therapeutic Class or Brand Name: Givlaari®

Applicable Drugs: N/A

Preferred: N/A

Non-preferred: N/A

Date of Origin: 2/24/2025

Date Last Reviewed / Revised: 2/24/2025

PRIOR AUTHORIZATION CRITERIA

(May be considered medically necessary when criteria I through V are met)

I. Documented diagnosis of acute hepatic porphyria (AHP) and criteria A through B are met (see Appendix Table 1):
   A. Elevated aminolevulinic acid (ALA) and/or porphobilinogen (PBG) at time of diagnosis.
   B. Active disease within the past year defined as at least two of the following i through iii:
      i. Hospitalization
      ii. Urgent healthcare visit
      iii. Intravenous hemin administration

II. Minimum age requirement of 18 years.

III. Treatment must be prescribed by or in consultation with a dermatologist, gastroenterologist, hematologist, hepatologist, or neurologist.

IV. Request is for a medication with the appropriate FDA labeling, or its use is supported by current clinical practice guidelines.

V. Refer to the plan document for the list of preferred products. If the requested agent is not listed as a preferred product, must have documented treatment failure or contraindication to the preferred product(s).

EXCLUSION CRITERIA

- Concurrent use with CYP1A2 and CYP2D6 substrates for which minimal concentration changes may lead to serious adverse effects (eg, doxorubicin, fezolinetant, mequitazine, thioridazine).

OTHER CRITERIA

- N/A

QUANTITY / DAYS SUPPLY RESTRICTIONS

- Givlaari (givosiran) 189 mg/mL (1 mL) single-dose vial:
  - 2.5 mg/kg subcutaneous injection once monthly.

Approval Length

- **Authorization:** 6 months
- **Re-Authorization:** 12 months, with an updated letter of medical necessity or progress notes showing improvement or maintenance with medication.
  Documentation that criteria 1 through 3 are met:
  1. Reduction in frequency of porphyria attacks requiring hospitalization, urgent healthcare visit, or intravenous hemin administration compared to baseline.
  2. Reduction in ALA and/or PBG levels compared to baseline.
  3. Assessment of liver function, renal function, and serum homocysteine (Hcy) through monitoring of the following a through c:
     a. LFTs, including ALT
     b. SCr or eGFR
     c. Hcy

Appendix

Table 1. Applicable Diagnoses for Acute Hepatic Porphyria (AHP)

Acute Hepatic Porphyria (AHP) Subtype and Gene Mutation	
Acute intermittent porphyria (AIP)	hydroxymethylbilane synthase gene (HMBS)
Hereditary coproporphyria (HCP)	coporphyrinogen oxidase (CPOX)
Variegate porphyria (VP)	protoporphyrinogen oxidase (PPOX)
ALA dehydratase deficient porphyria (ADP)	aminolevulinic acid dehydratase (ALAD)

References

1. Givlaari. Prescribing Information. Alnylam Pharmaceuticals, Inc.; 2024. Accessed January 9, 2025.
   https://www.alnylam.com/sites/default/files/pdfs/GIVLAARI-Prescribing-Information.pdf
2. Balwani M, Sardh E, Ventura P, et al. Phase 3 Trial of RNAi Therapeutic Givosiran for Acute Intermittent Porphyria. N Engl J Med. 2020;382(24):2289-2301. doi:10.1056/NEJMoa1913147. Accessed January 9, 2025.
   https://pubmed.ncbi.nlm.nih.gov/32521132/
3. Wang B, Rudnick S, Cengia B, Bonkovsky HL. Acute Hepatic Porphyrias: Review and Recent Progress. Hepatol Commun. 2018;3(2):193-206. Published 2018 Dec 20. doi:10.1002/hep4.1297. Accessed January 9, 2025.
   https://pubmed.ncbi.nlm.nih.gov/30766957/

DISCLAIMER: Medication Policies are developed to help ensure safe, effective and appropriate use of selected medications. They offer a guide to coverage and are not intended to dictate to providers how to practice medicine. Refer to Plan for individual adoption of specific Medication Policies. Providers are expected to exercise their medical judgement in providing the most appropriate care for their patients.