PHARMACY POLICY STATEMENT
Indiana Medicaid

DRUG NAME	Givlaari (givosiran)
BENEFIT TYPE	Medical
STATUS	Prior Authorization Required

Givlaari, approved by the FDA in 2019, is an aminolevulinate synthase 1-directed small interfering RNA indicated for the treatment of adults with acute hepatic porphyria (AHP). It works by causing degradation of aminolevulinate synthase 1 (ALAS1) mRNA in hepatocytes to lower induced ALAS1, thereby leading to reduced accumulation of neurotoxic intermediates aminolevulinic acid (ALA) and porphobilinogen (PBG) which are associated with AHP attacks and chronic manifestations.
In the pivotal phase 3 trial ENVISION, patients treated with Givlaari experienced an average of 70% fewer

If all the above requirements are met, the medication will be approved for 6 months.

For **reauthorization**:
1. Chart notes must document at least one of the following:
   a) Reduced number of porphyria attacks requiring hospitalization, urgent care, or Panhematin use
   b) Reduced severity of attack symptoms such as pain and decreased opioid use; AND
2. Member is not using Panhematin for attack prophylaxis (allowed for acute use only); AND
3. Member has not had and is not anticipating a liver transplant.

If all the above requirements are met, the medication will be approved for an additional 12 months.

CareSource considers Givlaari (givosiran) not medically necessary for the treatment of conditions that are not listed in this document. For any other indication, please refer to the Off-Label policy.

DATE	ACTION/DESCRIPTION
04/23/2020	New policy for Givlaari created.
12/20/2022	Transferred to new template. Updated J code. Updated and added references. Added diagnostic confirmation via biochemical testing. Added criterion for trigger avoidance. Added neurology and hematology to accepted prescriber specialties. Rephrased re-auth criteria and made attack reduction more specific; added symptom/pain reduction, added liver transplant exclusion.
01/26/2024	Added new reference (AGA 2023). Changed recurrent attack definition from clinical trial definition to guideline definition. Added that if they have already been receiving prophylactic hemin then they don't have to meet recurrent attack definition.

References:

1. Givlaari [package insert]. Summit, NJ: Celgene Corporation, November 2023.
2. Balwani M, Wang B, Anderson KE, et al. Acute hepatic porphyrias: Recommendations for evaluation and long-term management. Hepatology. 2017;66(4):1314–1322. doi:10.1002/hep.29313.
3. 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
4. Ventura P, Bonkovsky HL, Gouya L, et al. Efficacy and safety of givosiran for acute hepatic porphyria: 24-month interim analysis of the randomized phase 3 ENVISION study. *Liver Int*. 2022;42(1):161-172. doi:10.1111/liv.15090
5. Stölzel U, Doss MO, Schuppan D. Clinical Guide and Update on Porphyrias. *Gastroenterology*. 2019;157(2):365-381.e4. doi:10.1053/j.gastro.2019.04.050
6. Stein PE, Badminton MN, Rees DC. Update review of the acute porphyrias. *Br J Haematol*. 2017;176(4):527-538. doi:10.1111/bjh.14459
7. Majeed CN, Ma CD, Xiao T, Rudnick S, Bonkovsky HL. Spotlight on Givosiran as a Treatment Option for Adults with Acute Hepatic Porphyria: Design, Development, and Place in Therapy. *Drug Des Devel Ther*. 2022;16:1827-1845. Published 2022 Jun 16. doi:10.2147/DDDT.S281631

11. 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

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Revised date: 01/26/2024