PHARMACY POLICY STATEMENT
North Carolina Marketplace

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 porphyria attacks than the placebo group. Porphyrias are rare genetic disorders characterized by abnormally high levels of porphyrins in the body due to certain enzyme defects in the heme biosynthesis pathway. There are four types of acute hepatic porphyria (AHP), which are characterized by potentially life-threatening neurologic attacks. The most common and severe type is acute intermittent porphyria (AIP). Women of childbearing age are the most affected population, and the most common attack symptom is severe abdominal pain. Up to 8% of AHP patients have recurrent attacks, defined as more than 4 attacks per year. Givlaari is a treatment option for such patients. Commonly, IV hemin (Panhematin) has been used off label for attack prevention and is the mainstay for treating acute attacks.

Givlaari (givosiran) will be considered for coverage when the following criteria are met:

Acute Hepatic Porphyria (AHP)

For **initial** authorization:

1. Member is at least 18 years of age; AND
2. Medication must be prescribed by or in consultation with a neurologist, hematologist, gastroenterologist, or hepatologist; AND
3. Member has a documented diagnosis of Acute Hepatic Porphyria with one of the following types: acute intermittent porphyria (AIP), hereditary coproporphyria (HCP), variegate porphyria (VP), or aminolevulinic acid dehydratase deficiency porphyria (ADP); AND
4. Member's diagnosis must be confirmed by labs showing an elevated level of urinary ALA or PBG (≥4 times the upper limit of the normal) within the past year; AND
5. Member chart notes must include documentation of active recurrent porphyria attacks with at least 2 attacks in the last 6 months requiring hospitalization, urgent care visit, or intravenous hemin administration at home; AND
6. Member has been assessed for possible attack triggers such as certain drugs, smoking, alcohol, or low carb diets, and counseled to avoid these potential causative factors; AND
7. Member does NOT have any of the following:
   a) Prior or anticipated liver transplant
   b) Active HIV, hepatitis B, or hepatitis C infection; AND
8. Member will not be receiving concomitant prophylactic treatment with IV hemin (Panhematin). *Note: Hemin for treatment of acute attacks is permitted*.
9. **Dosage allowed/Quantity limit:** 2.5 mg/kg subcutaneous injection once monthly.

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.

References:

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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
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