Medical Policy

Utilization Management and Clinical Medical Policy

Policy Name:	Policy Number:	Scope:	Origination Date:	Effective Date:
Givosiran (Givlaari®)	**MP-RX-FP-195-26**	☒ **MMM MA** ☒ **MMM MultiHealth**	**10/21/2026** **Last Review Date:** **10/21/2026**	**10/21/2026** **Frequently Revision:** **Annual**

Service Category:

☐ Anesthesia
☐ Surgery
☐ Radiology Procedures
☐ Pathology and Laboratory Procedures
☐ Medicine Services and Procedures
☐ Evaluation and Management Services
☐ DME/Prosthetics or Supplies
☒ Other: Part B Drugs

Service Description:

This document addresses the use of *Givlaari® (givosiran),* aminolevulinate synthase 1 (ALAS1)-directed small interfering RNA indicated for the treatment of adults with acute hepatic porphyria (AHP).

Background Information:

Porphyria is a group of eight genetic disorders that cause defective production of heme, the oxygen-carrying component of red blood cells. Acute hepatic porphyria is a form of porphyria with 4 subtypes: acute intermittent porphyria (AIP), hereditary coproporphyria (HCP), variegate porphyria (VP), and ALA dehydratase-deficiency porphyria (ADP). In AHP, defective enzymes in the heme biosynthesis pathway allow aminolevulinic acid (ALA) and other neurotoxic heme intermediates to accumulate. This accumulation can trigger a porphyria attack.

AHP occurs primarily in women and has an onset in young adulthood. Porphyria attacks are characterized by severe abdominal and neuropathic pain, many nonspecific symptoms, hypertension, hyponatremia, and red urine. Attacks can last for days and can be lifethreatening. It can be triggered or exacerbated by factors that increase ALAS1 activity and ALA accumulation. This includes inadequate carbohydrate intake, stress, pain, female hormonal changes, smoking, excessive alcohol use, and drugs or substances that induce ALAS1 activity. Long-term complications of AHP include liver disease, hepatocellular carcinoma, chronic kidney disease, and hypertension.

Givlaari is the first FDA-approved treatment that prevents attacks of acute hepatic porphyria. It works by muting ALAS1 via RNA interference through monthly subcutaneous injections administered by a healthcare professional. Givlaari is not approved for other forms of porphyria, such as cutaneous forms of porphyria, where standard treatment typically includes regularly scheduled phlebotomies. Prior to Givlaari, the only approved treatment for recurrent porphyria attacks from AHP was the administration of Panhematin (hemin), an intravenous infusion, along with carbohydrate loading and supportive care. Although it has been known to be used off-label for preventative therapy, Panhematin is only FDA-approved for management of acute attacks.

Approved Indications

A. For the treatment of adults with acute hepatic porphyria (AHP).

Other Uses

A. None.

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Medical Necessity Guidelines:

When a drug is being reviewed for coverage under a member's medical benefit plan or is otherwise subject to clinical review (including prior authorization), the following criteria will be used to determine whether the drug meets any applicable medical necessity requirements for the intended/prescribed purpose.

givosiran (Givlaari®)

A. Criteria For Initial Approval (*Provider must submit documentation [such as office chart notes, lab results, pathology reports, imaging studies, and any other pertinent clinical information] supporting the patient's diagnosis for the drug and confirming that the patient has met **all** approval criteria.)*

Requests for initiation of Givlaari (givosiran) may be approved if the following criteria are met:

i. Individual is 18 years of age or older; **AND**
ii. Individual has a diagnosis of acute hepatic porphyria, and one of the following subtypes (APF):
    A. Acute intermittent porphyria (AIP); **OR**
    B. Hereditary coproporphyria (HCP), **OR**
    C. Variegate porphyria (VP); **OR**
    D. ALA dehydratase-deficiency porphyria (ADP); **AND**
iii. Documentation is provided that individual has an elevated urinary or plasma porphobilinogen (PBG) or delta-aminolevulinic acid (ALA) within the past year (Balwani 2019); **AND**
iv. Individual meets one of the following criteria:
    A. Individual has active symptomatic disease, with at least two porphyria attacks within the last six months, and documentation is provided (Balwani 2019); **OR**
    B. Individual is currently on prophylactic hemin treatment due to history of severe or frequent porphyria attacks.

B. Criteria For Continuation of Therapy

Requests for continuation of Givlaari (givosiran) may be approved if the following criteria are met:

i. Documentation is provided that individual has experienced a clinical response to therapy (for example, a reduction in the number of porphyria attacks, or a reduction in hemin requirements for acute attacks); **AND**
ii. Individual does not have severe or clinically significant transaminase elevations, defined as alanine aminotransferase (ALT) greater than 5 times the upper limit of normal (Balwani 2019).

C. Authorization Duration

i. Initial Approval Duration: Up to 6 months
ii. Reauthorization Approval Duration: Up to 12 months

D. Conditions Not Covered

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Any other use is considered experimental, investigational, or unproven, including the following (this list may not be all inclusive):

Givlaari (givosiran) may not be approved for the following (NCT03338816):

i. Concurrent use of prophylactic hemin treatment with Givlaari (givosiran); **OR**
ii. Liver transplantation is anticipated; **OR**
iii. Individual has a history of recurrent pancreatitis; **OR**
iv. Individual is requesting for other forms of porphyria, such as cutaneous porphyrias (for example, porphyria cutanea tarda [PCT]); **OR**
v. When the above criteria are not met and for all other indications.

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Limits or Restrictions:

A. Therapeutic Alternatives

The list below includes preferred alternative therapies recommended in the approval criteria and may be subject to prior authorization.

i. N/A

B. Quantity Limitations

Approvals may be subject to dosing limits in accordance with FDA-approved labeling, accepted compendia, and/or evidence-based practice guidelines. The chart below includes dosing recommendations as per the FDA-approved prescribing information.

Use	Recommended Dosing Schedule
Givlaari® injection 189 mg/mL single dose vial	• 2.5 mg/kg sc once monthly. ○ Dosing is based on actual body weight.
Exceptions	

• Monitor liver function prior to initiating treatment, every month during the first 6 months of treatment, and clinically indicated therafter.
  • In patients with significant transaminase elevations (3 times the upper limit of normal), who have dose interruption and subsequent improvement, reduce the dose to 1.25 mg/kg once monthly.
  • In patients who resume dosing at 1.25 mg/kg once monthly without recurrence of severe or clinically significant transaminase elevations, the dose may be increased to the recommended dose of 2.5 mg/kg once monthly.	

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Codes Information:

The following list(s) of procedure and/or diagnosis codes is provided for reference purposes only and may not be all inclusive. Inclusion or exclusion of a procedure, diagnosis or device code(s) does not constitute or imply member coverage or provider reimbursement policy. Benefit coverage for health services is determined by the member specific benefit plan document and applicable laws that may require coverage for a specific service. The inclusion of a code does not imply any right to reimbursement or guarantee claim payment. Other Policies and Guidelines may apply.

ICD-10 Diagnostic Codes:

Codes	Description
E80.20-E80.29	Other and unspecified porphyria
Z29.9	Encounter for prophylactic measures, unspecified

HCPCS Codes:

Codes	Description
J0223	Injection, givosiran, 0.5 mg

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Reference Information:

1. Alnylam Pharmaceuticals, Inc. Givlaari® (givosiran) prescribing information. Revised September 2025. Accessed August 25, 2026. https://www.alnylam.com/sites/default/files/pdfs/GIVLAARI-Prescribing-Information.pdf
2. Balwani M, Gouya L, Rees DC, et al. ENVISION, a Phase 3 Study to Evaluate the Efficacy and Safety of Givosiran, an Investigational RNAi Therapeutic Targeting Aminolevulinic Acid Synthase 1, in Acute Hepatic Porphyria Patients. April 13, 2019. European Association for the Study of the Liver (EASL) 54th Annual International Liver Congress. Vienna, Austria.
3. DailyMed. Package inserts. U.S. National Library of Medicine, National Institutes of Health website. http://dailymed.nlm.nih.gov/dailymed/about.cfm. Accessed: December 2, 2025.
4. DrugPoints® System [electronic version]. Truven Health Analytics, Greenwood Village, CO. Updated periodically.
5. Lexi-Comp ONLINE™ with AHFS™, Hudson, Ohio: Lexi-Comp, Inc.; Updated periodically
6. NCT03338816. ClinicalTrials.gov. U.S. National Library of Medicine. Available at https://clinicaltrials.gov/ct2/show/NCT03338816?term=nct03338816&draw=1&rank=1.
7. Porphyria. American Porphyria Foundation (APF). 2010-2025. Available at https://www.porphyriafoundation.org/for-healthcareprofessionals/porphyria/. Accessed on December 2, 2025.
8. The Porphyrias Consortium. Rare Diseases Clinical Research Network. National Institutes of Health. Available at https://www.rarediseasesnetwork.org/cms/porphyrias/Healthcare-Professionals/Disorder-Definitions.

Federal and state laws or requirements, contract language, and Plan utilization management programs or polices may take precedence over the application of this clinical criteria.

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Type of Review	Summary of Changes	P&T Approval Date	UM/CMPC Approval Date
Policy Inception	Elevance Health's Medical Policy adoption.	10/15/2026	10/21/2026