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Givosiran for Acute Hepatic Porphyria

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Disclaimer

Medical policies are a set of written guidelines that support current standards of practice. They are based on current generally accepted standards of and developed by nonprofit professional association(s) for the relevant clinical specialty, third-party entities that develop treatment criteria, or other federal or state governmental agencies. A requested therapy must be proven effective for the relevant diagnosis or procedure. For drug therapy, the proposed dose, frequency and duration of therapy must be consistent with recommendations in at least one authoritative source. This medical policy is supported by FDA-approved labeling and/or nationally recognized authoritative references to major drug compendia, peer reviewed scientific literature and generally accepted standards of medical care. These references include, but are not limited to: MCG care guidelines, DrugDex (IIa level of evidence or higher), NCCN Guidelines (IIb level of evidence or higher), NCCN Compendia (IIb level of evidence or higher), professional society guidelines, and CMS coverage policy.

Carefully check state regulations and/or the member contract.

Each benefit plan, summary plan description or contract defines which services are covered, which services are excluded, and which services are subject to dollar caps or other limitations, conditions or exclusions. Members and their providers have the responsibility for consulting the member's benefit plan, summary plan description or contract to determine if there are any exclusions or other benefit limitations applicable to this service or supply. **If there is a discrepancy between a Medical Policy and a member's benefit plan, summary plan description or contract, the benefit plan, summary plan description or contract will govern.**

Legislative Mandates

EXCEPTION: For HCSC members residing in the state of Ohio, § 3923.60 requires any group or individual policy (Small, Mid-Market, Large Groups, Municipalities/Counties/Schools, State Employees, Fully-Insured, PPO, HMO, POS, EPO) that covers prescription drugs to provide for the coverage of any drug approved by the U. S. Food and Drug Administration (FDA) when it is prescribed for a use recognized as safe and effective for the treatment of a given indication in one or more of the standard medical reference compendia adopted by the United States Department of Health and Human Services or in medical literature even if the FDA has not approved the drug for that indication. Medical literature support is only satisfied when safety and efficacy has been confirmed in two articles from major peer-reviewed professional medical journals that present data supporting the proposed off-label use or uses as generally safe and effective. Examples of accepted journals include, but are not limited to, Journal of

American Medical Association (JAMA), New England Journal of Medicine (NEJM), and Lancet. Accepted study designs may include, but are not limited to, randomized, double blind, placebo controlled clinical trials. Evidence limited to case studies or case series is not sufficient to meet the standard of this criterion. Coverage is never required where the FDA has recognized a use to be contraindicated and coverage is not required for non-formulary drugs.

Coverage

Initial Treatment

Givosiran **may be considered medically necessary** if the following conditions are met:

1. Individual is 18 years of age or older.
2. Individual has a diagnosis of acute hepatic porphyria (AHP) and confirmation of 1 of the following subtypes:
   a. Acute intermittent porphyria (AIP)
   b. Hereditary coproporphyria (HCP)
   c. Variegate porphyria (VP)
   d. Delta-aminolevulinic acid (ALA) dehydratase deficiency (ADP).
3. Documentation is provided that the individual has an elevated porphobilinogen (PBG)- or ALA in the urine or plasma within the past year.
4. Individual meets any 1 of the following criteria:
   a. Individual has documented active symptomatic disease with at least 2 porphyria attacks within the last 6 months.
   b. Individual is currently on prophylactic hemin treatment due to a history of severe or frequent porphyria attacks.
5. Individual will not be receiving prophylactic hemin treatment and givosiran concurrently.
6. Prescriber agrees to monitor liver function tests (LFTs).
7. Prescriber agrees to monitor renal function.

Initial authorization is for 12 months.

Continuation of Treatment

Incremental reauthorization for givosiran **may be considered medically necessary** if the following conditions are met:

1. Individual continues to meet the initial treatment criteria cited above.
2. Documentation is provided that the individual has experienced a clinical response to therapy (e.g., a reduction in rate of porphyria attacks or reduction in hemin requirements for acute attacks) since initiating therapy.
3. PBG or ALA concentration has not increased from baseline.
4. Individual does not have severe or clinically significant transaminase elevations, defined as alanine aminotransferase (ALT) greater than 5 times the upper limit of normal.

Reauthorization period is for 12 months.

Givosiran **is considered experimental, investigational and/or unproven** for all other indications.

Policy Guidelines

The recommended dose of givosiran is 2.5 mg/kg administered via subcutaneous injection once monthly by a healthcare professional, and medical support is readily available to appropriately manage anaphylactic reactions. Dosing is based on actual body weight.

In individuals with severe or clinically significant transaminase elevations, who have dose interruption and subsequent improvement, reduce the dose to 1.25 mg/kg once monthly. In individuals 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 2.5 mg/kg once monthly.

- Givosiran is a ready-to-use solution that does not require additional reconstitution or dilution prior to administration, supplied in single-dose vials of 189 mg/mL;
- Calculate volume required based on recommended dosage: individual weight in kg × 2.5 mg/kg × 1 mL/189 mg=mL of givosiran to administer;
- If the total volume of givosiran per dose is >1.5 mL, divide the dose into multiple injections of approximately equal volumes.

Transaminase elevations (ALT) of at least 3 times the upper limit of normal (ULN) were observed in 15% of individuals treated with givosiran in the ENVISION trial. It is recommended that the prescriber measure liver function tests prior to initiating treatment with givosiran, repeat every month during the first 6 months of treatment, and as clinically indicated thereafter.

Increases in serum creatinine levels and decreases in estimated glomerular filtration rate (eGFR) have been reported during treatment with givosiran. It is recommended that the prescriber monitor renal function during treatment as clinically indicated.

In the ENVISION trial, an individual was eligible for the study without genetic testing that identified a variant in a porphyria-related gene if the individual had both clinical features and diagnostic biochemical criteria consistent with AHP. This is reported to be < 5% of the total number of AHP cases.

Description

Acute hepatic porphyria (AHP) is a rare disease with a prevalence of 5 to 10 cases/100,000 people in the U.S. and effects primarily females (age range 15 to 45 years). The induction of the enzyme aminolevulinate synthase 1 (ALAS1) results in increased production and accumulation of toxic heme intermediates delta aminolevulinic acid and porphobilinogen in the plasma and urine. The accumulation of these toxic heme intermediates results in acute attacks

characterized by severe abdominal pain, muscle weakness, seizures, psychiatric dysfunction, irreversible neurologic damage, and increased risk of hepatic malignancy. Givosiran (Givlaari®) is a double-stranded small interfering RNA that causes degradation of ALAS1 mRNA in hepatocytes through RNA interference, reducing the elevated levels of liver ALAS1 mRNA. This leads to decreased circulating levels of neurotoxic intermediates aminolevulinic acid (ALA) and porphobilinogen (PBG), factors associated with attacks and other disease manifestations of acute hepatic porphyria.

Background

Acute Hepatic Porphyria

Porphyrias are inborn errors of metabolism that cause deficient activity within the 8-step heme synthetic pathway, leading to accumulation of heme precursors and subsequent clinical manifestations of disease. Porphyrias are generally classified in 1 of 2 ways: by main site of heme precursors (hepatic or erythropoietic) or cardinal clinical features (acute or cutaneous).

Acute hepatic porphyria (AHP) is a group of inherited diseases comprised of 4 subtypes: acute intermittent porphyria (AIP), hereditary coproporphyria (HCP), variegate porphyria (VP), and aminolevulinic acid (ALA) dehydratase-deficiency (ADP) porphyria. Three (i.e., AIP, HCP, and VP) arise from autosomal dominant mutations of genes that control normal hepatic heme biosynthesis; AIP is the most common. The fourth type (ADP porphyria) is an autosomal recessive condition that is very rare. Acute hepatic porphyria is a rare disease with a prevalence of 5 to 10 cases/100,000 people in the U.S. and affects primarily females (age range 15 to 45 years). The induction of enzyme aminolevulinate synthase 1 (ALAS1) results in increased production and accumulation of toxic heme intermediates delta ALA and porphobilinogen (PBG) in the plasma and urine. Clinically, the accumulation of toxic heme intermediates results in acute attacks characterized by severe abdominal pain, muscle weakness, seizures, psychiatric dysfunction, irreversible neurologic damage, and increased risk of hepatic malignancy. (2) Approximately 20% of patients with recurrent symptoms develop chronic and ongoing pain and other symptoms.

Porphyrias are rare disorders with nonspecific clinical manifestations similar to those of many other more common diseases. As a result, their diagnosis and appropriate treatment are often delayed. The condition is typically a diagnosis of exclusion and is usually considered only after several attack-related emergency department visits. First-line screening tests are sensitive for diagnosis of these disorders, and additional second-line testing readily differentiates the various types of porphyria. Diagnostic confirmation by DNA analysis is readily available. If suspected, establishing or ruling out an AHP diagnosis involves requesting a quantitative estimation of urine porphobilinogen (PBG), delta-aminolevulinic acid (ALA), and porphyrins via a spot sample, with results normalized to urine creatinine. In a symptomatic patient, a normal urine PBG excludes the 3 most common AHPs as the etiology of symptoms.

Treatment

The goal of therapy for an acute attack of AIP is to abate the attack as rapidly as possible and to provide appropriate supportive and symptomatic care. Hospitalization is usually required.

Treatment of attacks consists of hemin Panhematin®, which is an enzyme inhibitor derived from processed red blood cells. Other long-term management considerations include discontinuation of medications that are harmful to patients with AHP during acute attacks; avoiding cigarettes, alcohol, and marijuana; and maintaining a diet high in carbohydrates (60% to 70% of total calories). Liver transplant, when available, is also an option. (3)

Regulatory Status
On November 20, 2019, Givlaari® (givosiran) was approved by the U.S. Food and Drug Administration (FDA) for the treatment of adults with AHP.

Rationale

Medical policies assess the clinical evidence to determine whether the use of a technology improves the net health outcome. Broadly defined, health outcomes are length of life, quality of life, and ability to function including benefits and harms. Every clinical condition has specific outcomes that are important to patients and to managing the course of that condition. Validated outcome measures are necessary to ascertain whether a condition improves or worsens; and whether the magnitude of that change is clinically significant. The net health outcome is a balance of benefits and harms.

To assess whether the evidence is sufficient to draw conclusions about the net health outcome of a technology, 2 domains are examined: the relevance and the quality and credibility. To be relevant, studies must represent 1 or more intended clinical use of the technology in the intended population and compare an effective and appropriate alternative at a comparable intensity. For some conditions, the alternative will be supportive care or surveillance. The quality and credibility of the evidence depend on study design and conduct, minimizing bias and confounding that can generate incorrect findings. The randomized controlled trial (RCT) is preferred to assess efficacy; however, in some circumstances, nonrandomized studies may be adequate. Randomized controlled trials are rarely large enough or long enough to capture less common adverse events and long-term effects. Other types of studies can be used for these purposes and to assess generalizability to broader clinical populations and settings of clinical practice.

Acute Hepatic Porphyria
Clinical Context and Therapy Purpose
The purpose of givosiran in individuals who have acute hepatic porphyria (AHP) is to provide a treatment option that is an alternative to existing therapeutic management including pharmacologic (e.g., hemin) and/or non-pharmacologic (e.g., discontinuation of porphyrinogenic medications and carbohydrate loading) approaches.

The following PICO was used to select literature to inform this policy.

Populations

The relevant population(s) of interest is adults with AHP.

Interventions
The therapy being considered is givosiran. It is a small interfering ribonucleic acid (RNA) that causes degradation of aminolevulinate synthase 1 (ALAS1) mRNA in hepatocytes through RNA interference, eventually reducing elevated levels of porphobilinogen (PBG) and aminolevulinic acid (ALA). This leads to decreased circulating levels of the neurotoxic intermediates ALA and PBG, factors associated with attacks and other disease manifestations of AHP.

Comparators
The following therapies are currently being used to make decisions about the treatment of AHP: nonpharmacologic and pharmacologic approaches that treat symptoms. These include avoiding or discontinuing porphyrinogenic medications and maintenance of a balanced diet without prolonged fasting or crash dieting. In the early stages of an acute AHP attack, management includes oral administration of calories (i.e., carbohydrate loading) and rehydration as well as the potential administration of intravenous hemin. For patients who experience frequent recurrent attacks, which primarily involves women and may be associated with menstrual cycle changes, ovulatory suppression with a gonadotropin-releasing hormone analogue may be beneficial. Other medications may be necessary for symptom management on an individualized basis (e.g., opiates for pain).

Outcomes
The general outcomes of interest are symptoms, quality of life, hospitalizations, and resource utilization. Health outcome measures relevant to AHP in adults are summarized in Table 1.

Table 1. Health Outcome Measures Relevant to AHP in Adults

Outcome	Measure (Units)	Description and Administration	Thresholds for Improvement/Decline or Clinically Meaningful Difference
Annualized rate of porphyria attacks in patients with AIP	Time frame: 6 months	Porphyria attacks were defined as meeting all of the following criteria: an acute episode of neurovisceral pain in the abdomen, back, chest, extremities and/or limbs, no other medically determined cause, and required treatment with IV dextrose or hemin, carbohydrates, or analgesics, or other medications such as antiemetics at a dose or frequency beyond the	The annualized rate of porphyria attacks is a composite endpoint, which included porphyria attacks requiring hospitalization, urgent healthcare visit, or IV hemin administration at home.

		participant's usual daily porphyria management.	

AHP: acute hepatic porphyria; AIP: acute intermittent porphyria; IV: intravenous.

Study Selection Criteria

Methodologically credible studies were selected using the following principles:

- To assess efficacy outcomes, comparative controlled prospective trials were sought, with a preference for RCTs;
- In the absence of such trials, comparative observational studies were sought, with a preference for prospective studies;
- To assess long-term outcomes and adverse events, single-arm studies that capture longer periods of follow-up and/or larger populations were sought;
- Consistent with a 'best available evidence approach', within each category of study design, studies with larger sample sizes and longer durations were sought;
- Studies with duplicative or overlapping populations were excluded.

Randomized Controlled Trials

The pivotal double-blind, placebo-controlled, phase 3 ENVISION trial (NCT03338816) evaluated the efficacy and safety of monthly givosiran as compared to placebo for 6 months in 94 symptomatic patients with AHP. (4) Key study characteristics of ENVISION are summarized in Table 2. Results are summarized in Table 3. Results were reported for the 89 patients with the acute intermittent porphyria (AIP) subtype of AHP only. Treatment with givosiran was associated with a significant reduction in the rate of porphyria attacks and improvement in other disease manifestations as compared to placebo. After the 6-month, double-blind period of ENVISION, all on-study patients were administered givosiran during an open-label extension. Long-term results from the patients in ENVISION who completed 24 months (5) and 36 months (6) of follow-up reported sustained improvement in symptoms of AHP, as well as median annualized attack rate. Proportions of patients with 0 attacks or 0 days of hemin use increased over time and patients showed continued improvement in physical/mental health and quality of life. Safety findings were consistent with those observed in the initial double-blind period.

Table 2. Summary of Key RCT Characteristics

Study	Countries	Sites	Dates	Participants	Interventions	
					Active	Comparator
ENVISION (2021) (4) (NCT03338816)	U.S., EU, Canada, Mexico, Australia, South Korea, Taiwan, Japan	36	2017-2021	Inclusion • Age ≥12 years • Documented AHP diagnosis[a] (AIP, HCP, VP, ADP) • Documentation of at least 2 composite porphyria	Givosiran 2.5 mg/kg subcutan-eously monthly for 6 months (n=48)	Placebo monthly for 6 months (n=46)

				attacks within 6 months before baseline Primary endpoint • Annualized rate of porphyria attacks that require hospitalization, urgent care visit, or in-home IV hemin administration		

[a] Diagnosis based on clinical features, at least 1 documented urinary or plasma PBG or ALA value ≥ 4 × ULN within the past year prior to or during screening, AND 1 of the following: Either documented genetic evidence of mutation in a porphyria-related gene, defined as ANY of the following: AIP (variant in *HMB gene* also referred to as the *PBGD* gene), HCP (variant in *CPOX* gene), VP (variant in PPOX gene) and ADP (variant in *ALAD* homozygous or compound heterozygous genes) OR if the results of a patient's genetic testing do not identify a variant in a porphyria-related gene (< 5% of cases), a patient may be eligible for the study if they have both clinical features and diagnostic biochemical criteria consistent with AHP.

ADP: ALA dehydratase-deficiency porphyria; AHP: acute hepatic porphyria; AIP: acute intermittent porphyria; ALA: aminolevulinic acid dehydratase; CPOX: coproporphyrinogen oxidase; EU: European Union; HCP: hereditary coproporphyria; HMBS: hydroxymethylbilane synthase; IV: intravenous; PBG: porphobilinogen; PBGD: porphobilinogen deaminase; PPOX: protoporphyrinogen oxidase; RCT: randomized controlled trial; ULN: upper limit of normal; VP: variegate porphyria; U.S.: United States.

Table 3. Summary of Key RCT Results: ENVISION

Study	**Givosiran (n=48)**	**Placebo (n=46)**
ENVISION (1)		
Mean rate (95% CI) of porphyria attacks[a]	1.9 (1.3, 2.8)	6.5 (4.5, 9.3)
Rate ratio[b] (95% CI) (givosiran/placebo)	0.3 (0.2, 0.4)	
p value	<0.0001	
Mean days (95% CI) of hemin use	4.7 (2.8, 7.9)	12.8 (7.6, 21.4)
Ratio[b] (95% CI) (givosiran/placebo)	0.3 (0.1, 0.5)	
p value	0.0002	

CI: confidence interval; RCT: randomized controlled trial.

[a] Attacks that require hospitalization, urgent healthcare visits, or intravenous hemin administration at home.

[b] Adjusted for prior hemin prophylaxis status and historical attack rates. A ratio <1 represents a favorable outcome for givosiran.

The purpose of the study limitations tables (see Table 4) is to display notable limitations identified in each study. This information is synthesized as a summary of the body of evidence following each table and provides the conclusions on the sufficiency of evidence supporting the position statement. A gap in relevance for ENVISION is related to the lack of data on individuals with non-AIP AHP. No major gaps were identified in study design and conduct.

Table 4. Study Relevance Limitations

Study	Population[a]	Intervention[b]	Comparator[c]	Outcomes[d]	Duration of Follow-up[e]
ENVISION (2021) (4, 1)	4. Enrolled populations do not reflect relevant diversity (80% White) 5. Other (limited data for non-AIP patients; of the 94 enrolled patients, 89 were AIP, 2 were VP, 1 was HCP, and 2 with no identified variant)				

AIP: acute intermittent porphyria; HCP: hereditary coproporphyria; VP: variegate porphyria.
The study limitations stated in this table are those notable in the current review; this is not a comprehensive gaps assessment.
[a] Population key: 1. Intended use population unclear; 2. Study population is unclear; 3. Study population not representative of intended use; 4, Enrolled populations do not reflect relevant diversity; 5. Other.
[b] Intervention key: 1. Not clearly defined; 2. Version used unclear; 3. Delivery not similar intensity as comparator; 4. Not the intervention of interest (e.g., proposed as an adjunct but not tested as such); 5: Other.
[c] Comparator key: 1. Not clearly defined; 2. Not standard or optimal; 3. Delivery not similar intensity as intervention; 4. Not delivered effectively; 5. Other.
[d] Outcomes key: 1. Key health outcomes not addressed; 2. Physiologic measures, not validated surrogates; 3. Incomplete reporting of harms; 4. Not establish and validated measurements; 5. Clinically

significant difference not prespecified; 6. Clinically significant difference not supported; 7. Other.
[e] Follow-Up key: 1. Not sufficient duration for benefit; 2. Not sufficient duration for harms; 3. Other.

Section Summary: Acute Hepatic Porphyria

Results from a single double-blind, placebo-controlled RCT (ENVISION) comparing givosiran to placebo for 6 months concluded that givosiran therapy was associated with a significant reduction in the rate of acute porphyria attacks and other disease manifestations in patients with AHP as compared to placebo. There was an increase in injection site reactions, nausea, fatigue, and hepatic- and renal-related adverse events with givosiran therapy. The efficacy benefits seen in the double-blind period of the ENVISION trial were confirmed in studies reporting long-term follow-up data up to 36 months with safety findings consistent with the initial ENVISION trial results.

Summary of Evidence

For individuals with acute hepatic porphyria (AHP) who receive givosiran, the evidence includes a randomized controlled trial (RCT) and data from a long-term extension of the RCT. Relevant outcomes are symptoms, quality of life, hospitalizations, and resource utilization. Results from the double-blind, placebo-controlled, ENVISION RCT revealed that patients administered givosiran monthly for 6 months experienced a significant improvement in daily worst pain score and significant reductions in porphyria attacks, hemin use, and urinary aminolevulinic acid (ALA) and porphobilinogen (PBG) levels as compared to placebo. The increased efficacy of givosiran was accompanied by an increased frequency of hepatic and renal adverse events. Results of long-term follow-up at 24- and 36-months confirmed the continuing benefits of givosiran therapy with safety findings consistent with the initial double-blind period. The evidence is sufficient to determine that the technology results in an improvement in the net health outcome.

Practice Guidelines and Position Statements

American Gastroenterological Association

The American Gastroenterological Association Institute Clinical Practice Updates Committee published best practice advice from a review of the published literature and from expert opinion on diagnosis and management of acute hepatic porphyrias (AHP). (7) The best practice advises on management of the disease include the following:

- Acute attacks of AHP that are severe enough to require hospital admission should be treated with intravenous hemin, given daily, preferably into a high-flow central vein.
- In addition to intravenous hemin, management of acute attacks of AHP should include pain control, antiemetics, management of systemic arterial hypertension, tachycardia, and hyponatremia, and hypomagnesemia, if present.
- Patients should be counseled to avoid identifiable triggers that may precipitate acute attacks, such as alcohol and porphyrinogenic medications.
- Prophylactic heme therapy or givosiran, administered in an outpatient setting, should be considered in patients with recurrent attacks (4 or more per year).
- Liver transplantation for AHP should be limited to patients with intractable symptoms and significantly decreased quality of life who are refractory to pharmacotherapy.

- Patients with AHP should be monitored annually for liver disease.
- Patients with AHP, regardless of the severity of symptoms, should undergo surveillance for hepatocellular carcinoma, beginning at age 50 years, with liver ultrasound every 6 months.
- Patients with AHP on treatment should undergo surveillance for chronic kidney disease annually with serum creatinine and estimated glomerular filtration rate.
- Patients should be counseled on the chronic and long-term complications of AHP, including neuropathy, chronic kidney disease, hypertension, and hepatocellular carcinoma, and need for long-term monitoring.

National Institute for Health and Care Excellence

On November 24, 2021, the National Institute for Health and Care Excellence (NICE) issued highly specialized technologies guidance on givosiran for treating AHP. (8) Givosiran is recommended as an option for treating AHP in adults and young people aged 12 and older, only if they have clinically confirmed severe recurrent attacks (4 attacks or more within 12 months) and the company provides it according to the commercial arrangement.

Ongoing and Unpublished Clinical Trials

Some currently ongoing trials that might influence this policy are listed in Table 5.

Table 5. Summary of Key Trials

NCT Number	Trial Name	Planned Enrollment	Completion Date
Ongoing			
NCT04883905[a]	ELEVATE, a Global Observational Longitudinal Prospective Registry of Patients With Acute Hepatic Porphyria (AHP)	150	Apr 2027

NCT: national clinical trial.

[a] Denotes industry-sponsored or cosponsored trial.

Coding

Procedure codes on Medical Policy documents are included **only** as a general reference tool for each policy. **They may not be all-inclusive.**

The presence or absence of procedure, service, supply, or device codes in a Medical Policy document has no relevance for determination of benefit coverage for members or reimbursement for providers. **Only the written coverage position in a Medical Policy should be used for such determinations.**

Benefit coverage determinations based on written Medical Policy coverage positions must include review of the member's benefit contract or Summary Plan Description (SPD) for defined coverage vs. non-coverage, benefit exclusions, and benefit limitations such as dollar or duration caps.

CPT Codes	None
HCPCS Codes	J0223

*Current Procedural Terminology (CPT®) ©2024 American Medical Association: Chicago, IL.

References

U.S. Food and Drug Administration Label:

1. Prescribing Label: Givlaari (givosiran) injection, for subcutaneous use. Initial U.S. Approval: 2019. Revised 4/2024. Available at <https://www.alnylam.com> (accessed June 17, 2025).

Other:

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8. National Institute for Health and Care Excellence. Givosiran for treating acute hepatic porphyria. Highly specialized technologies guidance. HST16. 2021. Available at <https://www.nice.org.uk> (accessed June 17, 2025).

Centers for Medicare and Medicaid Services (CMS)

The information contained in this section is for informational purposes only. HCSC makes no representation as to the accuracy of this information. It is not to be used for claims adjudication for HCSC Plans.

The Centers for Medicare and Medicaid Services (CMS) does not have a national Medicare coverage position. Coverage may be subject to local carrier discretion.

A national coverage position for Medicare may have been developed since this medical policy document was written. See Medicare's National Coverage at <https://www.cms.hhs.gov>.

Policy History/Revision

Date	Description of Change
11/01/2025	Document updated with literature review. Coverage section completely revised. Added references 1-8; others removed. Title changed from “Givosiran”.

12/15/2024	Document updated with literature review. Coverage unchanged. No new references added; some updated.
07/01/2023	Reviewed. No changes.
01/15/2023	Document updated with literature review. Coverage unchanged. Reference 8 added, other references updated.
11/01/2021	Reviewed. No changes.
11/15/2020	New medical document. Givosiran (Givlaari™) may be considered medically necessary for the treatment of individuals with acute hepatic porphyria (AHP) who meet the following criteria: individuals 18 years of age and older; and patient has a confirmed diagnosis of acute hepatic porphyria (AHP) [i.e., acute intermittent porphyria (AIP), variegate porphyria (VP), hereditary coproporphyria (HCP), delta-aminolevulinic acid dehydratase deficient porphyria (ADP)]; and patient has active disease with at least two documented porphyria attacks within the 6 months prior to initiation (requiring hospitalization, urgent healthcare visit, or intravenous hemin administration at home). Givosiran (Givlaari™) is considered experimental, investigational, and/or unproven for all other indications.