Givosiran (Givlaari®)

NDC CODE(S) 71336-1001-xx GIVLAARI 189MG/ML Solution (ALNYLAM PHARMACEUTICALS)

DESCRIPTION

Givosiran is a double-stranded small interfering RNA that causes degradation of aminolevulinate synthase 1 (ALAS1) mRNA in hepatocytes through RNA interference, reducing the elevated levels of liver ALAS1 mRNA. This leads to reduced circulating levels of neurotoxic intermediates aminolevulinic acid (ALA) and porphobilinogen (PBG), factors associated with attacks and other disease manifestations of acute hepatic porphyria (AHP).

POLICY

- Givosiran for the treatment of acute hepatic porphyria (AHP) is considered ***medically necessary*** if the medical appropriateness criteria are met. **(See Medical Appropriateness below.)**

- Givosiran for the treatment of other conditions/diseases is considered ***investigational***

MEDICAL APPROPRIATENESS

INITIAL APPROVAL

- Patient is at least 18 years of age; **AND**

Universal Criteria

- Patient will avoid known triggers of porphyria attacks (i.e., alcohol, smoking, exogenous hormones, hypocaloric diet/fasting, certain medications such as barbiturates, hydantoins, sulfa-antibiotics, anti-epileptics, etc.); **AND**
- Patient has not had or is not anticipating a liver transplant; **AND**

Acute Hepatic Porphyria (AHP)

- Patient has a definitive diagnosis of acute hepatic porphyria* (including acute intermittent porphyria, variegate porphyria, hereditary coproporphyria, or ALA dehydratase deficient porphyria) as evidenced by one of the following:
  - Patient has had elevated urinary or plasma PBG (porphobilinogen) and ALA (delta-aminolevulinic acid) levels within the previous year; **OR**
  - Patient has a mutation in an affected gene as identified on molecular genetic testing; **AND**
- Patient has a history of at least two documented porphyria attacks (i.e., requirement of hospitalization, urgent healthcare visit or intravenous administration of hemin) **OR** one severe attack with CNS involvement (e.g., hallucinations, seizures, etc.) during the previous six months; **AND**
- Patients currently receiving prophylactic intravenous hemin therapy will discontinue hemin within 3 to 6 months following initiation of givosiran

*Acute Hepatic Porphyria	Urine delta-aminolevulinic acid (ALA)	Urine porphobilinogen (PBG)	Urine porphyrins	Gene
Acute Intermittent Porphyria (AIP)	Elevated	Elevated	Increased uroporphyrin	*HMBS*
Hereditary Coproporphyria (HCP)	Elevated	Elevated	Increased coproporphyrin	*CPOX*

Variegate Porphyria (VP)	Elevated	Elevated	Increased coproporphyrin	*PPOX*
ALA Dehydratase-Deficiency Porphyria (ADP)	Elevated	Normal	Increased coproporphyrin	*ALAD*

RENEWAL CRITERIA

- Patient continues to meet universal and other indication-specific relevant criteria such as concomitant therapy requirements (not including prerequisite therapy), performance status, etc. identified in Initial Approval Criteria; **AND**
- Absence of unacceptable toxicity from the drug. Examples of unacceptable toxicity include the following: anaphylactic reactions, severe hepatic toxicity, severe renal toxicity, severe injection site reactions, etc.; **AND**
- Disease response as evidenced by a decrease in the frequency of acute porphyria attacks, and/or hospitalizations/urgent care visits, and/or a decrease requirement of hemin intravenous infusions for acute attacks; **AND**
- Patient has a reduction/normalization of biochemical markers (i.e., ALA, PBG) compared to baseline; **AND**
- Patient will not use in combination with prophylactic intravenous hemin therapy; **AND**

DOSAGE/ADMINISTRATION

INDICATION	DOSE
Acute Hepatic Porphyria (AHP)	**For administration by a healthcare professional as a subcutaneous injection only.** • Administer 2.5 mg/kg via subcutaneous injection once monthly. Dosing is based on actual body weight.

LENGTH OF AUTHORIZATION

Coverage will be provided for 6 months initially and may be renewed annually thereafter.

DOSING LIMITS

Max Units (per dose and over time) [HCPC Unit]:

- 576 billable units every month

APPLICABLE TENNESSEE STATE MANDATE REQUIREMENTS

BlueCross BlueShield of Tennessee's Medical Policy complies with Tennessee Code Annotated Section 56-7-2352 regarding coverage of off-label indications of Food and Drug Administration (FDA) approved drugs when the off-label use is recognized in one of the statutorily recognized standard reference compendia or in the published peer-reviewed medical literature.

IMPORTANT REMINDER

We develop Medical Policies to provide guidance to Members and Providers. This Medical Policy relates only to the services or supplies described in it. The existence of a Medical Policy is not an authorization, certification, explanation of benefits or a contract for the service (or supply) that is referenced in the Medical Policy. For a determination of the benefits that a Member is entitled to receive under his or her health plan, the Member's health

plan must be reviewed. If there is a conflict between the Medical Policy and a health plan, the express terms of the health plan will govern.

ADDITIONAL INFORMATION

For appropriate chemotherapy regimens, dosage information, contraindications, precautions, warnings, and monitoring information, please refer to one of the standard reference compendia (e.g., the NCCN Clinical Practice Guidelines in Oncology (NCCN Guidelines®) published by the National Comprehensive Cancer Network®, Drugdex Evaluations of Micromedex Solutions at Truven Health, or The American Hospital Formulary Service Drug Information).

SOURCES

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3. Anderson KE. Porphyrias: An overview. Mahoney DH, Means RT, ed. UpToDate. Waltham, MA: UpToDate Inc. https://www.uptodate.com/contents/porphyrias-anoverview?search=Acute%20Hepatic%20Porphyria&sectionRank=2&usage_type=default&anchor=H148718266&source=machineLearning&selectedTitle=1~123&display_rank=1#H148 718266 (Accessed on November 24, 2020).
4. Balwani M, Gouya L, Rees D, et al. GS-14-ENVISION, a phase 3 study to evaluate efficacy and safety of givosiran, an investigational RNAi therapeutic targeting aminolevulinic acid synthase 1, in acute hepatic porphyria patients. J Hepatology: Apr 2019; Vol 70; Iss. 1, Suppl;pps e81–e82
5. Balwani M, Sardh E, Ventura P,et al.; ENVISION Investigators. Phase 3 Trial of RNAi Therapeutic Givosiran for Acute Intermittent Porphyria. N Engl J Med. 2020 Jun 11;382(24):2289-2301.
6. Lexicomp Online. (2020, March). AHFS DI. Givosiran. Retrieved December 28, 2020 from Lexicomp Online with AHFS.
7. MICROMEDEX Healthcare Series. Drugdex Evaluations. (2020, March). Givosiran. Retrieved December 28, 2020 from MICROMEDEX Healthcare Series.

EFFECTIVE DATE 6/2/2021

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