Givlaari® (givosiran)
(Subcutaneous)

Document Number: SHP-0514

Last Review Date: 01/04/2022
Date of Origin: 12/13/2019
Dates Reviewed: 12/2019, 01/2021, 01/2022

I. Length of Authorization

Coverage will be provided for 12 months initially and may be renewed annually thereafter.

II. Dosing Limits

A. Quantity Limit (max daily dose) [NDC Unit]:

- Givlaari 189 mg/mL in a single-dose vial for injection: 2 vials every month

B. Max Units (per dose and over time) [HCPS Unit]:

- 576 billable units every month

III. Initial Approval Criteria[1]

Coverage is provided in the following conditions:

> Submission of medical records (chart notes) related to the medical necessity criteria is REQUIRED on all requests for authorizations. Records will be reviewed at the time of submission. Please provide documentation related to diagnosis, step therapy, and clinical markers (i.e. genetic and mutational testing) supporting initiation when applicable. Medical records may be submitted via direct upload through the PA web portal or by fax.

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

Universal Criteria [1,3-5]

- 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) † Φ [1,3-5]

- 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**
- **ONE** of the following:
    - Patient has a history of at least two documented porphyria attacks during the previous six months; **OR**
    - Patient has a history of one severe attack with CNS, PNS, or ANS involvement (e.g., hallucinations, seizures, etc.) during the previous six months; **OR**
    - Patient is currently receiving off-label hemin for attack prophylaxis; **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*

† FDA Approved Indication(s); ‡ Compendium Recommended Indication(s); Φ Orphan Drug

IV. Renewal Criteria [1]

Coverage can be renewed based upon the following 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 section III; **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

V. Dosage/Administration [1]

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.

VI. Billing Code/Availability Information

HCPCS Code:

- J0223 – Injection, givosiran, 0.5 mg: 1 billable unit=0.5 mg

NDC:

- Givlaari 189 mg/mL in a single-dose vial for injection: 71336-1001-xx

VII. References

1. Givlaari [package insert]. Cambridge, MA; Alnylam Pharm., Inc., October 2021. Accessed November 2021.
2. Whatley SD, Badminton MN. Acute Intermittent Porphyria. 2005 Sep 27 [Updated 2013 Feb 7]. In: Adam MP, Ardinger HH, Pagon RA, et al., editors. GeneReviews® [Internet]. Seattle (WA): University of Washington, Seattle; 1993-2019. Available from: https://www.ncbi.nlm.nih.gov/books/NBK1193/.
3. Anderson KE. Porphyrias: An overview. Mahoney DH, Means RT, ed. UpToDate. Waltham, MA: UpToDate Inc. https://www.uptodate.com/contents/porphyrias-an-overview?search=Acute%20Hepatic%20Porphyria&sectionRank=2&usage_type=default&anchor=H148718266&source=machineLearning&selectedTitle=1~123&display_rank=1#H148718266 (Accessed on November 19, 2021).
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. Balwani M, Wang B, Anderson KE. Acute hepatic porphyrias: Recommendations for evaluation and long-term management. Hepatology. Volume66, Issue4 October 2017. Pages 1314-1322. https://doi.org/10.1002/hep.29313

Appendix 1 – Covered Diagnosis Codes

ICD-10	ICD-10 Description
E80.20	Unspecified porphyria
E80.21	Acute intermittent (hepatic) porphyria
E80.29	Other porphyria

Appendix 2 – Centers for Medicare and Medicaid Services (CMS)

Medicare coverage for outpatient (Part B) drugs is outlined in the Medicare Benefit Policy Manual (Pub. 100-2), Chapter 15, §50 Drugs and Biologicals. In addition, National Coverage Determination (NCD), Local Coverage Determinations (LCDs), and Local Coverage Articles (LCAs) may exist and compliance with these policies is required where applicable. They can be found at: https://www.cms.gov/medicare-coverage-database/search.aspx. Additional indications may be covered at the discretion of the health plan.

Medicare Part B Covered Diagnosis Codes (applicable to existing NCD/LCD/LCA): N/A

Medicare Part B Administrative Contractor (MAC) Jurisdictions		
Jurisdiction	**Applicable State/US Territory**	**Contractor**
E (1)	CA, HI, NV, AS, GU, CNMI	Noridian Healthcare Solutions, LLC
F (2 & 3)	AK, WA, OR, ID, ND, SD, MT, WY, UT, AZ	Noridian Healthcare Solutions, LLC
5	KS, NE, IA, MO	Wisconsin Physicians Service Insurance Corp (WPS)
6	MN, WI, IL	National Government Services, Inc. (NGS)
H (4 & 7)	LA, AR, MS, TX, OK, CO, NM	Novitas Solutions, Inc.
8	MI, IN	Wisconsin Physicians Service Insurance Corp (WPS)
N (9)	FL, PR, VI	First Coast Service Options, Inc.
J (10)	TN, GA, AL	Palmetto GBA, LLC
M (11)	NC, SC, WV, VA (excluding below)	Palmetto GBA, LLC
L (12)	DE, MD, PA, NJ, DC (includes Arlington & Fairfax counties and the city of Alexandria in VA)	Novitas Solutions, Inc.
K (13 & 14)	NY, CT, MA, RI, VT, ME, NH	National Government Services, Inc. (NGS)
15	KY, OH	CGS Administrators, LLC