Givlaari® (givosiran)
(Subcutaneous)

Document Number: IC-0514

Last Review Date: 01/05/2023
Date of Origin: 12/13/2019
Dates Reviewed: 12/2019, 01/2021, 01/2022, 01/2023

I. Length of Authorization

Coverage will be provided for 6 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:

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

Universal Criteria [1,3-6]

- 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**

- 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*

† 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: anaphylactic reactions, severe hepatic toxicity, severe renal toxicity, severe injection site reactions, increase in blood homocysteine levels, 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., January 2022. Accessed November 2022.
2. Whatley SD, Badminton MN. Acute Intermittent Porphyria. 2005 Sep 27 [Updated 2019 Dec 5]. In: Adam MP, Everman DB, Mirzaa GM, et al., editors. GeneReviews® [Internet]. Seattle (WA): University of Washington, Seattle; 1993-2022. Available from: https://www.ncbi.nlm.nih.gov/books/NBK1193/.
3. Anderson KE. Porphyrias: An overview. In Means RT, Tirnauer JS (Eds), *UpToDate*. Last updated: March 11, 2022. Accessed on November 29, 2022. https://www.uptodate.com/contents/porphyrias-an-overview?search=Porphyrias:%20An%20overview&source=search_result&selectedTitle=1~150&usage_type=default&display_rank=1.
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

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- Qualified sign language interpreters
- Written information in other formats (large print, audio, accessible electronic formats, other formats)

Provides free language services to people whose primary language is not English, such as:

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Grievance Specialist
PreferredOne Community Health Plan
PO Box 59052
Minneapolis, MN 55459-0052
Phone: 1.800.940.5049 (TTY: 763.847.4013)
Fax: 763.847.4010
customerservice@preferredone.com

You can file a grievance in person or by mail, fax, or email. If you need help filing a grievance, a Grievance Specialist is available to help you.

You can also file a civil rights complaint with the U.S. Department of Health and Human Services, Office for Civil Rights, electronically through the Office for Civil Rights Complaint Portal, available at https://ocrportal.hhs.gov/ocr/portal/lobby.jsf, or by mail or phone at:

U.S. Department of Health and Human Services
200 Independence Avenue, SW
Room 509F, HHH Building
Washington, D.C. 20201
1-800-368-1019, 800-537-7697 (TDD)

Complaint forms are available at http://www.hhs.gov/ocr/office/file/index.html.

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U.S. Department of Health and Human Services
200 Independence Avenue, SW
Room 509F, HHH Building
Washington, D.C. 20201
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