Neighborhood Health Plan OF RHODE ISLAND™
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Givlaari™ (givosiran)
(Subcutaneous)

Effective date: 4/15/2020
Review date: 4/15/2020, 1/11/2021, 1/20/2022, 2/1/2023, 12/07/2023, 01/04/2024, 3/12/2025

Scope: Medicaid*, Exchange*, Medicare-Medicaid Plan (MMP)
***(Medication only available on the Medical Benefit)**

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) [HCPCS Unit]:

- 576 billable units every month

III. Summary of Evidence

Givlaari is an aminolevulinate synthase 1-directed small interfering RNA indicated for the treatment of adults with acute hepatic porphyria (AHP). Clinical trials evaluating the efficacy and safety of Givlaari have demonstrated significant reductions in the frequency of porphyria attacks, as well as improvements in pain, quality of life, and biochemical markers of disease activity. Givlaari has been shown to reduce levels of aminolevulinic acid (ALA) and porphobilinogen (PBG), key intermediates in the heme biosynthesis pathway, thereby reducing the burden of acute porphyria symptoms.

IV. Initial Approval Criteria[1,]

Coverage is provided in the following conditions:

MMP members who have previously received this medication within the past 365 days are not subject to Step Therapy Requirements

- 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

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 of initiation of givosiran

*Acute Hepatic Porphyria	Urine delta-aminolevulinic acid (ALA)	Urine porphobilinogen (PBG)	Urine prophyrins	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

V. 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, acute pancreatitis, 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

VI. 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.

VII. Billing Code/Availability Information

HCPCS:

- 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

VIII. References

1. Givlaari [package insert]. Cambridge, MA; Alnylam Pharm., Inc., February 2023. Accessed February 2025.
2. Sardh E, Barbaro M. Acute Intermittent Porphyria. 2005 Sep 27 [Updated 2024 Feb 8]. In: Adam MP, Feldman J, Mirzaa GM, et al., editors. GeneReviews® [Internet]. Seattle (WA): University of Washington, Seattle; 1993-2024. Available from: https://www.ncbi.nlm.nih.gov/books/NBK1193/
3. Anderson KE. Porphyrias: An overview. Mahoney DH, ed. UpToDate. Waltham, MA: UpToDate Inc. https://www.uptodate.com/contents/porphyrias-an-

overview?search=acute%20hepatic%20porphyria&source=search_result&selectedTitle=3~91&usage_type=default&display_rank=3 (Accessed on January 02, 2017.).

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:Apr2019;Vol70;Iss. 1, Suppl;pps e81–e82
5. Wang B, Bonkovsky HL, Kim, JK, et al. AGA Clinical Practice Update on Diagnosis and Management of Acute Hepatic Prophyrias: Expert Review. Gastroenterology. Volume 164, Issue 3, Pages 484-491. https://www.gastrojournal.org/article/S0016-5085(22)01356-7/fulltext

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) and Local Coverage Determinations (LCDs) may exist and compliance with these policies is required where applicable. They can be found at: http://www.cms.gov/medicare-coverage-database/search/advanced-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): 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

Medicare Part B Administrative Contractor (MAC) Jurisdictions		
Jurisdiction	**Applicable State/US Territory**	**Contractor**
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

Policy Rationale:

Givlaari was reviewed by the Neighborhood Health Plan of Rhode Island Pharmacy & Therapeutics (P&T) Committee. Neighborhood adopted the following clinical coverage criteria to ensure that its members use Givlaari according to Food and Drug Administration (FDA) approved labeling and/or relevant clinical literature. Neighborhood worked with network prescribers and pharmacists to draft these criteria. These criteria will help ensure its members are using this drug for a medically accepted indication, while minimizing the risk for adverse effects and ensuring more cost-effective options are used first, if applicable and appropriate. For INTEGRITY (Medicare-Medicaid Plan) members, these coverage criteria will only apply in the absence of National Coverage Determination (NCD) or Local Coverage Determination (LCD) criteria. Neighborhood will give individual consideration to each request it reviews based on the information submitted by the prescriber and other information available to the plan.