Clinical Policy Title:	givosiran
Policy Number:	RxA.623
Drug(s) Applied:	Givlaari®
Original Policy Date:	05/21/2020
Last Review Date:	03/09/2021
Line of Business Policy Applies to:	All lines of business

Background

Givlaari® is an aminolevulinate synthase 1-directed small interfering RNA indicated for the treatment of adults with acute hepatic porphyria (AHP).

Dosing Information

Drug Name	Indication	Dosing Regimen	Maximum Dose
givosiran (Givlaari®)	Acute hepatic porphyria	2.5mg/kg once monthly (subcutaneous)	250mg per month (1.3ml)

Dosage Forms

- 189mg/ml in a single-dose vial

Clinical Policy

Provider must submit documentation (such as office chart notes, lab results or other clinical information) supporting that member has met all approval criteria.

I. Initial Approval Criteria

A. Acute Hepatic Porphyria (AHP) (must meet all):

1. The member has a diagnosis of AHP (including acute intermittent porphyria (AIP), hereditary coproporphyria (HCP), variegate porphyria, or aminolevulinic acid (ALA) dehydratase deficient porphyria)
2. The member is an adult (≥18 years old).
3. The member has active disease which is defined as two documented porphyria attacks within the past 6 months. These can include:
   i Hospitalization
   ii Urgent healthcare visit
   iii Intravenous hemin administration at home
4. The dose requested does not exceed 250mg/month (1.3ml).

Approval Duration

Commercial: 3 months

Medicaid: 3 months

II. Continued Therapy Approval

A. Acute Hepatic Porphyria (AHP) (must meet all):

1. Currently receiving medication that has been authorized by RxAdvance or has previously met initial approval criteria.
2. The prescriber has evaluated effectiveness of the medication.
3. The member has responded positively to therapy with Givlaari®.

Approval Duration
Commercial: 3 months
Medicaid: 3 months

III. Appendices

APPENDIX A: Abbreviation/Acronym Key
AHP: Acute Hepatic Porphyria
AIP: Acute intermittent porphyria
HCP: Hereditary coproporphyria
ALA: Aminolevulinic acid

APPENDIX B: Therapeutic Alternatives
None

APPENDIX C: Contraindications/Boxed Warnings

- Contraindication(s):
  - Severe hypersensitivity to givorisan

- Boxed Warning(s):
  - None

APPENDIX D: General Information

- The acute hepatic porphyrias are a group of four inherited disorders, each resulting from a deficiency in the activity of a specific enzyme in the heme biosynthetic pathway. These disorders present clinically with acute neurovisceral symptoms which may be sporadic or recurrent and, when severe, can be life-threatening.
- Anaphylaxis has occurred with Givlaari® treatment t (<1% of patients in clinical trials). Ensure that medical support is available to appropriately manage anaphylactic reactions when administering Givlaari®. Monitor for signs and symptoms of anaphylaxis. If anaphylaxis occurs, immediately discontinue administration of Givlaari® and institute appropriate medical treatment.
- Measure liver function tests prior to initiating treatment with Givlaari®, repeat every month during the first 6 months of treatment, and as clinically indicated thereafter. Interrupt or discontinue treatment with Givlaari® for severe or clinically significant transaminase elevations.
- Increases in serum creatinine levels and decreases in estimated glomerular filtration rate (eGFR) have been reported during treatment with Givlaari®. Monitor renal function during treatment with Givlaari® as clinically indicated.

References

1. Givlaari® Prescribing Information. Cambridge, MA; Alnylam Pharmaceutical Inc: December 2020. Available at www.givlaari.com. Accessed January 27, 2021.
2. Balwani M, Wang B, Anderson KE, et al. Acute hepatic porphyrias: Recommendations for evaluation and long-term management. Hepatology. 2017;66(4):1314-1322.

3. Wang B, Rudnick S, Cengia B, Bonkovsky HL. Acute Hepatic Porphyrias: Review and Recent Progress. Hepatol Commun. 2019;3(2):193-206.

Review/Revision History	Review/Revision Date	P&T Approval Date
Policy established.	05/07/2020	05/21/2020
Policy was reviewed: 1. Clinical Policy Title was updated. 2. Line of Business Policy Applies to was updated to all lines of business. 3. APPENDIX D: General Information was updated by adding information. 4. Reference was updated.	1/28/2021	03/09/2021