



## SmartPA Criteria Proposal

<b>Drug/Drug Class:</b>	Givlaari Clinical Edit
<b>First Implementation Date:</b>	July 30, 2020
<b>Revised Date:</b>	TBD
<b>Prepared for:</b>	MO HealthNet
<b>Prepared by:</b>	MO HealthNet/Conduent
<b>Criteria Status:</b>	<input type="checkbox"/> Existing Criteria <input type="checkbox"/> Revision of Existing Criteria <input checked="" type="checkbox"/> New Criteria

### Executive Summary

**Purpose:** Ensure appropriate utilization and control of Givlaari™ (givosiran)

**Why Issue Selected:** Givlaari™ (givosiran) was FDA approved in November 2019, for the treatment of acute hepatic porphyria (AHP) in adults. Porphyria refers to a group of at least 8 inherited metabolic disorders that arise as a result of a malfunction in the synthesis of heme, which is essential for the transport of oxygen to cells in the body. AHP is comprised of four types of porphyrias: acute intermittent porphyria, hereditary coproporphyria, variegate porphyria and ALA dehydratase-deficiency porphyria. Symptoms of AHP vary widely but typically occur as intermittent attacks, which may be life-threatening due to neurologic complications such as seizures or paralysis. Approximately 20% of patients with recurrent symptoms develop chronic and ongoing pain and other symptoms, and approximately 3-5% of patients have frequent attacks, defined as more than 4 attacks per year, for a period of many years. Long-term complications of AHP include hypertension, chronic kidney disease, and liver disease (including hepatocellular carcinoma). Givlaari is a double-stranded small interfering RNA that causes degradation of aminolevulinic acid 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 AHP.

### Program-Specific Information:

Date Range FFS 1-1-2019 to 12-31-2019			
Drug	Claims	Cost per ml (MAC)	Cost per month (MAC)
Givlaari™ 189mg/ml vial	0	\$39,000.00	\$39,000.00 (participants ≤ 75kg)
			\$78,000.00 (participants > 75 kg and ≤ 150kg)

**Type of Criteria:** ☒ Increased risk of ADE  
☒ Appropriate Indications

☐ Preferred Drug List  
☒ Clinical Edit

**Data Sources:** ☐ Only Administrative Databases

☒ Databases + Prescriber-Supplied

## Setting & Population

- Drug class for review: Givlaari™ (givosiran)
- Age range: All appropriate MO HealthNet participants aged 18 years or older

## Approval Criteria

- Participant aged 18 years or older **AND**
- Prescribed by or in consultation with a hepatologist, gastroenterologist, or other specialist in the treated disease state **AND**
- Documented diagnosis of AHP in the past 2 years **AND**
- Documentation of labs used to verify AHP diagnosis (spot or 24 hour urine delta-aminolevulinic acid (ALA), porphobilinogen (PBG), and creatinine with results 4 times ULN) **AND**
- Documentation of active disease defined as at least 1 porphyria attack within the past 6 months (defined by hospitalization, urgent healthcare visit, or intravenous hemin therapy) **AND**
- Documentation of current LFTs and serum creatinine
- Renewal Criteria:
  - Initial approval of prior authorization is 6 months
  - Renewal of prior authorization may be up to 12 months following documentation of the following:
    - Documentation of stabilized or decreased AHP attack frequency (i.e. decreased hospitalizations, urgent healthcare visits, or hemin therapy) **AND**
    - Documentation of current LFTs < 3 times the ULN (monthly during the first 6 months of therapy and then at least once annually) **AND**
    - Documentation of current serum creatinine (at least once annually)

## Denial Criteria

- Therapy will be denied if no approval criteria are met

## Required Documentation

Laboratory Results:  
MedWatch Form:

X

Progress Notes:  
Other:

X
X

## Disposition of Edit

Denial: Exception code "0682" (Clinical Edit)  
Rule Type: CE

## Default Approval Period

6 months

## References

- GIVLAARI™ (givosiran) injection, [package insert]. Cambridge, MA: Alnylam Pharmaceuticals, Inc.; November 2019.
- PANHEMATIN® (hemin for injection) [package insert]. Raleigh, NC: Xellia Pharmaceuticals USA, LLC; July 2017

*SmartPA Clinical Proposal Form*

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- National Organization for Rare Disease. Porphyria. <https://rarediseases.org/rare-diseases/porphyria/>. Accessed December 9, 2019.
- Wang, B, et al. Acute Hepatic Porphyrias: Review and Recent Progress. *Hepatology Communications*, Vol 3, Issue 2. December 20, 2018. <https://doi.org/10.1002/hep4.1297>
- FDA Approves Givlaari. <https://www.drugs.com/newdrugs/fda-approves-givlaari-givosiran-acute-hepatic-porphyria-5109.html>. Accessed December 9, 2019.
- IPD Analytics. Hematologic: Porphyria. Accessed December 9, 2019.
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- Yarra, Pradeep, Faust, Denise, et. al. "Benefits of prophylactic heme therapy in severe acute intermittent porphyria." *Molecular Genetics and Metabolic Reports*. Published online 30 January 2019. Accessed 31 January 2020.