SmartPA Criteria Proposal

Drug/Drug Class:	Givlaari Clinical Edit
First Implementation Date:	July 30, 2020
Revised Date:	July 18, 2023
Prepared for:	MO HealthNet
Prepared by:	MO HealthNet/Conduent
Criteria Status:	☐Existing Criteria ☒Revision of Existing Criteria ☐New Criteria

Executive Summary

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

Why Issue Selected: Givlaari® (givosiran) was approved by the FDA 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 because of a malfunction in the synthesis of heme, which is essential for the transport of oxygen to cells in the body. There are two general categories of porphyria – erythropoietic porphyria, where pathway intermediates originate in the bone marrow and are transported through the bloodstream, and hepatic porphyria, where they accumulate in the liver. 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 usually involving the nervous system, which may be life-threatening due to 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 aminolevulinate 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.

Due to the high cost and specific approved indication, MO HealthNet will impose clinical criteria to ensure appropriate utilization of Givlaari.

Program-Specific Information:

Date Range FFS 1-1-2022 to 12-31-2022			
Drug	**Claims**	**Spend**	**Avg Spend Per Claim**
GIVLAARI 189 MG/ML VIAL	24	$1,400,266.86	$58,344.45

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 acute hepatic porphyria (AHP) **AND**
- Documentation of all of the following **random (spot) urine tests** ~~**labs**~~ used to verify AHP diagnosis:
    - **Porphobilinogen (PBG)**
    - **Delta-aminolevulinic acid (ALA)**
    - **Porphyrins AND**

  ~~**(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, serum creatinine, and blood homocysteine levels

- 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) **AND**
        - Documentation of current blood homocysteine levels (at least once annually)

Denial Criteria

- Therapy will be denied if all approval criteria are not met

Required Documentation

Laboratory Results:	X	Progress Notes:	X
MedWatch Form:		Other:	X

Disposition of Edit

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

Default Approval Period

6 months

References

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- 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
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- Yarra, Pradeep & Faust, Denise & Bennett, Mary & Rudnick, Sean & Bonkovsky, Herbert. (2019). Benefits of prophylactic heme therapy in severe acute intermittent porphyria. Molecular genetics and metabolism reports. 19. 100450. 10.1016/j.ymgmr.2019.01.002.