Clinical Criteria

Subject:	Givlaari (givosiran)		
Document #:	ING-CC-0154	**Publish Date:**	~~01/20/2020~~01/25/2021
Status:	~~New~~Revised	**Last Review Date:**	~~12/09/2019~~12/14/2020

Table of Contents

Overview

This document addresses the use of Givlaari (givosiran), aminolevulinate synthase 1 (ALAS1)-directed small interfering RNA indicated for the treatment of adults with acute hepatic porphyria (AHP).

Porphyria is a group of eight genetic disorders that cause defective production of heme, the oxygen-carrying component of red blood cells. Acute hepatic porphyria is a form of porphyria with 4 subtypes: acute intermittent porphyria (AIP), hereditary coproporphyria (HCP), variegate porphyria (VP), and ALA dehydratase-deficiency porphyria (ADP). In AHP, defective enzymes in the heme biosynthesis pathway allow aminolevulinic acid (ALA) and other neurotoxic heme intermediates to accumulate. This accumulation can trigger a porphyria attack.

AHP occurs primarily in women and has an onset in young adulthood. Porphyria attacks are characterized by severe abdominal and neuropathic pain, many nonspecific symptoms, hypertension, hyponatremia, and red urine. Attacks can last for days and can be life-threatening. It can be triggered or exacerbated by factors that increase ALAS1 activity and ALA accumulation. This includes inadequate carbohydrate intake, stress, pain, female hormonal changes, smoking, excessive alcohol use, and drugs or substances that induce ALAS1 activity. Long-term complications of AHP include liver disease, hepatocellular carcinoma, chronic kidney disease, and hypertension.

Givlaari is the first FDA-approved treatment that prevents attacks of acute hepatic porphyria. It works by muting ALAS1 via RNA interference through monthly subcutaneous injections administered by a healthcare professional. Givlaari is not approved for other forms of porphyria, such as cutaneous forms of porphyria, where standard treatment typically includes regularly scheduled phlebotomies. Prior to Givlaari, the only approved treatment for recurrent porphyria attacks from AHP was the administration of Panhematin (hemin), an intravenous infusion, along with carbohydrate loading and supportive care. Although it has been known to be used off-label for preventative therapy, Panhematin is only FDA-approved for management of acute attacks.

Clinical Criteria

When a drug is being reviewed for coverage under a member's medical benefit plan or is otherwise subject to clinical review (including prior authorization), the following criteria will be used to determine whether the drug meets any applicable medical necessity requirements for the intended/prescribed purpose.

Givlaari (givosiran)

Requests for initiation of Givlaari (givosiran) may be approved if the following criteria are met:

I. Individual is 18 years of age or older; **AND**
II. Individual has a diagnosis of acute hepatic porphyria, **and** confirmation of one of the following subtypes (APF 2010-2019):
   A. Acute intermittent porphyria (AIP); **OR**
   B. Hereditary coproporphyria (HCP), **OR**
   C. Variegate porphyria (VP); **OR**
   D. ALA dehydratase-deficiency porphyria (ADP); **AND**

III. Individual has documentation of elevated urinary or plasma porphobilinogen (PBG) or delta-aminolevulinic acid (ALA) within the past year (~~NCT03338816~~Balwani 2019); **AND**

IV. Individual meets one of the following criteria:

A. Individual has active symptomatic disease, with at least two documented porphyria attacks within the last six months (~~NCT03338816~~Balwani 2019); **OR**

~~IV.~~ B. Individual is currently on prophylactic hemin treatment due to history of severe or frequent porphyria attacks.

Requests for continuation of Givlaari (givosiran) may be approved if the following criteria are met:

I. Individual has experienced a clinical response to therapy (for example, a reduction in the number of porphyria attacks, or a reduction in hemin requirements for acute attacks); **AND**

II. Individual does not have severe or clinically significant transaminase elevations, defined as alanine aminotransferase (ALT) greater than 5 times the upper limit of normal (Balwani 2019).

Givlaari (givosiran) may not be approved for the following (NCT03338816):

I. Concurrent use of prophylactic hemin treatment with Givlaari (givosiran); **OR**

~~I.~~II. Liver transplantation is anticipated; **OR**

~~II.~~III. Individual has a history of recurrent pancreatitis; **OR**

~~III.~~IV. Individual is requesting for other forms of porphyria, such as cutaneous porphyrias (for example, porphyria cutanea tarda [PCT]); **OR**

~~IV.~~V. When the above criteria are not met and for all other indications.

Approval Duration:

Initial Requests: 6 months
Maintenance Requests: 12 months

Formatted: Indent: Left: 0.63", Don't add space between paragraphs of the same style, Tab stops: 1", Left

Formatted: Font: (Default) Arial, 9 pt

Formatted: Font: (Default) Arial, 9 pt

Formatted: Font: Bold

Formatted: Font: (Default) Arial, 9 pt

Formatted: Space After: 0 pt, Don't add space between paragraphs of the same style, Line spacing: single

Formatted: Font: Bold

Coding

The following codes for treatments and procedures applicable to this document are included below for informational purposes. Inclusion or exclusion of a procedure, diagnosis or device code(s) does not constitute or imply member coverage or provider reimbursement policy. Please refer to the member's contract benefits in effect at the time of service to determine coverage or non-coverage of these services as it applies to an individual member.

HCPCS

J0223	Injection, givosiran, 0.5 mg (Effective 7/1/2020)

ICD-10 Diagnosis

E80.20-E80.29	Hereditary porphyria
Z29.9	Encounter for prophylactic measures, unspecified

Document History

Revised: 12/14/2020
Document History:

- 12/14/2020 – Annual Review: Update criteria to allow for use in those who require prophylactic use of hemin. Update continuation criteria to add another example for clinical response, and update non-approvable criteria to restrict use of prophylactic hemin together with Givlaari. Update references. Coding Reviewed: Added ICD-10-CM Z29.9.
- 12/09/2019 – Annual Review: Add new clinical criteria document for Givlaari (givosiran). Coding Reviewed: Added J3490 J3590, C9399, C9056 HCPCS. Added E80.20-E80.29 ICD-10 dx codes. 3/31/2020 Deleted C9399, 4/1/2020 C9056. Coding Review 5/15/2020: Added HCPCS J0223 (Effective 7/1/2020). Delete 6/30/2020- J3490, J3590, C9056

References

1. Balwani M, Gouya L, Rees DC, et al. ENVISION, a Phase 3 Study to Evaluate the Efficacy and Safety of Givosiran, an Investigational RNAi Therapeutic Targeting Aminolevulinic Acid Synthase 1, in Acute Hepatic Porphyria Patients. April 13, 2019. European Association for the Study of the Liver (EASL) 54th Annual International Liver Congress. Vienna, Austria.

2. Clinical Pharmacology [database online]. Tampa, FL: Gold Standard, Inc.: 2020. URL: http://www.clinicalpharmacology.com. Updated periodically.
3. DailyMed. Package inserts. U.S. National Library of Medicine, National Institutes of Health website. http://dailymed.nlm.nih.gov/dailymed/about.cfm. Accessed: November 13, 2020.
4. DrugPoints® System [electronic version]. Truven Health Analytics, Greenwood Village, CO. Updated periodically.
5. Lexi-Comp ONLINE™ with AHFS™, Hudson, Ohio: Lexi-Comp, Inc.; 2020; Updated periodically.
6. NCT03338816. ClinicalTrials.gov. U.S. National Library of Medicine. Available at https://clinicaltrials.gov/ct2/show/NCT03338816?term=nct03338816&draw=1&rank=1.
7. Porphyria. American Porphyria Foundation (APF). 2010-2020. Available at https://www.porphyriafoundation.org/for-healthcare-professionals/porphyria/. Accessed on November 13, 2020.
8. The Porphyrias Consortium. Rare Diseases Clinical Research Network. National Institutes of Health. Available at https://www.rarediseasesnetwork.org/cms/porphyrias/Healthcare-Professionals/Disorder-Definitions. Accessed on November 13, 2020.

Federal and state laws or requirements, contract language, and Plan utilization management programs or polices may take precedence over the application of this clinical criteria.