

## Medical Policy:

### Givlaari® (givosiran) injection for subcutaneous use

POLICY NUMBER	LAST REVIEW	ORIGIN DATE
MG.MM.PH.203	February 29, 2024	

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The treating physician or primary care provider must submit to EmblemHealth, or ConnectiCare, as applicable (hereinafter jointly referred to as “EmblemHealth”), the clinical evidence that the member meets the criteria for the treatment or surgical procedure. Without this documentation and information, EmblemHealth will not be able to properly review the request preauthorization or post-payment review. The clinical review criteria expressed below reflects how EmblemHealth determines whether certain services or supplies are medically necessary. This clinical policy is not intended to pre-empt the judgment of the reviewing medical director or dictate to health care providers how to practice medicine. Health care providers are expected to exercise their medical judgment in rendering appropriate care. Health care providers are expected to exercise their medical judgment in rendering appropriate care.

EmblemHealth established the clinical review criteria based upon a review of currently available clinical information (including clinical outcome studies in the peer reviewed published medical literature, regulatory status of the technology, evidence-based guidelines of public health and health research agencies, evidence-based guidelines and positions of leading national health professional organizations, views of physicians practicing in relevant clinical areas, and other relevant factors). EmblemHealth expressly reserves the right to revise these conclusions as clinical information changes and welcomes further relevant information. Each benefit program defines which services are covered. The conclusion that a particular service or supply is medically necessary does not constitute a representation or warranty that this service or supply is covered and/or paid for by EmblemHealth, as some programs exclude coverage for services or supplies that EmblemHealth considers medically necessary.

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## Definitions

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.

GIVLAARI is indicated for the treatment of adults with acute hepatic porphyria (AHP).

## Length of Authorization

Coverage will be provided for 12 months and may be renewed.

## Dosing Limits [Medical Benefit]

Max Units (per dose and over time) 2.5 mg/kg administered by subcutaneous injection once monthly by a healthcare professional only.

**Max Units (per dose and over time) [HCPS Unit]:**

576 billable units every month

**Guideline**

**I. Initial Approval Criteria**

**1. Acute Hepatic Porphyria**

- A. Member has been diagnosed with **acute hepatic porphyria** (including acute intermittent porphyria, hereditary coproporphyria, variegate porphyria, ALA dehydratase deficient porphyria); **AND**
- B. Member is at least 18 years of age; **AND**
- C. Medication is prescribed by or in consultation with, a porphyria specialist (e.g. hepatologist, gastroenterologist, etc.); **AND**
- D. 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**
- E. Member has had elevated urinary or plasma PBG (porphobilinogen) or ALA (aminolevulinic acid) values within the past year; **AND**
- F. Patient has a mutation in an affected gene as identified on molecular genetic testing; **AND**
  - i. Active disease has been documented with at least 2 porphyria attacks requiring hospitalization, urgent healthcare visit, or intravenous hemin administration at home, within the past 6 months; **OR**
  - ii. Patient has a history of 1 severe attack with CNS, ANS or PNS involvement within the past 6 months(e.g. hallucinations, seizure, paralysis, respiratory failure, etc.); **AND**
- G. Individuals currently receiving prophylactic intravenous hemin therapy will discontinue hemin within 3 to 6 months of initiation with givosiran

**II. Renewal Criteria**

- 1. Individual continues to meet initial approval criteria; **AND**
- 2. Absence of unacceptable toxicity from the drug (e.g. anaphylactic reactions, severe hepatic toxicity, severe renal toxicity, etc.) ; **AND**
- 3. 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; **AND**
- 4. Patient has a reduction/normalization of biochemical markers (i.e., ALA, PBG) compared to baseline; **AND**
- 5. Patient will not use in combination with prophylactic intravenous hemin therapy

**Limitations/Exclusions**

- 1. Member has not or is not anticipating a liver transplant

**Applicable Procedure Codes**

Code	Description
J0223	Givlaari (givosiran sodium), 189mg/mL soln

**Applicable NDCs**

Code	Description
71336-1001-01	Givlaari (givosiran sodium), 189mg/ml single use vial

## ICD-10 Diagnoses

Code	Description
C82.00	Follicular lymphoma grade I unspecified site
C82.01	Follicular lymphoma grade I lymph nodes of head, face, and neck
C82.02	Follicular lymphoma grade I intrathoracic lymph nodes
C82.03	Follicular lymphoma grade I intra-abdominal lymph nodes
C82.04	Follicular lymphoma grade I lymph nodes of axilla and upper limb
C82.05	Follicular lymphoma grade I lymph nodes of inguinal region and lower limb
C82.06	Follicular lymphoma grade I intrapelvic lymph nodes
C82.07	Follicular lymphoma grade I spleen
C82.08	Follicular lymphoma grade I lymph nodes of multiple sites
C82.09	Follicular lymphoma grade I extranodal and solid organ sites
C82.10	Follicular lymphoma grade II unspecified site
C82.11	Follicular lymphoma grade II lymph nodes of head, face, and neck
C82.12	Follicular lymphoma grade II intrathoracic lymph nodes
C82.13	Follicular lymphoma grade II intra-abdominal lymph nodes
C82.14	Follicular lymphoma grade II lymph nodes of axilla and upper limb
C82.15	Follicular lymphoma grade II lymph nodes of inguinal region and lower limb
C82.16	Follicular lymphoma grade II intrapelvic lymph nodes
C82.17	Follicular lymphoma grade II spleen
C82.18	Follicular lymphoma grade II lymph nodes of multiple sites
C82.19	Follicular lymphoma grade II extranodal and solid organ sites
C82.20	Follicular lymphoma grade III unspecified site
C82.21	Follicular lymphoma grade III lymph nodes of head, face, and neck
C82.22	Follicular lymphoma grade III intrathoracic lymph nodes
C82.23	Follicular lymphoma grade III intra-abdominal lymph nodes
C82.24	Follicular lymphoma grade III lymph nodes of axilla and upper limb
C82.25	Follicular lymphoma grade III lymph nodes of inguinal region and lower limb
C82.26	Follicular lymphoma grade III intrapelvic lymph nodes
C82.27	Follicular lymphoma grade III spleen
C82.28	Follicular lymphoma grade III lymph nodes of multiple sites
C82.29	Follicular lymphoma grade III extranodal and solid organ sites
C82.30	Follicular lymphoma grade IIIa unspecified site
C82.31	Follicular lymphoma grade IIIa lymph nodes of head, face, and neck
C82.32	Follicular lymphoma grade IIIa intrathoracic lymph nodes
C82.33	Follicular lymphoma grade IIIa intra-abdominal lymph nodes
C82.34	Follicular lymphoma grade IIIa lymph nodes of axilla and upper limb
C82.35	Follicular lymphoma grade IIIa lymph nodes of inguinal region and lower limb
C82.36	Follicular lymphoma grade IIIa intrapelvic lymph nodes
C82.37	Follicular lymphoma grade IIIa spleen
C82.38	Follicular lymphoma grade IIIa lymph nodes of multiple sites
C82.39	Follicular lymphoma grade IIIa extranodal and solid organ sites
C82.40	Follicular lymphoma grade IIIb unspecified site
C82.41	Follicular lymphoma grade IIIb lymph nodes of head, face, and neck
C82.42	Follicular lymphoma grade IIIb intrathoracic lymph nodes

C82.43	Follicular lymphoma grade IIIb intra-abdominal lymph nodes
C82.44	Follicular lymphoma grade IIIb lymph nodes of axilla and upper limb
C82.45	Follicular lymphoma grade IIIb lymph nodes of inguinal region and lower limb
C82.46	Follicular lymphoma grade IIIb intrapelvic lymph nodes
C82.47	Follicular lymphoma grade IIIb spleen
C82.48	Follicular lymphoma grade IIIb lymph nodes of multiple sites
C82.49	Follicular lymphoma grade IIIb extranodal and solid organ sites
C82.50	Diffuse follicle center lymphoma unspecified site
C82.51	Diffuse follicle center lymphoma lymph nodes of head, face, and neck
C82.52	Diffuse follicle center lymphoma intrathoracic lymph nodes
C82.53	Diffuse follicle center lymphoma intra-abdominal lymph nodes
C82.54	Diffuse follicle center lymphoma lymph nodes of axilla and upper limb
C82.55	Diffuse follicle center lymphoma lymph nodes of inguinal region and lower limb
C82.56	Diffuse follicle center lymphoma intrapelvic lymph nodes
C82.57	Diffuse follicle center lymphoma spleen
C82.58	Diffuse follicle center lymphoma lymph nodes of multiple sites
C82.59	Diffuse follicle center lymphoma extranodal and solid organ sites
C82.60	Cutaneous follicle center lymphoma unspecified site
C82.61	Cutaneous follicle center lymphoma lymph nodes of head, face, and neck
C82.62	Cutaneous follicle center lymphoma intrathoracic lymph nodes
C82.63	Cutaneous follicle center lymphoma intra-abdominal lymph nodes
C82.64	Cutaneous follicle center lymphoma lymph nodes of axilla and upper limb
C82.65	Cutaneous follicle center lymphoma lymph nodes of inguinal region and lower limb
C82.66	Cutaneous follicle center lymphoma intrapelvic lymph nodes
C82.67	Cutaneous follicle center lymphoma spleen
C82.68	Cutaneous follicle center lymphoma lymph nodes of multiple sites
C82.69	Cutaneous follicle center lymphoma extranodal and solid organ sites
C82.80	Other types of follicular lymphoma unspecified site
C82.81	Other types of follicular lymphoma lymph nodes of head, face, and neck
C82.82	Other types of follicular lymphoma intrathoracic lymph nodes
C82.83	Other types of follicular lymphoma intra-abdominal lymph nodes
C82.84	Other types of follicular lymphoma lymph nodes of axilla and upper limb
C82.85	Other types of follicular lymphoma lymph nodes of inguinal region and lower limb
C82.86	Other types of follicular lymphoma intrapelvic lymph nodes
C82.87	Other types of follicular lymphoma spleen lymph nodes of multiple sites
C82.88	Other types of follicular lymphoma lymph nodes of multiple sites
C82.89	Other types of follicular lymphoma extranodal and solid organ sites
C82.90	Follicular lymphoma, unspecified site
C82.91	Follicular lymphoma, unspecified lymph nodes of head, face, and neck
C82.92	Follicular lymphoma, unspecified intrathoracic lymph nodes
C82.93	Follicular lymphoma, unspecified intra-abdominal lymph nodes
C82.94	Follicular lymphoma, unspecified lymph nodes of axilla and upper limb
C82.95	Follicular lymphoma, unspecified lymph nodes of inguinal region and lower limb
C82.96	Follicular lymphoma, unspecified intrapelvic lymph nodes
C82.97	Follicular lymphoma, unspecified spleen
C82.98	Follicular lymphoma, unspecified lymph nodes of multiple sites

C82.99	Follicular lymphoma, unspecified extranodal and solid organ sites
C83.00	Small cell B-cell lymphoma unspecified site
C83.01	Small cell B-cell lymphoma lymph nodes of head, face, and neck
C83.02	Small cell B-cell lymphoma intrathoracic lymph nodes
C83.03	Small cell B-cell lymphoma intra-abdominal lymph nodes
C83.04	Small cell B-cell lymphoma lymph nodes of axilla and upper limb
C83.05	Small cell B-cell lymphoma lymph nodes of inguinal region and lower limb
C83.06	Small cell B-cell lymphoma intrapelvic lymph nodes
C83.07	Small cell B-cell lymphoma spleen
C83.08	Small cell B-cell lymphoma lymph nodes of multiple sites
C83.09	Small cell B-cell lymphoma extranodal and solid organ sites
C83.80	Other non-follicular lymphoma unspecified site
C83.81	Other non-follicular lymphoma lymph nodes of head, face, and neck
C83.82	Other non-follicular lymphoma intrathoracic lymph nodes
C83.83	Other non-follicular lymphoma intra-abdominal lymph nodes
C83.84	Other non-follicular lymphoma lymph nodes of axilla and upper limb
C83.85	Other non-follicular lymphoma lymph nodes of inguinal region and lower limb
C83.86	Other non-follicular lymphoma intrapelvic lymph nodes
C83.87	Other non-follicular lymphoma spleen
C83.88	Other non-follicular lymphoma lymph nodes of multiple sites
C83.89	Other non-follicular lymphoma extranodal and solid organ sites
C85.80	Other specified types of non-Hodgkin lymphoma, unspecified site
C85.81	Other specified types of non-Hodgkin lymphoma, lymph nodes of head, face, and neck
C85.82	Other specified types of non-Hodgkin lymphoma, intrathoracic lymph nodes
C85.83	Other specified types of non-Hodgkin lymphoma, intra-abdominal lymph nodes
C85.84	Other specified types of non-Hodgkin lymphoma, lymph nodes of axilla and upper limb
C85.85	Other specified types of non-Hodgkin lymphoma, lymph nodes of inguinal region and lower limb
C85.86	Other specified types of non-Hodgkin lymphoma, intrapelvic lymph nodes
C85.87	Other specified types of non-Hodgkin lymphoma, spleen
C85.88	Other specified types of non-Hodgkin lymphoma, lymph nodes of multiple sites
C85.89	Other specified types of non-Hodgkin lymphoma, extranodal and solid organ sites
C88.4	Extranodal marginal zone B-cell lymphoma of mucosa-associated lymphoid tissue [MALT-lymphoma]
C91.10	Chronic lymphocytic leukemia of B-cell type not having achieved remission
C91.12	Chronic lymphocytic leukemia of B-cell type in relapse

## Revision History

Company(ies)	DATE	REVISION
EmblemHealth & ConnectiCare	2/29/2024	Annual Review: Updated dosing limits Initial Criteria: Acute Hepatic Porphyria: Added: Patient will avoid known triggers of porphyria attacks (i.e., alcohol, smoking, exogenous hormones, hypocaloric diet/fasting, certain medications such as barbiturates, hydantoin, sulfa-antibiotics, anti-epileptics, etc.); AND Patient has a mutation in an affected gene as identified on molecular genetic testing; AND” Removed: “Clinical presentation of disease has been documented (e.g. abdominal pain, constipation, nausea/vomiting, symptoms of ileus, tachycardia, hypertension, dark urine, skin photosensitivity or other

		cutaneous symptoms, disease-specific common laboratory abnormalities [hyponatremia, hypomagnesemia], seizures, CKD, etc.); AND Patient is currently receiving off-label hemin treatment for attack prophylaxis; OR” Updated timeframe from the past year to the past 6 months in the following statement: :Patient has a history of 1 severe attack with CNS, ANS or PNS involvement within the 6 months(e.g. hallucinations, seizure, paralysis, respiratory failure, etc.)” Renewal Criteria: Added: 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
EmblemHealth & ConnectiCare	6/5/2023	Annual Revision: 1. Updated exclusion criteria to include “or is not anticipating” a liver transplant 2. Updated the definition of patients with active, symptomatic disease by adding additional criteria: “Patient is currently receiving off-label hemin treatment for attack prophylaxis; <b>OR</b> Patient has a history of 1 severe attack with CNS, ANS or PNS involvement within the past year (e.g. hallucinations, seizure, paralysis, respiratory failure, etc.)”
EmblemHealth & ConnectiCare	6/17/2022	Transferred policy to new template
EmblemHealth & ConnectiCare	7/15/2019	Annual review

## References

1. Gazyva prescribing information. Genentech, Inc. South San Francisco, CA 2016.
2. Clinical Pharmacology Elsevier Gold Standard. 2017.
3. Micromedex® Healthcare Series: Thomson Micromedex, Greenwood Village, Co. 2017.
4. National Comprehensive Cancer Network. Cancer Guidelines and Drugs and Biologics Compendium. 2017.
5. AHFS Drug Information. American Society of Health-Systems Pharmacist or Wolters Kluwer Lexi-Drugs. Bethesda, MD. 2017.