Utilization Review Policy 240

POLICY: Panhematin Utilization Management Medical Policy

- Panhematin® (hemin injection for intravenous infusion – Recordati Rare Diseases)

EFFECTIVE DATE: 3/15/2021
LAST REVISION DATE: 09/16/2024

COVERAGE CRITERIA FOR: All UCare Plans

OVERVIEW

Panhematin, an enzyme inhibitor derived from processed red blood cells, is indicated for the **amelioration of recurrent attacks of acute intermittent porphyria** (AIP) temporally related to the menstrual cycle in susceptible women, after initial carbohydrate therapy is known or suspected to be inadequate.[1]

Safety and effectiveness in patients < 16 years of age have not been established.[1]

Disease Overview

Porphyria is a group of metabolic disorders caused by abnormalities in the chemical steps that lead to the production of heme.[2] Heme is necessary for the transport of oxygen to cells in the body. If synthesis of heme is hindered, an accumulation of porphyrins or porphyrin precursors (intermediate chemicals) accumulates in the cells, resulting in oxygen depletion. Acute hepatic porphyrias (AHPs) are a subgroup of porphyrias in which the enzyme deficiency occurs within the liver.[3] AHPs include AIP, variegate porphyria (VP), 5-aminolevulinic acid dehydratase deficiency porphyria (ALAD), and hereditary coproporphyria (HCP) and are characterized by acute neurovisceral symptoms with or without cutaneous manifestations.[3,4] Symptoms and treatments for AIP, VP, ALAD, and HCP are similar; however, VP and HCP patients often develop photosensitivity. Signs and symptoms of AHP usually occur intermittently and include abdominal pain, constipation, muscle weakness, pain in the arms and legs, insomnia, emotional complications, rapid pulse, and high blood pressure, along with elevated urinary aminolevulinic acid and porphobilinogen. Hospitalization is often required for acute attacks. Although most symptomatic patients with AHP have complete resolution of their symptoms between attacks, those with numerous recurrences may develop chronic pain. Due to the high prevalence of chronic kidney disease, serum creatinine and estimated glomerular filtration rate should be monitored annually for all symptomatic patients.

Dosing Information

The recommended dose of Panhematin is 1 to 4 mg/kg/day administered by intravenous infusion for 3 to 14 days based on the clinical signs.[1] The standard dose in clinical practice is 3 to 4 mg/kg/day. Do not exceed 6 mg/kg in any 24 hour period.

Guidelines

The Porphyrias Consortium of the National Institutes of Health's Rare Diseases Clinical Research Network has developed recommendations for evaluation and long-term management of AHPs (2017).[5] Initial assessments should include diagnostic confirmation by biochemical testing, subsequent genetic testing to determine the specific AHP, and a complete medical history and physical examination. Preventative measures should be taken to prevent attacks. Hemin therapy (e.g., Panhematin) is recommended for preventative management in AHP and treatment during acute attacks. Patients with ≥ four attacks per year are candidates for either prophylactic or "on demand" infusions. The need for ongoing prophylaxis should be assessed every 6 to 12 months. Repeated long-term treatment with hemin therapy can lead to iron overload and contribute to hepatic damage and fibrosis. Carbohydrate loading (glucose tablets or dextrose solutions) has been used in early stages of an acute attack, but there are no clear data showing a benefit. Women with AHP can develop cyclic attacks correlated with the menstrual cycle. Options to prevent these attacks include recognizing and removing exacerbating factors, a gonadotropin releasing-hormone analog, switching to a low dose hormonal contraceptive, or prophylactic hemin therapy infusions.

Safety
Panhematin is derived from human blood; therefore, there is a potential risk of the transmission of infectious agents (e.g., viruses) that may cause disease.[1] Because increased levels of iron and serum ferritin have been reported in post-marketing experience with Panhematin, providers should monitor iron and serum ferritin in patients receiving multiple doses.

POLICY STATEMENT

Prior Authorization is recommended for medical benefit coverage of Panhematin. Approval is recommended for those who meet the **Criteria** and **Dosing** for the listed indications. Extended approvals are allowed if the patient continues to meet the Criteria and Dosing. Requests for doses outside of the established dosing documented in this policy will be considered on a case-by-case basis by a clinician (i.e., Medical Director or Pharmacist). All approvals are provided for the duration noted below. Because of the specialized skills required for evaluation and diagnosis of patients treated with Panhematin as well as the monitoring required for adverse events and long-term efficacy, approval requires Panhematin to be prescribed by or in consultation with a physician who specializes in the condition being treated.

Automation: None.

RECOMMENDED AUTHORIZATION CRITERIA

Coverage of Panhematin is recommended in those who meet one of the following criteria:

FDA-Approved Indication

1. **Acute Intermittent Porphyria.** Approve for 1 year if the patient meets ALL of the following (A, B, C, and D):
   - **A)** Patient is ≥ 16 years of age; AND
   - **B)** Diagnosis of acute intermittent porphyria was confirmed by both of the following (i and ii):

i. Patient demonstrated clinical features associated with acute intermittent porphyria; AND
Note: Examples of clinical features associated with acute intermittent porphyria include neurovisceral symptoms, blistering lesions, hepatic involvement, peripheral neuropathy, abdominal pain, constipation, muscle weakness, pain in the arms and legs.

ii. Patient meets one of the following (a or b):

a) Elevated urinary aminolevulinic acid (ALA) greater than the upper limit of normal; OR

b) Elevated urinary porphobilinogen (PBG) greater than the upper limit of normal; AND

C) Acute intermittent porphyria is related to the menstrual cycle; AND

D) The medication is prescribed by or in consultation with a gastroenterologist, hepatologist, or a physician who specializes in acute intermittent porphyria.

Dosing. Approve up to 6 mg/kg administered by intravenous infusion once daily given no more frequently than 14 days per 30 days.

Other Uses with Supportive Evidence

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2. Acute Hepatic Porphyria. Approve for 1 year if the patient meets all of the following (A, B, and C):

A) Patient is ≥ 16 years of age; AND

B) Diagnosis of acute hepatic porphyria was confirmed by both of the following (i and ii):

i. Patient demonstrated clinical features associated with acute hepatic porphyria; AND
Note: Examples of clinical features associated with acute intermittent porphyria include neurovisceral symptoms, blistering lesions, hepatic involvement, peripheral neuropathy, abdominal pain, constipation, muscle weakness, pain in the arms and legs.

ii. Patient meets one of the following (a or b):

a) Elevated urinary aminolevulinic acid (ALA) greater than the upper limit of normal; OR

b) Elevated urinary porphobilinogen (PBG) greater than the upper limit of normal; AND

C) The medication is prescribed by or in consultation with a gastroenterologist, hepatologist, or a physician who specializes in acute hepatic porphyria.

Dosing. Approve up to 6 mg/kg given by intravenous infusion once daily no more frequently than 14 days per 30 days.

CONDITIONS NOT RECOMMENDED FOR APPROVAL

Coverage of Panhematin is not recommended in the following situations:

1. Coverage is not recommended for circumstances not listed in the Recommended Authorization Criteria. Criteria will be updated as new published data are available.

REFERENCES

1. Panhematin® intravenous infusion [prescribing information]. Lebanon, NJ: Recordati Rare Diseases; May 2020.
2. Porphyria. U.S. National Library of Medicine; National Institutes of Health; Department of Health and Human Services. Available at: https://ghr.nlm.nih.gov/condition/porphyria. Accessed on October 10, 2023.
3. Wang B, Rudnick S, Cengia B, et al. Acute hepatic porphyrias: review and recent progress. *Hepatol Commun.* 2018;3(2):193-206.
4. Bissell DM, Wang B. Acute hepatic porphyria. *J Clin Transl Hepat*. 2015;3(1):17-26.
5. Balwani M, Wang B, Anderson K, et al. Acute hepatic porphyrias: recommendations for evaluation and long term management. *Hepatology*. 2017;66(4):1314-1322.

HISTORY

Type of Revision	Summary of Changes	Review Date
Early Annual Revision	No criteria changes	10/19/2022
Annual Revision	No criteria changes.	10/18/2023
UCare P&T Review	Policy reviewed and approved by UCare P&T committee. Annual review process	09/16/2024