Clinical Policy: Hemin (Panhematin)

Reference Number: CP.PHAR.181
Effective Date: 02.01.16
Last Review Date: 02.24
Line of Business: Commercial, HIM, Medicaid

Coding Implications
Revision Log

See Important Reminder at the end of this policy for important regulatory and legal information.

Description

Hemin for injection (Panhematin®) is an enzyme inhibitor derived from processed red blood cells.

FDA Approved Indication(s)

Panhematin is indicated for 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.

Limitation(s) of use:

- Before administering Panhematin, consider an appropriate period of carbohydrate loading (i.e., 400 g glucose/day for 1 to 2 days).
- Attacks of porphyria may progress to a point where irreversible neuronal damage has occurred. Panhematin therapy is intended to prevent an attack from reaching the critical stage of neuronal degeneration. Panhematin is not effective in repairing neuronal damage.

Policy/Criteria

Provider must submit documentation (such as office chart notes, lab results or other clinical information) supporting that member has met all approval criteria.

It is the policy of health plans affiliated with Centene Corporation® that Panhematin is **medically necessary** when the following criteria are met:

I. Initial Approval Criteria

A. Acute Porphyria (must meet all)**:**

1. Diagnosis of acute porphyria (i.e., AIP, variegate porphyria [VP], or hereditary coproporphyria [HCP]) confirmed by both of the following (a and b):
   a. Presence of clinical symptoms (e.g., abdominal pain, pain in chest, legs or back, peripheral neuropathy, hyponatremia, tachycardia, sweating, tremor, dysuria, incontinence, constipation, nausea, vomiting);
   b. History of at least a four-fold increase of 5-aminolevulinic acid (ALA) or porphobilinogen (PBG) using a random urine sample within the past year (*see Appendix D*);
2. Age ≥ 16 years;
3. Documentation of member's current body weight (in kg);
4. Dose does not exceed 6 mg/kg in any 24-hour period.

Approval duration: 14 days

B. Other diagnoses/indications (must meet 1 or 2)**:**

1. If this drug has recently (within the last 6 months) undergone a label change (e.g., newly approved indication, age expansion, new dosing regimen) that is not yet reflected in this policy, refer to one of the following policies (a or b):
   a. For drugs on the formulary (commercial, health insurance marketplace) or PDL (Medicaid), the no coverage criteria policy for the relevant line of business: CP.CPA.190 for commercial, HIM.PA.33 for health insurance marketplace, and CP.PMN.255 for Medicaid; or
   b. For drugs NOT on the formulary (commercial, health insurance marketplace) or PDL (Medicaid), the non-formulary policy for the relevant line of business: CP.CPA.190 for commercial, HIM.PA.103 for health insurance marketplace, and CP.PMN.16 for Medicaid; or
2. If the requested use (e.g., diagnosis, age, dosing regimen) is NOT specifically listed under section III (Diagnoses/Indications for which coverage is NOT authorized) AND criterion 1 above does not apply, refer to the off-label use policy for the relevant line of business: CP.CPA.09 for commercial, HIM.PA.154 for health insurance marketplace, and CP.PMN.53 for Medicaid.

II. Continued Therapy

A. Acute Porphyria (must meet all)**:**

1. Member meets one of the following (a or b):
   a. Currently receiving medication via Centene benefit or member has previously met initial approval criteria;
   b. Member is currently receiving medication and is enrolled in a state and product with continuity of care regulations (*refer to state specific addendums for CC.PHARM.03A and CC.PHARM.03B);*
2. Member is responding positively to therapy;
3. Documentation of member's current body weight (in kg);
4. If request is for a dose increase, new dose does not exceed 6 mg/kg in any 24-hour period.

Approval duration: Up to 14 days

B. Other diagnoses/indications (must meet 1 or 2)**:**

1. If this drug has recently (within the last 6 months) undergone a label change (e.g., newly approved indication, age expansion, new dosing regimen) that is not yet reflected in this policy, refer to one of the following policies (a or b):
   a. For drugs on the formulary (commercial, health insurance marketplace) or PDL (Medicaid), the no coverage criteria policy for the relevant line of business: CP.CPA.190 for commercial, HIM.PA.33 for health insurance marketplace, and CP.PMN.255 for Medicaid; or
   b. For drugs NOT on the formulary (commercial, health insurance marketplace) or PDL (Medicaid), the non-formulary policy for the relevant line of business: CP.CPA.190 for commercial, HIM.PA.103 for health insurance marketplace, and CP.PMN.16 for Medicaid; or

2. If the requested use (e.g., diagnosis, age, dosing regimen) is NOT specifically listed under section III (Diagnoses/Indications for which coverage is NOT authorized) AND criterion 1 above does not apply, refer to the off-label use policy for the relevant line of business: CP.CPA.09 for commercial, HIM.PA.154 for health insurance marketplace, and CP.PMN.53 for Medicaid.

III. Diagnoses/Indications for which coverage is NOT authorized:

A. Non-FDA approved indications, which are not addressed in this policy, unless there is sufficient documentation of efficacy and safety according to the off label use policy – CP.CPA.09 for commercial, HIM.PA.154 for health insurance marketplace, and CP.PMN.53 for Medicaid, or evidence of coverage documents.

IV. Appendices/General Information

Appendix A: Abbreviation/Acronym Key

AIP: acute intermittent porphyria
ALA: 5-aminolevulinic acid
FDA: Food and Drug Administration
HCP: hereditary coproporphyria
PBG: prophobilinogen
VP: variegate porphyria

Appendix B: Therapeutic Alternatives

Not applicable

Appendix C: Contraindications/Boxed Warnings

- Contraindication(s): known hypersensitivity to Panhematin
- Boxed warning(s): none reported

Appendix D: ALA and PBG Laboratory Testing

Concentrations of ALA or PBG in a random urine sample greater than four times the upper limit of normal establish the diagnosis of AHP (Wang 2019). Variations in reference ranges and reporting (e.g., with or without creatinine correction) may differ across U.S. laboratories; however, four times the upper limit of normal based on a random urine sample remains an appropriate evaluative tool.

Examples of laboratory reporting variations:*

**ALA/PBG values below are chosen for demonstration purposes only and do not reflect actual required values.*

- Corrected for creatinine:*
  **Additional units applicable here include mg/mmol creatinine.*
  - ALA = 38 mg/g creatinine (reference range 0-7 mg/g creatinine);
  - PBG = 85 mg/g creatinine (reference range 0-4 mg/g creatinine).

  See Wang et al (2019) for additional information.
- Uncorrected for creatinine:*
  **Additional units applicable here include mcmol/L.*
  - ALA = 40 mg/L (reference range 0.0-5.4 mg/L);
  - PBG = 90 mg/L (reference range 0.0-2.0 mg/L).

  See LabCorp (www.labcorp.com) and Mayo Medical Laboratories (www.mayoclinicalabs.com) testing information for additional information.

Wang B, Rudnick S, Cengia B, Bonkovsky HL. Acute hepatic porphyrias: Review and recent progress. Hepatology Communications, 2019; 3(2): 193:206.

V. Dosage and Administration

Indication	Dosing Regimen	Maximum Dose
Amelioration of recurrent attacks of AIP	1 to 4 mg/kg/day IV for 3 to 14 days based on the clinical signs. The standard dose in clinical practice is 3 to 4 mg/kg/day. Repeat dose in more severe cases no earlier than every 12 hours. Do not exceed 6 mg/kg in any 24-hour period.	6 mg/kg in any 24-hour period.

VI. Product Availability

Single-dose lyophilized powder vial: 350 mg

VII. References

1. Panhematin. Prescribing Information. Lebanon, NJ: Recordati Rate Disease, Inc. May 2020. Available at https://www.panhematin.com/pdf/Panhematin-PI-May-2020.pdf. Accessed November 10, 2023.
2. Stein P, Badminton M, Barth J et al. Best practice guidelines on clinical management of acute attacks of porphyria and their complications. Ann Clin Biochem. 2013 May;50(Pt 3):217-23. doi: 10.1177/0004563212474555.
3. Balwani M, Wang B, Anderson KE, et al. Acute hepatic porphyrias: Recommendations for evaluation and long term management. Hepatology 2017; 66(4):1314-1322.
4. Anderson KE, Bloomer JR, Bonkovsky HL, et al. Recommendations for the diagnosis and treatment of the acute porphyrias. *Ann Intern Med*. 2005; 142:439-450.
5. Wang B, Bonkovsky HL, Lim JK, and Balwani M. AGA Clinical practice update on diagnosis and management of acute hepatic porphyrias: Expert review. Gastroenterology 2023;164:484-491.

Coding Implications

Codes referenced in this clinical policy are for informational purposes only. Inclusion or exclusion of any codes does not guarantee coverage. Providers should reference the most up-to-date sources of professional coding guidance prior to the submission of claims for reimbursement of covered services.

HCPCS Codes	Description
J1640	Injection, hemin, 1 mg

Reviews, Revisions, and Approvals	Date	P&T Approval Date
1Q 2020 annual review: no significant changes; added HIM line of business; references reviewed and updated.	10.21.19	02.20

Reviews, Revisions, and Approvals	Date	P&T Approval Date
1Q 2021 annual review: no significant changes; references to HIM.PHAR.21 revised to HIM.PA.154; references reviewed and updated.	11.25.20	02.21
1Q 2022 annual review: no significant changes; added requirement for documentation of member's weight for dose calculation purposes, as a previously Corporate P&T-approved approach to ensure appropriate dosing; references reviewed and updated.	11.23.21	02.22
Template changes applied to other diagnoses/indications and continued therapy section.	10.03.22	
1Q 2023 annual review: required labs for diagnosis of porphyria revised to align with Givlaari (CP.PHAR.457); added Appendix D ALA and PBG Laboratory Testing; references reviewed and updated.	11.14.22	02.23
1Q 2024 annual review: no significant changes; corrected "hypernatremia" to "hyponatremia" in examples of clinical symptoms of acute porphyria in section I.A.1.a. references reviewed and updated.	02.09.24	02.24

Important Reminder

This clinical policy has been developed by appropriately experienced and licensed health care professionals based on a review and consideration of currently available generally accepted standards of medical practice; peer-reviewed medical literature; government agency/program approval status; evidence-based guidelines and positions of leading national health professional organizations; views of physicians practicing in relevant clinical areas affected by this clinical policy; and other available clinical information. The Health Plan makes no representations and accepts no liability with respect to the content of any external information used or relied upon in developing this clinical policy. This clinical policy is consistent with standards of medical practice current at the time that this clinical policy was approved. "Health Plan" means a health plan that has adopted this clinical policy and that is operated or administered, in whole or in part, by Centene Management Company, LLC, or any of such health plan's affiliates, as applicable.

The purpose of this clinical policy is to provide a guide to medical necessity, which is a component of the guidelines used to assist in making coverage decisions and administering benefits. It does not constitute a contract or guarantee regarding payment or results. Coverage decisions and the administration of benefits are subject to all terms, conditions, exclusions and limitations of the coverage documents (e.g., evidence of coverage, certificate of coverage, policy, contract of insurance, etc.), as well as to state and federal requirements and applicable Health Plan-level administrative policies and procedures.

This clinical policy is effective as of the date determined by the Health Plan. The date of posting may not be the effective date of this clinical policy. This clinical policy may be subject to applicable legal and regulatory requirements relating to provider notification. If there is a discrepancy between the effective date of this clinical policy and any applicable legal or

regulatory requirement, the requirements of law and regulation shall govern. The Health Plan retains the right to change, amend or withdraw this clinical policy, and additional clinical policies may be developed and adopted as needed, at any time.

This clinical policy does not constitute medical advice, medical treatment or medical care. It is not intended to dictate to providers how to practice medicine. Providers are expected to exercise professional medical judgment in providing the most appropriate care, and are solely responsible for the medical advice and treatment of members. This clinical policy is not intended to recommend treatment for members. Members should consult with their treating physician in connection with diagnosis and treatment decisions.

Providers referred to in this clinical policy are independent contractors who exercise independent judgment and over whom the Health Plan has no control or right of control. Providers are not agents or employees of the Health Plan.

This clinical policy is the property of the Health Plan. Unauthorized copying, use, and distribution of this clinical policy or any information contained herein are strictly prohibited. Providers, members and their representatives are bound to the terms and conditions expressed herein through the terms of their contracts. Where no such contract exists, providers, members and their representatives agree to be bound by such terms and conditions by providing services to members and/or submitting claims for payment for such services.

Note: For Medicaid members, when state Medicaid coverage provisions conflict with the coverage provisions in this clinical policy, state Medicaid coverage provisions take precedence. Please refer to the state Medicaid manual for any coverage provisions pertaining to this clinical policy.