Preemptive policy: This is a P&T approved policy and can be used after the drug is FDA approved until it is superseded by an updated policy

CENTENE® Corporation

Clinical Policy: Bitopertin (Brand Name)

Reference Number: CP.PHAR.758
Effective Date: FDA Approval Date
Last Review Date: 11.26
Line of Business: Commercial, HIM/ICHRA, Medicaid

Revision Log

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

INTERIM POLICY AND INFORMATION IS SUBJECT TO CHANGE

Description

Bitopertin (Brand Name®/™) is a glycine transporter 1 (GlyT1) inhibitor.

FDA Approved Indication(s) [Pending]

Bitopertin is indicated for the treatment of patients aged 12 years and older with erythropoietic protoporphyria (EPP), including X-linked protoporphyria (XLP).

Limitation(s) of use: [XXX]

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 bitopertin is **medically necessary** when the following criteria are met:

I. Initial Approval Criteria*

**Criteria will mirror the clinical information from the prescribing information once FDA-approved*

A. Erythropoietic Protoporphyria and X-Linked Protoporphyria (must meet all)**:**

1. Diagnosis of EPP or XLP confirmed by both of the following tests (a and b):*
   a. Elevated total erythrocyte protoporphyrin (e.g., 300 to 5,000 mcg/dL vs. normal at 80 mcg/dL);
   b. Erythrocyte fractionation shows ≥ 50% metal-free vs. zinc protoporphyrin (certified laboratories include University of Texas Medical Branch at Galveston - Porphyria Center, and Mayo Medical Laboratories);
2. Prescribed by or in consultation with a dermatologist;
3. Age ≥ 12 years;*
4. Evidence of EPP/XLP-associated acute non-blistering cutaneous reactions (e.g., pain, stinging, redness, swelling, blanching) following exposure to sun;*
5. Sun avoidance and use of sunscreen, protective clothing, and pain medication have proven inadequate in controlling EPP/XLP-associated painful skin reactions;*
6. Member does not have any of the following (a, b, c, or d):
   a. Aspartate aminotransferase and alanine transaminase ≥ 2 times upper limit of normal (ULN);
   b. Total bilirubin ≥ ULN;

c. History of liver transplantation;
d. An inherited or acquired red cell disease associated with anemia (e.g., sickle cell anemia, iron-deficiency anemia, aplastic anemia, autoimmune hemolytic anemia, thalassemias);

7. Bitopertin is not prescribed concurrently with Scenesse®;*
8. Dose does not exceed 60 mg per day.*

Approval duration: 12 months

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/ICHRA) 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/ICHRA, and CP.PMN.255 for Medicaid; or
   b. For drugs NOT on the formulary (commercial, health insurance marketplace/ICHRA) 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/ICHRA, 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/ICHRA, and CP.PMN.53 for Medicaid.

II. Continued Therapy*

**Criteria will mirror the clinical information from the prescribing information once FDA-approved*

A. Erythropoietic Protoporphyria and X-Linked Protoporphyria (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 as evidenced by any of the following (a or b):
   a. Reduction in acute non-blistering cutaneous reactions (e.g., pain, stinging, redness, swelling, blanching) following exposure to sun;
   b. Increase in pain-free period during direct sunlight exposure;
3. Bitopertin is not prescribed concurrently with Scenesse;
4. If request is for a dose increase, new dose does not exceed 60 mg per day.*

Approval duration: 12 months

INTERIM POLICY AND INFORMATION IS SUBJ... CHANGE

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/ICHRA) 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/ICHRA, and CP.PMN.255 for Medicaid; or
   b. For drugs NOT on the formulary (commercial, health insurance marketplace/ICHRA) 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/ICHRA, 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/ICHRA, 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 policies – CP.CPA.09 for commercial, HIM.PA.154 for health insurance marketplace/ICHRA, and CP.PMN.53 for Medicaid or evidence of coverage documents.

IV. Appendices/General Information

Appendix A: Abbreviation/Acronym Key

EPP: erythropoietic protoporphyria
FDA: Food and Drug Administration
GlyT1: glycine transporter 1
ULN: upper limit of normal
XLP: X-linked protoporphyria

Appendix B: Therapeutic Alternatives

Not applicable

Appendix C: Contraindications/Boxed Warnings [Pending]

- Contraindication(s): pending
- Boxed warning(s): pending

V. Dosage and Administration [Pending]

Indication	Dosing Regimen	Maximum Dose
EPP*	Pending	60 mg/day*

VI. Product Availability [Pending]

Tablets: 10 mg, 30 mg*

INTERIM POLICY AND INFORMATION IS SUBJECT TO

VII. References

1. ClinicalTrials.gov. Study of Bitopertin to evaluate the safety, tolerability, efficacy, and PPIX concentrations in participants with EPP. Available at: https://clinicaltrials.gov/study/NCT05308472. Accessed July 21, 2026.
2. Anzctr.org. A phase 2, randomized, open label study of bitopertin administered orally to evaluate the safety, tolerability, efficacy, and protoporphyrin IX (PPIX) concentrations in participants with erythropoietic protoporphyria (EPP). Available at: https://anzctr.org.au/Trial/Registration/TrialReview.aspx?ACTRN=12622000799752. Accessed July 21, 2026.
3. Dickey A, Keel S, Bonkovsky HL, et al. Results from the Aurora study: A phase 2, randomized, double-blind, placebo-controlled study of Bitopertin in erythropoietic protoporphyria. Blood 2024;144(s1):1089-1090.
4. Minder A, Kluijver LG, Barman-Aksozen J, Minder EI, Langendonk JG. Erythropoietic protoporphyrias: Pathogenesis, diagnosis, and management. Liver International 2025;45:e16027.
5. Dickey AK, Naik H, Keel SB et al. Evidence-based consensus guidelines for the diagnosis and management of erythropoietic protoporphyria and x-linked protoporphyria. J Am Acad Demeratol 2023;89(6):1227-37.

Reviews, Revisions, and Approvals	Date	P&T Approval Date
Policy created pre-emptively	11.04.25	12.25
4Q 2026 annual review: added ICHRA line of business; no significant changes as drug is not yet FDA-approved; references reviewed and updated.	07.10.26	11.26

INTERIM POLICY AND INFORMATION SUBJECT TO CHANGE

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.

©2025 Centene Corporation. All rights reserved. All materials are exclusively owned by Centene Corporation and are protected by United States copyright law and international copyright law. No part of this publication may be reproduced, copied, modified, distributed, displayed, stored in a retrieval system, transmitted in any form or by any means, or otherwise published without the prior written permission of Centene Corporation. You may not alter or remove any trademark, copyright or other notice contained herein. Centene® and Centene Corporation® are registered trademarks exclusively owned by Centene Corporation.

INTERNAL POLICY AND INFORMATION IS SUBJECT TO CHANGE