Clinical Policy: Pegloticase (Krystexxa)

Reference Number: CP.PHAR.115
Effective Date: 06.01.13
Last Review Date: 02.26
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

Pegloticase (Krystexxa®) is a PEGylated uric acid specific enzyme.

FDA Approved Indication(s)

Krystexxa is indicated for the treatment of chronic gout in adult patients refractory to conventional therapy.

Limitation(s) of use: Krystexxa is not recommended for the treatment of asymptomatic hyperuricemia.

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

I. Initial Approval Criteria

A. Chronic Gout (must meet all)**:**

1. Diagnosis of chronic gout;
2. Age ≥ 18 years;
3. Positive for symptomatic gout with one or more of the following:
   a. At least 3 gout flares in the previous 18 months;
   b. At least 1 gout tophus;
   c. Chronic gouty arthritis;
4. Failure to normalize uric acid to < 6 mg/dL with allopurinol and febuxostat at maximally indicated doses, each used for at least 3 months unless clinically significant adverse effects are experienced or both are contraindicated;
5. Failure of one uricosuric agent (e.g., probenecid), at maximally indicated doses, in combination with allopurinol or febuxostat, unless clinically significant adverse effects are experienced or all are contraindicated;
6. Krystexxa is co-administered with weekly oral methotrexate and folic acid or folinic acid, unless clinically significant adverse effects are experienced or all are contraindicated;
7. Krystexxa is not prescribed concurrently with oral urate-lowering agents (e.g., allopurinol, febuxostat, probenecid) or injectable urate-lowering agents (e.g., pegadricase);

8. Dose does not exceed 8 mg (uricase protein) every two weeks.

Approval duration:
Medicaid/HIM – 12 months
Commercial – 6 months or to the member's renewal date, whichever is longer

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. Chronic Gout (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 a decrease in plasma uric acid levels;
3. Krystexxa is co-administered with weekly oral methotrexate and folic acid or folinic acid, unless clinically significant adverse effects are experienced or all are contraindicated;
9. Krystexxa is not prescribed concurrently with oral urate-lowering agents (e.g., allopurinol, febuxostat, probenecid) or injectable urate-lowering agents (e.g., pegadricase);
4. If request is for a dose increase, new dose does not exceed 8 mg (uricase protein) every two weeks.

Approval duration:
Medicaid/HIM – 12 months
Commercial – 6 months or to the member's renewal date, whichever is longer

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 2 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 policies – 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
FDA: Food and Drug Administration
G6PD: glucose-6-phosphate dehydrogenase

Appendix B: Therapeutic Alternatives
This table provides a listing of preferred alternative therapy recommended in the approval criteria. The drugs listed here may not be a formulary agent for all relevant lines of business and may require prior authorization.

Drug Name	Dosing Regimen	Dose Limit/ Maximum Dose
allopurinol (Zyloprim®)	100 mg PO QD; may be increased by 100 mg every 2 to 4 weeks until serum urate concentration is ≤ 6 mg/dL or until maximum of 800 mg/day is reached	800 mg/day
Uloric® (febuxostat)	40 mg PO QD	80 mg/day
probenecid	250 mg PO BID for the first week, then 500 mg PO BID	2 gm/day
methotrexate	15 mg PO weekly	varies

Therapeutic alternatives are listed as Brand name® (generic) when the drug is available by brand name only and generic (Brand name®) when the drug is available by both brand and generic.

Appendix C: Contraindications/Boxed Warnings

- Contraindication(s): glucose-6-phosphate dehydrogenase (G6PD) deficiency
- Boxed warning(s): anaphylaxis and infusion reactions; G6PD deficiency-associated hemolysis and methemoglobinemia

V. Dosage and Administration

Indication	Dosing Regimen	Maximum Dose
Chronic gout	8 mg IV every 2 weeks, co-administered with weekly PO methotrexate 15 mg. Krystexxa alone may be used in patients for whom methotrexate is contraindicated or not clinically appropriate.	8 mg/2 weeks

VI. Product Availability

Vial: 8 mg of uricase protein/1 mL

VII. References

1. Krystexxa Prescribing Information. Lake Forest, IL: Horizon Pharma USA, Inc.; July 2022. Available at: https://www.accessdata.fda.gov/drugsatfda_docs/label/2022/125293s104lbl.pdf. Accessed: November 14, 2025.
2. Khanna D, Fitzgerald, JD, Khanna PP, et al. 2012 American College of Rheumatology guidelines for management of gout. Part 1: systematic nonpharmacologic and pharmacologic therapeutic approaches to hyperuricemia gout. Arthritis Care Res. October 2012; 64(10): 1431-1446.
3. FitzGerald JD, Dalbeth N, Mikuls T, et al. 2020 American College of Rheumatology Guideline for the Management of Gout. Arthritis Care & Research. June 2020; 0 (0): 1-17.
4. DRUGDEX® System [Internet database]. Greenwood Village, Colo: Thomson Healthcare. Updated periodically. Accessed November 14, 2025.

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
J2507	Injection, pegloticase, 1 mg

Reviews, Revisions, and Approvals	Date	P&T Approval Date
1Q 2022 annual review: no significant changes; references reviewed and updated	11.20.21	02.22
Template changes applied to other diagnoses/indications and continued therapy section.	09.30.22	
1Q 2023 annual review: RT4: no addition of co-administration with methotrexate criteria; updated dosing in Appendix B; updated	11.28.22	02.23

Reviews, Revisions, and Approvals	Date	P&T Approval Date
template language for continued therapy and other diagnoses/indication sections; references reviewed and updated.		
1Q 2024 annual review: updated "Uloric" to generic "febuxostat" to clarify generic redirection is preferred; references reviewed and updated.	11.12.23	02.24
1Q 2025 annual review: no significant changes; references reviewed and updated	10.23.24	02.25
1Q 2026 annual review: removed losartan as a uricosuric agent as its place in therapy is an antihypertensive alternative to HCTZ; added combination use with MTX per labeling; added prevention of concomitant use with pegadricase; extended initial approval duration from 6 to 12 months for Medicaid and HIM; references reviewed and updated.	11.14.25	02.26

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.