Clinical Policy: Pegloticase (Krystexxa)

Reference Number: CP.PHAR.115
Effective Date: 06.01.13
Last Review Date: 02.18
Line of Business: Commercial, Medicaid

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 (which may include office chart notes and lab results) 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. ≥ 3 gout flares in the previous 18 months;
   b. ≥ 1 gout tophus;
   c. Chronic gouty arthritis;
4. Failure to normalize uric acid to < 6 mg/dL with at least 3 months each of allopurinol and febuxostat (at maximumally indicated doses) unless contraindicated or clinically significant adverse effects are experienced;
5. Failure of one uricosuric agent (e.g., probenecid or losartan) at up to maximally indicated doses, in combination with allopurinol or febuxostat unless contraindicated or clinically significant adverse effects are experienced;
6. Has tested negative for glucose-6-phosphate dehydrogenase (G6PD) deficiency;
7. Dose does not exceed 8 mg (uricase protein) every two weeks.

Approval duration:
Medicaid – 6 months
Commercial – Length of Benefit

B. Other diagnoses/indications

1. Refer to the off-label use policy for the relevant line of business if diagnosis is NOT specifically listed under section III (Diagnoses/Indications for which coverage is NOT authorized): CP.CPA.09 for commercial, HIM.PHAR.21 for health insurance marketplace, and CP.PMN.53 for Medicaid.

II. Continued Therapy

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

1. Currently receiving medication via Centene benefit or member has previously met initial approval criteria;
2. Member is responding positively to therapy (e.g., demonstrated decrease in plasma uric acid levels);
3. Member is not concurrently taking any oral urate-lowering agents (e.g., allopurinol, febuxostat, probenecid);
4. If request is for a dose increase, new dose does not exceed 8 mg (uricase protein) every two weeks.

Approval duration:
Medicaid – 12 months
Commercial – Length of Benefit

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

1. Currently receiving medication via Centene benefit and documentation supports positive response to therapy.
   Approval duration: Duration of request or 6 months (whichever is less); or
2. Refer to the off-label use policy for the relevant line of business if diagnosis is NOT specifically listed under section III (Diagnoses/Indications for which coverage is NOT authorized): CP.CPA.09 for commercial 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 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

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®)	400-600 mg PO QD	600 mg/day

Drug Name	Dosing Regimen	Dose Limit/ Maximum Dose
Uloric® (febuxostat)	40 mg PO QD	80 mg/day
probenecid	500 mg PO BID	2 gm/day
losartan (Cozaar®)*	50 mg PO QD	50 mg/day

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.
**Off-label*

V. Dosage and Administration

Indication	Dosing Regimen	Maximum Dose
Chronic gout	8 mg IV every 2 weeks	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.; September 2016. Available at: https://hznp.azureedge.net/public/KRYSTEXXA_Prescribing_Information.pdf. Accessed September 22, 2017.
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. DRUGDEX® System [Internet database]. Greenwood Village, Colo: Thomson Healthcare. Updated periodically. Accessed September 22, 2017.

Reviews, Revisions, and Approvals	Date	P&T Approval Date
Simplified medical necessity algorithm by removing monitoring questions related to administration of the drug	06.14	06.14
Modified algorithm to included discontinuing oral urate-lowering therapies Added Appendix D: Oral Urate-Lowering Therapies	04.15	05.15
Policy converted to new template. Requests for documentation are removed. Age added per PI. PI indication criteria “chronic [and symptomatic] gout” is modified per ACR guidelines (symptomatic gout despite therapy: recent acute gout attacks, tophi, chronic gouty arthritis) and PI clinical trial inclusion criteria (uric acid	04.16	05.16

Reviews, Revisions, and Approvals	Date	P&T Approval Date
of at least 8 mg/dL, gout with at least 3 gout flares in the previous 18 months or 1 gout tophus or gouty arthritis). Removed Appendix B, "clinical features of chronic gout." Indication criteria "refractory to conventional therapy" is modified per PI clinical trial inclusion criteria and ACR guidelines, replacing Appendix C, reasons for not completing trial of XOI. Gout flare prophylaxis, use of pre-infusion medications, and administration in a healthcare setting are added under "therapeutic plan" criteria per PI. Max dose added per PI. Decreased uric acid levels added as efficacy criteria		
Under renewal criteria, added "baseline" to "decrease in plasma uric acid levels".	04.17	05.17
- Converted to new template. - Added requirement to fail one uricosuric agent in combination with a xanthine oxidase inhibitor, after failure of xanthine oxidase inhibitors alone, per treatment guidelines. - Added age limit per package labeling. - Removed requirement for concomitant gout flare prophylactic therapy. - For continued approval, added the requirement to confirm the absence of concurrent oral urate-lowering agents. - Changed approval durations from 3 and 6 months to 6 and 12 months for initial and continued approvals, respectively.	09.22.17	11.17
1Q18 annual review: - No significant changes - Policies combined for Medicaid and Commercial lines of business - References reviewed and updated.	11.22.17	02.18

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.