Clinical Policy: Pegloticase (Krystexxa)

Reference Number: ERX.SPA.197
Effective Date: 01.11.17
Last Review Date: 02.21 Revision Log
Line of Business: Commercial, Medicaid

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.

Health plan approved formularies should be reviewed for all coverage determinations. Requirements to use preferred alternative agents apply only when such requirements align with the health plan approved formulary.

It is the policy of health plans affiliated with Envolve Pharmacy Solutions™ 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 Uloric® at up to maximally indicated doses, each used for 3 months unless clinically significant adverse effects are experienced or both are contraindicated;
5. Failure of one uricosuric agent (e.g., probenecid or losartan) at up to maximally indicated doses, in combination with allopurinol or Uloric unless clinically significant adverse effects are experienced or all are contraindicated;
6. Krystexxa is not prescribed concurrently with oral urate-lowering agents (e.g., allopurinol, Uloric, probenecid);
7. Dose does not exceed 8 mg (uricase protein) every two weeks.

Approval duration: 6 months

B. Other diagnoses/indications

1. Refer to ERX.PA.01 if diagnosis is NOT specifically listed under section III (Diagnoses/Indications for which coverage is NOT authorized).

II. Continued Therapy

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

1. Currently receiving medication via a health plan affiliated with Envolve Pharmacy Solutions or member has previously met initial approval criteria;

2. Member is responding positively to therapy as evidenced by a decrease in plasma uric acid levels;
3. Krystexxa is not prescribed concurrently with oral urate-lowering agents (e.g., allopurinol, Uloric, probenecid);
4. If request is for a dose increase, new dose does not exceed 8 mg every two weeks.

Approval duration: 12 months

B. Other diagnoses/indications (must meet 1 or 2)**:**
1. Currently receiving medication via a health plan affiliated with Envolve Pharmacy Solutions and documentation supports positive response to therapy.
   Approval duration: Duration of request or 6 months (whichever is less); or
2. Refer to ERX.PA.01 if diagnosis is NOT specifically listed under section III (Diagnoses/Indications for which coverage is NOT authorized).

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 – ERX.PA.01 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 and may require prior authorization.

Drug Name	Dosing Regimen	Dose Limit/ Maximum Dose
allopurinol (Zyloprim®)	400-600 mg PO QD	600 mg/day
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*

Appendix C: Contraindications/Boxed Warnings
- Contraindication(s): 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	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 2018. Available at: https://hznp.azureedge.net/public/KRYSTEXXA_Prescribing_Information.pdf. Accessed November 16, 2020.
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 16, 2020.

Reviews, Revisions, and Approvals	Date	P&T Approval Date
Policy created	12.16	01.17
4Q17 Annual Review - 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. References reviewed and updated.	11.22.17	02.18
1Q 2019 annual review: removed the requirement for G6PD deficiency testing; references reviewed and updated.	11.06.18	02.19
1Q 2020 annual review: no significant changes; references reviewed and updated.	10.28.19	02.20
1Q 2021 annual review: no significant changes; added requirement in continued therapy that member is not concurrently taking other oral urate-lowering therapy to Section I for initial approval; references reviewed and updated.	11.16.20	02.21

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.

This Clinical Policy is not intended to dictate to providers how to practice medicine, nor does it constitute a contract or guarantee regarding payment or results. 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 policy is the property of Envolve Pharmacy Solutions. Unauthorized copying, use, and distribution of this Policy or any information contained herein is strictly prohibited. By accessing this policy, you agree to be bound by the foregoing terms and conditions, in addition to the Site Use Agreement for Health Plans associated with Envolve Pharmacy Solutions.