Medical Drug Clinical Criteria

Subject:	Krystexxa (pegloticase)		
Document #:	CC-0057	**Publish Date**:	07/01/2024
Status:	Reviewed	**Last Review Date**:	05/17/2024

Table of Contents

Overview | Coding | References

Clinical criteria | Document history

Overview

This document addresses the use of Krystexxa (pegloticase). Krystexxa is a recombinant uricase enzyme that achieves its therapeutic effect by catalyzing the oxidation of uric acid to allantoin, thereby lowering serum uric acid.

Krystexxa is approved by the Food and Drug Administration for the treatment of chronic gout in adults that are refractory to conventional therapy. In the clinical trials that supported the approval of Krystexxa, chronic refractory gout was defined as three or more self-reported gout flares during the previous 18 months, one or more tophi or gouty arthropathy defined clinically or radiographically as joint damage due to gout. Krystexxa should be co-administered with weekly methotrexate and folic acid/folinic acid supplementation unless contraindicated or not clinically appropriate. Methotrexate co-administration decreases anti-drug antibody incidence rate and titers, therefore allowing for increased Krystexxa exposure levels.

The 2020 American College of Rheumatology (ACR) guidelines for the management of gout strongly recommend allopurinol as the preferred first-line agent for individuals starting urate-lowering therapy (ULT), including those with chronic kidney disease (CKD) stage ≥3. The guidelines also strongly recommend a xanthine oxidase inhibitor over probenecid for those with CKD stage ≥3. For individuals on ULT, the ACR recommends targeting a serum urate level <6 mg/dL. The guidelines strongly recommend switching to Krystexxa in individuals for whom xanthine oxidase inhibitors, uricosurics and other interventions have failed to achieve the serum urate target and who continue to have frequent gout flares (≥2 flares/year) or who have nonresolving subcutaneous tophi.

Krystexxa has a black box warning for anaphylaxis and infusion reactions and glucose-6-phosphate dehydrogenase (G6PD) deficiency associated hemolysis and methemoglobinemia. Krystexxa should be administered in a healthcare setting and by healthcare providers prepared to manage anaphylaxis and infusion reactions. Individuals should be pre-medicated with antihistamines and corticosteroids for each infusion and closely monitored for symptoms of anaphylaxis. Monitor serum uric acid levels prior to infusions and consider discontinuing treatment if levels increase to above 6 mg/dL, particularly when two consecutive levels above 6 mg/dL are observed. Individuals at risk for G6PD deficiency (including African, Mediterranean and Southern Asian ancestry) should be screened prior to starting Krystexxa. Hemolysis and methemoglobinemia have been reported with Krystexxa in individuals with G6PD deficiency. Do not administer Krystexxa to individuals with G6PD deficiency.

Clinical Criteria

When a drug is being reviewed for coverage under a member's medical benefit plan or is otherwise subject to clinical review (including prior authorization), the following criteria will be used to determine whether the drug meets any applicable medical necessity requirements for the intended/prescribed purpose.

Krystexxa (pegloticase)

Initial requests for Krystexxa (pegloticase) may be approved if the following criteria are met:

I. Individual is 18 years of age or older; **AND**
II. Individual has a diagnosis of chronic gout demonstrated by one or more of the following (Sundy 2011):
    A. Three or more gout flares in the previous 18 months; **OR**
    B. One or more tophus present; **OR**
    C. History of chronic gouty arthropathy, defined clinically or radiographically as joint damage due to gout.

AND

III. Documentation is provided that individual has a baseline serum uric acid of 6 mg/dL or greater prior to initiating Krystexxa (pegloticase) (FitzGerald 2020); **AND**
IV. Documentation is provided that individual has failed to respond to, is intolerant of, or has a medical contraindication to 1 or more of the following conventional therapies (FitzGerald 2020):

A. A xanthine oxidase inhibitor (allopurinol or febuxostat); **OR**
B. Combination therapy of 1 xanthine oxidase inhibitor given with a uricosuric agent (for example, probenecid); **AND**

V. Krystexxa (pegloticase) will be administered in combination with methotrexate and folic acid/folinic acid supplementation unless contraindicated or not clinically appropriate.

Continuation requests for Krystexxa (pegloticase) may be approved if the following criterion is met:

I. There is clinically significant improvement in clinical signs and symptoms of disease (including but not limited to reduction in serum uric acid level, gout flare reduction, tophus resolution, reduction in joint pain) (Sundy 2011); **AND**
II. Krystexxa (pegloticase) will be administered in combination with methotrexate and folic acid/folinic acid supplementation unless contraindicated or not clinically appropriate.

Krystexxa (pegloticase) may not be approved for the following:

I. Individual has asymptomatic hyperuricemia; **OR**
II. Individual has a known glucose-6-phosphate dehydrogenase (G6PD) deficiency; **OR**
III. Individual is using in combination with oral urate-lowering therapy (including but not limited to allopurinol, febuxostat, probenecid); **OR**
IV. For continuation requests, the two most recent serum uric acid levels have been 6 mg/dL or greater; **OR**
V. May not be approved when the above criteria are not met and for all other indications.

Quantity Limits

Krystexxa (pegloticase) Quantity Limit

Drug	Limit
Krystexxa (pegloticase) 8 mg/mL single dose vial	2 vials per 28 days

Coding

The following codes for treatments and procedures applicable to this document are included below for informational purposes. Inclusion or exclusion of a procedure, diagnosis or device code(s) does not constitute or imply member coverage or provider reimbursement policy. Please refer to the member's contract benefits in effect at the time of service to determine coverage or non-coverage of these services as it applies to an individual member.

HCPCS

J2507	Injection, pegloticase, 1mg [Krystexxa]

ICD-10 Diagnosis

M1A.00X0-M1A.9XX1	Chronic gout
M10.00-M10.9	Gout

Document History

Reviewed: 5/17/2024
Document History:

- 5/17/2024 – Annual Review: No changes. Coding Reviewed: No changes.
- 04/01/2024 – Add quantity limit.
- 05/19/2023 – Annual Review: Add criteria for combination use with methotrexate, may not approve criteria for combination use with oral urate-lowering therapy and may not approve criteria for repeated elevated serum uric acid levels. Wording and formatting changes. Coding Reviewed: No changes.
- 05/20/2022 – Annual Review: Wording and formatting changes. Coding Reviewed: No changes.
- 08/01/2021 – Administrative update to add documentation.
- 05/21/2021 – Annual Review: Update guideline references. Coding Reviewed: No changes.
- 05/15/2020 – Annual Review: Addition of continuation criteria. Wording and formatting changes. Coding Reviewed: No changes.
- 05/17/2019 – Annual Review: Wording and formatting changes. Coding reviewed: no changes.
- 11/16/2018 – Select Review: Initial P&T Review of Krystexxa (pegloticase). Update criteria with off-label references. Minor wording and formatting changes. HCPCs and ICD-10 Review: No changes.

References

1. DailyMed. Package inserts. U.S. National Library of Medicine, National Institutes of Health website. http://dailymed.nlm.nih.gov/dailymed/about.cfm. Accessed: April 5, 2024.
2. DrugPoints® System [electronic version]. Truven Health Analytics, Greenwood Village, CO. Updated periodically.
3. FitzGerald JD, Dalbeth N, Mikuls T, et al. 2020 American College of Rheumatology Guideline for the Management of Gout. *Arthritis Rheumatol.* 2020;72(6):879-895. Available at: https://onlinelibrary.wiley.com/doi/epdf/10.1002/art.41247.
4. 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. *Arthritis Care Res.* 2012; 64: 1431-46.
5. Lexi-Comp ONLINE™ with AHFS™, Hudson, Ohio: Lexi-Comp, Inc. Updated periodically.
6. Sundy JS, Baraf HS, Yood RA, et al. Efficacy and tolerability of pegloticase for the treatment of chronic gout in patients refractory to conventional treatment: two randomized controlled trials. *JAMA*. 2011; 306:711–720.

Federal and state laws or requirements, contract language, and Plan utilization management programs or polices may take precedence over the application of this clinical criteria.