Blue Cross Blue Shield Blue Care Network of Michigan

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P&T Date: 06/05/2025

Krystexxa® (pegloticase)

HCPCS: J2507

Policy:

Requests must be supported by submission of chart notes and patient specific documentation.

A. Coverage will be provided if ALL of the following are met:
   a. FDA approved age
   b. Diagnosis of chronic gout
   c. Patient has at least one of the following:
      i. Two or more gouty flares in previous 12 months
      ii. Presence of one or more tophi
      iii. Chronic gouty arthritis (defined clinically or radiographically as joint damage due to gout)
   d. Serum uric acid > 6 mg/ dL
   e. Member has undertaken appropriate lifestyle modifications, (i.e. limiting alcohol consumption, discontinuing or changing other medications known to precipitate gout attacks when possible)
   f. Treatment with maximally titrated or maximally tolerated dose of a xanthine oxidase inhibitor (i.e. allopurinol or febuxostat) has been ineffective or is contraindicated.
   g. Treatment with an uricosuric agent (example: probenecid) in combination with a xanthine oxidase inhibitor unless contraindicated, not tolerated, or has been ineffective.
      i. If xanthine oxidase inhibitor therapy is contraindicated or not tolerated, probenecid can be used unless contraindicated itself
   h. Krystexxa will NOT be used concomitantly with oral urate-lowering therapies (examples: allopurinol, febuxostat, probenecid)
   i. Coverage will NOT be provided for the following indications:
      i. Hyperuricemia not associated with gout
      ii. Asymptomatic hyperuricemia
   j. Trial and failure, contraindication, OR intolerance to the preferred drugs as listed in BCBSM/BCN's utilization management medical drug list

B. Quantity Limitations, Authorization Period and Renewal Criteria
   a. Quantity Limits: Align with FDA recommended dosing
   b. Authorization Period: One year at a time
   c. Renewal Criteria: Clinical documentation must be provided to confirm that current criteria are met and that the medication is providing clinical benefit.

***Note: Coverage and approval duration may differ for Medicare Part B members based on any applicable criteria outlined in Local Coverage Determinations (LCD) or National Coverage Determinations (NCD) as determined by Center for Medicare and Medicaid Services (CMS). See the CMS website at http://www.cms.hhs.gov/. Determination of coverage of Part B drugs is based on medically accepted indications which have supported citations included or approved for inclusion determined by CMS approved compendia.

Background Information:

- Gout is an inflammatory arthritis that results from hyperuricemia, which contributes to crystallization of monosodium urate monohydrate in the joints. It is one of the most common rheumatic diseases of adulthood with significant morbidity attributed to gout flares (i.e. severe pain, reduced quality of life, decreased physical function).

- One of the mainstays of gout treatment is patient education on diet, lifestyle modifications, and management of comorbidities with a goal of decreasing the risk and frequency of acute gout attacks and lowering serum urate levels. Dietary modifications include limiting consumption of purine-rich meat and seafood, alcohol, and beverages sweetened by high-fructose corn syrup, and encouraging the consumption of vegetables and low-/non-fat dairy products. Elimination of non-essential medications that may induce hyperuricemia should also be considered.

- The American College of Rheumatology (ACR) guidelines for the management of gout (2020) strongly recommend the use of pharmacologic urate-lowering therapy (ULT) in gout patients with any of the following:

    - ≥ 1 subcutaneous tophi

    - Evidence of radiographic damage attributable to gout (i.e., gouty arthropathy)

    - Frequent gout flares defined as ≥ 2 flares annually.

- A target-to-treat strategy is strongly recommended for all patients receiving ULT to optimize patient outcomes by achieving and maintaining a serum urate target of < 6 mg/dL. Dose titration and subsequent dosing should be individualized to the patient and guided by serial serum urate values to achieve the target level as opposed to utilizing a fixed standard-dose strategy for ULT.

- Per the updated guidelines, allopurinol, a xanthine oxidase inhibitor (XOI), is the preferred first-line treatment option for all patients requiring ULT, including those with moderate-to-severe chronic kidney disease (CKD) stage > 3. This recommendation is based on allopurinol's efficacy, safety, tolerability, and low cost. Treatment should be initiated with a lower starting dose (< 100 mg per day) to mitigate safety issues, and gradually titrated to a target serum urate (SU) level of < 6 mg/dL, not to exceed a maximum of 800 mg per day.

- If despite initial treatment with a maximally tolerated or maximally dosed XOI serum urate levels are persistently above target and a patient exhibits continued gout flares (> 2 per year) or has non-resolving subcutaneous tophi, the guidelines conditionally recommend switching to a second XOI (i.e. febuxostat (Uloric®)) over adding a uricosuric agent.

    - The conditional recommendation is due to the fact that no studies directly address the choice of switching to another xanthine oxidase inhibitor or adding a uricosuric agent (e.g., probenecid) when the ULT strategy requires a change.

    - The guidelines strongly recommend initiating febuxostat therapy with a low dose (< 40 mg/day), with subsequent dose titration guided by serum urate levels to a target of < 6 mg/dL, up to a maximum of 80 mg per day.

    - Febuxostat carries a boxed warning of an increased risk of cardiovascular death in gout patients with established cardiovascular disease. Switching to an alternative oral ULT agent is conditionally recommended by the guidelines for patients taking febuxostat with a history of cardiovascular disease (CVD) or a new CVD-related event if available and consistent with other guideline recommendations.

- The 2020 ACR guidelines did not include a formal vote on the indications for uricosuric agents like probenecid; however, they do concur with the 2012 guidelines that add-on therapy with a uricosuric agent to partially responsive XOI treatment can result in improved control of serum urate as demonstrated in several studies of lesinurad added to XOI therapy. Additionally, literature supports the use of probenecid as monotherapy if there is a contraindication or intolerance to XOIs as it provides an alternative mechanism for the treatment of gout. Of note, treatment with uricosuric agents like probenecid should be avoided in patients with a history of nephrolithiasis or moderate-to-severe CKD (stage > 3).

- Patients with gout for whom treatment with XOI, uricosurics, and other interventions have failed to achieve target serum urate levels, and who continue to have frequent gout flares (>2 per year) or who have non-resolving subcutaneous topi are strongly recommended to switch to pegloticase (Krystexxa), an intravenously administered PEGylated uric acid specific enzyme indicated for the treatment of chronic gout in adult patients refractory to conventional therapy. Per the guidelines, Krystexxa is strongly recommended against in the following situations:

    - As first-line therapy, in accordance with FDA approved labeling.

    - For patients with gout who have persistently elevated serum urate levels above target despite maximally tolerated treatments and interventions but have infrequent gout flares (< 2 per year) and no tophi.

- The safety and efficacy of Krystexxa was studied in two replicate randomized, double-blind, placebo-controlled, Phase III trials each conducted over 6 months (i.e. GOUT1 and GOUT2). Krystexxa demonstrated a significantly greater plasma urate lowering response (i.e. sUR < 6mg/dL) than placebo, thereby meeting the primary endpoint of the studies. Patients involved in the trial had a baseline serum uric acid of 8.0mg/dL or greater, had a contraindication to allopurinol or failed to normalize uric acid levels with the maximum appropriate dose of allopurinol, and had at least one of the following:

    - ≥ 3 gout flares in the previous 18 months

    - ≥ 1 tophus

    - Gouty arthropathy, defined clinically or radiographically as joint damage due to gout.

- Consistent with the FDA approved labeling, Krystexxa should not be used concomitantly with oral urate-lowering therapies and has not been evaluated to treat asymptomatic hyperuricemia or hyperuricemia not associated with gout.

References:

1. Reinders M, Jansen TL. New advances in the treatment of gout: review of pegloticase. Ther and Clin Risk Mgt 2010; 6: 543-550.
2. Sundy J, Baraf H, Yood R et al. Efficacy and tolerability of pegloticase for the treatment of chronic gout in patient's refractory to conventional treatment. JAMA 2011; 306 (7): 711-720.
3. Edwards Lawrence. Treatment-failure gout: A moving target. Arth & Rheum; 58 (9): 2587-2590.

4. Chao J, Terkeltaub R. [abstract] A critical reappraisal of allopurinol dosing, safety, and efficacy for hyperuricemia in gout. Curr Rheum Rep 2009 Apr; 11(2): 135-40.
5. Becker MA, Schumacher HR, MacDonald PA et al. [abstract] Clinical efficacy and safety of successful long-term urate lowering with febuxostat or allopurinol in subjects with gout. J Rheum 2009 Jun; 36 (6): 1273-82.
6. Krystexxa™ (pegloticase) [package insert]. Savient Pharmaceuticals. July 2018.
7. 2012 American College of Rheumatology Guidelines for Management of Gout. Part 1: Systematic Nonpharmacologic and Pharmacologic Therapeutic Approaches to Hyperuricemia. Arthritis care and Research. Vol 64, No. 10, October 2012: 1431-1446.
8. Tilleman JA, et al. Urate-Lowering Therapy for the Prevention and Treatment of Gout Flare. US Pharm. 2017;42(3):33-37.
9. Fitzgerald JD, et al. 2020 American College of Rheumatology Guideline for the Management of Gout. Arthritis Care and Research. Vol. 72, No. 6, June 2020:744-760.
10. Perez-Ruiz F. Pharmacologic urate-lowering therapy and treatment of tophi in patients with gout. In: UpToDate, Post TW (Ed), UpToDate, Waltham, MA. (Accessed May 10, 2021).

Policy History		
#	Date	Change Description
2.3	Effective Date: 06/05/2025	Annual review of criteria was performed, no changes were made
2.2	Effective Date: 06/06/2024	Annual review of criteria was performed, no changes were made
2.1	Effective Date: 06/08/2023	Annual review of criteria was performed, no changes were made
2.0	Effective Date: 06/09/2022	Annual review of criteria was performed, no changes were made
1.9	Effective Date: 06/10/2021	Policy updated to align with 2020 ACR guidelines for management of gout Criteria changes for the following: • Number of flares per year • Serum uric acid requirement • Change t/f of allopurinol to t/f of any XOI • Removal of dose requirement to instead reflect maximally tolerated or maximally titrated dose Probenecid use in combination with any XOI, not just allopurinol
1.8	Effective Date: 8/13/2020	Addition of preferred drug step; changed baseline serum uric acid requirement to reflect population studied in the trial. Updated supporting information.
1.7	Effective Date: 08/15/2019	Removal of Uloric from step therapy and change in step therapy, addition of not taking urate-lowering therapies and lifestyle modification
1.6	Effective Date: 05/09/2019	Annual Review of Medical Policy
1.5	Effective Date: 05/03/2018	Annual Review of Medical Policy

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<tr><td>1.4</td><td>Effective Date: 07/05/2017</td><td>UM medical management system update for BCNA and MAPPO
<table><tr><th>Line of Business</th><th>PA Required in Medical Management System (Yes/No)</th></tr><tr><td>BCBS</td><td>Yes</td></tr><tr><td>BCN</td><td>Yes</td></tr><tr><td>MAPPO</td><td>Yes</td></tr><tr><td>BCNA</td><td>Yes</td></tr></table></td></tr>
<tr><td>1.3</td><td>Effective Date: 05/04/2017</td><td>Changes: Annual Review/Medicare Disclaimer added</td></tr>
<tr><td>1.2</td><td>Effective Date: 08/11/2016</td><td>Annual Review of Medical Policy</td></tr>
<tr><td>1.1</td><td>Effective Date: 04/01/2014</td><td>UM medical management system update for BCBS
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<tr><td>1.0</td><td>Effective Date: 11/2011</td><td>New Drug Review. UM medical management system update for BCN
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** The prescribing information for a drug is subject to change. To ensure you are reading the most current information it is advised that you reference the most updated prescribing information by visiting the drug or manufacturer website or http://dailymed.nlm.nih.gov/dailymed/index.cfm*