Medicare Part B Krystexxa Prior Authorization

FDA APPROVED INDICATIONS AND DOSAGE[1]

Agent(s)	Indication(s)	Dosage
Krystexxa® (pegloticase) Intravenous injection	Treatment of chronic gout in adult patients refractory to conventional therapy Limitations of Use: Not recommended for the treatment of asymptomatic hyperuricemia	8 mg given as an intravenous infusion every two weeks The optimal treatment duration has not been established

CLINICAL RATIONALE

Gout

Gout, the most common form of inflammatory arthritis, is caused by accumulation of excess urate crystals (monosodium urate) in joint fluid, cartilage, bones, tendons, bursas, and other sites. Patients experience joint swelling and pain during gout attacks, known as acute gouty arthritis. In some patients, the frequency and duration of acute attacks increase over time and lead to chronic gout, which may be associated with deposits of uric acid crystals known as tophi. Risk factors for gout include hypertension, overweight or obesity, poor kidney function, alcohol intake, a diet rich in meat, seafood and high-fructose food or drinks, and diuretic use.[3]

Goals of therapy are to treat acute gout episodes, prevent the recurrence of gout flares, and to reverse prior signs of the disease by achieving and maintaining serum urate level below 6 mg/dL (which is below its saturation point in the blood).[5] Nonpharmacologic lifestyle modifications include weight loss, dietary changes, regular physical activity, and control of diabetes, hypertension, and/or other comorbidities.[3-5]

Guidelines recommend treatment with corticosteroids, nonsteroidal anti-inflammatory drugs (NSAIDs), or colchicine for patients with acute gout. Combinations of these agents can be used where response to monotherapy is insufficient.[3-5] Guidelines recommend against initiating long-term urate-lowering therapy in most patients after a first gout attack or in patients with infrequent attacks. Urate-lowering therapies include xanthine oxidase inhibitors (allopurinol, febuxostat), uricosuric agents (probenecid), and pegloticase. The main indications for pharmacologic urate-lowering therapy in patients with a diagnosis of gout are recurring attacks (≥2 attacks in 12 months); tophi; joint damage; renal impairment; diuretic therapy use; and primary gout starting at a young age.[3,4] The goal of urate lowering therapy is to achieve a serum urate level < 6 mg/dL.[5] During initiation of urate-lowering therapy, prophylactic treatment with colchicine or NSAIDs is recommended by guidelines to prevent gout flares.[3-5]

For most patients in whom urate-lowering is indicated, allopurinol is first-line urate lowering therapy.[4,5] Initial therapy is at low dose, usually 100 mg daily, with dose titration by 100 mg every two to four weeks to reach and maintain urate-lowering goal range < 6 mg/dL. This may require doses of allopurinol anywhere from 300-900 mg/day, depending on the patient. Febuxostat can be used as an alternative second-line xanthine oxidase inhibitor if patients are intolerant to allopurinol or have renal impairment preventing allopurinol dose escalation. Uricosuric agents can be used in patients who are resistant to, or intolerant of, xanthine oxidase inhibitors, OR used in combination with a xanthine oxidase inhibitor in patients who

do not achieve serum urate targets on xanthine oxidase monotherapy.[2,4,5] Pegloticase is an alternative for patients with severe gout in whom treatment with other urate-lowering agents has failed to be effective. It is used as an option for patients when gout is advanced and actively symptomatic or when other urate lowering therapies are contraindicated.[2,5]

Efficacy
Efficacy of Krystexxa was studied in two replicate, multicenter, randomized, double-blind, placebo-controlled studies of 6 months duration. Patients either received Krystexxa 8 mg every 2 weeks, every 4 weeks, or placebo (2:2:1 ratio). Studies were stratified for the presence of tophi (71% of patients had baseline tophi). Patients received prophylaxis for gout flares with non-steroidal anti-inflammatories (NSAIDs) or colchicine, or both, beginning at least one week prior to starting Krystexxa. The primary endpoint in both trials was the proportion of patients who achieved plasma uric acid less than 6 mg/dL for at least 80% of the time during month 3 and month 6. A greater proportion of patients treated with Krystexxa every 2 weeks achieved urate lowering to below 6 mg/dL than those on placebo [47% vs 0% in trial 1 (95% CI, p <0.001); 38% vs 0% in trial 2 (95% CI, P<0.001)]. Those receiving Krystexxa every 4 weeks also achieved urate lowering to below 6 mg/dL, but also experienced an increased frequency of anaphylaxis and infusion reactions and less efficacy with respect to tophi (a secondary efficacy endpoint- see prescribing information for further details).[1]

Serum urate values should be monitored prior to each infusion. Treatment with Krystexxa should be discontinued if serum urate values are above 6 mg/dL on two consecutive occasions.[1]

Safety[1]
Krystexxa carries the following black box warnings:

- Anaphylaxis and infusion reactions have been reported to occur during and after administration of Krystexxa
- Anaphylaxis may occur with any infusion, including a first infusion, and generally manifests within 2 hours of the infusion. However, delayed-type hypersensitivity reactions have also been reported
- Krystexxa should be administered in a healthcare setting by healthcare providers prepared to manage anaphylaxis and infusion reactions
- Patients should be premedicated with antihistamines and corticosteroids
- Patients should be closely monitored for an appropriate period of time for anaphylaxis after administration of Krystexxa
- Monitor serum uric acid levels prior to infusions and consider discontinuing treatment if levels increase to above 6 mg/dL, particularly when 2 consecutive levels above 6 mg/dL are observed
  Patients should be screened for Glucose-6-phosphate dehydrogenase (G6PD) deficiency prior to starting Krystexxa. Hemolysis and methemoglobinemia have been reported with Krystexxa in patients with G6PD deficiency. Do not administer Krystexxa to patients with G6PD deficiency

Krystexxa is contraindicated in patients with Glucose-6-phosphate dehydrogenase (G6PD) deficiency.

References

1. Krystexxa prescribing information. Horizon Therapeutics USA, Inc. March 2021.
2. Fitzgerald JD, Dalbeth N, et al. 2020 American College of Rheumatology Guidelines for Management of Gout. Arthritis Care & Research. June 2020;0(0):1-17.

3. Qaseem A, Harris RP, Forciea MA. Management of Acute and Recurrent Gout: A Clinical Practice Guideline From the American College of Physicians. Ann Intern Med. January 2017;166(1):58-68.
4. Hui M, Carr A, Cameron S, et al. The British Society for Rheumatology Guideline for the Management of Gout. *Rheumatology*. July 2017;56(7):e1–e20.
5. Richette P, Doherty M, Pascual E, et al. 2016 Updated European League Against Rheumatism (EULAR) Evidence-Based Recommendations for the Management of Gout. Ann Rheum Dis. 2017;76:29-42.

Document History
Original Prime Standard Part B criteria, approved by P&T UM Committee 12/2021

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Coverage and policy application are contingent on National Coverage Determinations (NCD) and Local Coverage Determinations (LCD). An NCD or LCD that is applicable to the drug or product must be used in lieu of applicable medical necessity criteria. Also, please note that Prior Authorization criteria cannot be stricter than an NCD or LCD with specified step therapy requirements.

TARGET AGENT(S)	PREREQUISITE AGENT(S)
Target and prerequisite agent(s) determined by client	Target and prerequisite agent(s) determined by client
Krystexxa (pegloticase)	Allopurinol

Brand (generic)	GPI	Multisource Code	HCPCS/ J Code
Krystexxa (pegloticase)			
8 mg/mL vial	68000050002020	M, N, O, or Y	J2507

CRITERIA FOR APPROVAL
Evaluation
Target Agent(s) will be approved when ALL of the following are met:

1. The requested agent is being used for ONE of the following:
    a. An FDA approved indication
    OR
    b. An indication in CMS approved compendia

    AND
2. ONE of the following:
    a. Information has been provided that indicates the patient has been treated with the requested agent in the past 365 days
    OR
    b. There is documentation that the patient has had an ineffective treatment response to the active ingredient(s) of ALL prerequisite agent(s)
    OR
    c. The patient has a documented intolerance, hypersensitivity, or FDA labeled contraindication to the active ingredient(s) of ALL prerequisite agent(s)
    OR
    d. The prescriber has submitted documentation indicating ALL prerequisite agent(s) are likely to be ineffective or are likely to cause an adverse reaction or other harm to the patient

    AND
3. The patient does NOT have any FDA labeled contraindications to the requested agent
    AND
4. The requested quantity (dose) is within FDA labeled dosing or supported in compendia for the requested indication

Length of Approval: up to 12 months