PRIOR AUTHORIZATION POLICY

POLICY: Gout – Krystexxa Prior Authorization Policy
- Krystexxa® (pegloticase intravenous infusion – Horizon Therapeutics)

REVIEW DATE: 05/04/2022; selected revision 11/09/2022

OVERVIEW

Krystexxa, a PEGylated uric acid specific enzyme, is indicated for treatment of **chronic gout refractory to conventional therapy**, in adult patients.[1] Krystexxa has a Boxed Warning due to concerns for hemolysis and methemoglobinemia, in patients with glucose-6-phosphate dehydrogenase (G6PD) deficiency.

Disease Overview

Gout results from a metabolic disorder called hyperuricemia caused by an overproduction or underexcretion of uric acid; however, asymptomatic patients with elevated uric acid levels do not have gout and do not require treatment.[2,3] Excessive amounts of uric acid in the blood lead to deposits of crystals in the joints and connective tissues and may cause excruciating pain. Lumps of urate crystals (tophi) may develop in soft tissues such as the elbow, ear, or distal finger joints. Some patients fail to normalize serum uric acid and have inadequate control of the signs and symptoms of gout with maximum medically appropriate doses or have a contraindication to urate-lowering therapies. Treatment-failure should be differentiated as those who are under-treated for gout or are non-compliant with gout therapy. Those with treatment-failure gout generally have a high prevalence of tophi, frequent and disabling gout flares, deforming arthropathy, diminished quality of life, and disability.

Guidelines

The American College of Rheumatology provide guidelines (2020) for the management of gout. Allopurinol is the preferred first-line urate-lowering therapy, including patients with moderate to severe gout.[3] Febuxostat and probenecid are conditionally recommended as alternative first-line therapies for specific patient populations. Titration of urate-lowering therapy should be guided by serum uric acid concentrations, with target of < 6 mg/dL. In patients with refractory disease, effective therapeutic options include combination therapy with a xanthine oxidase inhibitor (e.g., allopurinol or febuxostat) and a uricosuric agent (e.g., probenecid, fenofibrate, or losartan). Krystexxa is not recommended as first-line therapy, however it is appropriate in patients with severe gout disease burden and refractoriness to, or intolerance of, appropriately dosed oral urate-lowering therapies.

POLICY STATEMENT

Prior Authorization is recommended for prescription benefit coverage of Krystexxa. All approvals are provided for the duration noted below. In cases where the approval is authorized in months, 1 month is equal to 30 days. Because of the specialized skills required for evaluation and diagnosis of patients treated with Krystexxa as well as the monitoring required for adverse events and long-term efficacy, approval requires Krystexxa to be prescribed by or in consultation with a physician who specializes in the condition being treated.

Automation: None.

RECOMMENDED AUTHORIZATION CRITERIA

Coverage of Krystexxa is recommended in those who meet the following criteria:

FDA-Approved Indication

1. **Gout, Chronic.** Approve for the duration noted below if the patient meets ONE of the following conditions (A or B):
   - **A)** Initial Therapy. Approve for 6 months if the patient meets ALL of the following (i, ii, and iii):
     - **i.** Patient has at least one tophus OR a history of 2 previous flares in the past year (prior to the current flare); AND
     - **ii.** Patient meets one of the following conditions (a or b):
       - **a)** Patient had an inadequate response, defined as serum uric acid level that remained > 6 mg/dL following a 3-month trial of a xanthine oxidase inhibitor; OR
         Note: Examples of xanthine oxidase inhibitor include allopurinol and febuxostat.
       - **b)** Patient has a contraindication or has had an intolerance to a trial of allopurinol, as determined by the prescriber; AND
     - **iii.** Patient meets one of the following conditions (a or b):
       - **a)** Patient had an inadequate response, defined as serum uric acid level that remained > 6 mg/dL following a 3-month trial of a uricosuric agent; OR
         Note: Examples of uricosuric agents include probenecid, fenofibrate, and losartan.
       - **b)** According to the prescriber, the patient has renal insufficiency (e.g., decreased glomerular filtration rate); AND
     - **iv.** Krystexxa will be used in combination with ONE of the following (a, b, or c):
       - **a)** Methotrexate; OR
       - **b)** Leflunomide; OR
       - **c)** Azathioprine; AND
     - **v.** Krystexxa will not be used in combination with another uric acid lowering drug.
       Note: Examples of uric acid lower drugs include allopurinol, febuxostat, or probenecid.
     - **vi.** Krystexxa is prescribed by or in consultation with a rheumatologist or a nephrologist.
   - **B)** Patient is Currently Receiving Krystexxa. Approve for 1 year if the patient meets ALL of the following (i, ii, and iii):
     - **i.** Patient is continuing therapy with Krystexxa to maintain response/remission; AND
     - **ii.** Patient has responded to therapy with evidence of serum uric acid level < 6 mg/dL with continued Krystexxa treatments; AND
     - **iii.** Krystexxa is being used in combination with ONE of the following (a, b, or c):
       - **a)** Methotrexate; OR
       - **b)** Leflunomide; OR
       - **c)** Azathioprine; AND
     - **iv.** Krystexxa is not being used in combination with another uric acid lowering drug.
       Note: Examples of uric lower drugs include allopurinol, febuxostat, or probenecid.
     - **v.** Krystexxa is prescribed by or in consultation with a rheumatologist or a nephrologist.

CONDITIONS NOT RECOMMENDED FOR APPROVAL

Coverage of Krystexxa is not recommended in the following situations:

1. **Known Glucose-6-Phosphate Dehydrogenase (G6PD) Deficiency.** Because of risks of hemolysis and methemoglobinemia, Krystexxa is contraindicated in G6PD deficiency.[1] Patients at increased risk of this deficiency (e.g., those of African or Mediterranean ancestry) should be screened prior to initiation of therapy.

2. Coverage is not recommended for circumstances not listed in the Recommended Authorization Criteria. Criteria will be updated as new published data are available.

REFERENCES

1. Krystexxa™ intravenous infusion [prescribing information]. Lake Forest, IL: Horizon Therapeutics; July 2022.
2. Gout. Centers for Disease Control and Prevention [Web site]. Last reviewed July 27, 2020. Available at: http://www.cdc.gov/arthritis/basics/gout.html. Accessed on April 27, 2022.
3. FitzGerald JD, Dalbeth N, Mikuls T, et al. 2020 American College of Rheumatology Guideline for the Management of Gout. *Arthritis Care Res*. 2020 Jun;72(6):744-760.