VENTURA COUNTY
HEALTH CARE PLAN

UTILIZATION MANAGEMENT MEDICAL POLICY

POLICY: Gout – Krystexxa Utilization Management Medical Policy
- Krystexxa® (pegloticase intravenous infusion – Horizon Therapeutics)

REVIEW DATE: 05/04/2022

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/Clinical Data

Use of Krystexxa is supported for the following conditions:

- **Gout**: 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 probenacid 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., probenacid, 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.
- **Nephrolithiasis and/or Gouty Nephropathy:** Approximately 10% to 20% of patients with primary gout will develop kidney stones, with factors such as diet and genetic aspects playing a role in their development.[4] Even though clinical gout is not present, the condition resembles primary gout in many aspects, including a persistently low urine pH, a reduced fractional excretion of uric acid, and varying degrees of hyperuricemia.

POLICY STATEMENT

Prior Authorization is recommended for medical benefit coverage of Krystexxa. Approval is recommended for those who meet the **Criteria** and **Dosing** for the listed indications. Extended approvals are allowed if the patient continues to meet the Criteria and Dosing. Requests for doses outside of the established dosing documented in this policy will be considered on a case-by-case basis by a clinician (i.e., Medical Director

or Pharmacist). 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 one of the following criteria:

FDA-Approved Indication

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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 current symptoms of gout; AND
       Note: Examples of gout symptoms include gout flares, gout tophus, and gouty arthritis.
     - **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 at least ONE of the following agents: allopurinol, Uloric, or a uricosuric agent; OR
         Note: Examples of uricosuric agents include probenecid, fenofibrate, and losartan.
       - **b)** Patient has a contraindication or has had an intolerance to a trial of allopurinol, as determined by the prescriber; AND
     - **iii.** 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 prescribed by or in consultation with a rheumatologist or a nephrologist.

   Dosing. Approve 8 mg as an intravenous infusion every 2 weeks.

Other Uses with Supportive Evidence

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2. **Nephrolithiasis and/or Gouty Nephropathy.** 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 BOTH of the following conditions (i and ii):
     - **i.** Patient meets one of the following conditions (a or b):
       - **a)** Patient had an inadequate response, defined as a serum uric acid level that remained > 6 mg/dL following a 3-month trial of allopurinol or Uloric; OR
       - **b)** Patient has a contraindication or has had an intolerance to a trial of allopurinol, as determined by the prescriber; AND
     - **ii.** 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 prescribed by or in consultation with a rheumatologist or a nephrologist.

Dosing. Approve 8 mg as an intravenous infusion every 2 weeks.

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; May 2021.
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.
4. Wiederkehr MR, Moe OW. Uric Acid Nephrolithiasis: a systemic metabolic disorder. *Clin Rev Bone Miner Metab*. 2011;9(3-4):207-217.

HISTORY

Type of Revision	Summary of Changes	Review Date
Annual Revision	**Gout, Chronic:** For the exception applying to a patient with a contraindication or an intolerance to a trial of allopurinol, wording was updated to more generally allow this determination by the prescriber (criteria previously specified this was according to the prescribing physician). To align more with product labeling, **Dosing** was changed from administration "no sooner than every 2 weeks" to "every 2 weeks". **Nephrolithiasis and/or Gouty Nephropathy:** For the exception applying to a patient with a contraindication or an intolerance to a trial of allopurinol, wording was updated to more generally allow this determination by the prescriber (criteria previously specified this was according to the prescribing physician). To align more with product labeling, **Dosing** was changed from administration "no sooner than every 2 weeks" to "every 2 weeks".	05/12/2021
Annual Revision	No criteria changes.	05/04/2022