Policy and Procedure	
PHARMACY PRIOR AUTHORIZATION POLICY AND CRITERIA ORPTCANA024.0824	**MISCELLANEOUS PRODUCTS** **KRYSTEXXA®** (pegloticase for injection)
Effective Date: 10/1/2024	**Review/Revised Date**: 04/11, 04/12, 06/13, 10/13, 06/14, 06/15, 05/16, 05/17, 05/18, 05/19, 05/20, 05/21, 05/22, 07/23, 07/24 (KN)
Original Effective Date: 06/11	**P&T Committee Meeting Date**: 04/11, 04/12, 06/13, 10/13, 06/14, 06/15, 05/16, 05/17 , 05/18, 05/19, 06/20. 06/21, 06/22, 08/23, 08/24
Approved by: Oregon Region Pharmacy and Therapeutics Committee	

SCOPE:
Providence Health Plan, Providence Health Assurance, Providence Plan Partners, and Ayin Health Solutions as applicable (referred to individually as "Company" and collectively as "Companies").

APPLIES TO:
Commercial
Medicare Part B
Medicaid

POLICY CRITERIA:

COVERED USES:
All Food and Drug Administration (FDA) approved indications not otherwise excluded from the benefit.

REQUIRED MEDICAL INFORMATION:
For initial therapy, all the following criteria must be met:

1. Diagnosis of symptomatic chronic gout as defined by one or more of the following, despite therapies outlined in criterion 2 below:
    a. At least two gout flares per year
    b. Non-resolving tophi

2. Documentation of inadequate response, intolerance or contraindication to both of the following at maximum medically appropriate doses:
    a. Xanthine oxidase inhibitor (such as allopurinol)
    b. Uricosuric agent (such as probenecid)

    Note: Inadequate response is defined as inability to achieve uric acid levels of less than 6 mg/dL after at least three months of continuous therapy.

3. Documentation that patient will be using pegloticase in combination with methotrexate, unless contraindicated or clinically inappropriate.

Reauthorization requires documentation of a decreased uric acid level from baseline

EXCLUSION CRITERIA: N/A

AGE RESTRICTIONS: N/A

PRESCRIBER RESTRICTIONS:
Must be prescribed by or in consultation with a rheumatologist

COVERAGE DURATION:
Initial authorization and reauthorization will be approved for one year

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Requests for indications that were approved by the FDA within the previous six (6) months may not have been reviewed by the health plan for safety and effectiveness and inclusion on this policy document. These requests will be reviewed using the New Drug and or Indication Awaiting P&T Review; Prior Authorization Request ORPTCOPS047.

Requests for a non-FDA approved (off-label) indication requires the proposed indication be listed in either the American Hospital Formulary System (AHFS), Drugdex, or the National Comprehensive Cancer Network (NCCN) and is considered subject to evaluation of the prescriber's medical rationale, formulary alternatives, the available published evidence-based research and whether the proposed use is determined to be experimental/investigational.

Coverage for Medicaid is limited to a condition that has been designated a covered line item number by the Oregon Health Services Commission listed on the Prioritized List of Health Care Services.

Coverage decisions are made on the basis of individualized determinations of medical necessity and the experimental or investigational character of the treatment in the individual case.

INTRODUCTION:
Krystexxa® (pegloticase) is a PEGylated uric acid specific enzyme indicated for the treatment of chronic gout in adult patient's refractory to conventional therapy. Pegloticase mechanism of action is acting as a recombinant uricase to catalyze the oxidation of uric acid and lowering serum uric acid levels.

FDA APPROVED INDICATIONS:
Krystexxa® (pegloticase) is a PEGylated uric acid specific enzyme indicated for the treatment of chronic gout in adult patient's refractory to conventional therapy. Gout refractory to conventional therapy occurs in patients who have failed to normalize serum uric acid and whose signs and symptoms are inadequately controlled with xanthine oxidase inhibitors at the maximum medically appropriate dose or for whom these drugs are contraindicated.

Krystexxa® is not recommended for the treatment of asymptomatic hyperuricemia.

POSITION STATEMENT:
The 2020 American College of Rheumatology (ACR) guideline for the management of gout strongly recommends initiation urate-lowering therapy (ULT) in patients with any of the following:

1. One or more subcutaneous tophi
2. Radiographic damage (any modality) attributable to gout
3. Frequent gout flares (>2/year)

Treatment with allopurinol is strongly recommended as the first-line ULT agent, even in patients with moderate-to-severe chronic kidney disease. Anti-inflammatory prophylaxis therapy (e.g., colchicine, NSAIDs, prednisone/prednisolone) should be initiated concomitantly with ULT and continued for three to six months. Treatment with ULT is recommended to target a uric acid level of <6 mg/dL and it is recommended to continue treatment with ULTs indefinitely if well tolerated and not burdensome for the patient.

The guidelines recommend strongly against the use of pegloticase as a first-line therapy due to costs and adverse event profile. Additionally, the guideline only recommends switching to pegloticase therapy if the patient continues to have gout flares (at least two per year) or non-resolving tophi despite therapy with xanthine oxidase inhibitors (e.g., allopurinol, febuxostat) and uricosurics (e.g., probenecid).

Krystexxa® was studied in two multicenter, randomized, double-blind, placebo-controlled studies. Patients with chronic, symptomatic gout. This was defined as at least three gout flares in the previous 18 months, at least 1 gout tophus, or gouty arthritis. Patients had serum uric acid levels of at least 8 mg/dL despite therapy with allopurinol. Patients were randomized to receive pegloticase 8 mg every two weeks or every four weeks or placebo in a 2:2:1 ratio. The primary endpoint was the proportion of patients who achieved uric acid levels of less than 6 mg/dL for at least 80% of the time during months three and six. About 40% of patients receiving pegloticase achieved the primary endpoint compared to none in the placebo group. Of note, patients receiving every four week dosing regimens experienced a higher frequency of anaphylaxis and infusion reactions.

Patients with glucose-6-phosphate dehydrogenase (G6PD) deficiency are contraindicated for use of this therapy due to the risk of hemolysis and methemoglobinemia. Patients at higher risk for G6PD deficiency (e.g., those of African and Mediterranean ancestry) should be screened prior to treatment.

Krystexxa® has a boxed warning for anaphylaxis and infusion reactions. These reactions can occur with any infusion (including the first infusion) and generally manifests within two hours of administration.

The recommended dosage is Krystexxa 8 mg every two weeks given as an IV infusion, co-administered with weekly methotrexate 15 mg orally. Krystexxa alone may be used in patients for whom methotrexate is contraindicated or not clinically appropriate. Use of methotrexate in combination with Krystexxa aids in preventing the formation of anti-drug antibodies (ADAs) an increasing the duration of effective therapy with Krystexxa. The formation of ADAs has been shown to confer a loss of efficacy as well as an increase in infusion-related reactions.

REFERENCE/RESOURCES:

1. Krystexxa® Prescribing Information, Horizon Therapeutics; Dublin, Ireland: August 2023.
2. Reinders MK, Jansen TL. New Advances in the treatment of gout: review of pegloticase. Ther Clin Risk Mgt. 2010;6:543-550.
3. Hershfield. Treating gout with pegloticase, a PEGylated urate oxidase, provides insight into the importance of uric acid as an antioxidant in vivo. Proc Natl Acad Sci USA 2010 Aug 10;107(32):14351-14356.
4. American College of Rheumatology. 2020 American College of Rheumatology Guideline for the Management of Gout. Available at https://www.rheumatology.org/Portals/0/Files/Gout-Guideline-Final-2020.pdf (Accessed June 18, 2024).
5. Botson, JK, Tesser, JRP, Bennett R, et al. Pegloticase in Combination with Methotrexate in Patients with Uncontrolled Gout: A Multicenter, Open-label Study (MIRROR). *J Rheum* 2021;48(5):767-774.

Brand Name	Generic Name	HCPCS Code
Krystexxa®	pegloticase	J2507