Medical Policy

Healthcare Services Department

Policy Name	Policy Number	Scope
Krystexxa (pegloticase)	MP-RX-FP-50-23	☒ MMM MA ☒ MMM Multihealth

Service Category

☐ Anesthesia
☐ Surgery
☐ Radiology Procedures
☐ Pathology and Laboratory Procedures
☐ Medicine Services and Procedures
☐ Evaluation and Management Services
☐ DME/Prosthetics or Supplies
☒ Part B Drugs

Service Description

This document addresses the use of Krystexxa (pegloticase). Krystexxa is a recombinant uricase enzyme that achieves its therapeutic effect by catalyzing the oxidation of uric acid to allantoin, thereby lowering serum uric acid. Krystexxa is approved by the Food and Drug Administration for the treatment of chronic gout in adults that are refractory to conventional therapy.

Background Information

In the clinical trials that supported the approval of Krystexxa, chronic refractory gout was defined as three or more self-reported gout flares during the previous 18 months, one or more tophi or gouty arthropathy defined clinically or radiographically as joint damage due to gout. Krystexxa should be co-administered with weekly methotrexate and folic acid/folinic acid supplementation unless contraindicated or not clinically appropriate. Methotrexate co-administration decreases anti-drug antibody incidence rate and titers, therefore allowing for increased Krystexxa exposure levels.

The 2020 American College of Rheumatology (ACR) guidelines for the management of gout strongly recommend allopurinol as the preferred first-line agent for individuals starting urate-lowering therapy (ULT), including those with chronic kidney disease (CKD) stage >3. The guidelines also strongly recommend a xanthine oxidase inhibitor over probenecid for those with CKD stage >3. For individuals on ULT, the ACR recommends targeting a serum urate level <6 mg/dL. The guidelines strongly recommend switching to Krystexxa in individuals for whom xanthine oxidase inhibitors, uricosurics and other interventions have failed to achieve the serum urate target and who continue to have frequent gout flares (≥2 flares/year) or who have nonresolving subcutaneous tophi.

Krystexxa has a black box warning for anaphylaxis and infusion reactions and glucose-6-phosphate dehydrogenase (G6PD) deficiency associated hemolysis and methemoglobinemia. Krystexxa should be administered in a healthcare setting and by healthcare providers prepared to manage anaphylaxis and infusion reactions. Individuals should be pre-medicated with antihistamines and corticosteroids for each infusion and closely monitored for symptoms of anaphylaxis. Monitor serum uric acid levels prior to infusions and consider discontinuing treatment if levels increase to above 6 mg/dL, particularly when two consecutive levels above 6 mg/dL are observed. Individuals at risk for G6PD deficiency (including African, Mediterranean and Southern Asian ancestry) should be screened prior to starting Krystexxa. Hemolysis and methemoglobinemia have been

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reported with Krystexxa in individuals with G6PD deficiency. Do not administer Krystexxa to individuals with G6PD deficiency.

Approved Indications

A. Gout
B. Gouty arthritis
C. Symptomatic hyperuricemia

Applicable Codes

The following list(s) of procedure and/or diagnosis codes is provided for reference purposes only and may not be all inclusive. Inclusion or exclusion of a procedure, diagnosis or device code(s) does not constitute or imply member coverage or provider reimbursement policy. Benefit coverage for health services is determined by the member specific benefit plan document and applicable laws that may require coverage for a specific service. The inclusion of a code does not imply any right to reimbursement or guarantee claim payment. Other Policies and Guidelines may apply.

HCPCS	Description
J2507	Injection, pegloticase, 1mg [Krystexxa]

ICD-10	Description
M1A.00X0-M1A.9XX1	Chronic gout
M10.00-M10.9	Gout

Medical Necessity Guidelines

When a drug is being reviewed for coverage under a member's medical benefit plan or is otherwise subject to clinical review (including prior authorization), the following criteria will be used to determine whether the drug meets any applicable medical necessity requirements for the intended/prescribed purpose.

Provider must submit documentation (such as office chart notes, lab results or other clinical information) supporting that member has met all approval criteria.

Pegloticase (Krystexxa)

A. Criteria For Initial Approval

i. Individual is 18 years of age or older; **AND**

ii. Individual has a diagnosis of chronic gout demonstrated by one or more of the following (Sundy 2011):

a. Three or more gout flares in the previous 18 months; **OR**

b. One or more tophus present; **OR**

c. History of chronic gouty arthropathy, defined clinically or radiographically as joint damage due to gout.

AND

iii. Documentation is provided that individual has a baseline serum uric acid of 6 mg/dL or greater prior to initiating Krystexxa (pegloticase) (FitzGerald 2020); **AND**

iv. Documentation is provided that individual has failed to respond to, is intolerant of, or has a medical contraindication to 1 or more of the following conventional therapies (FitzGerald 2020):

a. A xanthine oxidase inhibitor (allopurinol or febuxostat); **OR**

b. Combination therapy of 1 xanthine oxidase inhibitor given with a uricosuric agent (for example, probenecid); **AND**

v. Krystexxa (pegloticase) will be administered in combination with methotrexate and folic acid/folinic acid supplementation unless contraindicated or not clinically appropriate.

B. Criteria For Continuation of Therapy

i. There is clinically significant improvement in clinical signs and symptoms of disease (including but not limited to reduction in serum uric acid level, gout flare reduction, tophus resolution, reduction in joint pain) (Sundy 2011); **AND**

ii. Krystexxa (pegloticase) will be administered in combination with methotrexate and folic acid/folinic acid supplementation unless contraindicated or not clinically appropriate.

C. Authorization Duration

a. Initial Approval Duration: 1 year

b. Reauthorization Approval Duration: 1 year

D. **Conditions Not Covered**

Any other use is considered experimental, investigational, or unproven, including the following (this list may not be all inclusive):

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i. Individual has asymptomatic hyperuricemia; **OR**
ii. Individual has a known glucose-6-phosphate dehydrogenase (G6PD) deficiency; **OR**
iii. Individual is using in combination with oral urate-lowering therapy (including but not limited to allopurinol, febuxostat, probenecid); **OR**
iv. For continuation requests, the two most recent serum uric acid levels have been 6 mg/dL or greater; **OR**
v. May not be approved when the above criteria (Section A) are not met and for all other indications.

Limits or Restrictions

A. Quantity Limitations:

Drug	Limit
Krystexxa (pegloticase) 8 mg/mL single dose vial	2 vials per 28 days

Approvals may be subject to dosing limits in accordance with FDA-approved labeling, accepted compendia, and/or evidence-based practice guidelines. The chart below includes dosing recommendations as per the FDA-approved prescribing information.

Reference Information

1. Krystexxa [package insert]. Deerfield, IL: Horizon Therapeutics USA, Inc.; 2022.
2. Clinical Pharmacology [database online]. Tampa, FL: Gold Standard, Inc.: 2023. URL: http://www.clinicalpharmacology.com. Updated periodically.
3. Centers for Medicare and Medicaid Services (2023, Abril 27). Local Coverage Determination (LCD). CMS. Retrieved July 6, 2023, from https://www.cms.gov/medicare-coverage-database/view/article.aspx?articleid=58812&ver=47&keyword=krystexxa&keywordType=starts&areaId=s46&docType=NCA,CAL,NCD,MEDCAC,TA,MCD,6,3,5,1,F,P&contractOption=all&sortBy=relevance&bc=1
4. Welcome to the Clinical Criteria Page (2023, May 20). Anthem. Retrieved July 6, 2023, from https://www.anthem.com/ms/pharmacyinformation/clinicalcriteria/Krystexxa.pdf

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Policy History

Revision Type	Summary of Changes	P&T Approval Date	MPCC Approval Date
Annual Review	Annual Review: Add quantity limit.	11/18/2024	12/17/2024
Policy Inception	Elevance Health's Medical Policy adopted.	N/A	11/30/2023

Revised: 09/23/2024