



Louisiana

pegloticase (Krystexxa™)

Policy # 00290

Original Effective Date: 04/13/2011

Current Effective Date: 07/11/2018

Applies to all products administered or underwritten by Blue Cross and Blue Shield of Louisiana and its subsidiary, HMO Louisiana, Inc. (collectively referred to as the "Company"), unless otherwise provided in the applicable contract. Medical technology is constantly evolving, and we reserve the right to review and update Medical Policy periodically.

When Services May Be Eligible for Coverage

Coverage for eligible medical treatments or procedures, drugs, devices or biological products may be provided only if:

- *Benefits are available in the member's contract/certificate, and*
- *Medical necessity criteria and guidelines are met.*

Based on review of available data, the Company may consider the use of pegloticase (Krystexxa™)† for the treatment of chronic gout in adult patients refractory to conventional therapy to be **eligible for coverage**.

Patient Selection Criteria

Coverage eligibility for the use of pegloticase (Krystexxa) for the treatment of chronic gout will be considered when all of the following patient selection criteria are met:

- Patient is > 18 years of age; and
- Patient has a diagnosis of chronic gout; and
- Patient has a documented failure of, contraindication to, or intolerance of 2 xanthine oxidase inhibitor agents (e.g. Uloric, Zyloprim) after 3 months of use; and
*(Note: This specific patient criterion is an additional Company requirement for coverage eligibility and will be denied as not medically necessary** if not met).*
- Patient has at least 3 gout flares in the last 18 months; and
*(Note: This specific patient criterion is an additional Company requirement for coverage eligibility and will be denied as not medically necessary** if not met).*
- Negative screening of G6PD deficiency in those of African and Mediterranean ancestry.

When Services Are Considered Investigational

Coverage is not available for investigational medical treatments or procedures, drugs, devices or biological products.

Based on review of available data, the Company considers the use of pegloticase (Krystexxa) when patient selection criteria are not met (with the exception of the criteria denoted above as **not medically necessary****) to be **investigational**.*

When Services Are Considered Not Medically Necessary

Based on review of available data, the Company considers the use of pegloticase (Krystexxa) in the absence of a documented failure of, contraindication to, or intolerance of 2 xanthine oxidase inhibitor agents after 3 months of use OR in the absence of at least 3 gout flares in the last 18 months to be **not medically necessary**.**

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Background/Overview

Krystexxa is the first PEGylated uric acid specific enzyme approved by the Food and Drug Administration (FDA) for treatment of chronic gout in adult patients' refractory to conventional therapy. Krystexxa is not recommended in patients who have asymptomatic hyperuricemia.

Drug therapy for acute gout is aimed at relieving pain and inflammation. Therapeutic options include NSAIDs, colchicine, and corticosteroids. All fast-acting NSAIDs are equally effective when given in optimum doses. In addition to an increased risk of peptic ulcers, bleeds, or perforations, NSAIDs can worsen renal insufficiency, heart failure, and blood pressure control. Colchicine is effective at reducing the severity of an acute attack but has a slower onset than NSAIDs. Corticosteroids are generally used for acute gout in patients who cannot tolerate NSAIDs or colchicine or who are refractory to these agents. Long-term therapy with a urate-lowering agent is usually initiated if a second attack or further attacks of gout occur within 1 year. Prior to the availability of Krystexxa, agents approved for long-term therapy of gout include xanthine oxidase inhibitors (allopurinol and febuxostat) which inhibit production of urate from hypoxanthine and xanthine; and probenacid, a uricosuric agent that promotes urate excretion. Allopurinol is generally recommended as the first-line drug for lowering SUA because of its efficacy, convenience, and benefit to risk ratio in both over producers and under excretors of urate.

Patients treated with Krystexxa are at risk of anaphylaxis and must be pre-treated with antihistamines and corticosteroids. Risk of anaphylaxis is further increased in those with serum uric acid (SUA) levels above 6 mg/dL. Uric acid (UA) levels should be monitored prior to infusion with consideration of discontinuing Krystexxa if UA levels increase above 6mg/dL, particularly if 2 consecutive levels >6mg/dL are observed.

Krystexxa was approved with a Risk Evaluation and Mitigation Strategy (REMS) program intended to inform healthcare providers about anaphylaxis, infusion reactions, and contraindications of use with Krystexxa. The REMS program is also intended to inform patients about the serious risks associated with Krystexxa.

FDA or Other Governmental Regulatory Approval

U.S. Food and Drug Administration

Pegloticase (Krystexxa) was FDA approved in 2010 for the treatment of chronic gout in adults patients refractory to conventional therapy. It is not recommended for the treatment of asymptomatic hyperurecemia.

Rationale/Source

This medical policy was developed through consideration of peer-reviewed medical literature generally recognized by the relevant medical community, FDA approval status, nationally accepted standards of medical practice and accepted standards of medical practice in this community, Blue Cross and Blue Shield Association technology assessment program (TEC) and other non-affiliated technology evaluation centers, reference to federal regulations, other plan medical policies, and accredited national guidelines.

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Pegloticase injection is a PEGylated uric acid specific enzyme approved by the FDA for treatment of chronic gout in adult patients refractory to conventional therapy. Pegloticase injection is made up of a recombinant modified mammalian uricase produced by a genetically modified strain of *Escherichia coli* which is covalently bonded to monomethoxypoly (ethylene glycol) [mPEG]. It achieves a therapeutic effect by catalyzing the oxidation of uric acid to allantoin. Allantoin is then eliminated, mainly by renal excretion, thus lowering SUA. The recommended dose of pegloticase injection is 8mg administered every 2 weeks over no less than 120 minutes as an intravenous infusion.

Treatment-failure gout (TFG) exists in a small population of patients with severe gout. These patients have failed to normalize SUA and have inadequate control of the signs and symptoms of gout with maximum medically appropriate doses of urate-lowering therapy (ULT) (e.g., allopurinol, febuxostat [Uloric®][†]) or have a contraindication to ULT. Treatment-failure gout should be differentiated from patients who are under-treated for gout or are non-compliant with gout therapy. Those with TFG generally have a high prevalence of tophi, frequent and disabling gout flares, deforming arthropathy, diminished quality of life, and disability. Treatment-failure gout commonly co-exists with other conditions, including hypertension, cardiovascular disease (CVD), diabetes mellitus, chronic kidney disease, obesity and hyperlipidemia. Although many patients with gout have concomitant cardiovascular (CV) co-morbidities, it is unknown if elevated SUA is a predictor or causative factor associated with CVD. Of the estimated 5million patients in the US with gout, it is believed that TFG affects approximately 50,000 patients though some reports indicate that as many as 300,000 patients may be afflicted.

Krystexxa demonstrated efficiency in reducing PUA in two Phase III trials in patients with TFG. Safety and efficacy were evaluated for up to 30 months in an open-label extension study and were found comparable to the pivotal trials. Krystexxa is the first PEGylated uric acid specific enzyme approved by the FDA for treatment of chronic gout in adult patients and is only indicated in patients who are refractory to conventional ULT (e.g., allopurinol, febuxostat). Krystexxa is the only ULT administered intravenously and must therefore be administered in a healthcare facility under the care of a healthcare professional trained to recognize and manage an infusion reaction and/or anaphylaxis (e.g., a rheumatologist or nephrologist). Patients with major cardiac conditions (unstable angina, uncontrolled arrhythmia, non-compensated CHF, uncontrolled HTN) were excluded from the pivotal studies; therefore, the safety of Krystexxa is expected to be utilized in the small percentage of the gout population who have advanced symptomatic gout without other available pharmacologic alternatives, many who have concomitant CV disease. Further long-term data are needed to determine Krystexxa's safety profile, especially in terms of serious events such as anaphylaxis and infusion reactions. Krystexxa's place in therapy will continue to evolve with more clinical research and experience.

References

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Policy History

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04/07/2011	Medical Policy Committee review
04/13/2011	Medical Policy Implementation Committee approval. New policy.
04/12/2012	Medical Policy Committee review
04/25/2012	Medical Policy Implementation Committee approval. Coverage eligibility unchanged.
04/04/2013	Medical Policy Committee review
04/24/2013	Medical Policy Implementation Committee approval. Cleaned up wording of criteria. Denoted between investigation and not medically necessary in the patient selection criteria. Reworded the When Services are Considered Investigational and When Services are Considered Not Medically Necessary sections. No coverage changes.
07/10/2014	Medical Policy Committee review
07/16/2014	Medical Policy Implementation Committee approval. No change to coverage.
06/25/2015	Medical Policy Committee review
07/15/2015	Medical Policy Implementation Committee approval. No change to coverage.
06/30/2016	Medical Policy Committee review
07/20/2016	Medical Policy Implementation Committee approval. No change to coverage.

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01/01/2017 Coding update: Removing ICD-9 Diagnosis Codes
07/06/2017 Medical Policy Committee review
07/19/2017 Medical Policy Implementation Committee approval. No change to coverage.
07/05/2018 Medical Policy Committee review
07/11/2018 Medical Policy Implementation Committee approval. No change to coverage.
Next Scheduled Review Date: 07/2019

Coding

The five character codes included in the Blue Cross Blue Shield of Louisiana Medical Policy Coverage Guidelines are obtained from Current Procedural Terminology (CPT®)†, copyright 2017 by the American Medical Association (AMA). CPT is developed by the AMA as a listing of descriptive terms and five character identifying codes and modifiers for reporting medical services and procedures performed by physician.

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CPT is a registered trademark of the American Medical Association.

Codes used to identify services associated with this policy may include (but may not be limited to) the following:

Code Type	Code
CPT	No codes
HCPCS	J2507
ICD-10 Diagnosis	M10.00 M10.011-M10.079 M10.08-M10.10 M10.111-M10.179
	M10.18-M10.20 M10.211-M10.279 M10.28-M10.29 M10.9
	M1A.00X0-M1A.00X1 M1A.0110-M1A.09X1 M1A.20X0-M1A.9XX1

*Investigational – A medical treatment, procedure, drug, device, or biological product is Investigational if the effectiveness has not been clearly tested and it has not been incorporated into standard medical practice. Any determination we make that a medical treatment, procedure, drug, device, or biological product is Investigational will be based on a consideration of the following:

- A. Whether the medical treatment, procedure, drug, device, or biological product can be lawfully marketed without approval of the U.S. FDA and whether such approval has been granted at the time the medical treatment, procedure, drug, device, or biological product is sought to be furnished; or
- B. Whether the medical treatment, procedure, drug, device, or biological product requires further studies or clinical trials to determine its maximum tolerated dose, toxicity, safety, effectiveness, or effectiveness as compared with the standard means of treatment or diagnosis, must improve health outcomes, according to the consensus of opinion among experts as shown by reliable evidence, including:

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1. Consultation with the Blue Cross and Blue Shield Association TEC or other nonaffiliated technology evaluation center(s);
2. Credible scientific evidence published in peer-reviewed medical literature generally recognized by the relevant medical community; or
3. Reference to federal regulations.

****Medically Necessary (or "Medical Necessity")** - Health care services, treatment, procedures, equipment, drugs, devices, items or supplies that a Provider, exercising prudent clinical judgment, would provide to a patient for the purpose of preventing, evaluating, diagnosing or treating an illness, injury, disease or its symptoms, and that are:

- A. In accordance with nationally accepted standards of medical practice;
- B. Clinically appropriate, in terms of type, frequency, extent, level of care, site and duration, and considered effective for the patient's illness, injury or disease; and
- C. Not primarily for the personal comfort or convenience of the patient, physician or other health care provider, and not more costly than an alternative service or sequence of services at least as likely to produce equivalent therapeutic or diagnostic results as to the diagnosis or treatment of that patient's illness, injury or disease.

For these purposes, "nationally accepted standards of medical practice" means standards that are based on credible scientific evidence published in peer-reviewed medical literature generally recognized by the relevant medical community, Physician Specialty Society recommendations and the views of Physicians practicing in relevant clinical areas and any other relevant factors.

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