Corporate Medical Policy

Pegloticase (Krystexxa®)

File Name:	pegloticase_krystexxa
Origination:	6/2020
Last CAP Review:	1/2021
Next CAP Review:	1/2022
Last Review:	2/2021

Description of Procedure or Service

Pegloticase (Krystexxa®) is a PEGylated uric acid specific enzyme indicated for the treatment of chronic gout in adult patients refractory to conventional therapy. Pegloticase is not recommended for the treatment of asymptomatic hyperuricemia.

Gout (monosodium urate [MSU] crystal deposition disease) is the most common form of inflammatory arthritis and is characterized by extracellular fluid urate saturation, exhibited by hyperuricemia defined as serum urate concentrations exceeding 6.8 mg/dL. Symptomatic presentations of gout resulting from urate crystal deposition can include recurrent flares of inflammatory arthritis, chronic arthropathy, accumulation of urate crystals as tophaceous deposits, and uric acid nephrolithiasis. Long-term maintenance therapy of subsaturating serum urate levels causes cessation of gout flares, resolution of tophi and improved patient function and quality of life.

Pharmacological management of gout consists of both acute treatment of gout attacks and prophylactic treatment for gout flares. Anti-inflammatory drugs (NSAIDs), corticosteroids, and colchicine are all used for acute management of gout attacks. Urate-lowering therapy (ULT) is standard for the prevention of recurrent gout flares and disease progression, and is indicated in gout patients with one or more tophi, at least two gout flares per year, or with evidence of gouty arthritis. ULTs include xanthine oxidase inhibitors (allopurinol and febuxostat), uricosuric agents [probenecid and lesinurad (voluntarily withdrawn from market in 2019)], and pegloticase. Treatment with allopurinol is preferred as first line over all other ULTs. ULTs should be initiated during an acute gout attack and concomitantly with anti-inflammatory prophylaxis therapy, as an increase in gout flares is frequently observed upon initiation of anti-hyperuricemic therapy.

Gout that is refractory to conventional therapy occurs in patients who have failed to normalize serum uric acid and whose signs and symptoms are not adequately controlled with xanthine oxidase inhibitors at the maximum medically appropriate dose or for whom these drugs are contraindicated.

Pegloticase (Krystexxa) is a uric acid specific enzyme that was approved by the U.S. Food and Drug Administration (FDA) in September 2010 for the treatment of chronic gout in adults refractory to conventional therapy. It is a recombinant uricase that works by catalyzing the oxidation of uric acid to allantoin, thus decreasing serum uric acid levels.

******Note: This Medical Policy is complex and technical. For questions concerning the technical language and/or specific clinical indications for its use, please consult your physician.***

Pegloticase (Krystexxa®)

Policy

BCBSNC will provide coverage for pegloticase (Krystexxa) when it is determined to be medically necessary because the medical criteria and guidelines noted below are met.

Benefits Application

This medical policy relates only to the services or supplies described herein. Please refer to the Member's Benefit Booklet for availability of benefits. Member's benefits may vary according to benefit design; therefore member benefit language should be reviewed before applying the terms of this medical policy.

When Pegloticase (Krystexxa) is covered

Initial Therapy

Pegloticase (Krystexxa) may be considered medically necessary for the treatment of adult patients with chronic gout when the following criteria are met:

1. The patient is an adult with a diagnosis of chronic gout AND the following criteria are met:
    a. The patient has a baseline serum uric acid level of greater than 6 mg/dL; **AND**
    b. The patient has one of the following:
        i. The patient has frequent gout flares (≥ 2 flares/year), **OR**
        ii. The patient has at least one subcutaneous tophi, **OR**
        iii. The patient has gouty arthritis; **AND**
2. One of the following:
    a. The patient is currently receiving prophylaxis for gout flares with NSAIDs (e.g., ibuprofen, naproxen, celecoxib), colchicine, or both; **OR**
    b. The patient has a clinical contraindication or intolerance to both NSAIDs and colchicine; **AND**
3. One of the following:
    a. The patient has tried and had an inadequate response (defined as uric acid levels > 6 mg/dL and/or presence of frequent gout flares [≥2 flares/year] or persistent unresolved subcutaneous tophi despite maximum therapeutic doses) to ALL of the following:
        i. Allopurinol at the maximum tolerated dose for ≥ 3 months
        ii. Febuxostat
        iii. Uricosuric agent (e.g., probenecid); **OR**
    b. The patient has a clinical contraindication or intolerance to ALL prerequisite agents (i.e. allopurinol, febuxistat, and uricosuric agents); **AND**
4. The patient will NOT be using pegloticase in combination with an oral urate-lowering agent (e.g., allopurinol, febuxistat, probenecid).

Initial authorization: 6 months

Continuation Therapy

Continuation of treatment with pegloticase (Krystexxa) beyond 6 months after initiation of therapy, and every 12 months thereafter, may be considered medically necessary for the treatment of chronic gout when the following criteria are met:

1. The patient is currently being treated with pegloticase, and continues to meet or would have met initial criteria for coverage at the time of therapy initiation; **AND**
2. The patient has had a positive clinical response with pegloticase treatment demonstrated by a current uric acid level that is 6 mg/dL or less.

When Pegloticase (Krystexxa) is not covered

Pegloticase (Krystexxa) is considered **investigational** and therefore not covered when the above criteria are not met, and for all other indications not listed above.

Pegloticase (Krystexxa) is considered **investigational** and therefore not covered when used for the treatment of asymptomatic hyperuricemia.

Policy Guidelines

The recommended dosing regimen for Krystexxa is 8 mg (uricase protein) administered as an intravenous infusion every two weeks. The optimal treatment duration with Krystexxa has not been established. Oral urate-lowering medications should be discontinued prior to initiating Krystexxa and should not be used while receiving Krystexxa therapy.

The risk of anaphylaxis and infusion-related reactions is higher in patients receiving Krystexxa who have lost therapeutic response (i.e., when uric acid level increases to above 6 mg/dL). Serum uric acid levels should be monitored prior to infusions and treatment should be discontinued if levels increase to above 6 mg/dL, particularly if two consecutive levels are observed above 6 mg/dL. Due to these risks, Krystexxa should be administered in a healthcare setting and by healthcare providers who are prepared to manage anaphylaxis and infusion reactions, and patients should be observed for an appropriate period of time after administration.

Use of Krystexxa is contraindicated in patients with glucose-6-phosphate deyhydrogenase (G6PD) deficiency due to the risk of life-threatening hemolytic reactions and methemoglobinemia.

An increase in gout flares may occur after initiating therapy with Krystexxa, as starting anti-hyperuricemic therapy may result in mobilization of urate from tissue deposits due to changes in serum uric acid levels. Gout flare prophylaxis with NSAIDs or colchicine is recommended for at least 6 months following Krystexxa initiation, unless not tolerated or contraindicated.

In clinical trials evaluating efficacy of pegloticase, adult patients with chronic gout were randomly assigned to pegloticase treatment or placebo who had a baseline serum uric acid level of at least 8 mg/dL; and who had symptomatic gout with 3 or more self-reported gout flares during the previous 18 months or at least one tophi or gouty arthropathy (defined clinically or radiographically as joint damage due to gout). In addition, patients included in the trials had either a contraindication to allopurinol treatment or a history of failure to normalize uric acid

levels despite ≥ 3 months of allopurinol treatment at the maximum medically appropriate dose. The primary endpoint was the proportion of patients who achieved plasma uric acid less than 6 mg/dL for at least 80% of the time during month 3 and month 6. Pegloticase administered either every 2 weeks or monthly produced a significantly greater percentage of patients with plasma uric acid levels of less than 6 mg/dL at months 3 and 6 compared to placebo. Results from the clinical trials demonstrated improved serum uric acid concentrations, low frequency of flares, reduction in tophi, and improved quality of life in these patients with frequent gout flares or non-resolving subcutaneous tophi receiving pegloticase. However, pegloticase demonstrated potential for serious allergic reactions.

Billing/Coding/Physician Documentation Information

This policy may apply to the following codes. Inclusion of a code in this section does not guarantee that it will be reimbursed. For further information on reimbursement guidelines, please see Administrative Policies on the Blue Cross Blue Shield of North Carolina web site at www.bcbsnc.com. They are listed in the Category Search on the Medical Policy search page.

Applicable codes: *J2507*

BCBSNC may request medical records for determination of medical necessity. When medical records are requested, letters of support and/or explanation are often useful, but are not sufficient documentation unless all specific information needed to make a medical necessity determination is included.

Scientific Background and Reference Sources

Horizon Therapeutics. Krystexxa (pegloticase) injection for intravenous infusion. Highlights of prescribing information. January 2020. Available at: https://www.hzndocs.com/KRYSTEXXA-Prescribing-Information.pdf. Last accessed June 2020.

Sundy JS, Baraf HS, Yood RA, et al. Efficacy and tolerability of pegloticase for the treatment of chronic gout in patients refractory to conventional treatment: two randomized controlled trials. JAMA. 2011;306(7):711-20.

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):744-60.

Medical Director review 6/2020

Blue Cross NC Pharmacy and Therapeutics Committee 1/5/2021

Medical Director review 2/2021

Policy Implementation/Update Information

6/30/20 New policy developed. Krystexxa is considered medically necessary for the treatment of adult patients with chronic gout when specified medical criteria and guidelines are met. Added HCPCS code J2507 to Billing/Coding section. References added. Medical Director review 6/2020. **Notification given 6/30/2020 for effective date 10/1/2020**. (krc)

2/23/21 Updated "When Covered" section to include the following under definition of inadequate response: "and/or presence of frequent gout flares [≥2 flares/year] or persistent unresolved subcutaneous tophi despite maximum therapeutic doses." Added the following to continuation criteria in "When Covered" section for clarity with no change to criteria intent: "or would have met initial criteria for coverage at the time of therapy initiation." Blue Cross NC Pharmacy and Therapeutics Committee 1/5/2021. Reference added. Medical Director review 2/2021. (krc)