Medical Policy Bulletin

Title:
Pegloticase (Krystexxa®)
Policy #:
MA08.060f

This Policy Bulletin document describes the status of CMS coverage, medical terminology, and/or benefit plan documents and contracts at the time the document was developed. This Policy Bulletin will be reviewed regularly and be updated as Medicare changes their regulations and guidance, scientific and medical literature becomes available, and/or the benefit plan documents and/or contracts are changed.

Policy

Coverage is subject to the terms, conditions, and limitations of the member's Evidence of Coverage.

The Company reserves the right to reimburse only those services that are furnished in the most appropriate and cost-effective setting that is appropriate to the member's medical needs and condition.

MEDICALLY NECESSARY

INITIAL THERAPY
Pegloticase (Krystexxa) is considered medically necessary and, therefore, covered for the treatment of symptomatic chronic gout in adult individuals when all of the following criteria, including Dosing and Frequency Requirements, are met:

- Failure to normalize uric acid levels to less than 6 mg/dL after at least three months of one xanthine oxidase inhibitor (XOI) (e.g., allopurinol or febuxostat) at the maximum recommended dose (alone or in combination with probenecid), unless the individual is intolerant to, has had a toxic reaction to, or has a contraindication to taking XOI.
- Individual has at least one of the following:
  - at least two gout flares in the previous 12 months
  - at least one gout tophus
  - gouty arthritis
- Dosing and Frequency: 8 mg IV infusion every two weeks

CONTINUATION THERAPY
Pegloticase (Krystexxa) is considered medically necessary and, therefore, covered for the continued treatment of symptomatic chronic gout in adult individuals when both of the following are met:

- There is documented improvement in clinical signs and symptoms, such as reduction of uric acid levels to less than 6 mg/dL, gout flare reduction, tophus reduction/resolution, reduction in joint pain/swelling
- Dosing and Frequency: 8 mg IV infusion every two weeks

DOSING AND FREQUENCY REQUIREMENTS

The Company reserves the right to modify the Dosing and Frequency Requirements listed in this policy to ensure

consistency with the most recently published recommendations for the use of pegloticase (Krystexxa). Changes to these guidelines are based on a consensus of information obtained from resources such as, but not limited to: the US Food and Drug Administration (FDA); Company-recognized authoritative pharmacology compendia; or published peer-reviewed clinical research. The professional provider must supply supporting documentation (i.e., published peer-reviewed literature) in order to request coverage for an amount of pegloticase (Krystexxa) outside of the Dosing and Frequency Requirements listed in this policy. For a list of Company-recognized pharmacology compendia, view our policy on off-label coverage for prescription drugs and biologics.

Accurate member information is necessary for the Company to approve the requested dose and frequency of this drug. If the member's dose, frequency, or regimen changes (based on factors such as changes in member weight or incomplete therapeutic response), the provider must submit those changes to the Company for a new approval based on those changes as part of the utilization management activities. The Company reserves the right to conduct post-payment review and audit procedures for any claims submitted for pegloticase (Krystexxa).

EXPERIMENTAL INVESTIGATIONAL

The use of pegloticase (Krystexxa) for non-adults or for individuals with asymptomatic hyperuricemia, is considered experimental/investigational and, therefore, not covered because the safety and/or effectiveness of this use cannot be established by review of the available published peer-reviewed literature.

All other uses for pegloticase (Krystexxa) are considered experimental/investigational and, therefore, not covered unless the indication is supported as an accepted off-label use, as defined in the Company medical policy on off-label coverage for prescription drugs and biologics.

REQUIRED DOCUMENTATION

The individual's medical record must reflect the medical necessity for the care provided. These medical records may include, but are not limited to: records from the professional provider's office, hospital, nursing home, home health agencies, therapies, and test reports.

The Company may conduct reviews and audits of services to our members, regardless of the participation status of the provider. All documentation is to be available to the Company upon request. Failure to produce the requested information may result in a denial for the drug.

When coverage of pegloticase (Krystexxa) is requested outside of the Dosing and Frequency Requirements listed in this policy, the prescribing professional provider must supply documentation (i.e., published peer-reviewed literature) to the Company that supports this request.

Guidelines

There is no Medicare coverage determination addressing pegloticase (Krystexxa); therefore, the Company policy is applicable.

BLACK BOX WARNINGS

Refer to the specific manufacturer's prescribing information for any applicable Black Box Warnings.

The risk of anaphylaxis and infusion reactions is higher in individuals who have lost therapeutic response. Monitor serum uric acid levels prior to infusions and consider discontinuing treatment if levels increase to above 6 mg/dL, particularly when 2 consecutive levels above 6 mg/dL are observed.

BENEFIT APPLICATION

Subject to the terms and conditions of the applicable Evidence of Coverage, pegloticase (Krystexxa) is covered under the medical benefits of the Company's Medicare Advantage products when the medical necessity criteria and Dosing and Frequency Requirements listed in this medical policy are met.

However, drugs that are identified in this policy as experimental/investigational are not eligible for coverage or reimbursement by the Company.

Certain drugs are available through either the member's medical benefit (Part B benefit) or pharmacy benefit (Part D benefit), depending on how the drug is prescribed, dispensed, or administered. This medical policy only addresses instances when pegloticase (Krystexxa) is covered under a member's medical benefit (Part B benefit). It does not address instances when pegloticase (Krystexxa) is covered under a member's pharmacy benefit (Part D benefit).

DRUG ADMINISTRATION

Pegloticase (Krystexxa) is administered by intravenous infusion; it should not be given as a push or bolus. Pegloticase (Krystexxa) is not recommended for the treatment of asymptomatic hyperuricemia.

U.S. FOOD AND DRUG ADMINISTRATION (FDA)

Pegloticase (Krystexxa) was approved by the FDA on September 14, 2010, for treatment of individuals with chronic gout that is refractory to conventional therapy.

PEDIATRIC USE

The safety and effectiveness of pegloticase (Krystexxa) in pediatric individuals have not been established.

Description

Pegloticase (Krystexxa) is an intravenously administered uric acid--specific enzyme. It is a recombinant uricase (PEGylated) indicated for the treatment of symptomatic chronic gout in adults (18 years and older) who are refractory to the conventional therapy of xanthine oxidase inhibitors (eg, allopurinol [Zyloprim] or febuxostat [Uloric]) at the maximum recommended dose, unless intolerant, toxic, or contraindicated. Pegloticase (Krystexxa) achieves its therapeutic effect by increasing the conversion of uric acid to allantoin, which lowers the serum uric acid level. The allantoin is then excreted by the kidneys.

BACKGROUND OF GOUT

Gout (monosodium urate crystal deposition disease) is a form of arthritis caused by a buildup of plasma uric acid (a by-product of protein metabolism). This uric acid buildup is known as hyperuricemia. There are two categories of hyperuricemia:

- Primary hyperuricemia: lasts indefinitely and occurs in the absence of comorbidities or drugs that alter uric acid production or its excretion.
- Secondary hyperuricemia: excessive urate production or decreased renal function resulting from disease, diet, drug, or toxin.

Individuals diagnosed with gout have usually had hyperuricemia for a considerable amount of time. Many individuals with hyperuricemia have no symptoms (asymptomatic hyperuricemia) for years. Gout manifests acutely with pain, inflammation, swelling, and, possibly, cellulitis. The knees and feet are usual sites of gout flares, but any joint is susceptible. Severe gout flares in the joints of the foot, especially the great toe, are referred to as podagra.

There are four stages of gout:

- Asymptomatic phase: individual has no overt symptoms of gout but does have hyperuricemia and crystalline deposits into tissues.
- Acute gouty arthritis: occurs after years of asymptomatic hyperuricemia.
- Intercritical (interval) gout: there is a gap between flares, but individual is otherwise symptom free and has no joint problems.
- Chronic recurrent and tophaceous (nodules composed of uric acid) gout: after many years of flares, this stage is disabling and involves permanent damage to joints and kidneys.

Gout may manifest as one or more of the following:

- Recurrent acute inflammatory arthritis flares
- Chronic arthropathy
- Formation of tophaceous deposits (urate crystals)
- Uric acid nephrolithiasis
- Chronic nephropathy (due to comorbid states)

Acute gout flares may be treated with dietary changes (eg, decreasing/abstinence from consumption of alcohol, fructose-sweetened drinks, meat, and seafood), non-steroidal anti-inflammatory drugs (NSAID), steroids and colchicine (Colcrys®). Chronic gout treatment usually includes antihyperuricemia medications.

PEER-REVIEWED LITERATURE

SUMMARY
The safety and effectiveness of pegloticase (Krystexxa) was demonstrated in two replicate, multicenter, randomized, double-blind, placebo-controlled studies. Inclusion criteria included: baseline serum uric acid (SUA) of at least 8 mg/dL, symptomatic gout with at least 3 gout flares in the previous 18 months or at least 1 gout tophus or gouty arthritis, and self-reported medical contraindication to allopurinol or medical history of failure to normalize uric acid (to less than 6 mg/dL) with at least 3 months of allopurinol treatment at the maximum medically appropriate dose. The primary endpoint of both studies was the achievement of a plasma uric level of less than 6 mg/dL. Both studies reported a statistically significant lowering of the plasma uric levels (under 6 mg/dL) in those receiving pegloticase (Krystexxa), compared to those receiving placebo.

OFF-LABEL INDICATIONS

There may be additional indications contained in the Policy section of this document due to evaluation of criteria highlighted in the Company's off-label policy, and/or review of clinical guidelines issued by leading professional organizations and government entities.

References

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Coding

Inclusion of a code in this table does not imply reimbursement. Eligibility, benefits, limitations, exclusions, precertification/referral requirements, provider contracts, and Company policies apply.

The codes listed below are updated on a regular basis, in accordance with nationally accepted coding guidelines. Therefore, this policy applies to any and all future applicable coding changes, revisions, or updates.

In order to ensure optimal reimbursement, all health care services, devices, and pharmaceuticals should be reported using the billing codes and modifiers that most accurately represent the services rendered, unless otherwise directed by the Company.

The Coding Table lists any CPT, ICD-10, and HCPCS billing codes related only to the specific policy in which they appear.

CPT Procedure Code Number(s)
N/A

ICD - 10 Procedure Code Number(s)
N/A

ICD - 10 Diagnosis Code Number(s)
See Attachment A.

HCPCS Level II Code Number(s)
J2507 Injection, pegloticase, 1 mg

Revenue Code Number(s)
N/A

Cross Reference

Attachment A: Pegloticase (Krystexxa®)
Description: ICD-10 Codes and Narratives

Policy History

Revisions From MA08.060f:

02/14/2022	This version of the policy will become effective 02/14/2022. This policy was updated to clarify the Company's coverage criteria for Initial Therapy with pegloticase (Krystexxa), in accordance with 2020 American College of Rheumatology Guideline for the Management of Gout (FitzGerald et al). Probenecid was added as an option for prior therapies: one xanthine oxidase inhibitor (XOI) (e.g., allopurinol or febuxostat) at the maximum recommended dose (alone or in combination with probenecid). Coverage criteria for gout flares changed: **FROM:** at least three gout flares in the previous 18 months **TO:** at least two gout flares in the previous 12 months

Revisions From MA08.060e:

03/15/2021	This version of the policy will become effective 03/15/2021. This policy was updated to clarify the Company's coverage criteria for Continuation Therapy. An additional statement was added regarding the risk of anaphylaxis and infusion reactions in those who have lost therapeutic response.

Revisions From MA08.060d:

05/20/2020	This policy has been reissued in accordance with the Company's annual review process.
01/13/2020	This policy has been updated to communicate the Dosing and Frequency requirements for pegloticase (Krystexxa®).

Revisions From MA08.060c:

01/01/2019	This policy was updated to communicate the Company's coverage position for pegloticase (Krystexxa®).

Revisions From MA08.060b:

04/20/2016	This policy has been updated to convey the FDA package insert regarding the lack of studies in the pediatric population.

Revisions From MA08.060a:

01/15/2015	This policy has been updated to include a clinical trial summary and information about potential off-label indications.

Revisions From MA08.060:

01/01/2015	This is a new policy.

Version Effective Date:
02/14/2022
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Version Reissued Date:
N/A