BlueCross BlueShield of Arizona
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MEDICAL COVERAGE GUIDELINES
SECTION: DRUGS

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KRYSTEXXA™ (pegloticase)

Coverage for services, procedures, medical devices and drugs are dependent upon benefit eligibility as outlined in the member's specific benefit plan. This Medical Coverage Guideline must be read in its entirety to determine coverage eligibility, if any.

The section identified as "Description" defines or describes a service, procedure, medical device or drug and is in no way intended as a statement of medical necessity and/or coverage.

The section identified as "Criteria" defines criteria to determine whether a service, procedure, medical device or drug is considered medically necessary or experimental or investigational.

State or federal mandates, e.g., FEP program, may dictate that any drug, device or biological product approved by the U.S. Food and Drug Administration (FDA) may not be considered experimental or investigational and thus the drug, device or biological product may be assessed only on the basis of medical necessity.

Medical Coverage Guidelines are subject to change as new information becomes available.

For purposes of this Medical Coverage Guideline, the terms "experimental" and "investigational" are considered to be interchangeable.

Description:

Krystexxa® is a pegylated uric acid specific enzyme indicated for the treatment of chronic gout in adults refractory to conventional therapy. Gout refractory to conventional therapy occurs in individuals 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.

Treatment with Krystexxa will be or is used in conjunction with an oral antihistamine, intravenous (IV) corticosteroid and acetaminophen to reduce the incidence of infusion related side effects.

Gout flare prophylaxis with a non-steroidal anti-inflammatory drug (NSAID) or colchicine is started at least 1 week before initiation of Krystexxa therapy and lasting at least 6 months, unless medically contraindicated or not tolerated.

Krystexxa is given as an IV infusion of 8 mg every two weeks.

KRYSTEXXA (pegloticase) (cont.)

Criteria:

- Initial treatment with Krystexxa is considered ***medically necessary*** in adults age 18 and above for treatment of chronic gout refractory to conventional therapy with documentation of **ALL** of the following:

    1. Baseline serum uric acid of at least 8 mg/dL
    2. History of symptomatic gout with at least 3 gout flares in the previous 18 months or at least 1 gout tophus or gouty arthritis
    3. 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 of 800 mg per day (if individual has a contraindication to allopurinol, treatment failure on other agents e.g., Uloric, sulfinpyrazone, Probenecid will be considered)
    4. Gout flare prophylaxis with non-steroidal anti-inflammatory drugs [NSAID] or colchicine
    5. Glucose-6-phosphate dehydrogenase deficiency has been ruled out in individuals at high risk for hemolysis and methemoglobinemia
    6. Concurrent use of urate lowering agents are ruled out before start of and while on Krystexxa therapy

- The following indications require review by the medical director and/or clinical advisor and/or clinical pharmacist:

    1. Requests for treatment continuation when serum uric acid levels increase to above 6 mg/dL while on Krystexxa [1]
    2. If the Krystexxa dosages have consistently been longer than every two weeks [2]

[1] During treatment, the risk of anaphylaxis is higher in individuals when uric acid levels increase above 6 mg/dL, particularly when 2 consecutive levels above 6 mg/dL are observed. Therefore, the monitoring of serum uric acid levels prior to infusions is required.

[2] Although the 4 week regimen demonstrated efficacy for the primary endpoint, this regimen was associated with increased frequency of anaphylaxis and infusion reactions and less efficacy with respect to tophi.

KRYSTEXXA (pegloticase) (cont.)

Criteria: (cont.)

- Krystexxa for all other indications not previously listed or if above criteria not met is considered ***experimental or investigational*** based upon:

1. Lack of final approval from the Food and Drug Administration, and
2. Insufficient scientific evidence to permit conclusions concerning the effect on health outcomes, and
3. Insufficient evidence to support improvement of the net health outcome, and
4. Insufficient evidence to support improvement of the net health outcome as much as, or more than, established alternatives, and
5. Insufficient evidence to support improvement outside the investigational setting.

These indications include, *but are not limited to:*

- Asymptomatic hyperuricemia

Resources:

FDA Product Approval Information for Krystexxa:

- FDA-approved indication: For the treatment of chronic gout in adult patients refractory to conventional therapy.

  The recommended dose and regimen of Krystexxa for adult patients is 8 mg (uricase protein) given as an intravenous infusion every two weeks. The optimal treatment duration with Krystexxa has not been established.

  Krystexxa should be administered in a healthcare setting by healthcare providers prepared to manage anaphylaxis and infusion related reactions. Patients should be pre-treated with antihistamines and corticosteroids. Anaphylaxis may occur with any infusion, including a first infusion, and generally manifests within 2 hours of the infusion. However, delayed type hypersensitivity reactions have also been reported. Patients should be closely monitored for an appropriate period of time for anaphylaxis after administration of Krystexxa. Patients should be informed of the symptoms and signs of anaphylaxis and instructed to seek immediate medical care should anaphylaxis occur after discharge from the healthcare setting.
  The safety and effectiveness of Krystexxa in pediatric patients less than 18 years of age have not been established.