ROCKY MOUNTAIN HEALTH PLANS®
We understand Colorado. We understand you.

UNIFORM PHARMACY PRIOR AUTHORIZATION REQUEST FORM

CONTAINS CONFIDENTIAL PATIENT INFORMATION

Complete this form in its entirety and send to Rocky Mountain Health Plans at 858-357-2538

☐ **Initial Request** ☐ **Renewal** ☐ **Appeal/Redetermination**[1]

☐ **Urgent**[2] ☐ **Non-Urgent**

Requested Drug Name: Krystexxa® (pegloticase) - MEDICARE Part B

Patient Information:	**Prescribing Provider Information:**
Patient Name:	Prescriber Name:
Member/Subscriber Number:	Prescriber Fax:
Policy/Group Number:	Prescriber Phone:
Patient Date of Birth (MM/DD/YYYY):	Prescriber Pager:
Patient Address:	Prescriber Address:
Patient Phone:	Prescriber Office Contact:
Patient Email Address:	Prescriber NPI:
	Prescriber DEA:
Prescription Date:	Prescriber Tax ID:
	Specialty/Facility Name (If applicable):
	Prescriber Email Address:

Prior Authorization Request for Drug Benefit

Patient Diagnosis and ICD Diagnostic Code(s):

Drug(s) Requested (with J-Code, if applicable):

Strength/Route/Frequency:

Unit/Volume of Named Drug(s):

Start Date and Length of Therapy:

Location of Treatment: (e.g. provider office, facility, home health, etc.) including name, Type 2 NPI (if applicable), address and tax ID:

Clinical Criteria for Approval, Including other Pertinent Information to Support the Request, other Medications Tried, Their Name(s), Duration, and Patient Response:

Krystexxa® (pegloticase)

Diagnosis (documentation supportive of diagnosis is required for approval)

☐ Chronic gout refractory to conventional therapy (i.e. xanthine oxidase inhibitors)

☐ Other (please state): _____

Clinical Consideration (for approval, please indicate and provide documentation of the following):

☐ Initial Request (approval is granted for 4 months)

- ☐ Failure of conventional therapy (*defined as failure to normalize serum uric acid (<6 mg/dL) plus inadequate clinical response in spite of treatment with allopurinol AND febuxostat (Uloric®) at the maximum medically appropriate dose for at least three months)*
- ☐ Patient has documented intolerance to xanthine oxidase inhibitor therapy (allopurinol and febuxostat)
- ☐ One or more of the following criteria must be met *(indicate all that apply)*:
  - ☐ Three or more gout flares within the previous 18 months
  - ☐ One or more tophi
  - ☐ Gouty arthropathy
- ☐ Baseline serum UA is 8.0 mg/dL or greater

☐ Continued Approval Request

- ☐ Uric acid levels **consistently LESS than 6mg/dL**
- ☐ Course of disease significantly improved (i.e. resolution of symptoms or tophi)
- ☐ Greater than 4 weeks has not lapsed since the last IV infusion of Krystexxa®

Physician Specialty (diagnosis made by)

☐ Rheumatologist
☐ Nephrologist
☐ Other (please state): _____

☐ For use in clinical trial? (If yes, provide trial name and registration number):

Drug Name (Brand Name and Scientific Name)/Strength:

Dose:	Route:	Frequency:
Quantity:	Number of Refills:	

Product will be delivered to: ☐ Patient's Home ☐ Physician Office Other:

Prescriber or Authorized Signature: Date:

Dispensing Pharmacy Name and Phone Number:

☐ **Approved** ☐ **Denied**

If denied, provide reason for denial, and include other potential alternative medications, if applicable, that are found in the formulary of the carrier:

1. Appeal/redetermination requests can be made for this medication within 60 calendar days from the date on the faxed/written denial notice you received at the time of the original request.

2. A request for prior authorization that if determined in the time allowed for non-urgent requests could seriously jeopardize the life or health of the covered person or the ability of the covered person to regain maximum function, or subject the person to severe pain that cannot be adequately managed without the drug benefit contained in the prior authorization request.

Krystexxa® (pegloticase)

CLASSIFICATION

- Anti-gout, Enzyme

DESCRIPTION

- Pegloticase is a uric acid specific enzyme that consists of recombinant, modified, mammalian urate oxidase made with a genetically modified Escherichia coli strain that is then covalently conjugated to monomethoxypolyethylene glycol (mPEG). It achieves its therapeutic effect by catalyzing the oxidation of uric acid to allantoin, which is readily eliminated primarily by renal excretions, resulting in the lowering of serum uric acid.
- It is indicated for the treatment of chronic gout in adult patients refractory to conventional therapy (i.e. xanthine oxidase inhibitors). It is not recommended for the treatment of asymptomatic hyperuricemia.
- Two replicate, 6 month, randomized, double-blind, placebo-controlled trials (n=225) were conducted at 56 rheumatology practices in the US, Canada, and Mexico, in patients with severe gout (symptomatic and at least 3 flares in the previous 18 months or at least one gout tophus or gouty arthritis), allopurinol intolerance or refractoriness, and serum uric acid concentration ≥ 8mg/dL. The mean baseline serum uric acid was 10 mg/dL and 71% of participants had baseline tophi. During months 3 and 6, the percentage of patients achieving serum uric acid (SUA) levels <6 mg/dL for at least 80% of the time (primary outcome) was significantly greater in the patients treated with pegloticase 8 mg every 2 weeks (47% in trial 1 (95% CI, 31% to 62%; p <0.001 for both) and 38% in trial 2 (95% CI, 24% to 54%; p <0.001 for both)) compared with placebo (0% of patients in both trials). Pegloticase 8 mg every 4 weeks demonstrated efficacy (response rates of 20% (p<0.04) and 49% (p<0.001) for trial 1 and 2, respectively); however, this regimen was associated with an increased frequency of anaphylaxis and infusion reactions. Infusion-related reactions were reported in 26%, 42%, and 5% of patients in the pegloticase biweekly, pegloticase monthly, and placebo groups, respectively. Posthoc analysis revealed that most infusion reactions (79%) were associated with a loss of response to pegloticase.
- Treatment on tophi was assessed as a secondary outcome. Complete response, defined as 100% resolution of at least one target tophus, no new tophi appearing, and no single tophus showing progression, was achieved in 45%, 26%, and 8% of patients in the pegloticase biweekly, pegloticase monthly, and placebo groups, respectively (p=0.002 and p=0.2, respectively).
- Within 24 hours following the first dose of Krystexxa®, the mean uric acid levels were 0.7mg/dL compared to 8.2mg/dL with placebo. This initial response does not necessarily predict whether or not the patient will be a responder.
- Serum uric acid monitoring serves as a marker for both efficacy and safety, generally known within 4 months.
- Two consecutive uric acid levels >6mg/dL indicate loss of therapeutic response with Krystexxa and increase the risk of anaphylaxis and infusion reactions due to development of antibodies against Krystexxa®.
- Anti-pegloticase antibodies developed in 92% of patients treated with Krystexxa® compared to 28% for those treated with placebo. High anti-pegloticase antibody titer was associated with a failure to maintain pegloticase-induced normalization of uric acid.
- Adverse events occurring in at least 5% of patients treated with Krystexxa® are gout flares, infusion reactions, nausea, contusion or ecchymosis, nasopharyngitis, constipation, chest pain, anaphylaxis and vomiting.
- Krystexxa® concentrations are expressed as concentrations of uricase protein. Each mL of Krystexxa contains 8mg of uricase protein.

FORMULARY COVERAGE

Prior authorization: Required
Good Health Formulary: Tier 6
Commercial Formulary: Tier 6
Medicare Part D coverage: Tier 5

COVERAGE CRITERIA

Krystexxa® (pegloticase) meets the definition of **medical necessity** for the following:

Chronic gout refractory to conventional therapy (i.e. xanthine oxidase inhibitors).

- Failure of conventional therapy *defined as failure to normalized serum uric acid (<6mg/dL) plus inadequate clinical response in spite of treatment with allopurinol AND febuxostat (Uloric®) at the maximum medically appropriate dose for at least three months;* OR
- Patient has documented intolerance to xanthine oxidase inhibitor therapy (allopurinol and febuxostat). This may include allergic reaction, toxicity, intolerance, drug interaction, or severe renal dysfunction (allopurinol only).
- Additionally, one or more of the following criteria must be met:
  - Three or more gout flares within the previous 18 months; OR
  - One or more tophi; OR
  - Gouty arthropathy
- Baseline serum UA is 8.0mg/dL or greater.
- Krystexxa will be administered in a healthcare setting by healthcare providers who are prepared to manage anaphylaxis and infusion reactions.
- Uric acid levels will be monitored prior to each infusion.
  - Two consecutive uric acid levels >6mg/dL indicate loss of therapeutic response with Krystexxa and increases the risk of anaphylaxis and infusion reactions due to development of antibodies against Krystexxa®. Treatment should be discontinued.
- Patient will be screened for glucose 6-phosphate dehydrogenase (G6PD) deficiency due to risk of hemolysis and methemoglobinemia. Documentation of negative results required for high risk individuals (i.e. African or Mediterranean ancestry).

Providing coverage criteria are met, initial approval will be for 4 months (8 treatments). Continued approval will require documentation of 2 or more uric acid levels <6mg/dL and clinical notes indicating course of disease is significantly improved.

Krystexxa® (pegloticase) is considered **experimental** for the following:

- Any condition or diagnosis not FDA approved or Compendia supported
  - Use is not recommended for the treatment of asymptomatic hyperuricemia
  - Safety and efficacy of pegloticase in the treatment of chemotherapy-induced hyperuricemia is unknown

Required Provider Specialty:

- Approval is limited to Rheumatology and Nephrology

DOSAGE/ADMINISTRATION

Note: Krystexxa® should be administered in a healthcare setting by healthcare providers who are prepared to manage anaphylaxis and infusion reactions.

Adult Dosing (safety and efficacy has not been determined for pediatric patients less than 18 years):

- Gout, refractory to conventional therapy: 8mg IV infusion over no less than 120 minutes via gravity feed, syringe-type pump, or infusion pump, every 2 weeks.
- Premedicate with antihistamines and corticosteroids
    - Premedication in clinical trials consisted of: fexofenadine 60mg PO the evening before and again before infusion; acetaminophen 1000mg the morning of infusion; and hydrocortisone 200mg IV immediately before infusion.
- Gout flare prophylaxis with an NSAID or colchicines should be started one week before initiation of Krystexxa® therapy.
- Dose adjustment not necessary for renal impairment.

PRECAUTIONS

Black Box Warning:

- Anaphylaxis and infusion reactions have been reported to occur during and after administration of pegloticase. 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 pegloticase. Monitor serum uric acid levels prior to infusions. The risk of anaphylaxis and infusion reactions is higher in patients whose uric acid level increases to above 6mg/dL, particularly when 2 consecutive levels above 6 mg/dL are observed.

Contraindications:

- Glucose-6-phosphate dehydrogenase (G6PD) deficiency; risk of hemolysis and methemoglobinemia

Precautions:

- Anaphylaxis (e.g. wheezing, perioral or lingual edema, or hemodynamic instability, with or without urticaria or rash), immediate (within 2 hours) or delayed, have been reported in patients, including patients who received pretreatment with oral antihistamine, IV corticosteroid, and/or acetaminophen; it may occur with any pegloticase infusion, including the first infusion; monitoring recommended
- Infusion reactions (e.g. urticaria, dyspnea, chest discomfort, chest pain, erythema and pruritus), at any time during the course of treatment, have been reported in patients who received pretreatment with oral antihistamine, IV corticosteroid, and/or acetaminophen; monitoring recommended and rate adjustment or discontinuation of infusion may be necessary
- Congestive heart failure exacerbations occurred in clinical trials; use caution and monitor closely following infusion
- Re-treatment after a drug-free interval of more then 4 weeks may increase the risk of anaphylaxis and infusion reactions due to immunogenicity; monitoring recommended
- Increase gout flares are frequently observed (up to 80% of Krystexxa® treated patients) upon initiation of anti-hyperuricemic therapy, due to changing serum uric acid levels resulting in mobilization of urate from tissue deposits. Prophylaxis recommended. Start one week prior to start of therapy and continue for at least 6 months. Flares taper off with continued therapy in responders.

Billing/Coding information

HCPCS Coding:

J2507	Injection, pegloticase, 1mg (for billing prior to 1/1/12 use J3590 or C9281)

COST

- AWP (January 2012): Krystexxa® 8mg IV (1 vial): $2,760.00

COMMITTEE APPROVAL

- January 2012

GUIDELINE UPDATE INFORMATION

January 2012	Medical Policy created

REFERENCES

- DRUGDEX®, accessed 01/15/12.
- Product Information: Krystexxa® (pegloticase), Injection, for intravenous infusion. Savient Pharmaceuticals, Inc., East Brunswick, NJ, 2010.
- 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.