CLINICAL POLICY	
Department: Medical Management	**Document Name:** Krystexxa®
Page: 1 of 6	**Reference Number:** NH.PHAR.115
Effective Date: 06/13	**Replaces Document:**
Retired:	**Reviewed:** 08/16, 07/17
Specialist Review: No	**Revised:** 06/14
Product Type: All	**Committee Approval:** 06/13, 06/14

IMPORTANT REMINDER

This Clinical Policy has been developed by appropriately experienced and licensed health care professionals based on a thorough review and consideration of generally accepted standards of medical practice, peer-reviewed medical literature, government agency/program approval status, and other indicia of medical necessity.

The purpose of this Clinical Policy is to provide a guide to medical necessity. Benefit determinations should be based in all cases on the applicable contract provisions governing plan benefits ("Benefit Plan Contract") and applicable state and federal requirements, as well as applicable plan-level administrative policies and procedures. To the extent there are any conflicts between this Clinical Policy and the Benefit Plan Contract provisions, the Benefit Plan Contract provisions will control.

Clinical policies are intended to be reflective of current scientific research and clinical thinking. This Clinical Policy is not intended to dictate to providers how to practice medicine, nor does it constitute a contract or guarantee regarding payment or results. Providers are expected to exercise professional medical judgment in providing the most appropriate care, and are solely responsible for the medical advice and treatment of members.

Subject

Medical necessity criteria for the approval of Krystexxa® (pegloticase)

Description

The intent of the criteria is to ensure that patients follow selection elements established by Centene® medical policy.

Table 1. Krystexxa Indication[1,2]

Medication	Generic Name	FDA-Approved Indication
Krystexxa®	pegloticase	Treatment of chronic gout in adult patients refractory to conventional therapy

Management Challenge

Gout is a painful and potentially disabling form of arthritis.[3] The initial symptoms usually include intense episodes of painful swelling in a single joint, most often in the feet (especially the big toe).[3] Gout is a major health problem in the United States that affects 8.3 million people.[4] Despite a good understanding of its pathogenesis and the availability of effective treatment, gout is often misdiagnosed or the diagnosis is delayed, and even when correctly diagnosed, treatment is often suboptimal.[5] The prevalence of gout increases with age and is more common in men than women.[6]

The rising incidence and prevalence of gout are likely due to the aging population, increasing levels of obesity, and changes in diet.[6]

Policy/Criteria

It is the policy of Health Plans affiliated with Centene Corporation® that Krystexxa is **medically necessary** for members when meeting the following algorithm criteria:

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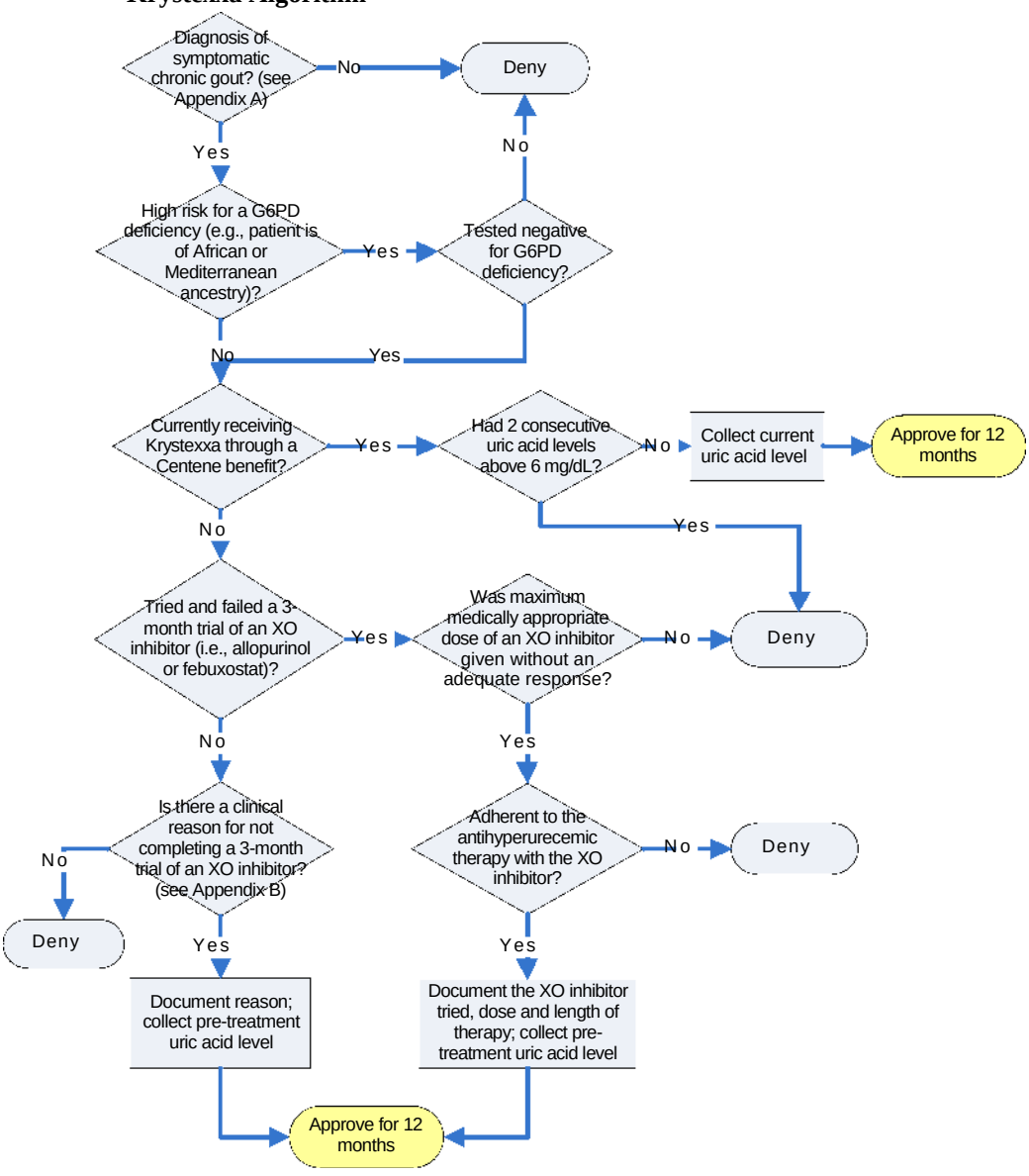
Krystexxa Algorithm



Background

Gout can present in different clinical phases: acute gout, intercritical gout (ie, intervals between attacks), or advanced gout (ie, chronic tophaceous gout).[4] Chronic tophaceous gout often involves polyarticular attacks, symptoms between attacks, and crystal deposition (tophi) in soft tissues or joints.[6] Gout is diagnosed by the presence of urate crystals in the synovial fluid or in a tophus by

polarized light microscopy.[7] Hyperuricemia (uric acid level greater than 6.8 mg/dL) is the single most important risk factor for the development of gout.[6,7] Uric acid is poorly soluble at serum concentrations greater than 6.8 mg/dL.[8] The reduction of serum uric acid levels below the saturation point for monosodium urate (≤ 6 mg/dL) can prevent urate crystal formation and enhance crystal dissolution.[5,6] The goal is to prevent acute gout attacks, tophus formation and tissue damage.[7]

Optimal treatment of gout requires both nonpharmacologic and pharmacological modalities.[4,5] Therapy should be tailored to specific risk factors (urate levels, previous attacks, radiographic signs), clinical phase, and general risk factors (age, sex, obesity, alcohol consumption, urate-raising drugs, drug interactions, and comorbidity).[4,5] Non-pharmacologic measures should be started in every patient.[4,5] Urate-lowering pharmacologic therapy can be considered for patients who have recurrent attacks (more than one attack in a given year), chronic arthropathy, tophi, nephrolithiasis, or radiographic changes of gout.[4]

There are three classes of uric acid-lowering agents for the treatment of chronic gout: xanthine oxidase inhibitors, uricosuric agents, and uricase agents.[6] The use of uric acid-lowering therapy may precipitate a gout attack, and initiation of therapy should be delayed for one to two weeks after inflammation from an acute attack has settled.[7] Prophylaxis of acute attacks with colchicine or nonsteroidal anti-inflammatory drugs can be given for the first months of urate-lowering therapy.[5] Initial treatment with allopurinol is appropriate for long-term urate-lowering therapy.[5,7] Other xanthine oxidase inhibitors (e.g., Uloric [febuxostat]), a uricosuric agent such as probenecid, or allopurinol desensitization (in cases of mild rash) can be considered if allopurinol toxicity occurs.[5]

Refractory gout occurs in patients with recurrent gout flares, progressive tophaceous deposits, chronic arthritis, and when target urate concentrations cannot be achieved.[8] A patient with treatment-failure gout may experience chronic joint pain and swelling, impaired function, chronic pain, and reduced quality of life.[8] Krystexxa is indicated for the treatment of chronic gout in adult patients refractory to conventional therapy.[1] Krystexxa is a PEGylated uricase agent that catalyzes the oxidation of uric acid to allantoin.[1] Allantoin is more water-soluble and more readily eliminated from the body than urate.[9] Krystexxa is administered by intravenous infusion and has a significant risk profile.[4] Potential candidates should be referred to health care professionals with expertise in the use of Krystexxa.[4]

Safety

A major component of this policy for the use of Krystexxa is to ensure necessary safety concerns are addressed prior to initiating therapy. Information from the product labeling, FDA MedWatches, and primary literature are considered. For a summary of safety concerns, refer to Table 2.

Table 2. Safety Concerns for Krystexxa[1]

Safety Parameters
Anaphylaxis and infusions reactions (boxed warning)
Caution in congestive heart failure
Contraindicated in patients with G6PD deficiency due to risk of hemolysis and methemoglobinemia
~~Gout flares during initiation of treatment~~

Abbreviations

G6PD: glucose-6-phosphate dehydrogenase
NSAID: non-steroidal anti-inflammatory drug
XO: xanthine oxidase

Appendices

Appendix A: Clinical Features of Chronic Gout[5]

- Tophi
- Gouty arthropathy
- Radiographic changes of gout
- Multiple joint involvement
- Associated uric acid nephrolithiasis

Appendix B: Clinical Reasons for Not Completing a 3 Month Trial of a Xanthine Oxidase Inhibitor[2,5,7]

- Patient experienced a severe allergic reaction to the agent
- Patient experienced toxicity with or could not tolerate the agent
- Significant drug interaction
- Severe renal dysfunction (for allopurinol only)

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Revision Log	Date
Simplified medical necessity algorithm by removing monitoring questions related to administration of the drug	06/14
Changed approval time frame from 6 months to 12 months	07/15
Annual Review. No Changes	08/16
Annual Review. No Changes	07/17