Formulary Review: Krystexxa®
Generic Name: Pegloticase
Manufacturer: Savient Pharmaceuticals.
Prepared by: University of Utah Drug Information Services
Updated by: Brandi C. LaFrance, PharmD, BCPS

Executive Summary

Introduction

Pegloticase is a pegylated urate oxidase enzyme labeled for treating adult patients with chronic gout uncontrolled by xanthine oxidase inhibitors, or patients with contraindications to xanthine oxidase inhibitors. It is not labeled for treating asymptomatic hyperuricemia. Pegloticase has not been studied in pediatric patients and patients with renal and/or hepatic impairment.

Pharmacology/Pharmacokinetics

Pegloticase oxidizes uric acid formic allantoin, thereby decreasing serum uric acid levels. Allantoin is an inactive metabolite that is readily excreted by the kidneys. Pegloticase plasma concentrations and area under the curve (AUC) increase proportionate to the administered dose. Pegloticase has a plasma half-life of 12.5 ± 0.9 days at the labeled dose.

Clinical Efficacy

A single published dose-finding study examined pegloticase for treating patients with gout unresponsive to conventional therapy. The primary outcome, maintaining plasma uric acid levels ≤ 6mg/dL during 80% of the treatment period, was achieved in 87.5% of patients receiving the labeled dose of pegloticase. In pegloticase responders, serum urate concentrations fell to ≤ 6mg/dL within 6 hours of administration.

Two identical, experimental placebo-controlled trials evaluating the efficacy of pegloticase are reported in the product labeling. The primary endpoint was defined as maintaining plasma uric acid concentrations <6mg/dL during 80% of the third and sixth months of treatment. The primary endpoint was achieved for the labeled pegloticase dose in 47% (trial 1) and 38% (trial 2) of patients, compared to no patients in the placebo groups ($p<0.001$ in each trial).

Adverse Drug Reactions

The most common adverse event with pegloticase is gout flare. Gout flare occurred during the first 3 months of therapy in 74% of patients receiving pegloticase, compared to 51% of patients receiving placebo. Infusion reactions (26%) and anaphylaxis (6.5%) are also common despite pre-treatment with an antihistamine and a corticosteroid with or without acetaminophen. Pegloticase has a ***black boxed warning*** for anaphylaxis and infusion reactions. Pegloticase is contraindicated in glucose-6-phosphate dehydrogenase (G6PD) deficient patients.

Drug Interactions

No formal drug-drug interaction studies have been conducted.

Dosage and Administration

Pegloticase is administered as 8mg intravenously every 2 weeks, infused over at least 120 minutes. Pegloticase must be administered in a healthcare setting prepared for treating anaphylaxis. Patients must be monitored throughout the infusion and for at least 1 hour after the infusion is complete. Monitor serum uric acid concentrations prior to each pegloticase infusion because patients with urate levels >6mg/dL despite pegloticase treatment are at a higher risk for anaphylaxis and infusion reactions.

Summary

Pegloticase is a pegylated enzyme approved for treating adult patients with unmanageable chronic gout despite conventional therapy with xanthine oxidase inhibitors. To date, pegloticase has not been compared to other anti-gout agents. Pegloticase decreases urate levels and contributes to resolution and prevention of tophi in patients with gout.

Cost

$2800/8mg vial ($5600/month)

Look-alike/sound-alike potential

None at this time

Status

Formulary; restricted to use in the outpatient setting