ATTACHMENT C: JOURNAL INFORMATION PIECE

Important Information on the Safe Use of KRYSTEXXA® (pegloticase)

Osaka Pharmaceuticals LLC is providing this Important Information on the Safe Use of KRYSTEXXA® (pegloticase) as part of our commitment to the safe and appropriate use of KRYSTEXXA.

KRYSTEXXA is a Fc-glylated uric acid specific enzyme for administration by intravenous infusion for the treatment of chronic gout in adult patients refractory to conventional therapy.

Decision to use KRYSTEXXA must balance the potential benefits with the potential risks of therapy based upon your patient’s individual needs. Please review the key safety information below and the product labeling carefully before initiating therapy.

The US Food and Drug Administration (FDA) has approved KRYSTEXXA with a Risk Evaluation and Mitigation Strategy (REMS) to ensure the benefits of the drug outweigh the risks of anaphylaxis and infusion reactions and contraindication of use of KRYSTEXXA in patients with glucose-6-phosphate dehydrogenase (G6PD) deficiency.

WARNING: ANAPHYLAXIS AND INFUSION REACTIONS

- Anaphylaxis and infusion reactions have been reported to occur during and after administration of KRYSTEXXA.
- 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.
- KRYSTEXXA should be administered in healthcare settings and by healthcare providers prepared to manage anaphylaxis and infusion reactions.
- Patients should be premedicated with antihistamines and corticosteroids.
- Patients should be closely monitored for an appropriate period of time for anaphylaxis after administration of KRYSTEXXA.
- 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.

Anaphylaxis

Intavenous administration of KRYSTEXXA may result in infusion reactions, including anaphylaxis or other hypersensitivity reactions. Anaphylaxis was reported in 6-5% of patients administered KRYSTEXXA during premarketing clinical trials. All patients received premedication.

Infusion Reactions

Infusion reactions were reported in 26% of patients administered KRYSTEXXA every 2 weeks during premarketing clinical trials compared to 5% of patients treated with placebo. All patients received pre-medication. The most common reported signs and symptoms included urticaria (11%), dyspnea (7%), erythema (6%), and flushing (6%). The risk of infusion reaction is higher in patients who have lost therapeutic response.

Concomitant Use with Urate-lowering Agents

Concomitant use of KRYSTEXXA with oral urate-lowering therapies, including allopurinol and febuxostat, may prevent the detection of patients who have lost therapeutic response to KRYSTEXXA and increase the risk of infusion reactions and/or anaphylaxis. It is therefore recommended that before starting KRYSTEXXA patients discontinue oral urate-lowering medications and not institute therapy with oral urate-lowering agents while taking KRYSTEXXA.

Key Aspects of Recommended Management:

- Discontinue oral urate-lowering therapies before instituting KRYSTEXXA and do not institute oral urate-lowering therapy while the patient is on KRYSTEXXA therapy.
- Infusion reactions
  - Patients should receive pre-treatment medication prior to each infusion to minimize the risk of infusion reactions, including anaphylaxis.
  - Administer KRYSTEXXA in a healthcare setting prepared to manage anaphylaxis.
  - Observe patients for an appropriate period of time after administration.
- Serum uric acid
  - Monitor serum uric acid levels prior to infusions and consider discontinuing treatment if levels increase to above 6 mg/dL, particularly when 2 consecutive values above 6 mg/dL are observed.

Contraindication in Patients with G6PD Deficiency

Use of KRYSTEXXA is contraindicated in patients with G6PD deficiency due to the risk of hemolysis and methemoglobinemia. It is recommended that patients at higher risk for G6PD deficiency (e.g., patients of African or Mediterranean ancestry) be screened for G6PD deficiency prior to starting KRYSTEXXA.

Additional information: gout refractory to conventional therapy occurs in patients 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.

If you have any questions regarding KRYSTEXXA please contact Creatax Pharmaceuticals LLC Medical Information at 1-888-KRYSTEXXA (1-888-597-8639).