### INFUSION REACTION PROPHYLAXIS

Individual physician orders may vary.

<table>
<thead>
<tr>
<th><strong>PREINFUSION MEDICATIONS</strong>¹</th>
<th><strong>CLASS</strong></th>
<th><strong>DRUG(S)</strong></th>
<th><strong>DOsing</strong></th>
<th><strong>TIMING IN RELATION TO INFUSION</strong></th>
</tr>
</thead>
<tbody>
<tr>
<td>IV corticosteroids*†</td>
<td>Methylprednisolone, hydrocortisone, Other:__________</td>
<td>Prior to each infusion</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Antihistamines*†</td>
<td>Allegra® (fexofenadine), Claritin® (loratadine), Benadryl® (diphenhydramine)</td>
<td>Dose determined by healthcare provider</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Oral analgesic*†</td>
<td>Tylenol® (acetaminophen)</td>
<td>Night before infusion, and/or can administer concomitantly with infusion</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

*To be given to the patient by nurse on day of infusion.
†Infusion reactions may occur despite pretreatment.

### GOUT FLARE PROPHYLAXIS

Because all patients taking KRYSTEXXA experience an initial drop in serum uric acid, it is recommended to take steps to proactively manage gout flares.¹‡

<table>
<thead>
<tr>
<th><strong>CLASS</strong></th>
<th><strong>DRUG(S)</strong></th>
<th><strong>DOsing</strong></th>
<th><strong>TIMING IN RELATION TO INFUSION</strong></th>
</tr>
</thead>
<tbody>
<tr>
<td>Anti–gout flare agent</td>
<td>Colcrys® (colchicine)</td>
<td>Daily, treatment initiated 1 week prior to initiation of KRYSTEXXA and lasting at least 6 months, unless medically contraindicated or not tolerated</td>
<td></td>
</tr>
<tr>
<td>Oral NSAIDs</td>
<td>Advil®, Aleve®</td>
<td>Patient may take any one of these drugs, as indicated</td>
<td></td>
</tr>
<tr>
<td>Corticosteroids</td>
<td>Prednisone, prednisolone</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

NSAIDs=nonsteroidal anti-inflammatory drugs.
‡Patients may still experience flares despite flare prophylaxis.

The drop in uric acid causes mobilization of uric acid crystals from stores in the body. Gout flares can be a sign that KRYSTEXXA is working to lower the uric acid in the blood.¹
INDICATION AND IMPORTANT SAFETY INFORMATION

INDICATIONS AND USAGE
KRYSTEXXA® (pegloticase) is indicated for the treatment of chronic gout in adult 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.

Important Limitations of Use: KRYSTEXXA is not recommended for the treatment of asymptomatic hyperuricemia.

IMPORTANT SAFETY INFORMATION

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.

The risk of anaphylaxis and infusion reactions is higher in patients who have lost therapeutic response. Concomitant use of KRYSTEXXA and oral urate-lowering agents may blunt the rise of sUA levels. Patients should discontinue oral urate-lowering agents and not institute therapy with oral urate-lowering agents while taking KRYSTEXXA.

In the event of anaphylaxis or infusion reaction, the infusion should be slowed, or stopped and restarted at a slower rate. Inform patients of the symptoms and signs of anaphylaxis, and instruct them to seek immediate medical care should anaphylaxis occur after discharge from the healthcare setting.

CONTRAINDICATIONS: G6PD DEFICIENCY ASSOCIATED HEMOLYSIS AND METHEMOGLOBINEMIA

Screen patients for G6PD deficiency prior to starting KRYSTEXXA. Hemolysis and methemoglobinemia have been reported with KRYSTEXXA in patients with G6PD deficiency. Do not administer KRYSTEXXA to these patients.

GOUT FLARES

An increase in gout flares is frequently observed upon initiation of anti-hyperuricemic therapy, including treatment with KRYSTEXXA. If a gout flare occurs during treatment, KRYSTEXXA need not be discontinued. Gout flare prophylaxis with a non-steroidal anti-inflammatory drug (NSAID) or colchicine is recommended starting at least 1 week before initiation of KRYSTEXXA therapy and lasting at least 6 months, unless medically contraindicated or not tolerated.

CONGESTIVE HEART FAILURE

KRYSTEXXA has not been studied in patients with congestive heart failure, but some patients in the clinical trials experienced exacerbation. Exercise caution when using KRYSTEXXA in patients who have congestive heart failure and monitor patients closely following infusion.

ADVERSE REACTIONS

The most commonly reported adverse reactions in clinical trials with KRYSTEXXA are gout flares, infusion reactions, nausea, contusion or ecchymosis, nasopharyngitis, constipation, chest pain, anaphylaxis and vomiting.

To report SUSPECTED ADVERSE REACTIONS, contact Horizon Pharma Rheumatology LLC at 1-866-479-6742 or the FDA at 1-800-FDA-1088 or www.fda.gov/medwatch.

Please see Full Prescribing Information, including Boxed Warning.

Reference: 1. KRYSTEXXA [prescribing information]. Horizon Pharma Rheumatology LLC.

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