RISK EVALUATION AND MITIGATION STRATEGY (REMS)

I. GOALS:
The goal of the KRYSTEXXA Risk Evaluation and Mitigation Strategy (REMS) is:

- To inform healthcare providers about anaphylaxis, infusion reactions, and contraindication of use of KRYSTEXXA in patients with glucose 6-phosphate dehydrogenase (G6PD) deficiency.

II. REMS ELEMENTS:

A. Communication Plan

Crealta Pharmaceuticals LLC (Crealta) will implement a communication plan to healthcare providers to support implementation of this REMS.

Crealta Pharmaceuticals LLC (Crealta) will implement a communication plan for healthcare providers who are expected to be the predominant clinicians who prescribe, administer and dispense KRYSTEXXA.

The communication plan will disseminate risk information about anaphylaxis and infusion reactions, including increased risk of anaphylaxis and infusion reactions with concomitant use of KRYSTEXXA and oral urate-lowering therapy, and the contraindication of use of KRYSTEXXA in patients with glucose 6-phosphate dehydrogenase (G6PD) deficiency.

Elements of the communication plan are:

1. A Dear Healthcare Provider/ Dear Infusion Site Medical Personnel Letter (DHCP/DISMP) (see Attachment A) will be distributed by Crealta representatives at least once between September 14, 2013 and September 14, 2014, to rheumatologist offices and infusion sites where KRYSTEXXA may be prescribed, administered and dispensed.

New healthcare prescribers and infusion site customers purchasing KRYSTEXXA from Distributors or Pharmacies will also receive the DHCP/DISMP Letter and the approved Prescribing Information. Between the date of approval of the 2013 REMS modification and September 14, 2014, Crealta will mail the DHCP/DISMP letter within one month of each initial shipment of KRYSTEXXA. New prescribers and infusion site customers will be identified using the sales and distributor databases.

The approved Prescribing Information, which includes the Medication Guide, will also be distributed with this letter.
2. Crealta will distribute the DHCP/DISMP Letter with Prescribing Information, which includes the Medication Guide, at the American College of Rheumatology Annual Meeting for an additional year (2014 Annual Meetings).

3. The DHCP/DISMP Letter will also be available through a REMS-dedicated link from the www.KRYSTEXXA.com website (See attached web page in Attachment B). Only FDA approved materials will be included on the REMS dedicated website. This REMS-dedicated link will exist throughout the 7 year time period. The KRYSTEXXA REMS webpage will also be accessible through a search engine.

4. Crealta will publish journal information pieces about risks of anaphylaxis, infusion reactions, including increased risk of anaphylaxis and infusion reactions with concomitant use of KRYSTEXXA and oral urate-lowering therapy, and the contraindicated use of KRYSTEXXA in patients with glucose 6-phosphate dehydrogenase (G6PD) deficiency, with key aspects of management. These announcements will appear in the following professional societies’ journals: American College of Rheumatology and the Infusion Nurses Society.
   - Arthritis and Rheumatism – Official monthly journal of the American College of Rheumatology.
   - Journal of Infusion Nursing – Official bi-monthly journal of the Infusion Nurses Society

   These announcements will be published in the fourth year after product approval (September 14, 2013 to September 14, 2014). (See Attachment C)

B. Timetable for Submission of Assessments

Crealta will submit REMS Assessments to the FDA at 1 year, 2 years, 3 years, 5 years and 7 years from the date of the approval of the REMS (September 14, 2010).

To facilitate inclusion of as much information as possible while allowing reasonable time to prepare the submission, the reporting interval covered by each assessment should conclude no earlier than 60 days before the submission date for that assessment. Crealta will submit each assessment so that it will be received by the FDA by the due date (14 September).