

**Food and Drug Administration**  
**Center for Drug Evaluation and Research**  
**Oncologic Drugs Advisory Committee (ODAC) Meeting**  
FDA White Oak Campus, Building 31, the Great Room, White Oak Conference Center  
(Rm. 1503), Silver Spring, MD

September 14, 2011

**QUESTION**

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**NDA 021825**  
**Ferriprox (deferiprone) film-coated tablets**

**APPLICANT: ApoPharma, Inc.**  
**represented by Cato Research Ltd.**  
(authorized U.S. agent)

**PROPOSED INDICATION:** for the treatment of patients with transfusional iron overload when current chelation therapy is inadequate

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Patients with some inherited anemias, most notably  $\beta$ -thalassemia, require chronic red blood cell transfusions for their disease and consequently develop iron overload (transfusional hemosiderosis). The iron deposits in tissues, mainly heart and liver, and results in morbidity and mortality. Iron chelation therapy (with deferoxamine) to remove iron from the body improves survival in these patients. ApoPharma (a division of Apotex, Inc) has submitted a New Drug Application (NDA) for deferiprone for the treatment of patients with transfusional iron overload when current chelation therapy is inadequate. Deferiprone has been marketed in the European Union (EU) (since 1999) and other countries for a similar indication.

In support of its application, the applicant provided the report and data from a single, retrospective, uncontrolled, multi-institutional study (LA36-0310) entitled "Analysis of Data from Clinical Studies of Ferriprox to Evaluate its Efficacy in Patients with Iron Overload for Whom Previous Chelation Therapy Has Been Inadequate". The study selected from the total clinical trial database for deferiprone those patients who had failed prior treatment with an iron chelator as assessed based on (1) serum ferritin >2500  $\mu\text{g/L}$ , (2) liver iron concentration (LIC) >7 g iron/g dry weight and/or (3) cardiac MRI T2\* value <20 milliseconds [taken as reflecting elevated cardiac iron content]. This retrospective, non-randomized study showed that over a treatment period of up to 1 year (76% of patients 6 months or longer; 27% of patients, 1 year or longer) 52% of study patients had a 20% or greater decrease in serum ferritin, consistent with a decrease in body iron load. LIC in the study patients evaluable for that parameter also declined and Cardiac MRI T2\* change was in a direction consistent with a beneficial effect of deferiprone. The major safety concern identified was agranulocytosis which occurred in 1.7% of patients in the clinical studies. While agranulocytosis is generally reversible with deferiprone discontinuation, there have been deaths in the post-EU approval marketing experience.

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**QUESTION (cont.)**

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1. **VOTE:** Is there a favorable benefit/risk profile for deferiprone in the treatment of patients in whom current chelation therapy is inadequate?