CENTER FOR DRUG EVALUATION AND RESEARCH

APPLICATION NUMBER:

021825Orig1s000

CHEMISTRY REVIEW(S)

ONDQA Division Director's Memo
NDA 21825, FERRIPROX (deferiprone) tablets, 500 mg
Date: 12-OCT-2011

Introduction

FERRIPROX (deferiprone) tablets are immediate-release, film-coated tablets supplied in one strength (500 mg). FERRIPROX is indicated for the treatment of patients with excessive body iron stores due to chronic transfusion therapy. The dose is 25-33 mg/kg body weight, taken orally three times daily for a total dose of 75-(b) (4) mg/kg body weight. The maximum safe dose is (b) (4) mg/kg body weight/day.

ONDQA recommends approval of this NDA. There are no outstanding CMC deficiencies for this NDA.

Administrative

The current submission is a Class 2 Resubmission to the Agency's 30-NOV-2009 Complete Response action. The Chemistry, Manufacturing and Controls assessment for the current cycle is captured in Chemistry Review #3 (dated 26-SEP-2011), the ONDQA Biopharmaceutics Review (dated 16-SEP-2011), and the ONDQA Biopharmaceutics Memorandum (25-SEP-2011). Primary CMC review of drug substance and drug product information, as well as biopharmaceutics information, confirm an approval recommendation, and all primary reviews confirm that there are no outstanding CMC deficiencies.

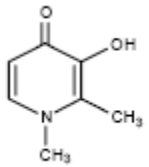
At the time of primary review completion, an overall recommendation from the Office of Compliance was still pending. An overall acceptable recommendation was issued by the Office of Compliance on 07-OCT-2011. This pending issue is now resolved.

This NDA is recommended for approval from a Chemistry, Manufacturing and Controls standpoint.

Insert the following language into the approval letter: "Based on the stability data provided in your application, the drug product is granted a 24-month expiry when stored at USP controlled room temperature 20-25ºC (68-77ºF); excursions permitted to 15-30ºC (59-86ºF)."

Drug Substance (Deferiprone)

Chemical Name: 1,2-dimethyl-3-hydroxypyrid-4-one



Deferiprone is a new chemical entity. Deferiprone is a bidentate iron chelator that preferentially binds ferric ions into a 3:1 (deferiprone: iron) complex at low pH. Bulk drug substance is a white to pink crystalline powder. (b) (4) Deferiprone is highly soluble in water at pH 1-7.5 and has high permeability, thus is a BCS class 1 drug. Structural elucidation studies show the material is prepared (b) (4) .

Manufacture is by a (b) (4) . Manufacture and control of bulk process at each proposed site is described in Apotex, Inc.'s type II DM 10867. During the CMC review, the DMF was reviewed and was found adequate to support approval of this application.

The CMC review grants a re-test period of (b) (4) for the Apotex Pharmachem and (b) (4) sites, and a retest period of (b) (4) for the (b) (4) site when stored under controlled room temperature. This is in agreement with what the Applicant proposes, and not additional action is needed.

Drug Product (Deferiprone Tablets, 500 mg)

The drug product is a scored tablet manufactured (b) (4) . All excipients used in the formulation are compendial and are conventional for solid oral dosage forms. The release specification includes testing for identity, average tablet weight, dissolution, content uniformity/assay, and degradants (unspecified and total). The CMC review confirms that the tests are adequate to establish identify, purity and strength of the drug product. The methods for assay and related substances were revised after NDA submission. Descriptions of the analytical methods are complete and provided in sufficient detail. Representative spectra and chromatograms have been provided. Validation studies for the non-compendial methods are complete and establish the methods as adequate for the intended use.

The proposed commercial presentation is 100 tablets in a 120cc round, white HDPE bottle. There is no carton for the bottle. Suppliers and materials of construction for each packaging component are identified and an acceptance specification for each component is provided. All Type III DMFs for the component suppliers and their materials of construction were evaluated as acceptable to support this NDA.

The CMC review grants a 24-month expiration dating period when stored at USP controlled room temperature 20-25ºC (68-77ºF); excursions permitted to 15-30ºC (59-86ºF).

Insert the following language into the approval letter:
"Based on the stability data provided in your application, the drug product is granted a 24-month expiry when stored at USP controlled room temperature 20-25ºC (68-77ºF); excursions permitted to 15-30ºC (59-86ºF)."

This is a representation of an electronic record that was signed electronically and this page is the manifestation of the electronic signature.

/s/

RICHARD T LOSTRITTO
10/12/2011

NDA 21-825

Ferriprox®

ApoPharma, Inc.

William M. Adams
Review Branch I
Division of New Drug Quality Assessment I
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For the Division of Hematology Products

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