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APPLICATION NUMBER:

021825Orig1s000

CLINICAL PHARMACOLOGY AND BIOPHARMACEUTICS REVIEW(S)

ONDQA BIOPHARMACEUTICS REVIEW ADDENDUM

NDA#:	21-825/(N-000)
Submission Dates:	09/22/11, 09/23/11
Brand Name:	Ferriprox
Generic Name:	Deferiprone
Formulation:	Immediate release (IR) tablet
Strength:	500 mg (one strength)
Applicant:	ApoPharma
Type of submission:	Applicant's Response to Information Requests
Reviewer:	Tien-Mien Chen, Ph.D.

REVIEW

This document is an Addendum to the Biopharmaceutics review in DARRTS dated September 16, 2011, addressing the Applicant responses submitted on September 22, 2011, for the Biopharmaceutics comments conveyed to them on the Information Request (IR) Letters dated August 10, 2011 and September 19, 2011, for NDA 21-825 for Ferriprox IR tablet 500 mg.

RECOMMENDATION

ONDQA- Biopharmaceutics had evaluated the information provided by the Applicant and considers that their response to the Biopharmaceutics comments included in the IR Letter dated August 10, 2011 is adequate.

Based on the evaluation of the dissolution data provided by the Applicant on September 22nd in response to the Agency's IR Letter dated September 19th, Biopharmaceutics agrees with the Applicant that the provided dissolution data support an acceptance criterion of Q= (b) (4) in 45 minutes. Therefore, it is recommended that this criterion be set for their product.

The above recommendation was conveyed to the Applicant on September 23rd, and on the same day ApoPharma agreed to implement the recommended dissolution criterion. Therefore, the approved dissolution method and acceptance criterion for Ferriprox IR Tablets are as follow:

Apparatus:	**USP Apparatus II (Paddle)**
Rotation Speed:	**50 rpm**
Dissolution Medium:	**1,000 mL of 0.1 N HCl at 37ºC**
Acceptance Criterion:	**Q = (b) (4) at 45 min**

OVERALL ASSESSMENT: From the Biopharmaceutics perspective, NDA 21-825 is recommended for approval.

Tien-Mien Chen, Ph.D.
Biopharmaceutics Reviewer
Office of New Drug Quality Assessment

Angelica Dorantes, Ph.D.
Biopharmaceutics Team Leader
Office of New Drug Quality Assessment

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/s/

ANGELICA DORANTES
09/25/2011

ONDQA BIOPHARMACEUTICS REVIEW

NDA#:	21-825/(N-000)
Submission Date:	04/13/11, 06/22/11,
Brand Name:	Ferriprox
Generic Name:	Deferiprone
Formulation:	Immediate release (IR) tablet
Strength:	500 mg (one strength)
Applicant:	ApoPharma
Type of submission:	Resubmission (6-month review)
Reviewer:	Tien-Mien Chen, Ph.D.

SUMMARY

Background: Deferiprone was developed under IND 45,724 by ApoPharma as an oral treatment for chronic iron overload in transfusion-dependent anemias. Ferriprox (deferiprone) is a 500-mg, film-coated, IR tablet (one strength only).

Submission: ApoPharma submitted NDA 21-825 for Ferriprox in 2006 and was granted an orphan drug status. A Complete Response (CR) letter was sent to the sponsor on 11/30/09. The applicant submitted on 04/13/11 through its US Agent, Cato Research Ltd., a full response to the CR letter. The review time clock is 6 months.

Biopharmaceutics Review: The dissolution development report, dissolution data/profiles, the proposed dissolution method, and the specifications are formally reviewed here.

Prior to resubmission on 04/13/11, the revised dissolution method and Acceptance criterion as previously agreed upon between the Agency and the applicant are shown below.

Apparatus: **USP Apparatus II (Paddle)**
Rotation Speed: **50 rpm**
Dissolution Medium: **1,000 mL of 0.1 N HCl at 37ºC**
Acceptance Criterion: (b) (4)

After a formal review by the Biopharmaceutics team on the dissolution development report, dissolution data/profiles, it is concluded that the dissolution method is acceptable. However, since (b) (4) of drug is dissolved in (b) (4), the data clearly support a tighter value and the above dissolution criterion should be further revised as follows:

Acceptance Criterion:
Change from Q = (b) (4)
to Q = (b) (4)

RECOMMENDATION

From the Biopharmaceutics perspective, information is lacking and the resubmission of NDA 21-825 is not recommended for approval at this time. The following deficiencies/comments need to be conveyed to the applicant.

COMMENTS: (Need to be sent to the applicant)

1. An information request was sent on 08/10/11 asking you to clarify if the dissolution medium used for the dissolution testing was (b) (4) instead of the proposed 0.1 N HCl medium. No response has been received yet. We request that you address this question adequately.

2. Your proposed dissolution method as shown below has been accepted:

   Apparatus: **USP Apparatus II (Paddle)**
   Rotation Speed: **50 rpm**
   Medium: **1,000 mL of 0.1 N HCl at 37°C**

   However, after a further evaluation on the dissolution profiles/data we consider that the previously agreed dissolution value needs further revision since (b) (4) of the drug is dissolved in (b) (4). Please revise the dissolution acceptance criterion as follows:

   Change from Q = (b) (4)
   to Q = (b) (4)

   Provide an updated specification sheet for your product including the revised criterion for the dissolution test.

_____ 09/16/11
Tien-Mien Chen, Ph.D. Date
Biopharmaceutics Reviewer
Office of New Drug Quality Assessment

_____ 09/16/11
Angelica Dorantes, Ph.D. Date
Biopharmaceutics Team Leader
Office of New Drug Quality Assessment

CC: NDA
Tien-Mien Chen

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