

First Committee Meeting Summary - RiaSTAP

Date: August 8, 2008 **Time:** 2:30 PM

From: Vasantha Kumar

To: STN 125317/0

Re: First Committee Meeting for CSLB's Human Fibrinogen Concentrate, RiaSTAP

FDA Participants:

Vasantha Kumar

Laura Wood

Nisha jain

Roman Drews

La'Nissa Brown

Boris Zaslavsky

Rebecca Olin

Loan Nguyen

Christine Drabick

Iftekhar Mahmood

Craig Zinderman

Tim Lee

Lisa Stockbridge

Faith Barash

Nannette Cagungun

Background:

Fibrinogen for intravenous use was marketed in the United States by several companies in the twentieth century. It was used to treat not only congenital fibrinogen deficiency, but also to treat obstetric (post-partum) bleeding. The FDA revoked all licenses for fibrinogen concentrates in 1977 because of the risk for hepatitis infection and a suspected lack of effectiveness in obstetric use. Several fibrin sealants are currently licensed in the U.S., but no fibrinogen for intravenous use is currently licensed. When licensed, RiaSTAP™ will have orphan drug status in the U.S. The B LA was submitted under the Accelerated Approval procedure.

Human fibrinogen concentrate, pasteurized (HFCP) is a concentrated form of human fibrinogen (coagulation factor I) derived from human plasma. The proposed indication for HFCP is for the treatment of patients with congenital fibrinogen deficiency, which comprises congenital afibrinogenemia, hypofibrinogenemia and dysfibrinogenemia.

Determination of patients' fibrinogen levels is recommended prior to and during treatment with HFCP, to maintain fibrinogen levels. The usual starting dose for adults is 1-2 grams, to obtain a replacement level or at or above .5-.8 g/L. Normal levels range from 200 – 450 mg/dl. If the fibrinogen level is unknown, the recommended dose is 70 mg/kg. HFCP is supplied as lyophilized powder and, after reconstitution, administered by slow, intravenous infusion. The labeled amount of HFCP is 1 g of fibrinogen with the

actual potency for each lot indicated on the vial label and carton. The proposed trade name for HFCEP is RiaSTAP.

Congenital fibrinogen deficiency is a very rare bleeding disorder. Hereditary afibrinogenemia affects an estimated 150-300 people in the US, based on published prevalence data. The prevalence of hypofibrinogenemia and dysfibrinogenemia are unknown. Patients with any of these conditions are treated for bleeding either by substitution with a cryoprecipitate or fresh frozen plasma. There are no fibrinogen concentrate products currently approved in the US.

Discussion:

The purpose and the outcome of this meeting are presented below:

- *To ensure the submission is complete.*

The submission was accepted to be complete.

- *To ensure a reviewer is assigned to review each section of the supplement.*

A reviewer from each discipline was assigned to review their respective sections and all the reviewers had received the modules for their respective disciplines

- *To identify if consult reviewers are needed in the review process.*

No consult reviewer seemed to be needed at this point

- *To identify follow up activities to be completed before the next meeting (Filing Meeting). The Filing Meeting is scheduled for 29-August-2008.*

Information requests from PK reviewer and APLB reviewer to be sent to the sponsor

- *To share the review findings to date and advice if there are any actions required at this time.*

Information requests for PK data and Pharmacovigilance plans were discussed. This submission had been granted an Orphan Drug designation and a fast Track designation was granted for a priority review based on serious life threatening condition (congenital afibrinogenemia) and unmet medical needs. The PLR team would review the package insert at the earliest. It was decided that this submission had to be discussed at the BPAC meeting scheduled for 9 Jan 2009. The review team was alerted that because of the new requirements under FDAAA and because there are Post Marketing Requirements, the approval letter and the labeling have to be submitted to the CBER and CDER Safety Working Groups by 16 December 2008.

- *To advise if others need to be included in this review.*

No other reviewer was found necessary at this point of time

List of Reviewers:

Discipline	Reviewer	Modules
Clinical	Nisha Jain	Modules 1 & 2, Module 5
	Laura Wood (Chair)	
CMC	Ze Peng Tim Lee	Full set
Additional CMC	Roman Drews	Modules 1 & 2, Module 3
Pharm/Tox	La'Nissa Brown	Modules 1 & 2, Module 4

Biostatistician	Boris Zaslavsky	Modules 1 & 2, Module 5
DMPQ	Rebecca Olin	Full set
	Loan Nguyen	
APLB	Lisa Stockbridge	Modules 1 & 2
BIMO	Chris Drabick	Modules 1 & 2, Module 5
PK	Iftekhar Mahmood	Modules 1 & 2 , Module 5
	Craig	
OBE	Zinderman Faith Barash	Modules 1 & 2, Module 5
RPM	Vasanthan Kumar	Full set (share with Iftekhar)
Archival		Full set