

QUICK SUMMARY

for the
BLOOD PRODUCTS ADVISORY COMMITTEE
84th Meeting –Sept 29, 2005

The agenda for this meeting included Product Approval of NDA 21-882 Exjade and discussion and approval of the DH lab site visit report of Feb 25, 2005.

Dr. George Mills, Director, Division of Medical Imaging and Hematology Products, CDER offered welcome comments, followed by discussion of Exjade from the Sponsor, Novartis Pharmaceutical Corp. Dr. Narang, Vice President, Global Head Drug Regulatory Affairs, Oncology Business Unit, Novartis introduced the topic, followed by discussion of the disease by Professor John Porter, University College London, Department of Hematology, UK. The efficacy and safety data for drug was presented by Peter Marks, M.D., Ph.D., Senior Director, Oncology Business Unit, Novartis and conclusions on benefits and risk were presented by Elliott Vichinsky, M.D. of Children's Hospital and Research Center at Oakland. Next George Shashaty, M.D., Medical Officer, CDER presented the FDA review of the drug application. Questions were deferred by the Committee Chair until after the Open Public Hearing. There were 13 written statements including a petition of support for the drug application signed by 1800 individuals that were submitted to the committee. 12 Open Public Speakers requested to speak and an additional 2 speakers requested to speak at the meeting. Lunch was followed by vigorous discussion over the topic. Questions were presented to the committee for their vote and comment. They are as follows:

- Do you believe that a reduction in LIC is an acceptable efficacy endpoint for approval? If not, what efficacy endpoint would you recommend? Vote was 14 Yes, 0 No. There was discussion that LIC does not take into account iron stored in heart. Also Ferritin was discussed.
- Does the demonstrated ability of Exjade to lower LIC in patients from their baseline to their end study value provide evidence for clinical efficacy. Vote was 14 Yes, 0 No. Comments that this was true for high dose of Exjade.
- Can safety and efficacy in the population of patients with LIC < 7mg Fe/g dw be extrapolated from patients with LIC \geq 7 mg Fe/g dw who were treated at doses of Exjade 20 or 30 mg/kg/day? If not, should these patients be further studied? The committee did not take a vote of this issue. They indicated that they did not see convincing data yet.
- Is the available information sufficient to direct initial and maintenance dosing? If yes, what does regimen and monitoring would you recommend? Should a liver biopsy to determine LIC be recommended as part of the selection and monitoring

- criteria? The committee did not vote on this issue, but the majority did not want to see mandatory liver biopsies.
- Does the safety database provide an adequate characterization of the safety of Exjade to allow adequate benefit/risk assessment and adequate labeling? Dr. Schreiber voted No. Other 13 voted yes, but wanted to see post marketing studies.

 - Should Exjade be approved with for the indicated population of beta-thalassemia patients with transfusional hemosiderosis? Vote: 14 Yes, 0 No

 - Should Exjade be approved for a broader indication of transfusional hemosiderosis? Vote: 14 Yes, 0 No. Discussion of efficacy of Sickle Cell Anemia patients.

 - Have adequate safety and efficacy data been presented to support labeling in pediatric patients (at least 2 years of age)?
Vote: 4 Yes, 10 No if 2 years; Unanimous Yes if greater than 6 years old.

The second topic included research presentations of Laboratory of Plasma Derivatives and Laboratory of Hemostasis in the Department of Hematology. The site visit report of these labs from Feb 25, 2005 was discussed in closed session. Approval of the report was unanimous.

This quick summary is provided as an unofficial overview of the committee discussions. Please refer to the meeting transcripts for a detailed account of the meeting