CENTER FOR DRUG EVALUATION AND RESEARCH

APPLICATION NUMBER:

216157Orig1s000

NON-CLINICAL REVIEW(S)

MEMORANDUM

TO: File for NDA 213137 and 216157

FROM: Pedro L. Del Valle, PhD., FATS
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DATE: December 9, 2021

SUBJECT: SDN 326 (SUPPL 6 - 6/25/2021) & SDN 1 (6/25/2021)

Voxelotor (GBT440) is being developed for the treatment of sickle cell disease (SCD) in adult and adolescent patients. OXBRYTA™ (voxelotor) oral tablets, 500 mg, was approved in November 2019 under accelerated approval for the treatment of sickle cell disease in adults and pediatric patients 12 years of age and older and can be administered alone or in combination with hydroxyurea. Supplement 6 for Efficacy (SDN 326) submitted on June 25, 2021 include the proposed indication for the treatment of SCD in adults and pediatric patients 4 years of age and older. The quality-related information for the new, age-appropriate dispersible tablet dosage form is provided in NDA 216157 (SDN 1).

The Applicant had two SPA for carcinogenicity studies under IND 121691 one each in mice and rats and submitted the final carcinogenicity study report in mice with the original NDA application. The Applicant submitted the final study report for a 104-week carcinogenicity study in Hsd:Sprague Dawley®SD® rats late in the review cycle (September 24, 2019) of the original NDA submission (SDN 27) and it is being reviewed under Supplement 6. No other nonclinical studies were submitted under NDA 213137 or NDA 216157.

Review of the carcinogenicity in rats and the statistical analysis for trend and pairwise comparison is completed, however, results and interpretation should be first discussed by ECAC. Once ECAC final conclusion is issued to the Applicant, the full carcinogenicity study in rats will be submitted to DARTTS. Labeling language in Section 13.1 was tentatively approved as proposed by the Applicant and will be revised based on ECAC conclusion. A supplement request letter asking the Applicant to insert specific language is an option to incorporate ECAC conclusion reflecting findings in the carcinogenicity study in rats.

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/s/

PEDRO L DELVALLE
12/09/2021 03:30:22 PM