CENTER FOR DRUG EVALUATION AND RESEARCH

APPLICATION NUMBER:

218466Orig1s000

NON-CLINICAL REVIEW(S)

MEMORANDUM

Date: April 18, 2024
From: G. Sachia Khasar, PhD
Pharmacology/Toxicology Reviewer
Division of Hematology Oncology Toxicology for Division of Oncology 2
Through: Claudia P. Miller, PhD
Supervisory Pharmacologist
Division of Hematology Oncology Toxicology for Division of Oncology 2
To: File for NDA 218466 and 215039 supplement 2
Product: VIJOICE granules
Re: Pharmacology and Toxicology

The FDA approved VIJOICE (Alpelisib) film-coated tablets (FCTs; 50 mg, 125 mg, and 200 mg) for the treatment of adult and pediatric patients, 2 years of age and older, with severe manifestations of PIK3CA-Related Overgrowth Spectrum (PROS) in 2022 under NDA 215039. Alpelisib is a kinase inhibitor of phosphatidylinositol-3-kinase (PI3K), with inhibitory activity predominantly against the α-isoform, PI3Kα. Gain-of-function mutations in the gene encoding the catalytic α-subunit of PI3K (PIK3CA) leads to activation of PI3Kα and downstream Akt-signaling that can promote cellular growth as well as transformation and generation of tumors in in vitro and in vivo models.

According to the Applicant, the FCTs may not be optimal for patients who may have difficulty swallowing. Therefore, the Applicant developed a new dosage form of the 50 mg FCT as 50 mg granules and submitted NDA 218466 for VIJOICE (alpelisib) Granules (submitted also to NDA 215039 supplement 2). The Applicant states that the 50 mg granule and 50 mg FCT dosage forms are bioequivalent in the fed state. No new nonclinical data were provided in the current application. The Applicant cross-referenced genetic toxicology data under NDA 212526 for PIQRAY (alpelisib), approved for breast cancer, to support the original approval of VIJOICE (NDA 215034; 2022). In the current application, the Applicant suggested, and we agreed to delete (b) (4) in Section 13.1 of the label to align with description of genetic toxicology results in PIQRAY label.

From a pharmacology/toxicology perspective, there are no outstanding issues, therefore, the application has been recommended for approval.

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/s/

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04/18/2024 12:30:10 PM

CLAUDIA P MILLER
04/18/2024 12:34:06 PM