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Attachment Two

Previous Suitability Petition Letter 2023-P-4291

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October 1, 2023

VIA ELECTRONIC SUBMISSION 10/1/23

Division of Dockets Management
Food and Drug Administration (HFA-305)
Department of Health and Human Services
5630 Fishers Lane, Room 1061
Rockville, MD 20852

CITIZEN PETITION

Dear Sir or Madam:

The undersigned submits this petition, pursuant to Section 505Q)(2)(C) of the Federal Food, Drug, and Cosmetic Act, and in accordance with 21 CFR 10.30 on behalf of a clieot requesting the Commissioner of the Food and Drug Administration to declare that the drug product, Lacosamide Orally Disintegrating Tablets, in strengths of 50 mg, 100 mg, 150 mg and 200 mg are suitable for consideration in an abbreviated new drug application (ANDA}.

A. Action Requested

The petitioner requests that the Commissioner of the Food and Drug Administration declare that, Lacosamide Orally Disintegrating Tablets, in strengths of 50 mg, 100 mg, 150 mg and 200 mg are suitable for submission as an ANDA. The reference-listed drug product (RLD), upon which this petition is based, is Vimpat (lacosamide) Tablets 200 mg, subject of NDA 22253 held by UBS Inc as designated in the Orange Book (see copy of the page from the current Electronic Edition of the *Approved Drug Products with Therapeutic Equivalence Evaluations* (Attachment 1)}. In addition, Vimpat is also approved in strengths of 50 mg, 100 mg and 150 mg. Therefore, the petitioner seeks a change in dosage form from immediate release tablets to orally disintegrating tablets for all approved strengths of Vimpat tablets.

B. Statement of Grounds

The Federal Food, Drug, and Cosmetic Act provides for the submission of an Abbreviated New Drug Application for a drug product that differs in dosage form from that of the listed drug provided the FDA has approved a petition that proposed filing such an application.

The RLD, Vimpat (lacosamide) Tablets by USB Inc. is a tablet product containing 200 mg of lacosamide in each tablet. As noted above, Vimpat is also approved in strengths of 50 mg, 100 mg, and 150 mg tablets. The proposed drug product will be an orally disintegrating tablet dosage form, containing 200 mg, 150 mg, 100 mg, or 50 mg of Lacosamide. This petition is thus seeking a change in dosage form to an orally disintegrating tablet of the same strengths as the approved tablet version of Vimpat, the RLD.

The proposed change in dosage form represents changes that are consistent with the dosing recommendations of the RLD's approved labeling. The current dosing instructions in the approved labeling of the RLD are as follows:

> Dosage and Administration - Usual Adult Dose:
>
> Vimpat can be administered with or without food.

Partial-Onset Seziures

VIMPAT can be initiated with either oral or intravenous administration. The initial dose should be 50 mg twice daily (100 mg per day). VIMPAT can be increased at weekly intervals by 100 mg/day given as two divided doses up to the recommended maintenance dose of 200 to 400 mg/day, based on individual patient response and tolerability. In clinical trials, the 600 mg daily dose was not more effective than the 400 mg daily dose, and was associated with a substantially higher rate of adverse reactions.

Pediatric Use

The safety and effectiveness of VIMPAT in pediatric patients <17 years have not been established.

The proposed orally disintegrating tablets would allow the same dosing instructions that of the RLD. However, there may be greater ease of administration than RLD (no water necessary to be taken with the product), especially for patients that have difficulty in swallowing tablets or have dysphagia.

The dosing strengths proposed in this petition are exactly the same as those of the RLD and would thus would provide the ability to reach all recommended doses suggested in the RLD label and could provide appropriate options for physicians to treat patients that have difficulty in swallowing tablets.

There are no proposed changes in labeling with the exception of the obvious changes in in dosage form and directions for use of the orally disintegrating tablet strength sought in this petition. Such a label change is permitted in accordance with the regulations based on an approval of an ANDA suitability petition for a permitted change. The uses, indications, warnings and directions for use will remain the same as that of the RLD. Draft labeling for the proposed products is included in Attachment 2, and the RLD's approved labeling is provided in Attachment 3.

Therefore, the petitioner's request for the Commissioner to find that a change in dosage form tablets to orally disintegrating tablets should raise no questions of safety or effectiveness, and the Agency should approve the petition.

Pediatric Waiver Request

In September of 2007, Congress reauthorized the Pediatric Research Equity Act of 2003 (PREA) that amended the Federal Food, Drug, and Cosmetic Act to provide the Agency authority to require drug firms to study drugs in pediatric patients, if the Agency concludes that such study would provide beneficial health data for that patient population. The Act specifically requires that a request for a new dosage form is subject to a pediatric evaluation. The act also provides for a waiver from such requirement if the drug:

(I) does not represent a meaningful therapeutic benefit over existing therapies for pediatric patients; and

(11) is not likely to be used in a substantial number of pediatric patients.

The proposed product will contain labeling that permits dosing for all patients for whom the drug is indicated (down to 17 years of age). The RLD labeling discusses the potential for adverse effects on CNS development and thus this product would not likely be utilized in children under the age of 17 due to potential impact on such development. While the product labeling does not cite any contraindications, it does warn that:

Lacosamide has been shown in vitro to interfere with the activity of CRMP-2, a protein involved in neuronal differentiation and control of axonal outgrowth. Potential adverse effects on CNS development cannot be ruled out. Administration of lacosamide to rats during the neonatal and juvenile periods of postnatal development resulted in decreased brain weights and long-term neurobehavioral changes (altered open field performance, deficits in learning and memory). The no-effect dose for developmental neurotoxicity in rats was associated with a plasma lacosamide exposure (AUC) approximately 0.5 times the human plasma AUC at the maximum recommended human dose of 400 mg/day.

Because of the potential for adverse CNS development, and the fact that there are other available AED treatments approved for pediatric patients, it is unlikely that the proposed product will be prescribed for or used by pediatric patients and therefore the petitioner hereby requests that a full waiver from the conduct of pediatric studies be granted for the approval of this petition to permit subsequent ANDA filing.

C. Environmental Impact

The petitioner claims a categorical exclusion under 21 CFR 25.31.

D. Economic Impact

The petitioner does not believe that this is applicable in this case, but will agree to provide such an analysis, if requested by the Agency.

E. Certification

The undersigned certifies that to the best knowledge and belief of the undersigned, this petition includes all information and views on which the petition relies, and that it includes representative data and information known to the petitioner, which are unfavorable to the petition.

Resoectfullv submitted,

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Attachments:
1. Approved Drug Products with Therapeutic Equivalence Evaluations, Electronic Orange Book listing, accessed 9/12/23
2. Draft insert labeling for proposed product
3. Approved labeling for reference-listed drug, Vimpat (lacosamide) Tablets