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April 15, 2024

VIA ELECTRONIC SUBMISSION 4/15/24

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 505(j)(2)(C) of the Federal Food, Drug, and Cosmetic Act, and in accordance with 21 CFR 10.30 requesting the Commissioner of the Food and Drug Administration to declare that the drug product, Escitalopram Oxalate Orally Disintegrating Tablets, 5 mg, 10 mg, 15 mg and 20 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, Escitalopram Oxalate Orally Disintegrating Tablets, 5 mg, 10 mg, 15 mg and 20 mg are suitable for submission as an ANDA. The reference-listed drug product (RLD), upon which this petition is based, is Lexapro (Escitalopram) Tablets 20 mg, subject of NDA 021323 held by Abbvie 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**)}. Lexapro tablets are approved in strengths of 5 mg, 10 mg and 20 mg. Therefore, the petitioner seeks a change in dosage form from immediate release tablets to orally disintegrating tablets for all approved strengths of Escitalopram tablets. In addition, the petitioner also seeks to add a 15 mg strength orally disintegrating tablet to its ANDA as an additional strength representing both a change in strength and dosage form from the RLD.

The dosing instructions are 10 mg to 20 mg once daily in the approved labeling of the RLD-see Table 1 on following page (also see **Attachment 3**). Lexapro Tablets 5 mg are not scored but the 10 mg and 20 mg Lexapro Tablets are scored. The existing scoring configuration for Lexapro Tablets was likely devised to give practitioners multiple options to provide a patient with a 15 mg dose as approved labeling does not recommend a dose less than 10 mg. This is precisely why the petitioner is seeking to add a 15 mg strength as none of our proposed ODT products will be scored. Because the proposed products will be offered in 5 mg, 10 mg, 15 mg and 20 mg strengths, the proposed products will give practitioners all of the approved dosing options that are available with the current Lexapro tablets.

> "Depending on clinical response and tolerability, dosage may be increased to the maximum recommended dosage of 20 mg once daily…."

The recommended time for dose adjustment varies based on indication with adjustment periods ranging from 1 week to 3 weeks. Availability of Lexapro Tablets available as an unscored 5 mg tablet clearly contemplates dose adjustments between the 10 mg starting dose and the 20 mg maximum dose. Availability of Escitalopram Oxalate ODT, 15 mg will permit patients to take a single tablet product when consistent administration of a 15 mg dose is appropriate for the patient based on clinical response and tolerability and can eliminate the need for tablet breaking to reach the 15mg dose..

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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 strength and dosage form from that of the listed drug provided the FDA has approved a petition that proposed filing such an application.

The RLD, Lexapro (Escitalopram) Tablets by Abbvie Inc., is a tablet product containing 20 mg of escitalopram in each tablet. As noted above, Lexapro Tablets is also approved in strengths of 5 mg and 10 mg. The proposed drug product will be an orally disintegrating tablet (ODT) dosage form, containing 5 mg, 10 mg, 15 mg and 20 mg of Escitalopram. This petition is thus seeking a change in dosage form from a solid oral tablet to an orally disintegrating tablet of the same strengths as the approved tablet version of Lexapro, the RLD along with the addition of a new strength, 15 mg.

The proposed change in dosage form and strength for the 15 mg ODT product represent changes that are consistent with the dosing recommendations of the RLD's approved labeling and give the practitioner more flexibility to titrate doses for their patients and make it easier for the patient to reach a 15mg intermediate dose. The current dosing instructions in the approved labeling of the RLD are as follows:

Dosage and Administration - Usual Adult Dose:

Escitalopram Oxalate is a selective serotonin reuptake inhibitor (SSRI) indicated for the:

- treatment of major depressive disorder (MDD) in adults and pediatric patients 12 years of age and older (1)
- treatment of generalized anxiety disorder (GAD) in adults and pediatric patients 7 years and older (1)

Table 1

Indication and Population	Recommended Dosage
MDD in Adults (2.1)	Initial: 10 mg once daily Recommended: 10 mg once daily Maximum: 20 mg once daily
MDD in Pediatric Patients 12 years and older (2.1)	Initial: 10 mg once daily Recommended: 10 mg once daily Maximum: 20 mg once daily
GAD in Adults (2.2)	Initial: 10 mg once daily Recommended: 10 mg once daily Maximum: 20 mg once daily
GAD in Pediatric Patients 7 years and older (2.2)	Initial: 10 mg once daily Recommended: 10 mg once daily Maximum: 20 mg once daily

The proposed orally disintegrating tablets allow dosing instructions consistent with the RLD (along with additional option provided by the proposed 15 mg strength) and may increase ease of administration compared to the RLD especially for patients that have difficulty in swallowing tablets or have dysphagia as the proposed ODT does not require water for administration. In addition, it may reduce the need for a patient taking a 15mg dose from having to break tablets to obtain the desired dose.

Three of the strengths (5 mg, 10 mg and 20 mg) proposed in this petition are the same as those of the RLD, and the 15 mg strength is an intermediate strength that falls between the 10 mg and 20 mg strengths of Lexapro Tablets, where labeling for Lexapro Tablets already contemplates administration of a single 15 mg dose. The proposed products will provide the practitioner all of the currently available dosing options while offering an alternate dosage form to ease administration.

The proposed changes in labeling are related to the changes proposed in this petition for the change in dosage form and the additional 15 mg strength, as well as directions for use of the orally disintegrating tablet. Such minor differences in labeling are permitted in accordance with the regulations at 21 CFR 314.94(a)(8)(iv) when made in accordance with approval of a suitability petition for the permitted change(s). The uses, indications, warnings and directions for use will remain the same as that of the RLD with only the the additions required for the changes sought in the petition. 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 from tablets to orally disintegrating tablets for the 5 mg, 10 mg and 20 mg products and a change in strength and dosage form for the 15 mg product should raise no questions of safety or effectiveness, and the Agency should approve the petition.

B. 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 safety and efficacy of Escitalopram for the treatment of major depressive disorder have been established in pediatric patients 12 years of age and older. In a 24-week, open label safety study was performed in pediatric patents aged 7 to 11 years old, the safety findings were consistent with the known safety and tolerability profile for Escitalopram.

The safety and effectiveness of Lexapro for the treatment of generalized anxiety disorder have been established in pediatric patients 7 years of age and older.

Furthermore, our request for a full waiver of the requirements under PREA is consistent with previous Agency action for a Suitability Petition. FDA granted a full waiver of the PREA requirements in the context of FDA's evaluation and approval of Suitability Petition FDA-2004-P-0415 (legacy petition 2004P-0247) on March 29, 2005 which was subsequently posted to Regulations.gov on April 1, 2005. Suitability Petition FDA 2004-P-0415, submitted by Frommer Lawrence & Haug LLP, requested a change in dosage form from tablets to capsules and therefore is consistent with the type of change, a change in dosage form, that triggers PREA for this petition. It is also noted that Suitability Petition FDA 2004-P-0415 ultimately served as the Basis of Submission for ANDA 077660 which was approved by the Office of Generic Drugs on July 31, 2007 for Escitalopram Oxalate Capsules, 5 mg, 10 mg, and 20 mg.

Based on the studies performed to date, FDA precedence for granting a full PREA waiver for the proposed change, and the fact that neither the dosage form change request to orally disintegrating tablets or additional strength change will have an impact on safety or efficacy, the petitioner 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 1t includes representative data and information known to the petitioner, which are unfavorable to the petition.

Respectfully submitted,

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Attachments:

1. Approved Drug Products with Therapeutic Equivalence Evaluations, Electronic Orange Book listing, accessed 4/12/24
2. Draft insert labeling for proposed product
3. Approved labeling for reference-listed drug, Lexapro (escitalopram oxalate) Tablets