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June 18, 2007

OVERNIGHT COURIER 6/18/07

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, in quadruplicate, pursuant to Section 505(j)(2)(C) of the Federal Food, Drug and Cosmetic Act, and in accordance with 21 CFR 10.30 on behalf of a client requesting the Commissioner of the Food and Drug Administration to declare that the drug product, Escitalopram Oxalate Orally Dissolving Film Strips, 5 mg, 10 mg and 20 mg, is 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 the product Escitalopram Oxalate Orally Dissolving Film Strips, 5 mg, 10 mg and 20 mg, is suitable for consideration in an abbreviated new drug application (ANDA). The reference-listed drug (RLD) product upon which this petition is based is Lexapro[®] (escitalopram oxalate tablets), 20 mg, NDA 21-323. Lexapro[®] Tablets are also approved in the 5 mg and 10 mg strength. (See copy of the page from the current Electronic Edition of the *Approved Drug Products with Therapeutic Equivalence Evaluations*, Attachment 1.) The petitioner seeks a change in dosage form (from the approved dosage form of an oral tablet to an orally dissolving film strip) from that of the RLD product.

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, Lexapro[®] by Forest Laboratories, Inc. is currently available as 5 mg, 10 mg and 20 mg oral tablets. The proposed drug product subject to this petition represents an orally dissolving film strip, also in the 5 mg, 10 mg and 20 mg dosage strengths. The petition is thus seeking a change in dosage form from that of the RLD (i.e., from a tablet to an orally dissolving strip). The proposed drug product is consistent with the currently approved RLD product's labeling with the exception of the dosage form and directions for administration (because of the difference in dosage form). Although we are not aware of any FDA approved drug products presently marketed in an orally dissolving strip dosage form, there are a number of products that are marketed over-the-counter that utilize this dissolving film technology. The proposed dosage form will contain inactive ingredients that are generally recognized as safe (GRAS) or have been approved in other marketed approved drug products. The orally dissolving strip is designed to be placed on the tongue and will dissolve within a few seconds after contact. This proposed dosage form is directly analogous to a fast dissolving and fast disintegrating tablet that has been previously approved

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by the FDA. Each dosage unit (strip) will contain either 5 mg, 10 mg or 20 mg of escitalopram oxalate and the petitioner will demonstrate bioequivalence to the RLD. Additionally, we note that the FDA has approved at least one petition permitting the submission of an ANDA for an orally dissolving strip (Docket #2004P-0353 approved July 5, 2005).

The proposed product will provide an alternate dosage form that may prove to be more convenient for patients who have difficulty swallowing a tablet or do not have access to water when a dose is needed. The proposed product will be labeled in accordance with the approved labeling of the RLD product upon which this petition is based and the FDA guidance on Medication Guides for Antidepressant Drugs Issued on May 2, 2007. Any difference in the labeling will relate only to the difference in dosage form and the method of administration (dissolving the strip on the tongue as opposed to swallowing the tablet) and those differences that may be necessary because the products are made by different manufacturers or because of patent or exclusivity protections. The uses, indications, warnings and directions for use will remain the same as that of the RLD. Draft labeling for the proposed product is included in Attachments 2 and 3, and the RLD's approved labeling is provided in Attachment 4.

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

Pediatric Waiver Request

In December 2003, Congress passed 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
- (II) is not likely to be used in a substantial number of pediatric patients.

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.

The reference-listed drug product that is the subject of this petition is an immediate-release tablet. Escitalopram oxalate was first approved for use in 2002. According to FDA's list of issued written requests, no written requests have been issued by the Agency to the innovator for pediatric studies for escitalopram oxalate. Furthermore, we note that the initial approval letter for Lexapro[®] did not request any additional pediatric studies. We also note that the review package for the original application indicates that a 'deferral' to pediatric studies was granted (see excerpt below) since FDA was reviewing results of pediatric studies for the parent compound, citalopram (Celexa[®] also by Forest Laboratories, Inc.).

This pediatric deferral was discussed at the pre-NDA meeting for NDA 21-323 held on November 14, 2000. The division noted that such a deferral would be acceptable and pointed out that the pediatric development plan for escitalopram would also be dependent on the results and FDA action on the pediatric studies currently being conducted with Celexa (citalopram). The Pediatric Study Request Letter (dated April 28, 1999) for Celexa requested that the results of the pediatric studies be submitted by April 28, 2002. After the FDA has reviewed the results of the Celexa studies Forest will negotiate with the Division regarding an optimal pediatric development program for escitalopram and the final date for the submission of pediatric study reports.

However, subsequent to the original approval of Lexapro[®], FDA determined that any pediatric exclusivity granted to citalopram would also extend to its enantiomer, escitalopram since the studies conducted used the racemate formulation (i.e., since escitalopram was present in the compound used in the studies, exclusivity would also extend to escitalopram). We note in the approval package for Supplement 1, to the RLD, Lexapro[®] (NDA 21-323), the Agency states the following:

Pediatric studies were conducted using the racemate formulation, Celexa (citalopram HBr) tablets, and submitted as pediatric efficacy supplements to NDA 20-822/SE5-016 (Celexa tablets) and 21-046/SE5-002 (Celexa solution). Pediatric exclusivity was granted for these applications on 7-12-02.

In a ruling by General Counsel, it was decided that pediatric exclusivity would extend to the enantiomer formulation, escitalopram, once approved if the racemate, citalopram, was granted pediatric exclusivity. The Agency has approved the parent NDA 21-323 in an approval letter dated 8-14-02, and the relapse prevention NDA (Type 6 NDA) was approved on 8-29-02. Pediatric exclusivity was granted for the racemate, citalopram, in an action dated 7-12-02.

As a result of this ruling, Forest Laboratories, Inc. has been awarded a 6-month period of pediatric exclusivity for all of their escitalopram oxalate products (Lexapro[®]) indicating that pediatric studies have been conducted on the drug. Additionally, we note that in the approval letter for Supplement 1 to RLD, Lexapro[®] (NDA 21-323/S-001, approved August 29, 2002), that Agency states that pediatric studies have been fulfilled (see excerpt below).

“Pediatrics

Be advised that, as of April 1, 1999, all applications for new active ingredients, new dosage forms, new indications, new routes of administration, and new dosing regimens are required to contain an assessment of the safety and effectiveness of the product in pediatric patients unless this requirement is waived or deferred (63 FR66632). We note that you have fulfilled the pediatric study requirement at this time.”

We also note the approval letter for Supplement 7 to NDA 21-323 (Lexapro[®]) on December 18, 2003, which provided for an additional indication, generalized anxiety disorder, the Agency once again did not request any further pediatric studies.

Thus, the fulfillment of the requirement for pediatric studies by Forest Laboratories, Inc. (indicated by the granted pediatric exclusivity) and the lack of request for additional pediatric studies in subsequent supplemental approval letters for Lexapro[®] indicate that additional pediatric studies are no longer needed for escitalopram oxalate. Therefore, the introduction of an alternate dosage form that can be used in a similar manner as the RLD, Lexapro[®] will not represent a meaningful therapeutic benefit over existing therapies for pediatric patients.

C. Environmental Impact

The petitioner claims a categorical exclusion under 21 CFR 25.31.

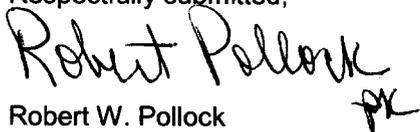
D. Economic Impact

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.

Respectfully submitted,

Handwritten signature of Robert W. Pollock in black ink, with the initials 'pk' written below the signature.

Robert W. Pollock
Senior Vice President
Lachman Consultant Services, Inc.

RWP/pk

cc: Craig Kiester (OGD)

- Attachments:
1. Approved Drug Products with Therapeutic Equivalence Evaluations, accessed June 11, 2007
 2. Draft Insert Labeling Proposed for Escitalopram Oxalate Orally Dissolving Film Strips
 3. Draft Medication Guide for Escitalopram Oxalate Orally Dissolving Film Strips
 4. Labeling for the reference-listed drug, Lexapro[®], revised May 2007 and FDA Medication Guide

Lexapro[®] and Celexa[®] are registered trademarks of Forest Laboratories, Inc.

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