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April 23, 2004

OVERNIGHT COURIER 4/23/04

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:

This petition is submitted in quadruplicate under 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 Divalproex Sodium Extended-Release Tablets, 750 mg is suitable for submission in an abbreviated new drug application (ANDA).

A. Action Requested

The petitioner requests that the Commissioner of the Food and Drug Administration make a determination that Divalproex Sodium Extended-Release Tablets, 750 mg, are suitable for submission in an ANDA. The reference-listed drug product upon which this petition is based is Depakote® ER (Divalproex Sodium) Extended-Release Tablets, 500 mg, which appears in the 24th edition of the Electronic Orange Book (see Attachment 1). The listed drug product is also approved in the 250 mg strength. Additionally, a petition submitted April 24, 2003 for a new, higher strength of 1000 mg was approved on August 13, 2003 [(Docket No. 03P-0178/CP1) see petition approval letter Attachment 2]. Therefore, the petitioner seeks a change in strength (from 250 mg and 500 mg tablets to include 750 mg tablets, a new, higher strength) from that of the listed drugs.

B. Statement of Grounds

The Federal Food, Drug and Cosmetic Act provides for the submission of an ANDA for a new drug that differs in strength from a listed drug provided the FDA has approved a petition that proposed the filing of such an application. Depakote® ER (Divalproex Sodium) Extended-Release Tablets, the reference-listed drug upon which this petition is based, are available in tablet dosage form and available in differing strengths containing 250 mg and 500 mg of Divalproex Sodium. Additionally, a petition submitted April 24, 2003 for a new, higher strength of 1000 mg was approved on August 13, 2003 (Docket No. 03P-0178/CP1). The proposed drug product represents the same dosage form and route of administration, differing only in strength from the reference-listed drug.

The recommended dose of Depakote® ER (Divalproex Sodium) Extended-Release Tablets is as follows:

- 500 mg once daily for 1 week, thereafter increasing to 1000 mg once daily in migraine. In epilepsy, therapy is initiated at 10-15 mg/kg/day and goes up to 60 mg/kg/day (750 mg – 3500 mg once daily in accordance with the conversion chart provided in the approved labeling of the RLD).

It is clear that each patient must be titrated to an effective dose of the drug product specific to the individual patient's needs and response to the medication. The availability of the proposed 750 mg tablet strength will provide for patients who take multiple tablets to achieve a single dose, more convenient

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single tablet dosage. It will also provide prescribing physicians a greater degree of flexibility in selecting proper individualized maintenance doses for specific patient needs.

There should be no question of safety or efficacy raised regarding the requested new drug product as the uses, dose, dosage form and route of administration of the proposed drug product are the same as that of the listed drug product. The approved labeling of the reference-listed drug (Attachment 3) indicates that each patient must be titrated to an effective dose of the drug product specific to the individual patient's needs and response to the medication. The proposed strength of 750 mg represents an intermediate strength within the dosing range for all indications. Labeling of the proposed product (Attachment 4) will be the same as the approved labeling of the reference-listed drug product with exception to the introduction of the 750 mg strength in the "Description" and "How Supplied" sections.

C. Environmental Impact

An environmental assessment on the action requested in this petition qualifies for a categorical exclusion under 21 CFR 25.31.

D. Economic Impact

Pursuant to 21 CFR 10.30 (b), economic impact information is to be submitted only when requested by the Commissioner. We will gladly provide such information, if so requested.

E. Certification

The undersigned certifies that to the best of its knowledge, 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 is unfavorable to the petition.

Respectfully submitted,


Leon Lachman
President
Lachman Consultant Services, Inc.
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LL/pk

cc: Emily Thakur (Office of Generic Drugs)

Attachments:

1. 24th Edition of the Orange Book
2. Petition Approval Letter, dated August 18, 2003
3. Approved Labeling
4. Labeling of the Proposed Product

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