LACHMAN CONSULTANT SERVICES, INC.

CONSULTANTS TO THE PHARMACEUTICAL AND ALLIED INDUSTRIES

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July 10, 2013

OVERNIGHT COURIER 07/10/13

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 C.F.R. § 10.30 on behalf of a client requesting the Commissioner of the Food and Drug Administration to declare that the drug product, Tizanidine Hydrochloride Tablets, 8 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 drug product, Tizanidine Hydrochloride Tablets, 8 mg, is suitable for submission as an ANDA. The reference listed drug product (RLD), upon which this petition is based, is Zanaflex® (Tizanidine Hydrochloride) Tablets, 4 mg, NDA 020397, currently held by Acorda as designated in the Orange Book. Therefore, the petitioner seeks a change in strength (from 4 mg to 8 mg), from that of the listed drug 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 strength from that of the listed drug provided the FDA has approved a petition that proposed filing such an application.

The RLD, Zanaflex® Tablets by Acorda is a tablet product containing 4 mg of tizanidine hydrochloride. See product listing for NDA 020397 from the electronic Orange Book also known as the *Approved Drug Products with Therapeutic Equivalence Evaluations*, accessed July 9, 2013, which lists the approval of the RLD. (Attachment 1) The proposed drug product also represents a tablet dosage form, but containing 8 mg of tizanidine hydrochloride. The petition is thus seeking a change in strength of tizanidine hydrochloride (from 4 mg to 8 mg) from that of the RLD. Please note that the proposed change in strength represents a dosage strength that is consistent with the dosing recommendations of the RLD's approved labeling.

Specifically, the dosing instructions in the approved labeling of the RLD state to titrate patients to a single dose of 8 mg of tizanidine, which can be repeated every 6 to 8 hours. The approved package insert for Zanaflex is included in Attachment 2. The pertinent excerpt from the Dosage and Administration section of the approved RLD labeling is as follows:

> "A single dose of 8 mg of tizanidine reduces muscle tone in patients with spasticity for a period of several hours. The effect peaks at approximately 1 to 2 hours and dissipates between 3 and 6 hours. Effects are dose related.
>
> Although single doses of less than 8 mg have not been demonstrated to be effective in controlled clinical studies, the dose-related nature of tizanidine's common adverse events make it prudent to begin treatment with single oral doses of 4 mg. Increase the dose gradually (2 to 4 mg steps) to optimum effect (satisfactory reduction of muscle tone at a tolerated dose).

> The dose can be repeated every 6 to 8 hours, as needed, to a maximum of three doses in 24 hours. The total daily dose should not exceed 36 mg."

Thus, once titrated, patients prescribed Zanaflex® must take two tablets, as a single dose, every 6 to 8 hours. The proposed 8 mg dosage strength offers patients greater convenience by providing that single dose in one tablet. In addition, the proposed 8 mg dosage strength will reduce the number of tablets a patient must ingest each day, thereby potentially improving a patient's compliance with the drug product's dosing regimen.

In summary, the proposed change in strength of tizanidine hydrochloride from 4 mg to 8 mg will not raise questions of safety or efficacy for the proposed product. The indication remains unchanged and the proposed dosing is consistent with that recommended in the labeling of the approved reference listed drug product. Therefore, the Agency should conclude that clinical investigations are not necessary to demonstrate the proposed product's safety or effectiveness.

There are no proposed changes in labeling with the exception of the obvious changes in strength sought in this petition. 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 Attachment 3.

Therefore, the petitioner requests that the Commissioner find that a change in strength from 4 mg to 8 mg in the proposed Tizanidine Hydrochloride Tablets, 8 mg, raises no questions of safety or effectiveness, and the Agency should approve the petition.

Inapplicability of the Pediatric Research Equity Act ("PREA"). PREA, which is codified at FDC Act § 505B, does not apply to a new strength, such as the one proposed in this Petition. (See FDC Act § 505B(a)(1)(A).) As such, PREA should not serve as an impediment to the Agency's granting of this Petition.

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,

Joan Janulis, R.A.C.
Vice President

cc: Martin Shimer (OGD)

JJ/pk

Attachments:
1. Approved Drug Products with Therapeutic Equivalence Evaluations, Electronic Orange Book listing accessed July 9, 2013
2. Approved labeling for reference listed drug product (RLD), Zanaflex (Acorda), updated June 2010
3. Draft Insert Labeling Proposed for Tizanidine Hydrochloride Tablets, 8 mg

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