LACHMAN CONSULTANT SERVICES, INC.

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June 4, 2013

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OVERNIGHT COURIER 06/04/13

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, Tramadol Hydrochloride 37.5 mg and Acetaminophen 300 mg Tablets, 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 Tramadol Hydrochloride 37.5 mg and Acetaminophen 300 mg Tablets, is suitable for submission as an ANDA. The reference listed drug product (RLD), upon which this petition is based, is Ultracet® (Tramadol and Acetaminophen) 37.5 mg/325 mg Tablets, NDA 021123, currently held by Janssen Pharmaceuticals as designated in the Orange Book. Therefore, the petitioner seeks a change in strength of the acetaminophen component (from 325 mg to 300 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, Ultracet® Tablets by Janssen is a tablet product containing 325 mg of Acetaminophen and 37.5 mg of Tramadol Hydrochloride. See product listing for NDA 021123 from the electronic Orange Book also known as the *Approved Drug Products with Therapeutic Equivalence Evaluations*, accessed June 4, 2013, which lists the approval of the RLD. (Attachment 1) The proposed drug product also represents a tablet dosage form, but containing 300 mg of acetaminophen in combination with 37.5 mg of Tramadol Hydrochloride. The petition is thus seeking a change in strength of only the acetaminophen component (from 325 mg to 300 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.

The current dosing instructions in the approved labeling of the RLD are as follows:

> "2 tablets every 4 to 6 hours as needed for pain relief, up to a maximum of 8 tablets per day."

Total Maximum Acetaminophen Exposure = 2.6 g/day, well below the maximum 4 g permissible daily exposure level. The approved package insert for Ultracet Tablets (tramadol hydrochloride 37.5 mg and acetaminophen 325 mg tablets) is included in Attachment 2.

The dosage for the proposed product (Attachment 3) is "2 tablets every 4 to 6 hours as needed for pain relief, up to a maximum of 8 tablets per day." Total Maximum Acetaminophen Dose = 2.40 g/day. This dosage is consistent with the dosage approved in the reference listed drug product's labeling.

In further support of approval of Acetaminophen at a 300 mg dosage level, FDA has approved 300 mg as a safe and effective dose in other combination products, such as Acetaminophen and Butalbital Tablets,

Acetaminophen and Codeine Phosphate Tablets, Acetaminophen and Hydrocodone Bitartrate Tablets, and Acetaminophen and Oxycodone Hydrochloride Tablets. Please see Attachment 4.

In summary, the proposed change in strength of the non-narcotic component from that of the reference listed drug (i.e., a change of acetaminophen from 325 mg to 300 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's request for the Commissioner to find that a change in strength from 325 mg to 300 mg of acetaminophen in the proposed Tramadol Hydrochloride and Acetaminophen Tablets, 37.5 mg/300 mg, should raise 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
Vice President

JJ/pk

Attachments:

1. Approved Drug Products with Therapeutic Equivalence Evaluations, Electronic Orange Book listing accessed June 4, 2013
2. Approved labeling for reference listed drug product (RLD), Ultracet Tablets (Janssen), updated February 2013
3. Draft Insert Labeling Proposed for Tramadol Hydrochloride, 37.5 mg and Acetaminophen, 300 mg Tablets
4. List of products approved in Electronic Orange Book with 300 mg dosage strength of Acetaminophen, accessed June 4, 2013

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