LACHMAN CONSULTANT SERVICES, INC.

CONSULTANTS TO THE PHARMACEUTICAL AND ALLIED INDUSTRIES

1600 STEWART AVENUE, WESTBURY, NY 11590
(516) 222-6222 • FAX (516) 683-1887

July 9, 2013

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OVERNIGHT COURIER 07/09/2013

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, to request that the Commissioner of the Food and Drug Administration declare that the drug product, Hydromorphone HCl Extended-Release Tablets, 24 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 declare that Hydromorphone HCl Extended-Release Tablets, 24 mg, is suitable for submission in an ANDA. The reference listed drug product (RLD), upon which this petition is based, is EXALGO® (hydromorphone HCl) Extended Release Tablets, 32 mg, NDA 021217, held by Mallinckrodt. (EXALGO® is also approved in dosage strengths of 8, 12, and 16 mg. These strengths constitute listed drugs which are also supportive of this petition.) Therefore, the petitioner seeks a change in strength from that of the Reference Listed Drug, to provide for an intermediate, 24 mg strength.

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, EXALGO® is an extended-release tablet for oral administration, containing 32 mg of hydromorphone HCl. EXALGO® is also available in dosage strengths of 8, 12, and 16 mg. (See Attachment 1 - product listing for NDA 021217 from the electronic Orange Book also known as the *Approved Drug Products with Therapeutic Equivalence Evaluations,* updated as of July 9, 2013.) The proposed product is also an extended-release tablet for oral administration, but contains 24 mg of hydromorphone HCl. The petition is thus seeking a change in strength from that of the RLD.

The proposed 24 mg strength is consistent with and contemplated by the dosing recommendations of the RLD's current labeling. (Attachment 2) The labeling states that initiation of dosing with EXALGO® should take into account the patient;s prior analgesic experience, with close monitoring for respiratory depression especially during the first 24 – 72 hours following initiation of therapy. It also identifies additional factors should be taken into consideration in selecting the initial dose. For patients being converted from other oral hydromorphone formulations, a starting dose equivalent to the patient's total daily oral dose of hydromorphone may be administered once daily. For patients being converted from therapy with other oral opioids, a tabular listing of conversion ratios is provided to assist in calculating the equivalent oral, once daily dose of EXALGO®.

The labeling also acknowledges that there is substantial inter-patient variation in the relative potency of different opioid drugs and formulations, and advises that it is safer to underestimate a patient's 24-hour oral hydromorphone requirement and to provide rescue medication as needed, than to overestimate and manage an adverse reaction.

The availability of an intermediate, 24 mg strength will thus provide dosing flexibility to enable selection of an appropriate initial dose and titration to a maintenance dose that delivers adequate analgesia while minimizing adverse reactions. It will also allow for appropriate tapering of the dose prior to discontinuation of therapy, to prevent withdrawal symptoms in opioid-tolerant patients.

There are no proposed changes in the labeling for Hydromorphone Extended-Release Tablets, 24 mg, other than the change sought in this petition. (Draft labeling for the proposed product is provided as Attachment 3.)

Based upon the foregoing, Hydromorphone HCl Extended-Release Tablets, 24 mg should raise no questions of safety or effectiveness. Additionally, the requirements for conduct of pediatric assessments prescribed under the Pediatric Research Equity Act (PREA codified at Section 505(b) of the Act) do not apply to an application submitted under Section 505 of the Act for a different dosage strength. Therefore, PREA should not serve as an impediment to this petition.

For the foregoing reasons, the Petitioner respectfully request that the Agency find that the drug product, Hydromorphone HCl Extended-Release Tablets, 24 mg is suitable for submission under an ANDA.

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 is unfavorable to the petition.

Respectfully submitted,

Joan Janulis, RAC
Vice President

JJ/pk

Attachments:
1. Approved Drug Products with Therapeutic Equivalence Evaluations, Electronic Orange Book listing updated as of July 9, 2013
2. Current labeling for reference listed drug product (RLD), EXALGO® (hydromorphone HCl) Extended-Release Tablets (Revised 3/2013 and Accessed from Daily Med)
3. Draft Labeling Proposed for Hydromorphone Extended-Release Tablets, 24 mg

cc: Martin Shimer, OGD

Petition Hydromorphone ER

From: (516) 683-1881 Origin ID: RMEA
Westbury Office
LACHMAN CONSULTANT SERVICES
1600 STEWART AVE
SUITE 604
WESTBURY, NY 11590

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