

LACHMAN CONSULTANT SERVICES, INC.
CONSULTANTS TO THE PHARMACEUTICAL AND ALLIED INDUSTRIES

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

January 30, 2007

OVERNIGHT COURIER 1/30/07

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 MonoSolRx, LLC requesting the Commissioner of the Food and Drug Administration to declare that the drug product, Zolpidem Tartrate Orally-Dissolving Strips, 5 mg and 10 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 Zolpidem Tartrate Orally-Dissolving Strips, 5 mg and 10 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 Ambien® (Zolpidem Tartrate) Tablets, 5 mg and 10 mg, NDA 19-908. Both the 5 mg and 10 mg strengths of Ambien® Tablets are manufactured by Sanofi-Aventis US, LLC. (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 oral tablets to an orally-dissolving 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, Ambien® Tablets by Sanofi-Aventis US is currently available as 5 mg and 10 mg oral tablets. The proposed drug product represents an orally-dissolving strip, containing the same 5 mg and 10 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-dissintegrating tablet that has been previously approved by the FDA. Each dosage unit

2007P-0042
www.lachmanconsultants.com

LCS@lachmanconsultants.com

CP1

(strip) will contain either 5 mg or 10 mg of Zolpidem Tartrate 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. 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 Attachment 2, and the RLD's approved labeling is provided in Attachment 3.

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. Zolpidem, a product first approved for use in 1992, was not on the list of drug products for which additional pediatric information may produce health benefits in the pediatric population (May 2001) nor is Zolpidem on the current list of drugs for which pediatric studies are needed (April 2006). According to FDA's list of issued written requests, a written request was issued by the Agency to the innovator for pediatric studies for Zolpidem. However, we note that Sanofi-Aventis has been awarded a 6-month period of pediatric exclusivity for all of their Zolpidem Tartrate products (Ambien[®] and Ambien CR[™]) indicating that the written request for pediatric studies has been fulfilled. In that regard, because the requirements for the conduct of pediatric studies has been satisfied by those studies submitted by the innovator in response to the written request, there should be no need to repeat such studies or engage in additional studies for the product proposed by this petition seeking the same condition of use as that of the RLD product upon which this petition is based.

Additionally, we note that in the tentative approval letter for NDA 21-412 for Zolpidem Tartrate Orally-Disintegrating Tablets to Biovail Technologies issued on May 26, 2005, the Agency did not request any additional pediatric studies. Since the Biovail application was for a new dosage form, orally-disintegrating tablets, under PREA the Agency could have required additionally pediatric studies if they were needed. However, no additional studies were requested.

Thus, the fulfillment of the written request by Sanofi-Aventis (indicated by the granted pediatric exclusivity) and the lack of request for additional pediatric studies in the tentative approval letter for Zolpidem Tartrate Orally-Disintegrating Tablets indicate that additional pediatric studies are no longer needed for Zolpidem Tartrate. Therefore, the introduction of an alternate dosage form that can be used in a similar manner as the other approved Zolpidem Tartrate products will not represent a meaningful therapeutic benefit over existing therapies for pediatric patients. Based on the nature of the medication and its routine use, it is not likely that the product will be used in a substantial number of 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,


John Janulis, Director
Lachman Consultant Services, Inc.

JJ/pk

- Attachments:
1. Approved Drug Products with Therapeutic Equivalence Evaluations, accessed January 17, 2007
 2. Draft Labeling Proposed for Zolpidem Tartrate Orally-Dissolving Strips
 3. Labeling for the Reference-Listed Drug Ambien[®], June 2006

cc: Craig Kiester (OGD)

Ambien[®] and Ambien CR[™] are registered trademarks of Sanofi-Aventis US, LLC.

M45JD7030