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APPLICATION NUMBER:

21-997

OFFICE DIRECTOR MEMO

MEMORANDUM

DATE: March 12, 2009

FROM: Director
Division of Neurology Products/HFD-120

TO: NDA 21-997

SUBJECT: Action Memo for NDA 21-997, for the use of Edluar (zolpidem tartrate sublingual tablets) in the treatment of insomnia characterized by difficulty falling asleep

NDA 21-997, for the use of Edluar (zolpidem tartrate sublingual [SL] tablets) in the treatment of insomnia characterized by difficulty falling asleep, was submitted by Orexa AB on 5/13/08. The application was submitted under section 505(b)(2) of the Federal Food, Drug, and Cosmetic Act, with Ambien as the reference listed drug. The application contains the results of a pivotal bioequivalence (BE) study comparing a single 10 mg dose of Edluar to a single 10 mg dose of Ambien. The application also contains a bioequivalence study comparing the formulation of Edluar studied in the pivotal BE study to the to-be-marketed formulation, a 60 day open-label study evaluating the effects of the SL tablet on the oral mucosa, as well as a cross-over study comparing a single 10 mg dose of Edluar to a single 10 mg dose of Ambien in patients with chronic insomnia in which sleep latency was evaluated. Several other pharmacokinetic (PK) studies were also performed.

The application has been reviewed by Dr. Suhail Kasim, medical officer, Dr. Thomas Wong, chemist, Dr. Jagan Parepally, clinical pharmacologist, Ms. Melina Griffis, Division of Medication Error Prevention and Analysis, Dr. Alicja Lerner, Controlled Substances Staff, Dr. Leyla Sahin, Pediatric and Maternal Health Staff, Dr. Melissa Banks, pharmacologist, Dr. Sriram Subramaniam, Division of Scientific Investigations, and Dr. Ron Farkas, Acting Neurology Team Leader. The clinical team recommends that the application be approved.

I agree that the application should be approved. The sponsor has documented that Edluar and Ambien are bioequivalent, and that there are no safety issues that would preclude approval. Several issues are worth noting, however.

The Controlled Substances Staff has expressed concern that the rapid dissolution of the SL tablets and their high solubility in carbonated drinks could lead to misuse of this product in criminal acts. For this reason, they have proposed that the sponsor commit to increased post-marketing surveillance for such events. Specifically, they have recommended that the sponsor: 1) submit expedited reports of "Events of Interest" related to abuse/misuse, 2) include a discussion in their quarterly periodic reports related to these events, and 3)

review data from the Drug Abuse Warning Network and the Toxic Exposure Surveillance System prepared by the National Poison Data System; the sponsor has agreed to do so.

b(4)

We have agreed with the sponsor on the language for product labeling, which is almost identical to that for Ambien. For these reasons, I will issue the attached Approval letter, with appended product labeling.

Russell Katz, M.D.

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/s/

Russell Katz
3/13/2009 02:01:17 PM
MEDICAL OFFICER