CENTER FOR DRUG EVALUATION AND RESEARCH

APPLICATION NUMBER:

22-032

SUMMARY REVIEW(S)

MEMORANDUM

Department Of Health and Human Services
Food and Drugs Administration
Center for Drug Evaluation and Research

Date: **June 12, 2007**

From: **Andrea Leonard-Segal, M.D.**
Director, Division of Nonprescription Clinical Evaluation

Joyce Korvick, M.D.
Acting Director, Division of Gastroenterology Products

Subject: **NDA 22-032**
Omeprazole 20 mg Tablets

Sponsor: **Dexcel Pharma Technologies, Ltd.**

Background:
On December 8, 2006, the FDA issued an Approvable Letter to Dexcel Pharma Technologies, Ltd. (DPT) for NDA 22-032, a 505(b)(2) application for Omeprazole Delayed Release Tablets 20 mg. The product is indicated for the nonprescription treatment of frequent heartburn. The sponsor seeks the same indication and treatment regimen for their product as for Prilosec OTC™.

The Approvable Letter stated the following:

1. During a recent inspection of one _____ facility for this application, our field investigator issued a 483 Notice of Findings to the facility's representative. Satisfactory resolution of the deficiencies is required before this application may be approved. b(4)
2. During a recent inspection of one of the manufacturing facilities for this application, our field investigator verbally conveyed issues to the facility's representative requiring revision to specifications and analytical procedures. Our review of these revisions is required before this application may be approved.

The letter also informed the sponsor that they would need to make several revisions to their labeling, that they would need to provide a summary of adverse events for their product, and that they should provide an updated estimate of use for their product marketed in other countries.

On December 18, 2007, the sponsor submitted their complete response to the approvable letter.

Chemistry:
DPT submitted data that satisfied Drs. Ysern and Rhee that the inspection of all manufacturing facilities was acceptable and that the revised analytical methods were satisfactory. The chemistry reviewers concluded that all chemistry issues have been addressed and recommend that this NDA can be approved. Refer to their review dated February 22, 2007.

Clinical Pharmacology:
Refer to the review by Drs. Adebowale and Lee, dated June 1, 2007 and the e-mail exchange between Dr. Adebowale and Dr. Leonard-Segal entered into the Division Files System on June 5, 2007. The concerns related to the integrity of the clinical pharmacology data have been resolved. The sponsor submitted pharmacokinetics and statistical data that demonstrates the bioequivalence of their omeprazole delayed release 20 mg formulation with Prilosec OTC 20.6 mg omeprazole magnesium delayed release tablets.

Clinical Safety Update
Dr. Lolita Lopez reviewed the safety data provided by the sponsor in the original submission (see her review dated November 9, 2006) and the safety data submitted in the complete response. She notes that the DPT omeprazole formulation under review is not approved elsewhere; the enteric coat is different from the DPT omeprazole 20 mg tablets marketed in Israel and in the United Kingdom (U.K.).

For the safety update submission, the sponsor submitted safety data on their omeprazole formulation marketed in the U.K. and in Israel covering the period from June, 2006 to November, 2006, during which time there were ——— sold and an estimated ——— patients exposed. As of November 30, 2006 there have been at least ——— million patients exposed to DPT's omeprazole 20 mg in both the U.K. and in Israel. The sponsor reported that there have been no regulatory actions taken for safety related reasons for this product. b(4)

No new safety signals for omeprazole and no deaths or serious adverse events were reported in the safety data provided. Six patients reported a lack of effect and one reported diarrhea. One reported taking an excessive dose but did not experience an adverse event.

Dr. Lopez recommends that from a clinical safety standpoint, DPT's proposed omeprazole 20 mg delayed release tablet has an acceptable safety profile for OTC marketing for the sought indication and duration of use and should be approved.

The Prilosec OTC label has been updated to include drug interaction warnings for tacrolimus and for atazanivir. The sponsor was told that these drug interaction warnings should appear on the DPT omeprazole Drug Facts label and in the package insert.

Labeling:
The sponsor has responded to all labeling requests made by the Agency and there are no unresolved labeling issues.

Pediatric Studies:
As detailed in the reviews written by each of us during the first submission cycle of this NDA, we both agree that it is appropriate to grant a waiver for pediatric studies for this application.

Legal Issues:
On April 11, 2007 DPT submitted a document informing the FDA that on May 31, 2006 Astra Zeneca sued them under the Hatch-Waxman Act. The suit alleges patent infringement for formulation patents US 4,853,230, US 4,786,505, the subject of which is the subcoating layer in the omeprazole formulation, and for crystalline form patent US 6,150,380. Consequently, there is a 30-month stay of FDA approval (which began on May 31, 2006) of NDA 22-032. The sponsor did not inform us of this legal situation until after the first review cycle had ended and the sponsor had been issued their Approvable letter.

Conclusions:
There are no outstanding medical or scientific issues to be resolved prior to approving this NDA. However, the legal matters must be settled prior to final approval of this NDA.

Recommendations:
This NDA should receive a Tentative Approval action pending resolution of the lawsuit over the alleged patent infringement.

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/s/

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