

CMC BRANCH CHIEF MEMORANDUM

To: NDA 22-173
From: Ramesh Sood, Branch Chief, ONDQA
Date: 13-Nov-2008
Drug name: Zyprexa (olanzapine) for extended-release injectable suspension
Subject: **“Approval”** recommendation for NDA 22-173

This resubmission contained responses to CMC deficiencies communicated to the applicant on 30th January, 2008. The applicant has provided satisfactory response to all CMC issues. The review # 3 contains an evaluation of applicant’s responses. Based on the satisfactory review of these responses in review #3 and subsequent memorandum by the CMC reviewer dated 13-Nov-08 in DFS, this application is recommended for **“Approval”** from CMC perspective. The CDER Labeling and Nomenclature Committee has determined that the most appropriate established name for this product is **“(olanzapine) for extended release injectable suspension”**. This information should be relayed to the Applicant and incorporated in the final labeling.

Please refer to my first memorandum for additional drug substance and drug product details.

A tentative expiration period of 36-month and 24-month are being assigned to the olanzapine pamoate powder drug product and the vehicle, respectively, based on the submitted stability data.

All manufacturing sites have been found acceptable by the Office of Compliance.

**This is a representation of an electronic record that was signed electronically and
this page is the manifestation of the electronic signature.**

/s/

Ramesh Sood
11/13/2008 11:50:45 AM
CHEMIST

MEMORANDUM

DEPARTMENT OF HEALTH AND HUMAN SERVICES
PUBLIC HEALTH SERVICE
FOOD AND DRUG ADMINISTRATION
CENTER FOR DRUG EVALUATION AND RESEARCH

DATE: November 12, 2008

FROM: David J. Claffey, Ph.D., ONDQA

SUBJECT: **Final CMC recommendation for**
NDA 22-173, Zyprexa (olanzapine) for extended release injectable
suspension

At the completion of CMC Review #3 for NDA 22-173 an approval recommendation was made with the caveat that any subsequent changes in the drug product dissolution method or acceptance limits would necessitate a reevaluation of the provided stability data and expiry period.

On November 7, 2008 the OCP review team completed their evaluation of the proposed drug product dissolution specification. They recommended that the acceptance criterion for the 2-hour time point for the 210 mg strength be limited to a (b) (4) range rather than the proposed (b) (4) range.

With this in mind, the stability and batch analysis data were reevaluated by this reviewer. The primary stability data together with data from the clinical lots at the 2-hour time point for the 210 mg strength fell within a consistently narrow range (average 60% with *ca.* 4.0% standard deviation). Therefore, the recommended change will not impact the expiry period accepted for this product (36 months) or the prior overall approval recommendation from a CMC perspective.

However, it should be noted that the validation lot for the 210 mg strength (#A302103), manufactured at the same scale and site as the proposed commercial drug product had an average dissolution result of (b) (4) at the 2-hour time point. This lot will fail to meet specifications should the Applicant accept the recommended changes. It should be noted that, in the Applicant's recent extensive justification for their need for a (b) (4)-point range at this time point (November 3, 2008), they failed to mention this result as a reason for requesting the wider acceptance criterion.

**This is a representation of an electronic record that was signed electronically and
this page is the manifestation of the electronic signature.**

/s/

David Claffey
11/13/2008 08:47:21 AM
CHEMIST

Ramesh Sood
11/13/2008 10:43:40 AM
CHEMIST