CENTER FOR DRUG EVALUATION AND RESEARCH

APPLICATION NUMBER:

204150Orig1s000

SUMMARY REVIEW

M E M O R A N D U M

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

DATE: 4 March 2013

FROM: Mitchell V. Mathis, M.D.
Acting Director
Division of Psychiatry Products, HFD-130

TO: File NDA 204150 [29 Feb 2012 submission]

SUBJECT: Approval recommendation for desvenlafaxine (base) extended-release tablets for the treatment of major depressive disorder (MDD)

Background and Regulatory History
This is a 505(b)(2) application for a once daily extended-release formulation of desvenlafaxine base (DVS-base). The reference listed drug is Pristiq (desvenlafaxine succinate) which was approved for MDD in Feb 2008 (NDA 21992). The application consists of CMC and bioequivalence data from two pharmacokinetic studies.

A tentative approval (TA) letter was issued 21 Dec 2012 with the only outstanding issue preventing final approval being unexpired exclusivity protection for the RLD (exclusivity period ending 1 March 2013).

Chemistry Manufacturing and Controls (CMC)
The sponsor intends to market this drug in the same two strengths as the RLD: 50 mg and 100 mg. Dr. Duan reviewed an alcohol dose dumping study and the dissolution methodology and acceptance criteria and found the application acceptable. Dr. Sapru reviewed the CMC information submitted in support of the application. He identified several deficiencies for the drug substance and product, but was able to resolve these deficiencies by working with the sponsor during the review cycle. The CMC team now recommends approval of this product.

Nonclinical Pharmacology/Toxicology
There are no unresolved pharmacology/toxicology issues for this application.

Office of Clinical Pharmacology
Dr. Kumi reviewed two bioequivalence (BE) studies and found both doses to be bioequivalent to the RLD. The Office of Scientific Investigation (OSI) conducted inspections of the clinical and bioanalytical study sites (b) (4) and determined the data submitted are acceptable.

Clinical
Safety
Dr. Mannheim reviewed the safety data from the bioequivalence development program. There were no serious adverse events and no meaningful differences compared to what is known about and labeled for the RLD.

Reference ID: 3270474

Revised Labeling
Labeling has been negotiated and agreement reached; labeling is based upon the RLD.

Conclusions and Recommendations
The sponsor has provided adequate evidence that desvenlafaxine base is bioequivalent to the RLD. There were no new or unexpected clinical safety findings. The review team has recommended approval of this supplement and I agree with the team. There are no outstanding review or inspection issues. The period of exclusivity for the RLD has expired. Labeling has been negotiated and finalized.

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/s/

MITCHELL V Mathis
03/04/2013