

**CENTER FOR DRUG EVALUATION AND
RESEARCH**

APPLICATION NUMBER:

204683Orig1s000

SUMMARY REVIEW

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

DATE: 10 July 2013

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

TO: File NDA 204683 [13 Sep 2012 submission]

SUBJECT: Approval recommendation for desvenlafaxine base ER (Khedezla) for the treatment of major depressive disorder

Background and Summary

Desvenlafaxine is a serotonin norepinephrine reuptake inhibitor (SNRI) approved as Pristiq (desvenlafaxine succinate ER) for the treatment of major depressive disorder (MDD). This application was submitted under 505(b)(2) and cites the Pristiq approval for evidence of safety and efficacy. The sponsor is Osmotica and the development program consisted of demonstrating bioequivalence between this drug product and Pristiq. The most relevant review was from the Office of Clinical Pharmacology (OCP) and their summary findings were that Khedezla is bioequivalent to Pristiq for both doses (50 mg and 100 mg) under fasting conditions and to Pristiq 100 mg under fed conditions. The OCP team has recommended approval and I agree with them (See Dr. Kumi's review for details).

Chemistry Manufacturing and Controls (CMC)

CMC determined the submission to be adequate and acceptable. Site inspections were conducted and found acceptable.

Nonclinical Pharmacology/Toxicology

There are no pharmacology/toxicology data provided as part of this application. No new impurities, degradants, or novel excipients were identified.

Office of Clinical Pharmacology (OCP)

OCP has concluded that this product is bioequivalent to Pristiq. They evaluated three studies:

1. A Relative Bioavailability Study of desvenlafaxine ER 100 mg versus Pristiq 100 mg under Fed Conditions (Study OS230-1006).
2. A Randomized, Open Label, Two Treatment, Two Period, Two Sequence, Single Dose, Crossover, Oral Comparative Bioavailability Study Of desvenlafaxine ER 50mg and Pristiq 50mg conducted in fasting healthy adults (Study 11-VIN-478).

3. A Randomized, Open Label, Two Treatment, Two Period, Two Sequence, Single Dose, Crossover, Oral Comparative Bioavailability Study of desvenlafaxine ER 100mg and Pristiq conducted in fasted healthy adults (Study 11-VIN-479).

An *in vitro* alcohol dose dumping study was also conducted for this extended-release product and no dose dumping was observed. The test drug product was found to be bioequivalent to the RLD and OCP recommends approval with no postmarketing commitments. Section 12.3 of labeling has been adopted as recommended by OCP.

Clinical

There were no safety or efficacy studies conducted under this NDA. No new or unexpected safety signals were identified from the clinical pharmacology studies used to demonstrate bioequivalence.

Labeling

Labeling is in PLR format modeled after the RLD. Specific information from the BE trials is included in section 12.3 and the RLD is identified as desvenlafaxine succinate.

Postmarketing Requirements/Commitments

None have been identified. Pediatric trials will be deferred to the innovator.

Conclusions and Recommendations

Sufficient information has been submitted to conclude that this formulation of desvenlafaxine ER is bioequivalent to the approved product.

The labeling and Medication Guide has been negotiated to current Division standards.

The sponsor has agreed to labeling and this application should be approved by the PDUFA date.

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/s/

MITCHELL V Mathis
07/10/2013