

**CENTER FOR DRUG EVALUATION AND  
RESEARCH**

*APPLICATION NUMBER:*

**205208Orig1s000**

**SUMMARY REVIEW**

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

---

**DATE:** 10 October 2013

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

**TO:** File NDA 205208

**SUBJECT:** Approval recommendation for desvenlafaxine fumarate ER (DVF-ER) tablet 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 Teva and the development program consisted of demonstrating bioequivalence between this drug product and Pristiq and supplying Chemistry, Manufacturing, and Control (CMC) data to support approval. The most relevant review was from the Office of Clinical Pharmacology (OCP) and their summary findings were that DVF-ER is bioequivalent to Pristiq for both doses (50 mg and 100 mg) under fasting conditions and can be given with or without food. 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 DVF-ER is bioequivalent to Pristiq. They evaluated three studies:

1. A Relative Bioavailability Study of DVF-ER 50 mg versus Pristiq 50 mg under Fed and Fasting Conditions (Study 2012-2833).
2. A Randomized, Open Label, Two Treatment, Two Period, Two Sequence, Single Dose, Crossover, Oral Comparative Bioavailability Study Of desvenlafaxine ER 100mg and Pristiq 100mg conducted in fasting healthy adults (Study 53811).

3. A Randomized, Open Label, Two Treatment, Two Period, Two Sequence, Single Dose, Crossover, Oral Comparative Bioavailability Study of DVF-ER 100mg and Pristiq 100 mg conducted in fed healthy adults (Study 53711).

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.

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

/s/  
-----

MITCHELL V Mathis  
10/10/2013