CENTER FOR DRUG EVALUATION AND RESEARCH

APPLICATION NUMBER:

205583Orig1s000

PHARMACOLOGY REVIEW(S)

PHARMACOLOGY/TOXICOLOGY MEMO TO THE FILE

NDA 205583
Submission: SDN 1, serial number 0000, submitted 3/28/12, received on 3/28/12
Drug name: Desvenlafaxine (Fumarate) ER tablets (50mg and 100mg strength)
Sponsor: Sun Pharmaceuticals Global FZE
Indication: Major Depressive Disorder
Reviewer: Shiny V. Mathew, Ph.D., Pharmacologist.
HFD-130, Division of Psychiatry Products

RE: A new formulation of desvenlafaxine extended release tablets (as the fumarate salt); submitted under 505(b)(2).

Background: The current NDA is a 505 (b)(2) application for Desvenlafaxine Fumarate with PRISTIQ® (NDA 21992, approved on 02/29/2008) as the reference listed drug (RLD). The Sponsor of this NDA has manufactured Desvenlafaxine Fumarate Extended release tablets to be bioequivalent to 50 mg and 100 mg to PRISTIQ® ER. Desvenlafaxine, the major metabolite of venlafaxine, is a norepinephrine and serotonin reuptake inhibitor (SNRI) exhibiting limited inhibition of dopamine reuptake. Irrespective of the salt form, desvenlfaxine (base) is found in the blood and is measured in pharmacokinetic studies.

The current submission: This submission is a 505(b)(2) application for the fumarate salt of desvenlafaxine. The Sponsor of this NDA has provided clinical studies to demonstrate bioequivalence to the reference listed drug PRISTIQ® at both 50mg and 100mg doses. The Sponsor is relying on the Agency's previous findings of safety and efficacy for PRISTIQ®. Therefore, no new nonclinical data are submitted with this NDA. However, the Sponsor's nonclinical summary indicates that a literature search was conducted on four databases (Biosis Previews®, EMBASE®, MEDLINE® and Toxfile) on May 28, 2013 yielding six unique citations. The Sponsor reviewed these citations and found that there were no new data that could contribute significantly to nonclinical safety related information. These literature citations were not provided within the submission. The Sponsor does not propose any changes to nonclinical sections of the label other than replacing PRISTIQ® with Desvenlafaxine Fumarate Extended Release Tablets, where applicable.

No impurities, degradants, or novel excipients in Desvenlafaxine Fumarate Extended Release tablets that would require additional toxicological characterization have been identified at this time. Consequently, there are no Pharmacology/Toxicology issues with this NDA.

Conclusion: There are no Pharmacology/Toxicology issues that would prevent the approval of this NDA.

Signatures:

Shiny V. Mathew, Ph.D., Pharmacologist *{see appended electronic signature page}*
Linda H. Fossom, Ph.D., Supervisory Pharmacologist *{see appended electronic signature page}*

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

/s/

SHINY V MATHEW
12/17/2013

LINDA H FOSSOM
12/17/2013

PHARMACOLOGY/TOXICOLOGY FILING CHECKLIST FOR NDA/BLA or Supplement

NDA Number: 205583 **Applicant: Sun Pharma Global FZE** **Stamp Date: March 28, 2013**

Drug Name: Desvenlafaxine fumarate (ER) tablets **NDA Type: 505(b)(2)**

On **initial** overview of the NDA/BLA application for filing:

	Content Parameter	Yes	No	Comment
1	Is the pharmacology/toxicology section organized in accord with current regulations and guidelines for format and content in a manner to allow substantive review to begin?	X		This NDA is being submitted as a 505(b)(2) application. The Sponsor is relying on the Agency's previous findings of safety and efficacy for the innovator product PRISTIQ® (desvenlafaxine [succinate]) Extended-Release Tablets; therefore, no nonclinical studies have been conducted in support of the submission.
2	Is the pharmacology/toxicology section indexed and paginated in a manner allowing substantive review to begin?			N/A
3	Is the pharmacology/toxicology section legible so that substantive review can begin?	X		See Comment 1 above.
4	Are all required (*) and requested IND studies (in accord with 505 b1 and b2 including referenced literature) completed and submitted (carcinogenicity, mutagenicity, teratogenicity, effects on fertility, juvenile studies, acute and repeat dose adult animal studies, animal ADME studies, safety pharmacology, etc)?			N/A
5	If the formulation to be marketed is different from the formulation used in the toxicology studies, have studies by the appropriate route been conducted with appropriate formulations? (For other than the oral route, some studies may be by routes different from the clinical route intentionally and by desire of the FDA).			N/A
6	Does the route of administration used in the animal studies appear to be the same as the intended human exposure route? If not, has the applicant submitted a rationale to justify the alternative route?			N/A
7	Has the applicant submitted a statement(s) that all of the pivotal pharm/tox studies have been performed in accordance with the GLP regulations (21 CFR 58) or an explanation for any significant deviations?			N/A

File name: 5_Pharmacology_Toxicology Filing Checklist for NDA_BLA or Supplement 010908

PHARMACOLOGY/TOXICOLOGY FILING CHECKLIST FOR NDA/BLA or Supplement

	Content Parameter	Yes	No	Comment
8	Has the applicant submitted all special studies/data requested by the Division during pre-submission discussions?			N/A
9	Are the proposed labeling sections relative to pharmacology/toxicology appropriate (including human dose multiples expressed in either mg/m2 or comparative serum/plasma levels) and in accordance with 201.57?	X		This 505(b)(2) application will be relying on content from RLD (Wyeth Pharmaceutical's PRISTIQ®) for the current labeling text.
10	Have any impurity – etc. issues been addressed? (New toxicity studies may not be needed.)	X		There are no currently known issues regarding new excipients, impurities and/or degradants present that may need to be qualified. No filing issues have been identified by the Chemistry reviewer.
11	Has the applicant addressed any abuse potential issues in the submission?			N/A
12	If this NDA/BLA is to support a Rx to OTC switch, have all relevant studies been submitted?			N/A

IS THE PHARMACOLOGY/TOXICOLOGY SECTION OF THE APPLICATION FILEABLE? ___yes___

Please identify and list any potential review issues to be forwarded to the Applicant for the 74-day letter.

None at this time

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

/s/

SHINY V MATHEW
05/10/2013

LINDA H FOSSOM
05/10/2013