CENTER FOR DRUG EVALUATION AND RESEARCH

APPLICATION NUMBER:

204683Orig1s000

PHARMACOLOGY REVIEW(S)

PHARMACOLOGY/TOXICOLOGY MEMO TO THE FILE

NDA 204683
Submission: SDN 1, serial No. 000, submitted and received on 9/13/12
Drug name: KHEDEZLA tablets (desvenlafaxine extended release tablets as 50 mg and 100mg strengths)
Sponsor: Osmotica Pharmaceuticals
Indication: Major Depressive Disorder
Reviewer: Shiny V. Mathew, Ph.D., Pharmacologist.
HFD-130, Division of Psychiatry Products

Re: New formulation (base alone) of desvenlafaxine extended release tablets submitted under 505 (b)(2)

Background: KHEDEZLA is an extended release formulation of desvenlafaxine (base) for the treatment of MDD. Desvenlfaxine is a selective serotonin and norepinephrine reuptake inhibitor (SNRI). Desvenlafaxine (HCl) is currently marketed as PRISTIQ®. The currently approved dosage strength for PRISTIQ® is 50mg/day although clinical dose of up to 400mg has been tested. This NDA for KHEDEZLA tablets is a 505 (b)(2) application with PRISTIQ® as the reference listed drug.

The current submission: The Sponsor has demonstrated bioequivalence to the reference listed drug at dose of 50 mg and 100mg. For the non-clinical data to support this NDA, the Sponsor has relied on our previous finding of safety (and efficacy) for PRISTIQ®. Therefore, no new nonclinical data were submitted with this NDA.

No impurities, degradants, or novel excipients in desvenlafaxine (base) extended release tablets that would require additional toxicological characterization have been identified.

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., Team Leader *{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
05/29/2013

LINDA H FOSSOM
05/29/2013

PHARMACOLOGY/TOXICOLOGY FILING CHECKLIST FOR NDA/BLA or Supplement

NDA/BLA Number: 204683 **Applicant: Osmotica Pharmaceuticals Ltd.** **Stamp Date: September 13, 2012**

Drug Name: Desvenlafaxine (base) Extended release **NDA/BLA 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 Agency's previous findings of safety and efficacy for the innovator desvenlfaxine product (Pristiq®); 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

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___

If the NDA/BLA is not fileable from the pharmacology/toxicology perspective, state the reasons and provide comments to be sent to the Applicant.

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

None at this time

Shiny Mathew, Ph.D. {see appended electronic signature page}
Reviewing Pharmacologist Date

Linda Fossom, Ph.D. {see appended electronic signature page}
Team Leader/Supervisor Date

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

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
11/08/2012

LINDA H FOSSOM
11/08/2012