

**CENTER FOR DRUG EVALUATION AND  
RESEARCH**

*APPLICATION NUMBER:*

**204150Orig1s000**

**PHARMACOLOGY REVIEW(S)**

## PHARMACOLOGY/TOXICOLOGY MEMO TO THE FILE

### NDA 204150

**Submission:** SDN 1, serial number 0000, submitted 2/29/12, received on 2/29/12

**Drug name:** Desvenlafaxine (Base) ER tablets (50mg and 100mg strength)

**Sponsor:** Alembic Pharmaceuticals, Ltd

**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 base, without succinate salt); submitted under 505(b)(2).**

**Background:** The current NDA for Desvenlafaxine (Base) Extended-Release tablets is a 505(b)(2) application with Pristiq® (approved on 02/29/2008) as the reference listed drug (RLD). This extended release formulation contains desvenlafaxine (base) (i.e. O-desmethyl venlafaxine) as the active ingredient, as opposed to the desvenlafaxine succinate salt (i.e., O-desmethyl venlafaxine succinate monohydrate) used in Pristiq® (Wyeth Pharmaceuticals, Inc., NDA 21-992). Irrespective of whether the base or the salt form of desvenlafaxine is administered, the pharmacologically active moiety, desvenlafaxine (base) is found in the blood and is measured in pharmacokinetic studies. Desvenlafaxine, the major metabolite of venlafaxine, is a norepinephrine and serotonin reuptake inhibitor (SNRI) exhibiting limited inhibition of dopamine reuptake. Desvenlafaxine has been in clinical use for over 4 years for Major Depressive Disorder (MDD) and has a well-established efficacy and safety profile. The patent exclusivity for the innovator expires on March 1, 2013.

**The current submission:** This submission is a 505(b)(2) application for the base form 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. 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 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:

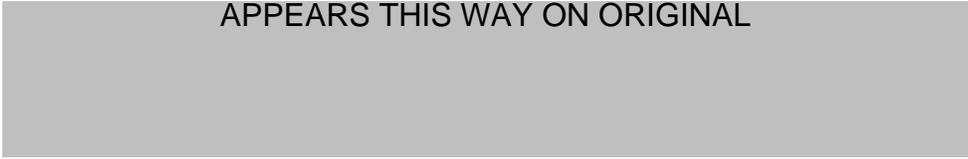
Shiny V. Mathew, Ph.D., Pharmacologist *{see appended electronic signature page}*

NDA 20-4150(Desvenlafaxine (Base) Extended release tablets)  
Shiny V. Mathew, Ph.D., Pharmacologist

page 2

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

APPEARS THIS WAY ON ORIGINAL



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/s/  
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SHINY V MATHEW  
12/06/2012

LINDA H FOSSOM  
12/10/2012

**PHARMACOLOGY/TOXICOLOGY FILING CHECKLIST FOR  
NDA/BLA or Supplement**

**NDA/BLA Number: 204150**

**Applicant: Alembic  
Pharmaceuticals, Ltd.**

**Stamp Date: February 29,  
2012**

**Drug Name: Desvenlafaxine  
(base) Extended release**

**NDA/BLA Type: 505(b)(2)**

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

	<b>Content Parameter</b>	<b>Yes</b>	<b>No</b>	<b>Comment</b>
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 desvenlafaxine 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 <u>submitted</u> a rationale to justify the alternative route?			N/A
7	Has the applicant <u>submitted</u> a statement(s) that all of the pivotal pharm/tox studies have been performed in accordance with the GLP regulations (21 CFR 58) <u>or</u> 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**

	<b>Content Parameter</b>	<b>Yes</b>	<b>No</b>	<b>Comment</b>
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 }  
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 Team Leader/Supervisor Date

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010908

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/s/  
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SHINY V MATHEW  
05/14/2012

LINDA H FOSSOM  
05/14/2012