

**CENTER FOR DRUG EVALUATION AND  
RESEARCH**

*APPLICATION NUMBER:*

**202133Orig1s000**

**PHARMACOLOGY REVIEW(S)**

## PHARMACOLOGY/TOXICOLOGY NDA REVIEW AND EVALUATION

**Application Number:** 202133

**Supporting Document:** SDN-1

**Applicant's Letter Date:** December 9, 2010

**CDER Stamp Date:** December 9, 2010

**Product:** Fluoxetine 60 mg Tablets

**Indication:** Major Depressive Disorder, Obsessive Compulsive Disorder, Bulimia Nervosa, and Panic Disorder

**Applicant:** Edgemont Pharmaceuticals, LLC

**Review Division:** Psychiatry Products

**Reviewer:** Antonia Dow, Ph.D.

**Team Leader:** Linda Fossom, Ph.D.

**Division Director:** Thomas Laughren, M.D.

**Project Manager:** Hiren Patel, Pharm.D.

### **Regulatory Background:**

Fluoxetine is a selective serotonin reuptake inhibitor initially approved for the treatment of Major Depressive Disorder on December 29, 1987. In addition to Major Depressive Disorder, fluoxetine is approved for Obsessive Compulsive Disorder, Bulimia Nervosa, and Panic Disorder. Currently, the dosing range for the listed indications is 10 – 80 mg/day.

Edgemont Pharmaceuticals filed this application as a 505(b)(2) NDA. The Sponsor is relying on the Agency's previous finding of safety and efficacy for the innovator fluoxetine product (Prozac® manufactured by Eli Lilly; NDA 18936). Therefore, no pharmacology/toxicology data was submitted in support of this application.

### **Review of Nonclinical Findings:**

Because no pharmacology/toxicology data was submitted in support of this application, there are no nonclinical data to review. The Sponsor's proposed indications and dose of 60 mg/day are supported by the current fluoxetine label. In addition; no new excipients, impurities, and/or degradants have been identified as being present in the drug product (please see the CMC review by Dr. Mohan Sapru dated 9/2/11 for further information).

### **Review of Label:**

The Sponsor's proposed labeling is based on the current Prozac® label. As a result, the nonclinical sections are adequate and no changes are being recommended.

### **Conclusions and Recommendations:**

From a pharmacology/toxicology perspective, this application is recommended for approval.

Antonia Dow, Pharmacologist *{see appended electronic signature page}*

Linda Fossom, Team Leader *{see appended electronic signature page}*

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/s/  
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ANTONIA L DOW  
09/06/2011

LINDA H FOSSOM  
09/06/2011

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

**NDA Number: 202133**

**Applicant: Edgemont  
Pharmaceuticals, LLC**

**Stamp Date: December 9, 2010**

**Drug Name: Fluoxetine HCl    NDA Type: Standard**

On **initial** overview of the NDA 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 effectiveness for the innovator fluoxetine product (Prozac®); therefore, no nonclinical studies have been conducted in support of this submission.
2	Is the pharmacology/toxicology section indexed and paginated in a manner allowing substantive review to begin?			Not applicable
3	Is the pharmacology/toxicology section legible so that substantive review can begin?			Not applicable
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)?	X		See Comment 1 above.
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).			Not applicable
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?			Not applicable
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?			Not applicable

**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?			Not applicable
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		Because this NDA is submitted as a 505(b)(2) application, the Sponsor is using the content from the RLD (Par Pharmaceutical Companies, Inc, ANDA 075755) for the current labeling text.
10	Have any impurity – etc. issues been addressed? (New toxicity studies may not be needed.)		X	I am not aware of any issues, but will be working with Chemistry during the review process to determine if there are any new excipients, impurities, and/or degradants present that may need to be qualified. The need to qualify new excipients, impurities, and/or degradants was communicated to the Sponsor in the pre-NDA Meeting Minutes dated 3/11/2010.
11	Has the applicant addressed any abuse potential issues in the submission?			Not applicable
12	If this NDA/BLA is to support a Rx to OTC switch, have all relevant studies been submitted?			Not applicable

**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.

Antonia Dow, Ph.D.

*{see appended electronic signature page}*

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Reviewing Pharmacologist

Date

Linda Fossom, Ph.D.

*{see appended electronic signature page}*

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Team Leader/Supervisor

Date

File name: 5\_Pharmacology\_Toxicology Filing Checklist for NDA\_BLA or Supplement

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/s/  
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ANTONIA L DOW  
01/31/2011

LINDA H FOSSOM  
01/31/2011