| *SUPPLEMENTAL NEW DRUG APPLICATION – PEDIATRIC INDICATIONS*<br>*BPCA SUMMARY REVIEW*<br>*OFFICE OF CLINICAL PHARMACOLOGY AND BIOPHARMACEUTICS* | | | |
|---|---|---|---|
| NDAs: | 20-151 | 20-699 | |
| SLRs: | 024 | 030 | |
| **Drug:**<br>**[Brand / Generic]** | Effexor Tablets<br>(Venlafaxine HCl) | Effexor XR<br>Extended Release Capsules<br>(Venlafaxine HCl) | |
| **Sponsor:** | Wyeth-Ayerst<br>Philadelphia, PA | **Correspondence Date:** | September 25, 2002 |

# 1 EXECUTIVE SUMMARY

## 1.1 RECOMMENDATION:

The Office of Clinical Pharmacology and Biopharmaceutics/Division of Pharmaceutical Evaluation I (OCPB/DPE-1) has reviewed NDA 20-699 S-029 submitted September 25, 2002, and finds the sponsor's submission acceptable.

## 1.2 PHASE IV COMMITMENTS

No phase IV commitments are requested.

# 2 SUMMARY OF CLINICAL PHARMACOLOGY AND BIOPHARMACEUTICS FINDINGS

The sponsor has applied for approval of the indication of General Anxiety Disorder in pediatric patients (GAD).

The efficacy studies for GAD were conducted with the ER formulation, whereas the initial pediatric pharmacokinetic studies were performed using the IR tablet formulation. Upon review of materials in a pre-NDA package OCPB requested a pediatric pharmacokinetic study with the ER formulation to assess if absorption of venlafaxine from an extended release formulation would be truncated before the end of the dosage interval. Collection of both of urine and feces was suggested to determine the fraction of the dose absorbed. In addition, since the youngest patients are most at risk for truncated absorption, and since the weight range in the protocols effectively excluded subjects less than 8 years old, the sponsor was requested to modify the weight range. In addition, and the sponsor was requested to study a minimum of 4 subjects in each of the following age brackets: 6 - 7 years old, 8 - 11 years old, and 12 - 17 years old.

The data submitted was sufficient to answer the most pertinent clinical pharmacology questions and the submission is therefore acceptable.

Results of the pharmacokinetic studies suggest that exposure to venlafaxine is slightly lower in adolescents as compared to adults when dosed at the same mg/kg dose. Whereas when children are given the same mg/kg dose, exposures drop sharply as age declines in preadolescents. The data with the ER formulation suggests that preadolescent children may need a much higher mg/kg dose as compared to adults. Inspection of the pharmacokinetic data suggests that pediatric patients may have been under-dosed in the pivotal efficacy studies.