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APPLICATION NUMBER:

22-104

PHARMACOLOGY REVIEW(S)

PHARMACOLOGY/TOXICOLOGY MEMO TO THE FILE

NDA 22-104.
Submission N-000, letter-dated 9/27/2007, stamp-dated 9/28/2006.

Drug: venlafaxine hyrdochloride, as extended-release oral tablets (37.5-, 75-, 150- and 225-mg strengths of venlafaxine).
Sponsor: Osmotica Pharmaceuticals Corp.
Indication: Treatment of Major Depressive Disorder, Social Anxiety Disorder — b(4)

Reviewer: Linda H. Fossom, Ph.D., Pharmacologist.
HFD-130, Division of Psychiatry Products.

RE: New extended-release formulation of venlafaxine HCl; submitted under 505(b)(2).

Background: Venlafaxine is an inhibitor of both serotonin and norepinephrine reuptake transporters. Venlafaxine (as the hydrochloride salt) has been approved since 1993 as an immediate-release tablet formulation, Effexor, for treatment of Major Depressive Disorder (MDD; NDA 20-151, sponsored by Wyeth). An extended-release capsule formulation, Effexor XR, was approved for treatment of MDD (NDA 20-699, also sponsored by Wyeth), with subsequent supplements approved for Generalized Anxiety Disorder (GAD), Social Anxiety Disorder (SAD), and Panic Disorder (PD). Effexor XR is approved at dosage strengths of 37.5-, 75-, and 150-mg, with a maximum recommended human dose of 225 mg per day for all indications.

The current submission: Osmotica has submitted the current NDA for a new extended-release tablet formulation of venlafaxine hydrochloride for treatment of MDD, SAD — b(4) under 505(b)(2), referencing the non-clinical data, as well as the clinical and some of the human pharmacokinetic data, to the innovator NDA 20-699 for Wyeth's Effexor XR. They have also conducted and submitted the reports for original studies to demonstrate clinical bioequivalence comparing their product with the innovator Effexor XR.

Osmotica has suggested that their new (extended-release) tablet formulation may be of benefit for patients who have trouble swallowing the innovator (extended-release) capsules. Additionally, they are providing a new dose-strength (225-mg) which is not available as Effexor XR.

Discussion: Osmotica has submitted this NDA under 505(b)(2), referencing the innovator Effexor XR (NDA 20-699, sponsored by Wyeth, the innovator). From a Pharmacology/Toxicology perspective, the non-clinical studies that supported the approval of the innovator product are considered adequate to support the current submission: 1) no new indications or patient populations are being proposed that have not already been approved for the innovator product; and 2) human exposures using the current formulation will not exceed those achieved using the innovator product, since the approval of this NDA will depend on demonstration of bioequivalence to the innovator product. Additionally, there are no chemistry issues (no impurities suspected to be genotoxic/carcinogenic or impurities specified over the threshold for qualification or novel excipients, etc.) that would require additional non-clinical studies for the current product (see CMC review, by Dr. Sherita McLamore, dated 8/20/07).

Recommendations: From a Pharmacology/Toxicology perspective, there are no issues that would prevent or delay the approval of this NDA.

The Pharmacology/Toxicology sections of labeling should be (and appear to be) the same as for Effexor XR.

b(4)

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

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/s/

Linda Fossom
9/7/2007 02:24:12 PM
PHARMACOLOGIST

Barry Rosloff
9/10/2007 04:19:32 PM
PHARMACOLOGIST