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BIOAVAILABILITY OF ONCE-DAILY VENLAFAXINE EXTENDED RELEASE COMPARED WITH THE IMMEDIATE-RELEASE FORMULATION IN HEALTHY ADULT VOLUNTEERS

STEVEN M. TROY,[1] CLIFFORD DILEA,[1] PATRICK T. MARTIN,[1] AMY S. ROSEN,[1] RICHARD J. FRUNCILLO,[2] AND SOONG T. CHIANG[1]

[1]*Wyeth-Ayerst Research, Philadelphia, and* [2]*Wyeth-Ayerst Research Clinical Pharmacology Unit, Graduate Hospital, Philadelphia, Pennsylvania*

ABSTRACT

Two open-label, randomized, crossover studies, one single- and one multiple-dose, were conducted to assess the relative bioavailability of two formulations of once-daily venlafaxine extended release (XR) 75 and 150 mg compared with the immediate-release (IR) formulation of venlafaxine. Healthy adults (12 men, 12 women) aged 18 to 45 years were enrolled in each study. Frequent blood samples were taken for determination of the plasma concentrations of venlafaxine and its active metabolite, O-desmethylvenlafaxine (ODV). In the single-dose study, the 2 × 75-mg XR formulation and the 150-mg XR formulation were bioequivalent with respect to the rate and extent of absorption of venlafaxine and the formation of ODV, and the area under the plasma concentration–time curve (AUC) of both XR formulations and the AUC of the IR formulation also were bioequivalent after normalization for dose. In the multiple-dose study, the three XR formulations were also bioequivalent with respect to the rate and extent of absorption of venlafaxine and formation of ODV, and the AUC of all three XR formulations compared with the AUC of the IR formulation also showed bioequivalence. Overall, the once-daily venlafaxine XR formulations provided the same total exposure (measured by AUC) to both venlafaxine and ODV. Thus it can be predicted that patients will obtain the same response with the XR formulations as with the IR formulations. *Key words:* venlafaxine, bioavailability, extended release, healthy volunteers.

INTRODUCTION

Venlafaxine hydrochloride (hereafter referred to as venlafaxine) is a unique antidepressant that differs structurally from other currently available antidepressants.[1] Venlafaxine and its active metabolite, O-desmethylvenlafaxine (ODV), inhibit the neuronal uptake of norepinephrine, serotonin, and, to a lesser degree, dopamine,[2,3] but have no monoamine oxidase inhibitory activity and a low affinity for brain musca-

Address correspondence to: Steven M. Troy, MS, Wyeth-Ayerst Research, P.O. Box 42528, Philadelphia, PA 19101.
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