

## Draft Guidance on Venlafaxine Hydrochloride

This draft guidance, when finalized, will represent the current thinking of the Food and Drug Administration (FDA, or the Agency) on this topic. It does not establish any rights for any person and is not binding on FDA or the public. You can use an alternative approach if it satisfies the requirements of the applicable statutes and regulations. To discuss an alternative approach, contact the Office of Generic Drugs.

**Active Ingredient:** Venlafaxine hydrochloride

**Dosage Form; Route:** Tablet/Oral

**Recommended studies:** Two Options: BCS or In-Vivo Studies

### I. BCS Waiver option:

It may be possible to request a waiver of in-vivo testing for all the strengths of this product provided that the appropriate documentation regarding high solubility, high permeability and rapid dissolution as detailed in the Guidance for Industry: *Waiver of In Vivo Bioavailability and Bioequivalence for Immediate – Release Solid Oral Dosage Forms Based on the Biopharmaceutics Classification System* is submitted in the application. You may use information contained in the approved labeling of the reference product. Peer reviewed articles may not contain the necessary details of the testing for the Agency to make a judgment regarding the quality of the studies. A decision regarding the acceptability of the waiver request can only be made upon review of the data submitted in the application.

### II. In vivo BE studies option

Type of study:	Fed
Design:	Single-dose, two-treatment, two-period crossover <i>in-vivo</i>
Strength:	50 mg
Subjects:	Normal healthy males and females, general population

Additional Comments: Bioequivalence studies under fasting conditions are not recommended due to safety concerns.

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**Analytes to measure:** Venlafaxine, and active metabolite O-desmethylvenlafaxine, in plasma.

Please submit the metabolite data as supportive evidence of comparable therapeutic outcome. For the metabolite, the following data should be submitted: individual and mean concentrations, individual and mean pharmacokinetic parameters, and geometric means and ratios of means for AUC and Cmax.

**Bioequivalence based on (90% CI):** Venlafaxine

**Waiver request of in-vivo testing:** 25 mg, 37.5 mg, 75 mg and 100 mg based on (i) acceptable bioequivalence studies on the 50 mg strength, (ii) proportionally similar across all strengths, and (iii) acceptable in vitro dissolution testing of all strengths.

**Dissolution test method and sampling times:** The dissolution information for this drug product can be found on the FDA-Recommended Dissolution Methods website available to the public at the following location: <http://www.accessdata.fda.gov/scripts/cder/dissolution/>. Conduct comparative dissolution testing on 12 dosage units each of all strengths of the test and reference products. Specifications will be determined upon review of the abbreviated new drug application (ANDA).