

Draft Guidance on Desvenlafaxine Fumarate

This draft guidance, when finalized, will represent the current thinking of the Food and Drug Administration (FDA, or the Agency) on this topic.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: Desvenlafaxine fumarate

Dosage Form; Route: Extended release tablet; Oral

Recommended Studies: Two studies

1. Type of study: Fasting
Design: Single-dose, two-treatment, two-period, crossover in vivo
Strength: EQ 100 mg Base
Subjects: Males and non-pregnant, non-lactating females, general population
Additional comments: None

2. Type of study: Fed
Design: Single-dose, two-treatment, two-period, crossover in vivo
Strength: EQ 100 mg Base
Subjects: Males and non-pregnant, non-lactating females, general population
Additional comments: None

Analyte to measure (in appropriate biological fluid): Desvenlafaxine in plasma

Bioequivalence based on (90% CI): Desvenlafaxine

Additional strengths: Bioequivalence of the EQ 50 mg Base strength to the corresponding reference product strength may be demonstrated based on principles laid out in the FDA guidance for industry, *Bioequivalence Studies with Pharmacokinetic Endpoints for Drugs Submitted Under an ANDA*.

Dissolution test method and sampling times: For modified release drug products, applicants should develop specific discriminating dissolution methods. Applicants may use the dissolution method set forth in any related official United States Pharmacopeia (USP) drug product monograph, or in the FDA's database (available at <http://www.accessdata.fda.gov/scripts/cder/dissolution/>), provided that applicants submit adequate dissolution data supporting the discriminating ability of such a method. If a new dissolution method is developed, the dissolution method development and validation report with the complete information/data supporting the proposed method should be submitted. Conduct comparative dissolution testing on 12 dosage units for each strength of the test and reference

products. Specifications will be determined upon review of the abbreviated new drug application.

In addition to the method above, dissolution profiles on 12 dosage units for each strength of the test and reference products generated using USP Apparatus 1 at 100 rpm and/or Apparatus 2 at 50 rpm in at least three dissolution media (pH 1.2, 4.5, 6.8 buffer) should be submitted in the application. Agitation speeds may be increased if appropriate. It is acceptable to add a small amount of surfactant, if necessary. Include early sampling times of 1, 2, and 4 hours and continue every 2 hours until at least 80% of the drug is released, to provide assurance against premature release of drug (dose dumping) from the formulation.

Alcohol dose dumping studies:

Due to a concern of dose dumping of drug from this drug product when taken with alcohol, the Agency currently requests that additional dissolution testing be conducted using various concentrations of ethanol in the dissolution medium as follows:

Testing Conditions: 900 mL, 0.1 N HCl, USP apparatus 1 (basket) at 100 rpm, with or without alcohol;

Test 1: 12 units tested according to the proposed method (with 0.1N HCl), with data collected every 15 minutes for a total of 2 hours

Test 2: 12 units analyzed by substituting 5% (v/v) of test medium with Alcohol USP and data collection every 15 minutes for a total of 2 hours

Test 3: 12 units analyzed by substituting 20% (v/v) of test medium with Alcohol USP and data collection every 15 minutes for a total of 2 hours

Test 4: 12 units analyzed by substituting 40% (v/v) of test medium with Alcohol USP and data collection every 15 minutes for a total of 2 hours

Both test and reference products should be tested accordingly, and data should be provided on individual unit, means, range and %CV.