

Draft Guidance on Dextroamphetamine Sulfate

This draft guidance, once finalized, will represent the Food and Drug Administration's (FDA's) current thinking on this topic. It does not create or confer any rights for or on any person and does not operate to bind FDA or the public. You can use an alternative approach if the approach satisfies the requirements of the applicable statutes and regulations. If you want to discuss an alternative approach, contact the Office of Generic Drugs.

Active Ingredient: Dextroamphetamine sulfate

Dosage Form; Route: Extended-release capsules; oral

Recommended Studies: Two studies

1. Type of study: Fasting
Design: Single-dose, two-way, crossover in vivo
Strength: 15 mg
Subjects: Healthy males and nonpregnant females, general population

2. Type of study: Fed
Design: Single-dose, two-way, crossover in vivo
Strength: 15 mg
Subjects: Healthy males and nonpregnant females, general population
Additional comments: Refer to the amantadine hydrochloride tablet draft guidance for additional information regarding fed studies

Analytes to measure (in appropriate biological fluid): Dextroamphetamine in plasma

Bioequivalence based on (90% CI): Dextroamphetamine

The 90% confidence intervals of the geometric mean test/reference (T/R) ratios for the four metrics (C_{max} , AUC_{0-4} , AUC_{4-t} , $AUC_{0-\infty}$) should fall within the bioequivalence (BE) limits of 80-125% for dextroamphetamine.

Waiver request of in vivo testing: 5 mg and 10 mg based on (i) acceptable BE studies on the 15 mg strength, (ii) acceptable in vitro dissolution testing of all strengths, and (iii) proportional similarity of the formulations across all strengths. Refer to the mirtazapine tablet draft guidance for additional information regarding waivers of in vivo testing.

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).

In addition to the method above, for modified-release products, dissolution profiles on 12 dosage units each of the test and reference products generated using U.S. Pharmacopoeia Apparatus I at 100 rpm and/or Apparatus II at 50 rpm in at least three dissolution media (pH 1.2, 4.5, and 6.8 buffer) should be submitted in the application. Agitation speeds may have to be increased if appropriate. It is acceptable to add a small amount of surfactant, if necessary. Please 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 the drug (dose dumping) from the formulation. Specifications will be determined upon review of the data submitted in the application.