Contains Nonbinding Recommendations

Draft Guidance on Guanfacine Hydrochloride

This draft guidance, when finalized, will represent the current thinking of the Food and Drug Administration (FDA, or the Agency) on this topic.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

Dosage Form; Route: Extended-release tablet; oral

Recommended Studies: Two studies

1. Type of study: Fasting
   Design: Single-dose, two-way crossover in vivo
   Strength: 4 mg
   Subjects: Healthy males and nonpregnant females, general population
   Additional comments: None

2. Type of study: Fed
   Design: Single-dose, two-way crossover in vivo
   Strength: 4 mg
   Subjects: Healthy males and nonpregnant females, general population
   Additional comments: None

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

Bioequivalence based on (90% CI): Guanfacine

Waiver request of in vivo testing: 1 mg, 2 mg, and 3 mg strengths based on (i) acceptable bioequivalence study on the 4 mg strength, (ii) acceptable in vitro dissolution testing of all strengths, and (iii) proportional similarity of the formulations across all strengths.

Dissolution test method and sampling times:

A Dissolution Methods Database is available to the public at the OGD Web site at http://www.accessdata.fda.gov/scripts/cder/dissolution/. The dissolution information for this product is available at this Web site. 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 application.

In addition to the method above, for modified-release products, dissolution profiles on 12 dosage units each of test and reference products generated using U.S. Pharmacopeia (USP) 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. 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. Specifications will be determined upon review of the data submitted in the application.