

Draft Guidance on Nisoldipine

This draft guidance, once finalized, will represent the Food and Drug Administration's (FDA's) current thinking on this topic.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 the 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: Nisoldipine

Dosage Form; Route: Extended release tablets; oral

Recommended Studies: Three studies

1. Type of study: Fasting
Design: Single-dose, two-way crossover in vivo
Strength: 40 mg
Subjects: Normal healthy males and females, general population
Additional comments: Carefully monitor the subjects' heart rates and blood pressure during the study, particularly over the first 10 hours.

2. Type of study: Fed
Design: Single-dose, two-way crossover in vivo
Strength: 40 mg
Subjects: Normal healthy males and females, general population
Additional comments: See above. Refer to the amantadine hydrochloride tablet draft guidance for additional information regarding fed studies.

3. Type of study: Fasting
Design: Single-dose, two-way crossover in vivo
Strength: 30 mg
Subjects: Normal healthy males and females, general population
Additional comments: See above.

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

Bioequivalence based on (90% CI): Nisoldipine

Waiver request of in vivo testing: 20 mg based on (i) acceptable bioequivalence studies on the 30 mg and 40 mg strengths, (ii) acceptable dissolution testing across all strengths, and (iii) proportional similarity in 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 Refer to the mirtazapine tablet draft guidance for additional information regarding waivers of in vivo testing.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).

For modified-release products, dissolution profiles generated using 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, water) 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. The following sampling times are recommended: one, two, and four hours and every two hours thereafter, until at least 80 percent of the drug is dissolved. Comparative dissolution profiles should include individual tablet data as well as the mean, range, and standard deviation at each time point for 12 tablets. Specifications will be determined upon review of the data submitted in the application.