

Draft Guidance on Nisoldipine

This draft guidance, once finalized, will represent the Food and Drug Administration's (FDA's) current thinking on this topic.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

1. Type of study: Fasting
Design: Single-dose, two-way crossover in vivo
Strength: 34 mg
Subjects: Healthy males and nonpregnant females, general population
Additional Comments:

2. Type of study: Fed
Design: Single-dose, two-way crossover in vivo
Strength: 34 mg
Subjects: Healthy males and nonpregnant females, general population
Additional Comments:

3. Type of study: Fasting
Design: Single-dose, two-way crossover in vivo
Strength: 17 mg
Subjects: Healthy males and nonpregnant females, general population
Additional Comments:

4. Type of study: Fasting
Design: Single-dose, two-way crossover in vivo
Strength: 8.5 mg
Subjects: Healthy males and nonpregnant females, general population
Additional Comments:

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

Bioequivalence based on (90% CI): Nisoldipine

Waiver request of in vivo testing: 25.5 mg based on (i) acceptable bioequivalence studies on the 34 mg strength, (ii) acceptable dissolution testing across 25.5 mg and 34 mg strengths, and (iii) proportional similarity in the formulations across 25.5 mg and 34 mg strengths.

Dissolution test method and sampling times:

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: 1, 2, and 4 hours and every 2 hours thereafter, until at least 80% 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 twelve tablets. Specifications will be determined upon review of the data submitted in the application.