

Draft Guidance on Minocycline Hydrochloride

This draft guidance, when finalized, will represent the current thinking of the Food and Drug Administration (FDA, or the Agency) on this topic.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

Dosage Form; Route: Tablet; extended-release, oral

Recommended Studies: Two studies

1. Type of study: Fasting
Design: Single-dose, two-way crossover in vivo
Strength: Eq 135 mg base
Subjects: Healthy males and nonpregnant females, general population
Additional comments: Solodyn 115 mg strength should be used as the reference product in the bioequivalence (BE) study if the 115 mg strength is the highest strength of the proposed generic product.

2. Type of study: Fed
Design: Single-dose, two-way crossover in vivo
Strength: Eq 135 mg base
Subjects: Healthy males and nonpregnant females, general population
Additional comments: Solodyn 115 mg strength should be used as the reference product in the BE study if the 115 mg strength is the highest strength of the proposed generic product. Refer to the amantadine hydrochloride draft guidance for additional information regarding fed studies.

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

Bioequivalence based on (90% CI): Minocycline

Waiver request of in vivo testing: Eq 115 mg base, Eq 105 mg base, Eq 90 mg base, Eq 80 mg base, Eq 65 mg base, Eq 55 mg base, and Eq 45 mg base strengths based on (i) acceptable BE studies on the Eq 135 mg base strength (or Solodyn Eq 115 mg base strength, if applicable), (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: The dissolution information for this drug product can be found on the FDA-Recommended Dissolution Methods Web site, 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 test and reference products 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) 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 drug (dose dumping) from the formulation. Specifications will be determined upon review of the data submitted in the application.