

Draft Guidance on Minocycline Hydrochloride

November 2025

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In general, FDA's guidance documents do not establish legally enforceable responsibilities. Instead, guidances describe the Agency's current thinking on a topic and should be viewed only as recommendations, unless specific regulatory or statutory requirements are cited. The use of the word *should* in Agency guidances means that something is suggested or recommended, but not required.

Active Ingredient: Minocycline hydrochloride

Dosage Form: Capsule, extended release

Route: Oral

Strength: EQ 40 mg Base

Recommended Studies: Two in vivo bioequivalence studies with pharmacokinetic endpoints

1. Type of study: Fasting
Design: Single-dose, two-treatment, two-period crossover in vivo
Strength: EQ 40 mg Base
Subjects: Healthy males and non-pregnant, non-lactating females
Additional comment: Exclude subjects with a history of drug hypersensitivity (e.g., hypersensitivity to tetracyclines) to prevent serious skin/hypersensitivity reactions.
2. Type of study: Fed
Design: Single-dose, two-treatment, two-period crossover in vivo
Strength: EQ 40 mg Base
Subjects: Healthy males and non-pregnant, non-lactating females
Additional comment: See comments above.

Analyte to measure: Minocycline in plasma

Bioequivalence based on (90% CI): Minocycline

Dissolution test method and sampling times: For modified release drug products, applicants should develop specific discriminating dissolution methods. Alternatively, applicants may use the dissolution method set forth in any related official United States Pharmacopeia (USP) drug product monograph, or in the FDA's database, <http://www.accessdata.fda.gov/scripts/cder/dissolution/>, provided that applicants submit adequate dissolution data supporting the discriminating ability of such a method. If a new dissolution method is developed, submit the dissolution method development and validation report with the complete information/data supporting the proposed method. Conduct comparative dissolution testing on 12 dosage units for each of the test product and reference listed drug (RLD). Specifications will be determined upon review of the abbreviated new drug application.

In addition to the method above, submit dissolution profiles on 12 dosage units for each of the test product and RLD generated using USP Apparatus 1 at 100 rpm and/or Apparatus 2 at 50 rpm in at least three dissolution media (e.g., pH 1.2, 4.5 and 6.8 buffer). Agitation speeds may 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.

Alcohol dose dumping studies: None

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