

Draft Guidance on Doxepin Hydrochloride

This draft guidance, once finalized, will represent the Food and Drug Administration's (FDA's) current thinking on this topic.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

Dosage Form/Route: Capsule; oral

Recommended Studies: Three studies

1. Type of study: Fasting
Design: Single-dose, two-treatment, two-period crossover in vivo
Strength: EQ 100 mg base
Subjects: Healthy males and nonpregnant females, general population
Additional comments: Due to the potential for serious adverse events, monoamine oxidase inhibitors should be discontinued at least two weeks prior to study initiation.

2. Type of study: Fed
Design: Single-dose, two-treatment, two-period crossover in vivo
Strength: EQ 100 mg base
Subjects: Healthy males and nonpregnant females, general population
Additional comments: Refer to the amantadine hydrochloride tablet draft guidance for additional information regarding fed studies

3. Type of study: Fasting
Design: Single-dose, two-treatment, two-period crossover in vivo
Strength: EQ 25 mg base
Subjects: Healthy males and nonpregnant females, general population
Additional comments: See comments above.

Analytes to measure (in appropriate biological fluid): Doxepin, and its active metabolite nordoxepin, in plasma

Bioequivalence based on (90% CI): Doxepin

Waiver request of in vivo testing: EQ 10 mg base based on (i) acceptable bioequivalence (BE) study on the EQ 25 mg base strength, (ii) acceptable in vitro dissolution testing of all strengths, and (iii) proportional similarity of the formulations across all strengths.

EQ 50 mg base and EQ 75 mg base based on (i) acceptable BE studies on the EQ 100 mg base strength, (ii) acceptable in vitro dissolution testing of all strengths, and (iii) proportional similarity of the formulations across all strengths.

Refer to the mirtazapine tablet draft guidance for additional information regarding waiver of in vivo testing.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).