Contains Nonbinding Recommendations

Draft Guidance on Doxycycline Hyclate

This draft guidance, when finalized, will represent the current thinking of the Food and Drug Administration (FDA, or the Agency) on this topic.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

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

Recommended Studies: Three studies (on 200 mg strength)

1. Type of study: Fasting
   Design: Single-dose, two-way crossover in vivo
   Strength: EQ 200 mg base at a dose of 200 mg (1x200 mg)
   Subjects: Males and nonlactating, nonpregnant females, general population
   Additional comments: None

2. Type of study: Fed
   Design: Single-dose, two-way crossover in vivo
   Strength: EQ 200 mg base at a dose of 200 mg (1x200 mg)
   Subjects: Males and nonlactating, nonpregnant females, general population
   Additional comments: None

3. Type of study: Fasting, sprinkle
   Design: Single-dose, two-way crossover in vivo
   Strength: EQ 200 mg base at a dose of 200 mg (1x200 mg)
   Subjects: Males and nonlactating, nonpregnant females, general population
   Additional comments: Administer the dose by carefully breaking up the tablet and sprinkling the tablet contents on a spoonful of applesauce, in accordance with the approved labeling of the reference listed drug.

Recommended Studies: Two studies (on 120 mg strength)

1. Type of study: Fasting
   Design: Single-dose, two-way crossover in vivo
   Strength: EQ 120 mg base at a dose of 120 mg (1x120 mg)
   Subjects: Males and nonlactating, nonpregnant females, general population
   Additional comments: None

2. Type of study: Fed
   Design: Single-dose, two-way crossover in vivo

Strength: EQ 120 mg base at a dose of 120 mg (1x120 mg)
Subjects: Males and nonlactating, nonpregnant females, general population
Additional comments: None

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

Bioequivalence based on (90% CI): Doxycycline

Waiver request of in vivo testing: EQ 50 mg base, EQ 75 mg base, EQ 80 mg base, EQ 100 mg base, and EQ 150 mg base based on (i) acceptable bioequivalence (BE) studies on the EQ 200 mg base strength, (ii) proportionally similar formulation across all strengths, and (iii) acceptable in vitro dissolution testing of all strengths

Waiver request of in vivo testing: EQ 60 mg base based on (i) acceptable bioequivalence studies on the EQ 120 mg base strength, (ii) proportionally similar across all strengths, and (iii) acceptable in vitro dissolution testing of 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).

Note that some of the above reference products are scored tablets. For additional information related to scored tablets, refer to the guidance *Tablet Scoring: Nomenclature, Labeling, and Data for Evaluation*, issued in March 2013 at http://www.fda.gov/downloads/Drugs/GuidanceComplianceRegulatoryInformation/Guidance s/UCM269921.pdf