Contains Nonbinding Recommendations

Draft Guidance on Amiodarone Hydrochloride

This draft guidance, once finalized, will represent the Food and Drug Administration's (FDA's) current thinking on this topic.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

Form/Route: Tablet/Oral

Recommended studies: 2 studies

1. Type of study: Fasting
   Design: Single-dose, two-way crossover in-vivo
   Strength: 200 mg
   Subjects: Healthy males and nonpregnant females, general population.
   Additional comments:

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2. Type of study: Fed
   Design: Single-dose, two-way crossover in-vivo
   Strength: 200 mg
   Subjects: Healthy males and nonpregnant females, general population.
   Additional Comments: Please refer to the Amantadine Hydrochloride Tablet Draft Guidance for additional information regarding fed studies.

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

Bioequivalence based on (90% CI): Amiodarone

Waiver request of in-vivo testing: 100 mg, 300 mg, and 400 mg based on (i) acceptable bioequivalence studies on the 200 mg strength, (ii) acceptable in-vitro dissolution testing of all strengths, and (iii) proportional similarity of the formulations across all strengths. Please refer to the Mirtazapine Tablet Draft Guidance for additional information regarding waivers of in-vivo testing.

Dissolution test method and sampling times:

Please note that a **Dissolution Methods Database** is available to the public at the OGD website at http://www.accessdata.fda.gov/scripts/cder/dissolution/. Please find the dissolution information for this product at this website. Please 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 application.

Information Regarding Long Half-Life Drugs

For an oral immediate release product with a long elimination half-life drug (>24 hrs), applicants can conduct a single-dose, crossover study, provided an adequate washout period is used. If the crossover study is problematic, BE applicants can use a BE study with a parallel design. For either a crossover or parallel study, sample collection time should be adequate to ensure completion of gastrointestinal transit of the drug product and absorption of the drug substance (which usually occurs within approximately 2 to 3 days). C_{max} and a suitable truncated AUC can be used to characterize peak and total drug exposure, respectively. For drugs that demonstrate low intrasubject variability in distribution and clearance, an AUC truncated at 72 hour ($AUC_{0\text{-}72hr}$) can be used in place of $AUC_{0\text{-}t}$ or $AUC_{0\text{-}inf}$. For drugs demonstrating high intrasubject variability in distribution and/or clearance, AUC truncation should not be used.