Contains Nonbinding Recommendations

Guidance on Digoxin

This guidance represents 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: Digoxin

Form/Route: Tablets/Oral

Recommended studies: 2 studies

1. Type of study: Fasting
   Design: Single-dose, two-way crossover *in-vivo*
   Strength: 0.25 mg
   Subjects: Normal healthy males and females, general population
   Additional Comments: If reliable blood drug levels cannot be obtained using a 1 x 0.25 mg dose, you may use a single dose of 2 x 0.25 mg tablets. Please carefully monitor the study subjects for adverse events. A washout period of about two weeks is suggested. Please continue sample collection for approximately 6 days, i.e., at least three or more terminal half-lives of the drug.

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2. Type of study: Fed
   Design: Single-dose, two-way crossover *in-vivo*
   Strength: 0.25 mg
   Subjects: Normal healthy males and females, general population
   Additional comments: Please see above comments.

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

Bioequivalence based on (90% CI): Digoxin

Waiver request of in-vivo testing: 0.125 mg based on (i) acceptable bioequivalence studies on the 0.25 mg strength, (ii) proportional similarity of the formuations across all strengths, and (iii) acceptable in vitro dissolution testing of all strengths.

Dissolution test method and sampling times:

Please conduct comparative dissolution testing on 12 dosage units of all strengths of the test and reference products using the following USP method.