Contains Nonbinding Recommendations

Draft Guidance on Dolasetron Mesylate

This draft guidance, once finalized, will represent the Food and Drug Administration's (FDA's) current thinking on this topic.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: Dolasetron Mesylate
Form/Route: Tablet/Oral
Recommended studies: 2 studies

1. Type of study: Fasting
   Design: Single-dose, two-way crossover in-vivo
   Strength: 100 mg
   Subjects: The bioequivalence study should be carried out in carefully screened, healthy volunteers who do not have a history of cardiac rhythm problems, a family history of Familial Prolonged QT Syndrome, or use of any medications known to interact with dolasetron mesylate.
   Additional Comments:
      a Specific prohibited concomitant medications should include any antiarrhythmic drug, azole antifungals, carbamazepine, phenothiazines, protease inhibitors, antidepressants, phenytoin, digoxin, barbiturates, CNS depressants, and warfarin.
      b All herbal preparations containing substances known to affect the cytochrome isoenzyme system should be prohibited.
      c Alcohol should be prohibited.

2. Type of study: Fed
   Design: Single-dose, two-way crossover in-vivo
   Strength: 100 mg
   Subjects: Please see comments above.
   Additional Comments: Please see comments above.

Analytes to measure (in appropriate biological fluid): Dolasetron and its metabolite, hydrodolasetron, in both studies. If Dolasetron plasma concentrations can be reliably measured and its pharmacokinetic parameters accurately determined, the dolasetron data should be analyzed using the confidence interval approach. The hydrodolasetron data can be used to provide supportive evidence of comparable therapeutic outcome.

Bioequivalence based on (90% CI): Dolasetron

If Dolasetron cannot be reliably measured, analyze the hydrodolasetron data obtained from these studies using the confidence interval approach.

Waiver request of in-vivo testing: 50 mg (i) acceptable bioequivalence studies on the 100 mg strength, (ii) acceptable in vitro dissolution testing for all strengths, and (iii) proportional similarity in the formulations across all strengths.

Dissolution test method and sampling times:
Please note that a Dissolution Method 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.

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