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Draft Guidance on Dolasetron Mesylate

October 2024

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Active Ingredient: Dolasetron mesylate

Dosage Form: Tablet

Route: Oral

Strengths: 50 mg, 100 mg

Recommended Study: One in vivo bioequivalence study with pharmacokinetic endpoints

1. Type of study: Fasting
   Design: Single-dose, two-treatment, two-period 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.

Analytes to measure: Dolasetron and its metabolite, hydrodolasetron. 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 study on the 100 mg strength, (ii) acceptable in vitro dissolution testing of both strengths, and (iii) proportional similarity in the formulations between both strengths

Dissolution test method and sampling times: The dissolution information for this drug product can be found in the FDA's Dissolution Methods database, http://www.accessdata.fda.gov/scripts/cder/dissolution. Conduct comparative dissolution testing on 12 dosage units for each of both strengths of the test product and reference listed drug (RLD).[1] Specifications will be determined upon review of the abbreviated new drug application.

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[1] If the RLD is not available, refer to the most recent version of the FDA guidance for industry on *Referencing Approved Drug Products in ANDA Submissions.*