Contains Nonbinding Recommendations

Draft Guidance on Memantine Hydrochloride

Active Ingredient: Memantine hydrochloride

Dosage Form; Route: Tablet; oral

Recommended Studies: Two options: Biopharmaceutics Classification System (BCS) or in vivo studies

I. BCS waiver option:

It may be possible to request a waiver of in vivo testing for all the strengths of this product provided that the appropriate documentation regarding high solubility, high permeability and rapid dissolution as detailed in the guidance for industry *Waiver of In Vivo Bioavailability and Bioequivalence for Immediate – Release Solid Oral Dosage Forms Based on the Biopharmaceutics Classification System* is submitted in the application. You may use information contained in the approved labeling of the reference product. Peer-reviewed articles may not contain the necessary details of the testing for the Agency to make a judgment regarding the quality of the studies. A decision regarding the acceptability of the waiver request can only be made upon review of the data submitted in the application.

II. In vivo option:

1. Type of study: Fasting
   Design: Single-dose, two-way crossover or parallel design in vivo
   Strength: 10 mg
   Subjects: Healthy males and nonpregnant females, general population
   Additional comments: Due to the long half-life of this drug, applicants may consider conducting a parallel study. Refer to the guidance for industry *Bioequivalence Studies with Pharmacokinetic Endpoints for Drugs Submitted Under an ANDA* (Dec 2013) for more information on long half-life drugs.

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2. Type of study: Fed
   Design: Single-dose, two-way crossover or parallel design in vivo
   Strength: 10 mg
   Subjects: Healthy males and nonpregnant females, general population
   Additional comments: See comment above

Analytes to measure: Memantine in plasma

Bioequivalence based on (90% CI): Memantine

Waiver request of in vivo testing: 5 mg based on (i) acceptable bioequivalence studies on the 10 mg strength, (ii) acceptable in vitro dissolution testing of all strengths, and (iii) proportional similarity of the formulations across all strengths.

Dissolution test method and sampling times: The dissolution information for this drug product can be found on the FDA-Recommended Dissolution Methods website 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).