Contains Nonbinding Recommendations

Draft Guidance on Rivastigmine Tartrate

This draft guidance, once finalized, will represent the Food and Drug Administration's (FDA's) current thinking on this topic.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

Form/Route: Capsules/Oral

Recommended studies: 3 studies

1. Type of study: Fasting
   Design: Single-dose, two-way crossover *in-vivo*
   Strength: 1.5 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: 1.5 mg
   Subjects: Healthy males and nonpregnant females, general population.
   Additional Comments:

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3. Type of study: Steady-State
   Design: Multiple-dose, two-way steady-state crossover *in-vivo*
   Strength: 6 mg
   Subjects: Patients currently taking the 6 mg of the RLD or patients with indications for rivastigmine therapy, using a slow titration to the intended dose as recommended in the product labeling. The firms may submit a protocol for review by the DBE prior to initiating the study.
   Additional Comments: It may be possible to request waiver of in-vivo testing for Rivastigmine Tartrate Capsules provided that the firms submit the appropriate documentation regarding solubility, permeability and dissolution as detailed in the Guidance for Industry: Waiver of In Vivo Bioavailability and Bioequivalence Studies for Immediate-Release Solid Oral Dosage Forms Based on a Biopharmaceutics Classification System. The firms may utilize 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.

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

Bioequivalence based on (90% CI): Rivastigmine

Waiver request of in-vivo testing: 3 mg and 4.5 mg based on (i) acceptable bioequivalence studies on the 6 mg strength, (ii) proportional similarity of the formulations across all strengths, and (iii) acceptable in vitro dissolution testing of all strengths.

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.fda.gov/cder/ogd/index.htm. 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.