Contains Nonbinding Recommendations

Draft Guidance on Galantamine Hydrobromide

This draft guidance, once finalized, will represent the Food and Drug Administration's (FDA's) current thinking on this topic.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

Form/Route: Extended Release Capsule/Oral

Recommended studies: 2 studies

1. Type of study: Fasting
   Design: Single-dose, two-way crossover *in-vivo*
   Strength: 8 mg
   Subjects: Normal healthy males and females, general population. Females should not be pregnant, and if applicable, should practice abstinence or contraception during the study.
   Additional Comments: The most frequent adverse events leading to drug discontinuation are nausea, vomiting, dizziness, and syncope. Please include appropriate safety precautions in your protocols. These include adequate monitoring of vital signs and adverse events, stopping criteria in the event of an unacceptable degree of hypotension or bradycardia, and appropriate evaluation and management of adverse events. Please assure that the investigator(s) will be vigilant in recognizing and managing any unacceptable clinical or laboratory findings.

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2. Type of study: Fed
   Design: Single-dose, two-way crossover *in-vivo*
   Strength: 8 mg
   Subjects: Normal healthy males and females, general population. Females should not be pregnant, and if applicable, should practice abstinence or contraception during the study.
   Additional comments: Please see comments above.

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

Bioequivalence based on (90% CI): Galantamine

Waiver request of in-vivo testing: 16 mg, 24 mg based on (i) acceptable bioequivalence studies on the 8 mg strength, (ii) proportionally similar 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.

In addition to the method above, for modified release products, dissolution profiles on 12 dosage units each of test and reference products generated using USP Apparatus I at 100 rpm and/or Apparatus II at 50 rpm in at least three dissolution media (pH 1.2, 4.5 and 6.8 buffer) should be submitted in the application. Agitation speeds may have to be increased if appropriate. It is acceptable to add a small amount of surfactant, if necessary. Please include early sampling times of 1, 2, and 4 hours and continue every 2 hours until at least 80% of the drug is released, to provide assurance against premature release of drug (dose dumping) from the formulation. Specifications will be determined upon review of the data submitted in the application.