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Draft Guidance on Donepezil Hydrochloride

October 2024

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Active Ingredient:	Donepezil hydrochloride
Dosage Form:	Tablet
Route:	Oral
Strength:	23 mg
Recommended Studies:	Two options: (1) Biopharmaceutics Classification System (BCS)-based biowaiver or (2) one in vivo bioequivalence study with pharmacokinetic endpoints

I. Option 1: BCS Class I-based biowaiver

A waiver request of in vivo testing for all the strengths of this product may be considered provided that the appropriate documentation regarding high solubility, high permeability and rapid dissolution of the test product and reference listed drugs (RLD) as detailed in the most recent version of the FDA guidance for industry on *M9 Biopharmaceutics Classification System-Based Biowaivers*[a] is submitted in the application. Applicants may use the information contained in the approved labeling of the RLD. 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 assessment of the data submitted in the application.

I. Option 2: One in vivo bioequivalence study with pharmacokinetic endpoints

1. Type of study: Fasting
   Design: Single-dose, two-treatment, two-period crossover in vivo
   Strength: 23 mg
   Subjects: Healthy males and non-pregnant non-lactating females
   Additional comments: An antiemetic drug may be administrated as needed during the in vivo bioequivalence study. Ensure that there is no drug-drug interaction between the antiemetic drug and donepezil, and that the antiemetic drug does not interfere with the bioanalytical method used to analyze donepezil plasma concentrations. Adequate monitoring of vital signs, adverse events, stopping criteria and appropriate evaluation and management of adverse events should be included. Ensure an adequate washout period between treatments in the crossover study due to the long elimination half-life of donepezil. Alternatively, a parallel study design may be considered.

Analyte to measure: Donepezil in plasma

Bioequivalence based on (90% CI): Donepezil

Waiver request of in vivo testing: Not applicable

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 the test product and RLD.[1] Specifications will be determined upon review of the abbreviated new drug application.

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[a] For the most recent version of a guidance, check the FDA guidance website at https://www.fda.gov/regulatory-information/search-fda-guidance-documents.

[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*.