

Draft Guidance on Memantine Hydrochloride

November 2024

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| Active Ingredient: | Memantine hydrochloride |
| Dosage Form: | Tablet, orally disintegrating ¹ |
| Route: | Oral |
| Strengths: | 5 mg, 10 mg |
| Recommended Studies: | Two options: (1) one in vivo bioequivalence study with pharmacokinetic endpoints using the designated reference standard (RS) for memantine hydrochloride tablets, or (2) one in vivo bioequivalence study with pharmacokinetic endpoints using the designated RS for memantine hydrochloride orally disintegrating tablets (ODTs) |
- I. Option 1: One in vivo bioequivalence study with pharmacokinetic endpoints using the designated RS for memantine hydrochloride tablets²**
1. Type of study: Fasting
Design: Single-dose, three-treatment, three-period crossover in vivo
Strength: 10 mg
Subjects: Healthy males and non-pregnant, non-lactating females
Additional comments: Conduct the study using a test product of memantine hydrochloride ODT administered with water and without water and a designated RS for memantine hydrochloride tablets with water. Ensure an adequate washout period between

¹ New dosage form identified is the subject of an approved suitability petition (FDA-2007-P-0061).

² The currently designated RS is the reference listed drug, NDA 021487, memantine hydrochloride tablets, 10 mg.

treatments in the crossover study due to the long elimination half-life of memantine. Alternatively, a parallel study design may be considered.

II. **Option 2: One in vivo bioequivalence study with pharmacokinetic endpoints using the designated RS for memantine hydrochloride ODT³**

1. Type of study: Fasting
Design: Single-dose, two-treatment, two-period crossover in vivo
Strength: 10 mg
Subjects: Healthy males and non-pregnant, non-lactating females
Additional comments: Conduct the study using a test product for memantine hydrochloride ODT administered without water and a designated RS for memantine hydrochloride ODT administered without water. Ensure an adequate washout period between treatments in the crossover study due to the long elimination half-life of memantine. Alternatively, a parallel study design may be considered.

Analyte to measure: Memantine in plasma

Bioequivalence based on (90% CI): Memantine

Waiver request of in vivo testing: 5 mg strength based on (i) an acceptable bioequivalence study on the 10 mg strength, (ii) acceptable in vitro dissolution testing of both strengths, and (iii) proportional similarity of 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 the RS. Specifications will be determined upon evaluation of the abbreviated new drug application.

Document History: Recommended November 2024

Unique Agency Identifier: PSG_021487-ODT

³ This option can be used when a petitioned ANDA for memantine hydrochloride ODT is approved and designated as the RS. There is currently no approved petitioned ANDA for memantine hydrochloride ODT.