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Draft Guidance on Primidone

December 2025

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Active Ingredient: Primidone

Dosage Form: Tablet, orally disintegrating[1]

Route: Oral

Strengths: 25 mg[1], 50 mg, 100 mg[1], 125 mg[1], 250 mg

Recommended Studies: Two options: (1) two in vivo bioequivalence studies with pharmacokinetic endpoints using the designated reference standard (RS) for primidone tablets, or (2) one in vivo bioequivalence study with pharmacokinetic endpoints using the designated RS for primidone orally disintegrating tablets (ODTs)

I. Option 1: Two in vivo bioequivalence studies with pharmacokinetic endpoints using the designated RS for primidone tablets[2]

1. Type of study: Fasting
   Design: Single-dose, three-treatment, three-period crossover in vivo
   Strength: 50 mg
   Subjects: Healthy males and non-pregnant, non-lactating females
   Additional comments:
   - Subjects should be evaluated prior to discharge for cognitive impairment such as somnolence and dizziness and instructed not to drive or operate machinery until their cognitive function returns to baseline level.

[1] New dosage form and strengths identified are the subject of an approved suitability petition (FDA-2009-P-0482).
[2] The currently designated RS is primidone tablets, 50 mg.

- Conduct the study by testing one primidone ODT of the test drug products, administered with and without water, compared to one primidone tablet of the RS with water.

2. Type of study: Fed
Design: Single-dose, two-treatment, two-period crossover in vivo
Strength: 50 mg
Subjects: Healthy males and non-pregnant, non-lactating females
Additional comments:
    - Subjects should be evaluated prior to discharge for cognitive impairment such as somnolence and dizziness and instructed not to drive or operate machinery until their cognitive function returns to baseline level.
    - Conduct the study by testing one primidone ODT of the test drug products administered without water, compared to one primidone tablet of the RS with water.

II. Option 2: One in vivo bioequivalence study with pharmacokinetic endpoints using the designated RS for primidone ODTs[3]

1. Type of study: Fasting
Design: Single-dose, two-treatment, two-period crossover in vivo
Strength: 50 mg
Subjects: Healthy males and non-pregnant, non-lactating females
Additional comments:
    - Subjects should be evaluated prior to discharge for cognitive impairment such as somnolence and dizziness and instructed not to drive or operate machinery until their cognitive function returns to baseline level.
    - Conduct the study by testing one primidone ODT of the test product, administered without water compared to one primidone ODT of the RS without water.

Analyte to measure: Primidone in plasma

Bioequivalence based on (90% CI): Primidone

Waiver request of in vivo testing: 25 mg, 100 mg, 125 mg and 250 mg strengths based on (i) acceptable bioequivalence studies on the 50 mg strength, (ii) acceptable in vitro dissolution testing of all the 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 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 all strengths of the test product and the RS. Specifications will be determined upon evaluation of the abbreviated new drug application.

[3] This option can be used when a petitioned ANDA for primidone ODT is approved and designated as the RS.

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