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Draft Guidance on Gabapentin

November 2023

This draft guidance, when finalized, will represent the current thinking of the Food and Drug Administration (FDA, or the Agency) on this topic. It does not establish any rights for any person and is not binding on FDA or the public. You can use an alternative approach if it satisfies the requirements of the applicable statutes and regulations. To discuss an alternative approach, contact the Office of Generic Drugs.

In general, FDA's guidance documents do not establish legally enforceable responsibilities. Instead, guidances describe the Agency's current thinking on a topic and should be viewed only as recommendations, unless specific regulatory or statutory requirements are cited. The use of the word *should* in Agency guidances means that something is suggested or recommended, but not required.

Active Ingredient: Gabapentin

Dosage Form: Tablet

Route: Oral

Strengths: 300 mg, 450 mg, 600 mg, 750 mg, 900 mg

Recommended Studies: Three in vivo bioequivalence studies with pharmacokinetic endpoints

1. Type of study: Fasting
   Design: Single-dose, two-treatment, two-period crossover in vivo
   Strength: 900 mg
   Subjects: Healthy males and non-pregnant, non-lactating females
   Additional comments: None

2. Type of study: Fed
   Design: Single-dose, two-treatment, two-period crossover in vivo
   Strength: 900 mg
   Subjects: Healthy males and non-pregnant, non-lactating females
   Additional comments: None

3. Type of study: Fed
   Design: Single-dose, two-treatment, two-period crossover in vivo
   Strength: 300 mg
   Subjects: Healthy males and non-pregnant, non-lactating females
   Additional comments: None

Analyte to measure: Gabapentin in plasma

Bioequivalence based on (90% CI): Gabapentin

Waiver request of in vivo testing: 450 mg, 600 mg, and 750 mg strengths based on (i) acceptable bioequivalence studies on the 900 mg strength, (ii) acceptable in vitro dissolution testing of all 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 and reference products. Specifications will be determined upon review of the abbreviated new drug application.

In addition to the method above, dissolution profiles on 12 dosage units each of test and reference products generated using U.S. Pharmacopeia (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. 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.

Alcohol dose dumping studies: Due to concerns of dose dumping of drug from this product when taken with alcohol, conduct additional in vitro dissolution testing using various concentrations of ethanol in the dissolution medium as follows:

Testing conditions: 900 mL, 0.1 N HCl, apparatus I (basket) @ 100 rpm, with and without the alcohol:

> Test 1: 12 units tested according to the proposed method (with 0.1 N HCl) with data collected every 15 minutes for a total of 2 hours
>
> Test 2: 12 units analyzed by substituting 5% of test medium (v/v) with Alcohol USP and data collected every 15 minutes for a total of 2 hours
>
> Test 3: 12 units analyzed by substituting 20% of test medium (v/v) with Alcohol USP and data collected every 15 minutes for a total of 2 hours
>
> Test 4: 12 units analyzed by substituting 40% of test medium (v/v) with Alcohol USP and data collected every 15 minutes for a total of 2 hours
>
> Conduct testing on both test and reference products accordingly, and provide data on individual unit, means, range, and %CV.

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