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Draft Guidance on Carbidopa; Levodopa

November 2021

This draft guidance, when finalized, will represent the current thinking of the Food and Drug Administration (FDA, or the Agency) on this topic.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.

This guidance, which interprets the Agency's regulations on bioequivalence at 21 CFR part 320, provides product-specific recommendations on, among other things, the design of bioequivalence studies to support abbreviated new drug applications (ANDAs) for the referenced drug product. FDA is publishing this guidance to further facilitate generic drug product availability and to assist the generic pharmaceutical industry with identifying the most appropriate methodology for developing drugs and generating evidence needed to support ANDA approval for generic versions of this product.

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In February 2010, FDA issued a draft product-specific guidance for industry on generic carbidopa; levodopa. We are now issuing revised draft guidance for industry that replaces the previously issued guidance.

Active Ingredients: Carbidopa; Levodopa

Dosage Form; Route: Tablet, orally disintegrating; oral

Recommended Studies: Two studies

1. Type of study: Fasting
   Design: Single-dose, two-treatment, two-period crossover in vivo
   Strength: 25 mg; 250 mg
   Subjects: Males and non-pregnant, non-lactating females, general population
   Additional comments: The orally disintegrating tablet should be placed on the tongue, allowed to disintegrate, and swallowed without water.

2. Type of study: Fed
Design: Single-dose, two-treatment, two-period crossover in vivo
Strength: 25 mg; 250 mg
Subjects: Males and non-pregnant, non-lactating females, general population
Additional comments: See comments above

Analytes to measure: Carbidopa and levodopa in plasma

Bioequivalence based on (90% CI): Carbidopa and levodopa

Waiver request of in vivo testing: 10 mg; 100 mg and 25 mg; 100 mg based on (i) acceptable bioequivalence studies on the 25 mg; 250 mg strength, (ii) acceptable dissolution among all strengths, and (iii) proportional similarity of 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.

Revision History: Recommended February 2010; Revised November 2021

Unique Agency Identifier: PSG_076699