

## Draft Guidance on Carbidopa; Entacapone; Levodopa

This draft guidance, once finalized, will represent the Food and Drug Administration's (FDA's) current thinking on this topic. It does not create or confer any rights for or on any person and does not operate to bind FDA or the public. You can use an alternative approach if the approach satisfies the requirements of the applicable statutes and regulations. If you want to discuss an alternative approach, contact the Office of Generic Drugs.

**Active ingredient:** Carbidopa; Entacapone; Levodopa

**Form/Route:** Tablet/Oral

**Recommended studies:** 3 studies

1. Type of study: Fasting  
Design: Single-dose, two-way crossover *in-vivo*  
Strength: (50 mg; 200 mg; 200 mg)  
Subjects: Healthy males and nonpregnant females, general population  
Additional Comments: Applicants may consider using a reference-scaled average bioequivalence approach for entacapone. Please refer to the Progesterone Draft Guidance for additional information regarding this bioequivalence approach.

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2. Type of study: Fed  
Design: Single-dose, two-way crossover *in-vivo*  
Strength: (50 mg; 200 mg; 200 mg)  
Subjects: Healthy males and nonpregnant females, general population  
Additional Comments: See comments above. Please refer to the Amantadine Hydrochloride Draft Guidance for additional information regarding fed studies.

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3. Type of study: Fasting  
Design: Single-dose, two-way crossover *in-vivo*  
Strength: (12.5 mg; 200 mg; 50 mg)  
Subjects: Healthy males and nonpregnant females, general population  
Additional Comments: See comments above.

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**Analytes to measure (in appropriate biological fluid):** Carbidopa, Entacapone and Levodopa in plasma

**Bioequivalence based on (90% CI):** Carbidopa, Entacapone and Levodopa

**Waiver request of in-vivo testing:** (37.5 mg; 200 mg; 150 mg), (31.25 mg; 200 mg; 125 mg), and (25 mg; 200 mg; 100 mg) based on (i) acceptable bioequivalence studies on the (50 mg; 200 mg; 200 mg) strength, (ii) acceptable in- vitro dissolution testing of the above strengths, and (iii)

proportional similarity in the formulations across the above strengths. Please refer to Mirtazapine Tablet Draft Guidance for additional information regarding waiver of in-vivo testing.

(18.75 mg; 200 mg; 75 mg) based on (i) acceptable bioequivalence studies on the (12.5 mg; 200 mg; 50 mg) strength, (ii) acceptable in-vitro dissolution testing of the above strengths, and (iii) proportional similarity in the formulations across the above strengths. Please refer to Mirtazapine Tablet Draft Guidance for additional information regarding waiver of in-vivo testing.

**Dissolution test method and sampling times:**

Please note that a **Dissolution Methods Database** is available to the public at the OGD website at <http://www.accessdata.fda.gov/scripts/cder/dissolution/>. Please find the dissolution information for this product at this website. Please conduct comparative dissolution testing on 12 dosage units each of all strengths of the test and reference products. Specifications will be determined upon review of the application.