

## Draft Guidance on Ropinirole Hydrochloride

This draft guidance, once finalized, will represent the Food and Drug Administration's (FDA's) current thinking on this topic.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:** Ropinirole Hydrochloride

**Form/Route:** Extended Release Tablets/Oral

**Recommended studies:** 2 studies

1. Type of study: Fasting  
Design: Single-dose, two-way crossover in-vivo  
Strength: 2 mg  
Subjects: Healthy males and nonpregnant females, general population.  
Additional Comments: Due to safety concerns, bioequivalence studies should be conducted using the 2 mg strength.

The subjects should remain in a comfortable recumbent position for up to 8 hours after dosing and remain under medical surveillance for up to 12 hours after dosing. Before they are allowed to ambulate, they should sit up with legs in a dependent position for one minute prior to standing up. While standing immobile, they should be closely observed for blood pressure changes and/or orthostatic symptoms, including nausea, dizziness, or faintness for at least three minutes.

- 
2. Type of study: Fed  
Design: Single-dose, two-way crossover in-vivo  
Strength: 2 mg  
Subjects: Healthy males and nonpregnant females, general population.  
Additional Comments: Please see comments above
- 

**Analytes to measure (in appropriate biological fluid):** Ropinirole in plasma

**Bioequivalence based on (90% CI):** Ropinirole

**Waiver request of *in-vivo* testing:** 4 mg, 8 mg and 12 mg based on (i) acceptable bioequivalence studies on the 2 mg strength, (ii) acceptable in vitro dissolution testing across all strengths, and (iii) proportional similarity across all strengths.

**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.

In addition to the method above, for modified release products, dissolution profiles on 12 dosage units each of test and reference products generated using USP Apparatus I at 100 rpm and/or Apparatus II at 50 rpm in at least three different pH dissolution media (e.g., pH 1.2, 4.5 and 6.8 buffer) and water 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. Please 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.

Due to concerns of dose dumping from this drug product when taken with alcohol, the Agency currently requests that additional in vitro dissolution testing be conducted using various concentrations of ethanol in the dissolution medium, as follows:

Testing Conditions: 500 mL, 0.1 N HCl, apparatus II (Paddle) @ 100 rpm, with and without the alcohol (see below):

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% (v/v) of test medium with Alcohol USP, and data collection every 15 minutes for a total of 2 hours.

Test 3: 12 units analyzed by substituting 20% (v/v) of test medium with Alcohol USP, and data collection every 15 minutes for a total of 2 hours.

Test 4: 12 units analyzed by substituting 40% (v/v) of test medium with Alcohol USP, and data collection every 15 minutes for a total of 2 hours.

All strengths of the test and the corresponding reference products must be tested accordingly and data must be provided on individual unit, means, range and %CV including f2 similarity values and dissolution plots.