

## Draft Guidance on Milnacipran Hydrochloride

This draft guidance, once finalized, will represent the Food and Drug Administration's (FDA's) current thinking on this topic.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

**Form/Route:** Tablet/Oral

**Recommended studies:** **2 Options: In Vivo or BCS Studies**

### I. In-Vivo option:

1. Type of study: Fasting  
Design: Single-dose, two-way crossover in vivo  
Strength: 50 mg  
Subjects: Normal healthy males and nonpregnant females, general population.  
Additional Comments: Due to safety concerns, the in vivo studies should be conducted on the 50 mg strengths. Females should not be breast-feeding, and if applicable, should practice abstention or contraception during the study.

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2. Type of study: Fed  
Design: Single-dose, two-way crossover in vivo  
Strength: 50 mg  
Subjects: Normal healthy males and nonpregnant females, general population.  
Additional Comments: Please see above comments
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**Analytes to measure (in appropriate biological fluid):** Milnacipran in plasma

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

**Waiver request of in vivo testing:** 12.5 mg, 25 mg, and 100 mg based on (i) acceptable bioequivalence studies on the 50 mg strength, (ii) proportional similarity of the 12.5 mg, 25 mg, 50 mg and 100 mg strengths, and (iii) acceptable in vitro dissolution testing of the 12.5 mg, 25 mg, 50 mg, and 100 mg strengths.

### II. BCS Waiver option:

It may be possible to request a waiver of in vivo testing for all the strengths of this product provided that the appropriate documentation regarding high solubility, high permeability and rapid dissolution as detailed in the Guidance for Industry: *Waiver of In Vivo Bioavailability and Bioequivalence for Immediate – Release Solid Oral Dosage Forms Based on the*

*Biopharmaceutics Classification System* is submitted in the application. You may use information contained in the approved labeling of the reference product. Peer reviewed articles usually do not contain the necessary detailed information about the testing for the Agency to make a judgment regarding the quality of the studies. A decision regarding the acceptability of the waiver request can only be made upon review of the data submitted in the application.

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**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/index.cfm>. 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.