Contains Nonbinding Recommendations

Draft Guidance on Metoprolol Tartrate

This draft guidance, when finalized, will represent the current thinking of the Food and Drug Administration (FDA, or the Agency) on this topic.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

Active Ingredient: Metoprolol tartrate

Dosage Form; Route: Tablet; oral

Recommended Studies: Two options: BCS or in vivo study

I. **Biopharmaceutics Classification System (BCS) Class 1 waiver option:**

A waiver request of in vivo testing for all the strengths of this product may be considered 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. You may use information contained in the approved labeling of the reference product. Peer reviewed articles may not contain the necessary details of the testing for the Agency to make a judgment regarding the quality of the studies. A decision regarding the acceptability of the waiver request will be made upon review of the data submitted in the application.

II. In vivo bioequivalence study option:

1. Type of study: Fasting
   Design: Single-dose, two- treatment, two-period crossover in vivo
   Strength: 100 mg
   Subjects: Males and non-pregnant, non-lactating females, general population
   Additional comments: None

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2. Type of study: Fed
   Design: Single-dose, two- treatment, two-period crossover in vivo
   Strength: 100 mg
   Subjects: Males and non-pregnant, non-lactating females, general population
   Additional comments: None

Analyte to measure (in appropriate biological fluid): Metoprolol in plasma

Bioequivalence based on (90% CI): Metoprolol

Waiver request of in vivo testing: The 25 mg, 37.5 mg, 50 mg, and 75 mg strengths based on (i) acceptable bioequivalence studies on the 100 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 on the FDA-Recommended Dissolution Methods web site, available to the public at the following location: http://www.accessdata.fda.gov/scripts/cder/dissolution/. Conduct comparative dissolution testing on 12 dosage units for each strength of the test and reference products. Specifications will be determined upon review of the abbreviated new drug application.

If any strength of the tablet product has a functional score, additional dissolution profile testing should be conducted for each segment of the split tablet after manual and mechanical splitting as per Guidance for Industry on *Tablet Scoring: Nomenclature, Labeling, and Data for Evaluation*.