Contains Nonbinding Recommendations

Draft Guidance on Metoprolol Tartrate

This draft guidance, once finalized, will represent the Food and Drug Administration's (FDA's) current thinking on this topic.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

Active Ingredient: Metoprolol tartrate

Dosage Form; Route: Tablet; oral

Recommended Studies: Two options: BCS or In vivo study

I. 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 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 can only be made upon review of the data submitted in the application.

II. In vivo BE studies option

1. Type of study: Fasting
   Design: Single-dose, two-way crossover in vivo
   Strength: 100 mg
   Subjects: Healthy males and nonpregnant females, general population.
   Additional comments: None

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2. Type of study: Fed
   Design: Single-dose, two-way crossover in vivo
   Strength: 100 mg
   Subjects: Healthy males and nonpregnant females, general population.
   Additional comments: None

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

Bioequivalence based on (90% CI): Metoprolol

Waiver request of in vivo testing: 25 mg and 50 mg 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 website available to the public at the following location: http://www.accessdata.fda.gov/scripts/cder/dissolution/. 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 abbreviated new drug application (ANDA).