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Draft Guidance on Labetalol Hydrochloride

March 2021

This draft guidance, when finalized, will represent the current thinking of the Food and Drug Administration (FDA, or the Agency) on this topic.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

This guidance, which interprets the Agency's regulations on bioequivalence at 21 CFR part 320, provides product-specific recommendations on, among other things, the design of bioequivalence studies to support abbreviated new drug applications (ANDAs) for the referenced drug product. FDA is publishing this guidance to further facilitate generic drug product availability and to assist the generic pharmaceutical industry with identifying the most appropriate methodology for developing drugs and generating evidence needed to support ANDA approval for generic versions of this product.

The contents of this document do not have the force and effect of law and are not meant to bind the public in any way, unless specifically incorporated into a contract. This document is intended only to provide clarity to the public regarding existing requirements under the law. FDA guidance documents, including this guidance, should be viewed only as recommendations, unless specific regulatory or statutory requirements are cited. The use of the word should in FDA guidances means that something is suggested or recommended, but not required.

In April 2010, FDA issued a draft product-specific guidance for industry on generic labetalol hydrochloride. We are now issuing revised draft guidance for industry that replaces the previously issued guidance.

Active Ingredient:	Labetalol hydrochloride
Dosage Form; Route:	Tablet; oral
Recommended Studies:	Two options: Biopharmaceutics Classification System (BCS) or in vivo studies

I. BCS Class 1-based biowaiver option:

A waiver request of in vivo testing for 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 in the application. Applicants 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 assessing 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: 200 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: 200 mg
   Subjects: Males and non-pregnant, non-lactating females, general population
   Additional comments: None

Analyte to measure: Labetalol in plasma

Bioequivalence based on (90% CI): Labetalol

Waiver request of in vivo testing: 100 mg and 300 mg based on (i) acceptable bioequivalence studies on the 200 mg strength, (ii) proportional similarity of the formulations across all strengths, and (iii) acceptable in vitro dissolution testing of all strengths.

Dissolution test method and sampling times: The dissolution information for this drug product can be found in the FDA's Dissolution Methods database, 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.

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*.

Revision History: Recommended June 2009; Revised April 2010, March 2021

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