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Draft Guidance on Oseltamivir Phosphate

May 2022

This draft guidance, when finalized, will represent the current thinking of the Food and Drug Administration (FDA, or the Agency) on this topic.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

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In December 2009, FDA issued a draft product-specific guidance for industry on oseltamivir phosphate. We are now issuing revised draft guidance for industry that replaces the previously issued guidance.

Active Ingredient:	Oseltamivir phosphate
Dosage Form; Route:	Capsule; oral
Recommended Studies:	Two options: (1) Biopharmaceutics Classification System (BCS)-based biowaiver or (2) two in vivo bioequivalence studies with pharmacokinetic endpoints

I. Option 1: BCS Class III-based biowaiver

A waiver request of in vivo testing for this product may be considered provided that the appropriate documentation regarding high solubility, very rapid dissolution, and the test product formulation is qualitatively the same and quantitatively similar as detailed in the most recent version of the FDA guidance for industry on *M9 Biopharmaceutics Classification System-Based Biowaivers*[a] is submitted in the application. A decision

regarding the acceptability of the waiver request will be made upon assessing the data submitted in the application.

II. Option 2: Two in vivo bioequivalence studies with pharmacokinetic endpoints

1. Type of study: Fasting
   Design: Single-dose, two-treatment, two-period crossover in vivo
   Strength: EQ 75 mg Base
   Subjects: Males and non-pregnant, non-lactating females, general population
   Additional comments: None

2. Type of study: Fed
   Design: Single-dose, two-treatment, two-period crossover in vivo
   Strength: EQ 75 mg Base
   Subjects: Males and non-pregnant, non-lactating females, general population
   Additional comments: None

Analytes to measure: Oseltamivir and its active metabolite, oseltamivir carboxylate in plasma

Submit the metabolite data as supportive evidence of comparable therapeutic outcome. For the metabolite, the following data should be submitted: individual and mean concentrations, individual and mean pharmacokinetic parameters, and geometric means and ratios of means for AUC and Cmax.

Bioequivalence based on (90% CI): Oseltamivir

Waiver request of in vivo testing: EQ 30 mg Base and EQ 45 mg Base strengths based on (i) acceptable bioequivalence studies on the EQ 75 mg Base 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 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 ANDA.

Revision History: Recommended December 2009; Revised May 2022

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[a] For the most recent version of a guidance, check the FDA guidance web page at https://www.fda.gov/regulatory-information/search-fda-guidance-documents.