

Contains Nonbinding Recommendations

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Draft Guidance on Prednisone

August 2022

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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 November 2013, FDA issued a draft product-specific guidance for industry on generic prednisone. We are now issuing revised draft guidance for industry that replaces the previously issued guidance.

Active Ingredient: Prednisone

Dosage Form; Route: Tablet, delayed release; oral

Recommended Studies: Two in vivo bioequivalence studies with pharmacokinetic endpoints

1. Type of study: Fasting
Design: Single-dose, two-treatment, two-period crossover in vivo
Strength: 5 mg
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: 5 mg
Subjects: Males and non-pregnant, non-lactating females, general population
Additional comments: None

Analyte to measure: Prednisone in plasma

Bioequivalence based on (90% CI): Prednisone

Additional strengths: Bioequivalence of the 1 mg and 2 mg strengths to the corresponding reference product strengths may be demonstrated based on principles laid out in the most recent version of the FDA guidance for industry on *Bioequivalence Studies with Pharmacokinetic Endpoints for Drugs Submitted Under an Abbreviated New Drug Application*.^a

Dissolution test method and sampling times: For modified release drug products, applicants should develop specific discriminating dissolution methods. Alternatively, applicants may use the dissolution method set forth in any related official United States Pharmacopeia (USP) drug product monograph, or in the FDA's database, <http://www.accessdata.fda.gov/scripts/cder/dissolution/>, provided that applicants submit adequate dissolution data supporting the discriminating ability of such a method. If a new dissolution method is developed, submit the dissolution method development and validation report with the complete information/data supporting the proposed method. 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 ANDA.

Alcohol dose dumping studies:

Due to concerns of dose dumping of drug from this product when taken with alcohol, conduct additional dissolution testing on all strengths using various concentrations of ethanol in the dissolution medium as follows:

Testing Conditions: 500 mL, 0.1 N HCl, USP Apparatus 2 (paddle) at 100 rpm, with or without alcohol

Test 1: 12 units tested according to the proposed method (with 0.1N HCl) with data collected every 15 minutes for a total of 2 hours

Test 2: 12 units analyzed by substituting 5% (v/v) of test medium with Alcohol USP and data collection every 15 minutes for a total of 2 hours

Test 3: 12 units analyzed by substituting 20% (v/v) of test medium with Alcohol USP and data collection every 15 minutes for a total of 2 hours

Test 4: 12 units analyzed by substituting 40% (v/v) of test medium with Alcohol USP and data collection every 15 minutes for a total of 2 hours

Conduct testing on both test and reference products accordingly, and provide data on individual unit, means, range and %CV.

Revision History: Recommended November 2013; Revised August 2022

Unique Agency Identifier: PSG_202020

^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>.