Contains Nonbinding Recommendations

Draft – Not for Implementation

Draft Guidance on Lisdexamfetamine Dimesylate

August 2026

This draft guidance, when finalized, will represent the current thinking of the Food and Drug Administration (FDA, or the Agency) on this topic.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

In general, FDA's guidance documents do not establish legally enforceable responsibilities. Instead, guidances describe the Agency's current thinking on a topic and should be viewed only as recommendations, unless specific regulatory or statutory requirements are cited. The use of the word *should* in Agency guidances means that something is suggested or recommended, but not required.

Active Ingredient:	Lisdexamfetamine dimesylate
Dosage Form:	Capsule
Route:	Oral
Strengths:	10 mg | 20 mg | 30 mg | 40 mg | 50 mg | 60 mg | 70 mg
Reference Listed Drug:	NDA 021977
Recommended Studies:	Two options: (1) One in vivo bioequivalence study with pharmacokinetic endpoints or (2) alternative approach to establish bioequivalence

Option I: One in vivo bioequivalence study with pharmacokinetic endpoints

1. Class of study: Bioequivalence
   Type of study: Fasting
   Design: Single-dose, two-treatment, two-period crossover in vivo
   Strength: 70 mg
   Subjects: Healthy males and non-pregnant, non-lactating females

Analyte to measure: Lisdexamfetamine in plasma

Bioequivalence based on (90% CI): Lisdexamfetamine

Bioequivalence of additional strengths: Waiver request of in vivo testing of additional strength based on (i) an acceptable bioequivalence study on the 70 mg strength, (ii) acceptable comparative in vitro dissolution studies between additional strengths and the 70 mg strength using 12 units per strength, and (iii) proportional similarity of the formulations across all strengths

Dissolution: Dissolution tests should be included for quality control and to support waiver request of in vivo testing of additional strengths. Provide a dissolution method development report for the test product containing information and data that demonstrate appropriateness of the selected dissolution method[1] and sampling times, such as the discriminating ability to detect changes in critical quality attributes that could potentially impact drug product performance.

For drug products containing high solubility drug substances that meet the rapidly dissolving criteria, demonstration of discriminating ability may not be needed. For additional information, refer to the guidance for industry *Dissolution Testing and Acceptance Criteria for Immediate-Release Solid Oral Dosage Form Drug Products Containing High Solubility Drug Substances*.[a]

Option II: Alternative approach to establish bioequivalence

BCS-I waiver: Lisdexamfetamine may be eligible for a Biopharmaceutics Classification System (BCS) class I-based biowaiver. 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 of the test product and reference listed drug (RLD) as detailed in the guidance for industry *M9 Biopharmaceutics Classification System-Based Biowaivers*[a] is submitted in the application. Applicants may use information contained in the approved labeling of the RLD. Peer-reviewed articles may not contain the necessary details of the testing for the FDA to make a judgment regarding the quality of the studies. A decision regarding the acceptability of the waiver request will be made upon assessment of the data submitted in the application.

Document History: Recommended September 2008; Revised October 2017, October 2024, August 2026

[a] We update guidances periodically. For the most recent version of a guidance, refer to the FDA guidance webpage at https://www.fda.gov/regulatory-information/search-fda-guidance-documents.

[1] Applicant-developed, United States Pharmacopeia drug product monograph or Dissolution Methods database, https://www.accessdata.fda.gov/scripts/cder/dissolution/index.cfm