

Contains Nonbinding Recommendations

Draft - Not for Implementation

Draft Guidance on Selinexor

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This draft guidance, when finalized, will represent the current thinking of the Food and Drug Administration (FDA, or the Agency) on this topic.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

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 March 2021, FDA issued a draft product-specific guidance for industry on generic selinexor. We are now issuing revised draft guidance for industry that replaces the previously issued guidance.

Active Ingredient: Selinexor

Dosage Form; Route: Tablet; oral

Recommended Study: One in vivo pharmacokinetic bioequivalence study with pharmacokinetic endpoints

1. Design: Single-dose, two-treatment, two-period crossover in vivo
Strength: 60 mg
Subjects: Patients with diffuse large B-cell lymphoma already receiving selinexor in a stable regimen
Additional comments: On Day 1 of each week, patients should receive either the test or the reference product. After the Day 1 treatment, the patients should resume taking the therapeutic medication on Day 3 in their established dosing regimen. Blood sampling for bioequivalence should consist of appropriate sampling times following the dose on

Day 1. Design the study around each patient's existing selinexor regimen and do not change the dose or regimen for the purpose of conducting the bioequivalence study. Due to risk of embryo-fetal toxicity, females of reproductive potential and males with female partners of reproductive potential should use effective contraception during the study and for one week after the dose.

Analyte to measure: Selinexor in plasma

Bioequivalence based on (90% CI): Selinexor

Waiver request of in vivo testing: 20 mg, 40 mg, and 50 mg strengths based on (i) acceptable bioequivalence study on the 60 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 in the FDA's Dissolution Methods database, <http://www.accessdata.fda.gov/scripts/cder/dissolution/>. Conduct comparative dissolution testing on 12 dosage units for each of all strengths of the test and reference products. Specifications will be determined upon review of the ANDA.

Revision History: Recommended March 2021; Revised May 2022

Unique Agency Identifier: PSG_212306