

Contains Nonbinding Recommendations

Draft – Not for Implementation

Draft Guidance on Entrectinib

March 2021

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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.

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.

This is a new draft product-specific guidance for industry on generic entrectinib.

Active Ingredient: Entrectinib

Dosage Form; Route: Capsule; oral

Recommended Studies: Two studies

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: Exclude subjects with abnormal liver function tests and with risk factors for prolonged QTc interval and Torsades de Pointes. Subjects should be appropriately monitored for electrocardiogram changes during the study. Females of reproductive potential should use effective contraception during the study and for 5 weeks following the final dose of entrectinib. Males with female partners of reproductive potential should use effective contraception during the study and for 3 months following the final dose of entrectinib.

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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: See comments above.
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Analyte to measure: Entrectinib in plasma

Bioequivalence based on (90% CI): Entrectinib

Waiver request of in vivo testing: 100 mg based on (i) acceptable bioequivalence studies on the 200 mg strength, (ii) proportional similarity of the formulations between both strengths, and (iii) acceptable in vitro dissolution testing of both 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 both strengths of the test and reference products. Specifications will be determined upon review of the abbreviated new drug application.

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