

Contains Nonbinding Recommendations

Draft – Not for Implementation

Draft Guidance on Elexacaftor, Ivacaftor, Tezacaftor; Ivacaftor

March 2021

This draft guidance, when finalized, will represent the current thinking of the Food and Drug Administration (FDA, or the Agency) on this topic.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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This is a new draft product-specific guidance for industry on generic elexacaftor, ivacaftor, tezacaftor; ivacaftor.

Active Ingredients: Elexacaftor, Ivacaftor, Tezacaftor

Dosage Form; Route: Tablet; oral

Recommended Studies: Two studies

1. Type of study: Fasting
Design: Single-dose, two-treatment, two-period crossover in vivo
Strength: 100 mg; 75 mg; 50 mg
Subjects: Males and non-pregnant, non-lactating females, general population
Additional comments: Ensure an adequate washout period between treatments in the crossover study due to the long elimination half-life of elexacaftor. Alternatively, a parallel study design may be considered.

2. Type of study: Fed
Design: Single-dose, two-treatment, two-period crossover in vivo

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Strength: 100 mg; 75 mg; 50 mg
Subjects: Males and non-pregnant, non-lactating females, general population
Additional comments: See comments above.

Analytes to measure: Elexacaftor, ivacaftor, and tezacaftor in plasma

Bioequivalence based on (90% CI): Elexacaftor, ivacaftor, and tezacaftor

Waiver request of in vivo testing: Not applicable

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 the test and reference products. Specifications will be determined upon review of the ANDA.

Active Ingredient: Ivacaftor

Dosage Form; Route: Tablet; oral

Recommended Studies: Two studies

1. Type of study: Fasting
Design: Single-dose, two-treatment, two-period crossover in vivo
Strength: 150 mg
Subjects: Males and non-pregnant, non-lactating females, general population
Additional comments: None
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2. Type of study: Fed
Design: Single-dose, two-treatment, two-period crossover in vivo
Strength: 150 mg
Subjects: Males and non-pregnant, non-lactating females, general population
Additional comments: None
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Analyte to measure: Ivacaftor in plasma

Bioequivalence based on (90% CI): Ivacaftor

Waiver request of in vivo testing: Not applicable

If an ANDA applicant has an approved ANDA for the single entity of 150 mg ivacaftor tablet, the applicant may cross reference its approved ANDA for this co-packaged product.

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 the test and reference products. Specifications will be determined upon review of the ANDA.

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