

**Draft Guidance on Deutivacaftor; Tezacaftor; Vanzacaftor Calcium
December 2025**

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Active Ingredients:	Deutivacaftor; Tezacaftor; Vanzacaftor calcium
Dosage Form:	Tablet
Route:	Oral
Strengths:	50 mg; 20 mg; EQ 4 mg Base and 125 mg; 50 mg; EQ 10 mg Base
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: 125 mg; 50 mg; EQ 10 mg Base
Subjects: Healthy males and non-pregnant, non-lactating females
Additional comments:
 - Exclude subjects with abnormal liver function tests due to risk of drug-induced liver injury and liver failure. Monitor liver function tests during the study.
 - $AUC_{(0-72h)}$ may be used in place of $AUC_{(0-t)}$ for comparing the extent of absorption, due to the long half-life of tezacaftor and vanzacaftor. Ensure adequate washout periods between treatments in the crossover study. Alternatively, a parallel study design may be considered.
2. Type of study: Fed
Design: Single-dose, two-treatment, two-period crossover in vivo
Strength: 125 mg; 50 mg; EQ 10 mg Base
Subjects: Healthy males and non-pregnant, non-lactating females
Additional comments: See comments above.

Analytes to measure: Deutivacaftor, tezacaftor, and vanzacaftor in plasma

Bioequivalence based on (90% CI): Deutivacaftor, tezacaftor, and vanzacaftor

Waiver request of in vivo testing: 50 mg; 20 mg; EQ 4 mg Base strength based on (i) acceptable bioequivalence studies on the 125 mg; 50 mg; EQ 10 mg Base strength, (ii) acceptable in vitro dissolution testing of both strengths, and (iii) proportional similarity of the formulations between 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 all strengths of the test product and reference listed drug (RLD).¹ Specifications will be determined upon review of the abbreviated new drug application.

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Unique Agency Identifier: PSG_218730

¹ If the RLD is not available, refer to the most recent version of the guidance for industry *Referencing Approved Drug Products in ANDA Submissions*.