Contains Nonbinding Recommendations

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Draft Guidance on Tovorafenib

November 2025

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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: Tovorafenib

Dosage Form: Tablet

Route: Oral

Strength: 100 mg

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: 100 mg
   Subjects: Healthy males and healthy females not of reproductive potential
   Additional comments:
   - Exclude subjects with abnormal liver function tests. Males with female partners of reproductive potential should use effective contraception during the study and for 2 weeks after the last dose of the study. Subjects should be instructed to use appropriate sun protection during the study to prevent photosensitivity reactions.
   - $AUC_{(0\text{-}72h)}$ may be used in place of $AUC_{(0\text{-}t)}$ for comparing the extent of absorption, due to tovorafenib's long half-life. Ensure an adequate washout period 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: 100 mg
Subjects: Healthy males and healthy females not of reproductive potential
Additional comments: See comments above.

Analyte to measure: Tovorafenib in plasma

Bioequivalence based on (90% CI): Tovorafenib

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 each 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_217700

[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.*