

Draft Guidance on Talazoparib Tosylate

This draft guidance, when finalized, will represent the current thinking of the Food and Drug Administration (FDA, or the Agency) on this topic.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

Active Ingredient: Talazoparib tosylate

Dosage Form; Route: Capsule; oral

Recommended Studies: One study

1. Type of study: Fasting
Design: Multiple-dose, steady-state, two-way crossover in vivo
Strength: EQ 1 mg Base
Subjects: Non-pregnant and non-lactating female patients with deleterious or suspected deleterious germline BRCA-mutated (gBRCAm) HER2-negative locally advanced or metastatic breast cancer based on an FDA-approved companion diagnostic for talazoparib tosylate, who are already on established regimens of 1 mg once daily
Additional comments: 1) Applicants may consider a parallel in vivo study as an alternative bioequivalence approach due to the long half-life of talazoparib, 2) blood sampling should allow sufficient time on the test and reference products to reach steady state, 3) blood sampling should consist of appropriate sampling time over a 24-hour period following attainment of steady state confirmed with at least three consecutive trough concentrations, 4) submission of an Investigational New Drug Application is required prior to the conduct of a bioequivalence study for a cytotoxic product pursuant to 21 C.F.R § 320.31(a).

Analyte to measure (in appropriate biological fluid): Talazoparib in plasma

Bioequivalence based on (90% CI): Talazoparib

Submit the following pharmacokinetics data for the steady-state bioequivalence: $AUC_{0-\tau}$, and C_{maxSS} . In addition, submit C_{minSS} (concentration at the end of a dose interval), C_{avSS} (average concentration during a dosing interval), degree of fluctuation $[(C_{max}-C_{min})/C_{avSS}]$, swing $[(C_{maxSS}-C_{minSS})/C_{minSS}]$, and T_{max} .

Waiver request of in vivo testing: EQ 0.25 mg Base based on (i) acceptable bioequivalence study on the EQ 1 mg Base strength, (ii) proportional similarity of the formulations across both strengths, and (iii) acceptable in vitro dissolution testing of the both strengths

Dissolution test method and sampling times: The dissolution information for this drug product can be found on the FDA-Recommended Dissolution Methods web site, available to the

public at the following location: <http://www.accessdata.fda.gov/scripts/cder/dissolution/>. Conduct comparative dissolution testing on 12 dosage units for each strength of the test and reference products. Specifications will be determined upon review of the abbreviated new drug application.