

Draft Guidance on Olaparib

This draft guidance, when finalized, will represent the current thinking of the Food and Drug Administration (FDA, or the Agency) on this topic.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

Dosage Form; Route: Tablet; oral

Recommended studies: One study

1. Type of study: Steady state
Design: Two-way crossover *in vivo*
Strength: 150 mg
Subjects: Patients with established dosing regimen who already are receiving a stable dose of olaparib tablets, 150 mg
Additional Comments: Recruitment efforts should be targeted at patients with deleterious or suspected deleterious germline BRCA-mutated advanced ovarian cancer, or female patients with deleterious or suspected deleterious gBRCAm, HER2-negative metastatic breast cancer who have been treated with chemotherapy in the neoadjuvant, adjuvant, or metastatic setting.

Submission of an Investigational New Drug Application (IND) is required prior to the conduct of a bioequivalence study for this cytotoxic drug product (See 21 C.F.R § 320.31)

Analytes to measure (in appropriate biological fluid): Olaparib in Plasma

Bioequivalence based on (90% CI): Olaparib

In the evaluation of the steady-state bioequivalence study, the following pharmacokinetics data should be submitted for olaparib: $AUC_{0-\tau}$, and C_{maxSS} . In addition, report C_{minSS} (concentration at the end of a dosing 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: 100 mg based on (i) acceptable bioequivalence study on the 150 mg strength, (ii) proportionally similar formulation across all strengths, and (iii) acceptable in vitro dissolution testing of all strengths

Dissolution test method and sampling times: The dissolution information for this drug product can be found on the FDA-Recommended Dissolution Methods website available to the public at the following location: <http://www.accessdata.fda.gov/scripts/cder/dissolution/>.

Conduct comparative dissolution testing on 12 dosage units each of all strengths of the test and reference products.