*Contains Nonbinding Recommendations*

*Draft – Not for Implementation*

**Draft Guidance on Olaparib**

**November 2024**

This draft guidance, when finalized, will represent the current thinking of the Food and Drug Administration (FDA, or the Agency) on this topic.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

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.

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**Active Ingredient:** Olaparib

**Dosage Form:** Tablet

**Route:** Oral

**Strengths:** 100 mg, 150 mg

**Recommended Study:** One in vivo bioequivalence study with pharmacokinetic endpoints

1. Type of study: Steady state
   Design: Multiple-dose, two-treatment, two-period crossover
   Strength: 150 mg
   Subjects: Patients with established dosing regimen who are already receiving a stable dose of olaparib tablets based on the indications in the approved labeling
   Additional comments:
   - For the purpose of a bioequivalence study, patients should be administered with the drug product under the similar food conditions during both periods.
   - The test product should have the same product design as the reference listed drug (RLD) including the same type of polymer, and the quantity of the polymer should not differ by more than 10% (w/w) based on the total excipients from the RLD for the amorphous solid dispersion drug product intermediate. Alternatively, if there are differences in manufacturing techniques or formulation beyond specified above, provide supporting documentation to demonstrate that any potential product risks posed by these differences would not affect the safety or efficacy of the test product. Such documentation may include, but is not limited to, comparative dissolution data (tested in at least three dissolution media, e.g., 0.1 N HCl, pH 4.5 buffer, and pH 6.8 buffer), or physiologically based biopharmaceutics modeling.

- Exclude patients who require dosage modification or with expected changes in concomitant medications that may potentially affect the pharmacokinetics of olaparib during the study.
- Implement safety precautions and monitoring including effective contraception and complete blood count as recommended in the labeling.
- Submission of an investigational new drug application is required prior to the conduct of a bioequivalence study for a cytotoxic drug of olaparib pursuant to 21 CFR § 320.31.

**Analyte to measure:** Olaparib in plasma

**Bioequivalence based on (90% CI):** Olaparib

**Waiver request of in vivo testing:** 100 mg strength based on (i) an acceptable bioequivalence study on the 150 mg 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 and reference listed drug (RLD).[1] Specifications will be determined upon review of the abbreviated new drug application.

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