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Draft – Not for Implementation

Draft Guidance on Olaparib

August 2026

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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:	Olaparib
Dosage Form:	Tablet
Route:	Oral
Strengths:	100 mg | 150 mg | 200 mg (FDA-2024-P-2885) | 250 mg (FDA-2025-P-0031) | 300 mg (FDA-2024-P-2885)
Reference Listed Drug:	NDA 208558
Recommended Studies:	Two options: (I) One in vivo bioequivalence study with pharmacokinetic endpoints, or (II) one in vivo bioequivalence study with pharmacokinetic endpoints for suitability petition strengths

Option I: One in vivo bioequivalence study with pharmacokinetic endpoints

1. Class of study: Bioequivalence
   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
   Safety recommendations:
   - 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.

Study design recommendations:

- For the purpose of a bioequivalence study, patients should be administered with the drug product under the similar food conditions during both periods.
- Exclude patients who require dosage modification or with expected changes in concomitant medications that may potentially affect the pharmacokinetics of olaparib during the study.
- The test product should have the same product design as the reference listed drug (RLD) including the same type of polymer, and the amount of polymer and total excipients in the amorphous solid dispersion intermediate of the test product should not differ from the amount of polymer and total excipients in the amorphous solid dispersion intermediate of the RLD by more than 10%. 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 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.

Analyte to measure: Olaparib in plasma

Bioequivalence based on (90% CI): Olaparib

Bioequivalence of additional strengths: Waiver request of in vivo testing of additional strength of 100 mg based on (i) an acceptable bioequivalence study on the 150 mg strength, (ii) acceptable comparative in vitro dissolution studies between the additional strengths and 150 mg strength using 12 units per strength in at least three dissolution media, e.g., 0.1 N HCl, pH 4.5 buffer, and pH 6.8 buffer, (iii) proportional similarity of the formulations across all strengths and the same weight ratio of critical excipient(s) to active pharmaceutical ingredient (e.g., polymer in solid dispersion to olaparib) between the additional strengths and 150 mg strength, (iv) and utilization of the same manufacturing process between the additional strengths and 150 mg strength of test product

Option II: One in vivo bioequivalence study with pharmacokinetic endpoints for suitability petition strength

Eligibility: If an applicant intends to submit an abbreviated new drug application (ANDA) for both the RLD strengths of 100 mg and 150 mg and the suitability petition strengths of 200 mg (FDA-2024-P-2885), 250 mg (FDA-2025-P-0031), and 300 mg (FDA-2024-P-2885), conduct an in vivo bioequivalence study using the 300 mg strength of the test product and RLD strength of 150 mg (2 × 150 mg).

1. Class of study: Bioequivalence
   Type of study: Steady state
   Design: Multiple-dose, two-treatment, two-period crossover
   Strength: 300 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
   Safety recommendations: See recommendations under Option I, Study#1.
   Study design recommendations: See recommendations under Option I, Study#1.

Analyte to measure: Olaparib in plasma

Bioequivalence based on (90% CI): Olaparib

Bioequivalence of additional strengths: Waiver request of in vivo testing of additional strengths of 100 mg, 150 mg, 200 mg, and 250 mg based on (i) an acceptable bioequivalence study on the 300 mg strength, (ii) acceptable comparative in vitro dissolution studies between the additional strengths and 300 mg strength using 12 units per strength in at least three dissolution media (e.g., 0.1 N HCl, pH 4.5 buffer, and pH 6.8 buffer), (iii) proportional similarity of the formulations across all strengths and the same weight ratio of critical excipient(s) to active pharmaceutical ingredient (e.g., polymer in solid dispersion to olaparib) between the additional strengths and 300 mg strength, (iv) and utilization of the same manufacturing process between the additional strengths and 300 mg strength of test product

If an applicant holds an approved ANDA for the 100 mg and 150 mg strengths, the applicant may request biowaivers of the 200 mg, 250 mg, and 300 mg strengths. Provide adequate justification, including the manufacturing process, formulation proportionality, and comparable in vitro dissolution profiles across the strengths in at least three dissolution media.

Recommendations for both Options:

Dissolution: Dissolution test(s) should be included for quality control and to support a waiver request of in vivo testing of additional strengths. For the quality control dissolution method, provide a dissolution method development report for the test product containing information and data that demonstrate appropriateness of the selected dissolution method[1] and sampling times, such as the discriminating ability to detect changes in critical quality attributes that could potentially impact drug product performance.

Document History: Recommended September 2018; Revised November 2024, August 2026

[1] Applicant-developed, United States Pharmacopeia drug product monograph or Dissolution Methods database, https://www.accessdata.fda.gov/scripts/cder/dissolution/index.cfm