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Olaparib 100 mg & 150 mg film-coated tablets product-specific bioequivalence guidance

Draft Agreed by Pharmacokinetics Working Party (PKWP)	28 October 2021
Adopted by CHMP for release for consultation	11 November 2021
Start of public consultation	16 December 2021
End of consultation (deadline for comments)	31 March 2022
Agreed by Pharmacokinetics Working Party	08 June 2022
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Disclaimer:

This guidance should not be understood as being legally enforceable and is without prejudice to the need to ensure that the data submitted in support of a marketing authorisation application complies with the appropriate scientific, regulatory and legal requirements.

Requirements for bioequivalence demonstration (PKWP)*

BCS Classification	**BCS Class:** ☐ **I** ☐ **III** ☒ **Neither of the two** **Background:** Olaparib is a low solubility compound.
Bioequivalence study design *in case a BCS biowaiver is not feasible or applied*	**multiple dose** **cross-over**
	patients
	☐ **fasting** ☐ **fed** ☒ **both** ☐ **either fasting or fed** **Background:** The SmPC recommends intake of the reference medicinal product irrespective of food intake. For products with specific formulation characteristics like olaparib tablets (solid dispersion), bioequivalence studies performed under both fasted and fed conditions are required. If a different technology is used, a different food effect might occur. For patients participating in the fasted study, strict fasting conditions according to the 'Guideline on the investigation of bioequivalence' are not requested, but the tablets are recommended to be taken one hour before a meal and 2 hours after food intake.

	A standardised light meal is recommended for patients participating in the fed bioequivalence study. A waiver for this fed study may be applicable if the products are manufactured using the same technology and if excipients are qualitatively the same and quantitatively similar between test and reference product.
	Strength: 150 mg **Background:** Highest strength to be used for a drug with linear pharmacokinetics and low solubility but the clinical dose of 300 mg BID should be used. A lower dose is acceptable as long as the same dose is administered during the study.
	Number of studies: two multiple dose studies
	Other design aspects: Achievement of steady-state conditions should be demonstrated. Co-medication of medicines that could affect the pharmacokinetics of olaparib should be avoided in line with the SmPC, if possible, and should be documented.
Analyte	☒ **parent** ☐ **metabolite** ☐ **both**
	☒ **plasma/serum** ☐ **blood** ☐ **urine**
	Enantioselective analytical method: ☐ **yes** ☒ **no**
Bioequivalence assessment	**Main pharmacokinetic variables:** $AUC_{0\text{-}tau}$ and $C_{max,ss}$
	90% confidence interval: 80.00–125.00%

* As intra-subject variability of the reference product has not been reviewed to elaborate this product-specific bioequivalence guideline, it is not possible to recommend at this stage the use of a replicate design to demonstrate high intra-subject variability and widen the acceptance range of C_{max}. If high intra-individual variability (CV_{intra} > 30%) is expected, the applicants might follow respective guideline recommendations.