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Committee for Medicinal Products for Human Use (CHMP)

Trametinib film-coated tablet 0.5 and 2mg product-specific bioequivalence guidance

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Adopted by CHMP for release for consultation	22 February 2024
Start of public consultation	March 2024
End of consultation (deadline for comments)	30 June 2024
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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 (MWP)*

BCS Classification	**BCS Class:** ☐ **I** ☐ **III** ☒ **Neither of the two** **Background:** Trametinib dimethyl sulfoxide is considered a low solubility compound.
Bioequivalence study design *in case a BCS biowaiver is not feasible or applied*	**single dose** **cross-over** **healthy subjects (excluding those with ocular disorders as described below)** **Background:** Subjects with central serous retinopathy, retinal vein thrombosis, or any risk factors for these conditions, including uncontrolled glaucoma or a history of hyper viscosity or hyper coagulability syndromes, should be excluded from the bioequivalence study.
	☒ **fasting** ☐ **fed** ☐ **both** ☐ **either fasting or fed** **Background:** The SmPC recommends administration without food, at least 1 hour before or at least 2 hours after a meal.
	Strength: 2 mg **Background:** Highest strength to be used for a drug with linear pharmacokinetics and low solubility.

	Number of studies: One single dose study.
	Other critical aspects:
Analyte	☒ **parent** ☐ **metabolite** ☐ **both**
	☒ **plasma/serum** ☐ **blood** ☐ **urine**
	Enantioselective analytical method: ☐ **yes** ☒ **no**
Bioequivalence assessment	**Main pharmacokinetic variables:** AUC_{0-72} and C_{max}
	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.