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Committee for Medicinal Products for Human Use (CHMP)

Paliperidone prolonged-release tablet 1.5 mg, 3 mg, 6 mg, 9 mg and 12 mg product-specific bioequivalence guidance

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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)*

BE Study design**	**Single dose fasting:** all strength or bracketing, healthy volunteers. **Single dose fed:** 12 mg, healthy volunteers. **Multiple dose fasting:** highest tolerable strength in healthy volunteers or highest strength in patients. **Background:** single dose (fasting and fed) and multiple dose studies are required for prolonged release formulations with accumulation. Single dose fasting studies on all strengths are necessary for a prolonged release single unit formulation which can be administered with or without food according to the SmPC.
	cross-over
Analyte	☒ **parent** ☐ **metabolite** ☐ **both**
	☒ **plasma/serum** ☐ **blood** ☐ **urine**
	Enantioselective analytical method: ☐ **yes** ☒ **no**

Bioequivalence assessment	**Main pharmacokinetic variables:** **Single dose:** AUC_{0-t}, AUC_{0-inf}, and C_{max} **Multiple dose:** $AUC_{0-\tau}$, $C_{max,ss}$, and $C_{\tau,ss}$
	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}, $C_{\tau,ss}$, and partial AUC. If high intra-individual variability (CV_{intra} > 30%) is expected, the applicants might follow respective guideline recommendations.

** For prolonged release formulations: If a single-dose study with the highest strength has shown that there is low risk of accumulation (i.e. AUC_{τ} > 90% of AUC_{inf}), the multiple-dose study may be waived. If low degree of accumulation is expected, the applicants might follow respective guideline recommendations.