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2 EMA/CHMP/156358/2016
3 Committee for Medicinal Products for Human Use (CHMP)

4 Paliperidone prolonged-release tablet 1.5mg, 3mg, 6mg, 5 9mg and 12mg product-specific bioequivalence guidance

6 Draft

Draft Agreed by Pharmacokinetics Working Party	February 2016
Adoption by CHMP for release for consultation	1 April 2016
Start of public consultation	2 May 2016
End of consultation (deadline for comments)	31 July 2016

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Comments should be provided using this template. The completed comments form should be sent to PKWPsecretariat@ema.europa.eu.

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Keywords	***Bioequivalence, generics, paliperidone***

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

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:** Highest strength of 12 mg. Healthy volunteers. **Multiple dose fasting:** Highest tolerable strength in healthy volunteers or highest strength in patients. **Cross over studies** **Background:** Single dose fasting and fed studies are mandatory for a prolonged release formulation. Single dose fasting studies on all strengths for a prolonged release single unit formulation which can be administered with or without food. A multiple-dose study is necessary for prolonged release formulations with accumulation.
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}, C_{max} **Multiple dose:** $AUC_{0-\tau}$, $C_{max,ss}$, $C_{\tau,ss}$
	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 (CVintra > 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. $AUC\tau$ > 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.