1 21 July 2016
2 EMA/CHMP/474825/2016
3 Committee for Medicinal Products for Human Use (CHMP)

4 Paliperidone palmitate depot suspension for injection 25, 5 50, 75, 100 and 150 mg product-specific bioequivalence 6 guidance

7 Draft

Draft agreed by Pharmacokinetics Working Party	June 2016
Adopted by CHMP for release for consultation	21 July 2016
Start of public consultation	1 August 2016
End of consultation (deadline for comments)	31 October 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 palmitate depot suspension for injection 25, 50, 75, 100 and 150 mg 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)*

Bioequivalence study design**	**Multiple dose:** any dose/strength (if the test product has the same concentration of active substance as the reference for all the strengths), patients **Background:** single-dose studies in healthy volunteers are not considered feasible.
	cross-over or parallel
Analyte	☐ **parent** ☒ **metabolite** ☐ **both** **Background:** the prodrug, paliperidone palmitate, is not reliably measurable in plasma. Bioequivalence should be based on paliperidone.
	☒ **plasma/serum** ☐ **blood** ☐ **urine**
	Enantioselective analytical method: ☐ **yes** ☒ **no**
Bioequivalence assessment	**Main pharmacokinetic variables:** **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} $C_{T,ss}$, and partialAUC.. 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.