15 December 2016
EMA/CHMP/156358/2016
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

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
Agreed by Pharmacokinetics Working Party	October 2016
Adoption by CHMP	15 December 2016
Date for coming into effect	1 July 2017

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

30 Churchill Place ● Canary Wharf ● London E14 5EU ● United Kingdom
Telephone +44 (0)20 3660 6000 **Facsimile** +44 (0)20 3660 5555
Send a question via our website www.ema.europa.eu/contact

Paliperidone prolonged-release tablet 1.5 mg, 3 mg, 6 mg, 9 mg and 12 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)*

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.