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Committee for Medicinal Products for Human Use (CHMP)

Posaconazole oral suspension 40 mg/ml product-specific bioequivalence guidance*

Draft agreed by Pharmacokinetics Working Party (PKWP)	October 2013
Adoption by CHMP for release for consultation	24 October 2013
Start of public consultation	15 November 2013
End of consultation (deadline for comments)	15 February 2014
Agreed by Pharmacokinetics Working Party	March 2015
Adoption by CHMP	26 March 2015
Date for coming into effect	1 October 2015

*This guideline was previously published as part of a "compilation of individual product-specific guidance on demonstration of bioequivalence Rev.3 EMA/CHMP/736403/2014"

Keywords	<i>Bioequivalence, generics, posaconazole</i>
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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)*

BCS Classification**	BCS Class: <input type="checkbox"/> I <input type="checkbox"/> III <input checked="" type="checkbox"/> neither of the two Background: posaconazole may be considered a low solubility compound with complete absorption.
Bioequivalence study design <i>in case a BCS biowaiver is not feasible or applied</i>	single dose cross-over
	healthy volunteers
	<input type="checkbox"/> fasting <input checked="" type="checkbox"/> fed <input type="checkbox"/> both <input type="checkbox"/> either fasting or fed High fat meal as defined in the Guideline on the investigation of Bioequivalence (CPMP/EWP/QWP/1401/98 Rev. 1; section 4.1.4).
	Strength: 400 mg Background: most sensitive dose for an oral suspension of a low solubility drug.
	Number of studies: one single dose study

	Other critical aspects: significant intra-patient variability in the pharmacokinetic parameters of posaconazole has been reported. A replicate cross-over design study can be carried out as per the Guideline on the investigation of bioequivalence (CPMP/EWP/QWP/1401/98 Rev. 1; section 4.1.10).
Analyte	<input checked="" type="checkbox"/> parent <input type="checkbox"/> metabolite <input type="checkbox"/> both
	<input checked="" type="checkbox"/> plasma/serum <input type="checkbox"/> blood <input type="checkbox"/> urine
	Enantioselective analytical method: <input type="checkbox"/> yes <input checked="" type="checkbox"/> no
Bioequivalence assessment	Main pharmacokinetic variables: AUC_{0-72h} and C_{max}
	90% confidence interval: 80.00– 125.00%

* If high intra-individual variability ($CV_{intra} > 30\%$) is expected, the applicants might follow respective guideline recommendations.

** This tentative BCS classification of the drug substance serves to define whether *in vivo* studies seems to be mandatory (BCS class II and IV) or, on the contrary, (BCS Class I and III) the Applicant may choose between two options: *in vivo* approach or *in vitro* approach based on a BCS biowaiver. In this latter case, the BCS classification of the drug substance should be confirmed by the Applicant at the time of submission based on available data (solubility experiments, literature, etc.). However, a BCS-based biowaiver might not be feasible due to product specific characteristics despite the drug substance being BCS class I or III (e.g. *in vitro* dissolution being less than 85 % within 15 min (BCS class III) or 30 min (BCS class I) either for test or reference, or unacceptable differences in the excipient composition).