



EUROPEAN MEDICINES AGENCY
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Committee for Medicinal Products for Human Use (CHMP)

Voriconazole tablets 50, 200 mg and powder for 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	29 April 2015
Adoption by CHMP	21 May 2015
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Draft revision agreed by Methodology Working Party (MWP)	3 April 2025
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* This revision addresses textual changes for dosing recommendation in line with the ICH M13A guideline

Keywords	<i>Bioequivalence, generics, voriconazole</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 (MWP)*

BCS Classification**	BCS Class: <input type="checkbox"/> I <input type="checkbox"/> III <input checked="" type="checkbox"/> Neither of the two Background: Voriconazole is a low solubility compound.
Bioequivalence study design <i>in case a BCS biowaiver is not feasible or applied</i>	single dose
	cross-over
	healthy volunteers
	<input checked="" type="checkbox"/> fasting <input type="checkbox"/> fed <input type="checkbox"/> both <input type="checkbox"/> either fasting or fed
	Strength: 200 mg for the tablets. 40 mg/ml for the powder for the oral suspension (at a dose of 200 mg).

	Background: For drugs with a more than proportional increase in AUC with increasing dose over the therapeutic dose range, the bioequivalence study should in general be conducted at the highest strength.
	Number of studies: One single dose study for tablets, one single dose study for the oral suspension
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-t} and C _{max}
	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, at this stage it is not possible to recommend the use of a replicate design to demonstrate high intra-subject variability and widen the acceptance range of C_{max}. 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 seem 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).