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Committee for Medicinal Products for Human Use (CHMP)

Fingolimod capsules 0.25 and 0.5 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
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Date for coming into effect	1 July 2017**
Draft revision agreed by Methodology Working Party (MWP)	3 April 2025
Adopted by CHMP	10 June 2025
Date of coming into effect	1 January 2026

* This revision relates to the deletion of the reference to low solubility in accordance with the ICH M13A guideline
**As before as no change in requirements.

Keywords	***Bioequivalence, generics, fingolimod***

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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:** ☐ **I** ☐ **III** ☒ **Neither of the two** **Background:** Fingolimod may be considered a low solubility compound with complete absorption.
BE Study design *in case a BCS biowaiver is not feasible*	**single dose** **cross-over or parallel**
	healthy volunteers
	☒ **fasting** ☐ **fed** ☐ **both** ☐ **either fasting or fed**
	Strength: 0.5 mg. **Background:** Highest strength to be used for a drug with linear pharmacokinetics. Supra-therapeutic doses could be used for the study if considered necessary.
	Number of studies: One single dose study.

Analyte	☒ **parent** ☐ **metabolite** ☐ **both**
	☐ **plasma/serum** ☒ **blood** ☐ **urine**
	Enantioselective analytical method: ☐ **yes** ☒ **no**
Bioequivalence assessment	**Main pharmacokinetic variables:** AUC_{0-72}, 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, 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}. 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).