



EUROPEAN MEDICINES AGENCY
SCIENCE MEDICINES HEALTH

25 July 2019
EMA/CHMP/154812/2016/Rev.1*
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
Date for coming into effect	1 July 2017
Agreed by Pharmacokinetics Working Party	June 2019
Adoption by the CHMP	25 July 2019
Date for coming into effect	1 July 2017**

*This revision concerns the availability of a lower (0.25 mg) strength.

**As before as no change in requirements.

Keywords	<i>Bioequivalence, generics, fingolimod</i>
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Fingolimod capsules 0.25 and 0.5 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)*

BCS Classification**	BCS Class: <input type="checkbox"/> I <input type="checkbox"/> III <input checked="" type="checkbox"/> Neither of the two Background: Fingolimod may be considered a low solubility compound with complete absorption.
BE Study design <i>in case a BCS biowaiver is not feasible</i>	single dose
	cross-over or parallel
	healthy volunteers
	<input checked="" type="checkbox"/> fasting <input type="checkbox"/> fed <input type="checkbox"/> both <input type="checkbox"/> either fasting or fed
	Strength: 0.5 mg Background: highest strength to be used for a drug with linear pharmacokinetics and low solubility. Supra-therapeutic doses could be used for the study if considered necessary.
	Number of studies: one single dose study

Analyte	<input checked="" type="checkbox"/> parent <input type="checkbox"/> metabolite <input type="checkbox"/> both
	<input type="checkbox"/> plasma/serum <input checked="" 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 ₀₋₇₂ , 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).