EUROPEAN MEDICINES AGENCY
SCIENCE MEDICINES HEALTH

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Committee for Medicinal Products for Human Use (CHMP)

Repaglinide tablets 0.5, 1 and 2 mg Product-Specific Bioequivalence Guidance

Draft Agreed by Pharmacokinetics Working Party	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	22 October 2014
Adopted by CHMP	20 November 2014
Date for coming into effect	1 June 2015
Draft revision agreed by Methodology Working Party (MWP)	3 April 2025
Adopted by CHMP	14 April 2025
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* This revision incorporates studies conducted under either fasting or fed conditions, in accordance with the ICH M13A guideline

Keywords	***Bioequivalence, generics, repaglinide***

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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:** ☐ **I** ☐ **III** ☒ **Neither of the two** **Background:** Repaglinide is a low solubility compound.
BE Study design	**single dose** **cross-over**
	healthy volunteers
	☐ **fasting** ☐ **fed** ☐ **both** ☒ **either fasting or fed** The SmPC recommends intake preprandially so a fed study is acceptable. However, a fasted study is also acceptable but administration of a glucose solution should be considered.
	Strength: 2 mg **Background:** Highest strength to be used for a drug with linear pharmacokinetics.
	Number of studies: One single dose study.

Analyte	☒ **parent** ☐ **metabolite** ☐ **both**
	☒ **plasma** ☐ **blood** ☐ **urine**
	Enantioselective analytical method: ☐ **yes** ☒ **no**
Bioequivalence assessment	**Main pharmacokinetic variables:** AUC_{0-t}, Cmax
	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 (CVintra > 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)