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

Prasugrel hydrochloride film-coated tablets 5 mg and 10 mg product-specific bioequivalence guidance

Draft

Draft agreed by Pharmacokinetics Working Party (PKWP)	June 2017
Adoption by CHMP for release for consultation	20 July 2017
Start of public consultation	3 August 2017
End of consultation (deadline for comments)	31 October 2017

†This revision concerns the addition of 'hydrochloride' to the title and the section on BCS classification and the addition of an 'additional study under fed conditions' and 'other information' to the section on Bioequivalence study design.

Comments should be provided using this template. The completed comments form should be sent to PKWP@ema.europa.eu

Keywords	***Bioequivalence, generics, prasugrel***

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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:** Prasugrel hydrochloride may be considered a low solubility compound.
Bioequivalence study design *in case a BCS biowaiver is not feasible or applied*	**single dose** **cross-over**
	healthy volunteers
	☒ **fasting** ☐ **fed** ☐ **both** ☐ **either fasting or fed** An additional study under fed conditions is recommended if the generic product contains a different salt form than the originator or the free base of prasugrel.

	Strength: 10 mg **Background:** highest strength to be used for a drug with linear pharmacokinetics and low solubility.
	Number of studies: one single dose study
	Other information: it should be justified/demonstrated that the conversion from prasugrel salt to free base is not more than 70%.
Analyte	☐ **parent** ☒ **metabolite** ☐ **both** **Background:** the parent compound is not detected in human or animal plasma (or other biological matrix). Bioequivalence should be based on the first metabolite, R-95913.
	☒ **plasma/serum** ☐ **blood** ☐ **urine**
	Enantioselective analytical method: ☐ **yes** ☒ **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, 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).