1 25 June 2015
2 EMA/CHMP/PKWP/36761/2015
3 Committee for Medicinal Products for Human Use (CHMP)

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

6 Draft

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| **Draft Agreed by Pharmacokinetics Working Party** | April 2015 |
| Adoption by CHMP for release for consultation | 25 June 2015 |
| Start of public consultation | 15 July 2015 |
| End of consultation (deadline for comments) | 1 November 2015 |

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

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|---|---|
| **Keywords** | ***Bioequivalence, generics, Prasugrel*** |

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# Prasugrel film-coated tablets 5 and 10 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)*

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| **BCS Classification**** | **BCS Class:** ☐ **I** ☐ **III** ☒ **Neither of the two**<br>**Background:** prasugrel may be considered a low solubility compound. |
| **BE Study design**<br>*in case a BCS biowaiver is not feasible or applied* | **single dose**<br>**cross-over** |
| | **healthy volunteers** |
| | ☒ **fasting** ☐ **fed** ☐ **both** ☐ **either fasting or fed** |
| | **Strength:** 10 mg<br>**Background:** highest strength to be used for a drug with linear pharmacokinetics and low solubility. |
| | **Number of studies:** one single dose study. |

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| **Analyte** | ☐ **parent** ☒ **metabolite** ☐ **both**<br>**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:** $AUC_{0-t}$, $C_{max}$ |
| | **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 (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 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).