21 May 2015
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Committee for Medicinal Products for Human Use (CHMP)

Capecitabine film-coated tablets 150, 500 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 Working Party	29 April 2015
Adoption by CHMP	21 May 2015
Date for coming into effect	1 December 2015

Keywords	***Bioequivalence, generics, capecitabine***

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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:** absorption in humans is almost complete, but capecitabine is unstable in acidic medium. Therefore, the available data on solubility does not allow the BCS classification of capecitabine.
BE Study design *in case a BCS biowaiver is not feasible or*	**single dose** **cross-over**

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applied	**patients**
	☐ **fasting** ☒ **fed** ☐ **both** ☐ **either fasting or fed** Fed state recommended to minimise the risk of vomiting, for example standardized light meal for patients participating in the bioequivalence study.
	Strength: 500 mg **Background:** generally, highest strength to be used for a drug with linear pharmacokinetics with no information on solubility available.
	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-t}, Cmax
	90% confidence interval: 80.00 – 125.00%

* Since high intra-individual variability (CVintra > 30 %) is expected, the applicants might follow respective guideline recommendations.