EUROPEAN MEDICINES AGENCY
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Colchicine tablet 0.5 mg and 1 mg product-specific bioequivalence guidance

Draft

Draft Agreed by Pharmacokinetics Working Party (PKWP)	January 2019
Adopted by CHMP for release for consultation	28 February 2019
Start of public consultation	8 March 2019
End of consultation (deadline for comments)	30 June 2019

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

Keywords	***Bioequivalence, generics, colchicine***

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Colchicine tablet 0.5 mg and 1 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:** ☐ **I** ☒ **III** ☐ **Neither of the two** **Background:** Colchicine is highly soluble with incomplete absorption.
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**
	Strength: 1 mg **Background:** Highest strength recommended. However, it is also possible to use the lower strength for a drug with linear pharmacokinetics and high solubility.

	Number of studies: One
Analyte	☒ **parent** ☐ **metabolite** ☐ **both**
	☒ **plasma/serum** ☐ **blood** ☐ **urine**
	Enantioselective analytical method: ☐ **yes** ☒ **no**
Bioequivalence assessment	**Main pharmacokinetic variables:** C_{max}, AUC_{0-t} **Background/justification:**
	90% confidence interval: 80.00– 125.00% for C_{max} and 90.00-111.11% for AUC_{0-t}. **Background:** Colchicine is a narrow therapeutic index drug.

* 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.

** Applying for a BCS-based biowaiver is restricted to highly soluble drug substances with known human absorption and considered not to have a narrow therapeutic index (NTI). As colchicine is considered a NTI drug, a BCS biowaiver is not possible.