1 20 July 2017
2 EMA/CHMP/421315/2017
3 Committee for Medicinal Products for Human Use (CHMP)

Dimethyl fumarate gastro-resistant capsules 120 mg and 240 mg product-specific bioequivalence guidance

4 Draft

Draft agreed by Pharmacokinetics Working Party	April 2017
Adopted 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

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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, dimethyl fumarate***

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Dimethyl fumarate gastro-resistant capsules 120 mg and 240 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)*

Bioequivalence study design *in case a BCS biowaiver is not feasible or applied*	**Single-dose:** 120 mg strength for tolerability reasons in healthy subjects **Multiple dose:** N/A **Background:** multiple unit formulation **Cross-over**
Analyte	☐ **parent** ☒ **metabolite** ☐ **both** **Background:** The parent, DMF, is not quantifiable in plasma. Bioequivalence has to be based on MMF.
	☒ **plasma/serum** ☐ **blood** ☐ **urine**
	Enantioselective analytical method: ☐ **yes** ☒ **no**

Bioequivalence assessment	**Main pharmacokinetic variables:** **Single dose:** AUC_{0-t}, AUC_{inf}, C_{max} (t_{lag} and t_{max}) **Multiple dose:** N/A
	90% confidence interval: 80.00–125.00% for AUC_{0-t}, AUC_{inf}, C_{max}. Comparable median and range for t_{lag} and t_{max}.

* 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} $C_{T,ss}$, and partial AUC. If high intra-individual variability (CV_{intra} > 30%) is expected, the applicants might follow respective guideline recommendations.

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