



1 30 March 2023
2 EMA/CHMP/590937/2022
3 Committee for Medicinal Products for Human Use (CHMP)

4 **Bosutinib film-coated tablets 100, 400 and 500 mg**
5 **product-specific bioequivalence guidance**

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Draft agreed by Pharmacokinetics Working Party (PKWP) / Methodology Working Party (MWP)	February 2023
Adopted by CHMP for release for consultation	30 March 2023
Start of public consultation	June 2023
End of consultation (deadline for comments)	30 September 2023
Agreed by Methodology Working Party (MWP)	
Adopted by CHMP	
Date for coming into effect	

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Comments should be provided using this [template](#). The completed comments form should be sent to GenericsDG@ema.europa.eu

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Keywords	<i>Bioequivalence, generics, bosutinib</i>
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11 **Bosutinib film-coated tablets 100, 400 and 500 mg product-specific bioequivalence**
 12 **guidance**

14 Disclaimer:

15 *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*
 16 *a marketing authorisation application complies with the appropriate scientific, regulatory and legal requirements.*

17 **Requirements for bioequivalence demonstration (PKWP)***

BCS Classification**	BCS Class: <input type="checkbox"/> I <input type="checkbox"/> III <input checked="" type="checkbox"/> Neither of the two Background: Bosutinib is considered a low solubility compound with limited absorption.
Bioequivalence study design <i>in case a BCS biowaiver is not feasible or applied</i>	single dose cross-over
	healthy volunteers
	<input type="checkbox"/> fasting <input checked="" type="checkbox"/> fed <input type="checkbox"/> both <input type="checkbox"/> either fasting or fed
	Strength: 400 mg Background: Highest strength generally recommended to be used for a drug with linear pharmacokinetics in the therapeutic range and low solubility. However, there may be safety/tolerability issues with the highest strength (500 mg) if given to healthy volunteers. For this reason, it is recommended to use a lower strength (400 mg).

	Number of studies: one single dose study
	Other design aspects: N/A
Analyte	<input checked="" type="checkbox"/> parent <input type="checkbox"/> metabolite <input type="checkbox"/> both
	<input checked="" type="checkbox"/> plasma/serum <input type="checkbox"/> blood <input type="checkbox"/> urine
	Enantioselective analytical method: <input type="checkbox"/> yes <input checked="" type="checkbox"/> no
Bioequivalence assessment	Main pharmacokinetic variables: AUC _{0-72h} and C _{max}
	90% confidence interval: 80.00–125.00%

18 * As intra-subject variability of the reference product has not been reviewed to elaborate this product-specific bioequivalence guideline, it is not possible
19 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
20 intra-individual variability (CV_{intra} > 30%) is expected, the applicants might follow respective guideline recommendations.

21 ** This tentative BCS classification of the drug substance serves to define whether in vivo studies seem to be mandatory (BCS class II and IV) or, on the
22 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
23 latter case, the BCS classification of the drug substance should be confirmed by the Applicant at the time of submission based on available data
24 (solubility experiments, literature, etc.). However, a BCS-based biowaiver might not be feasible due to product specific characteristics despite the drug
25 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
26 reference, or unacceptable differences in the excipient composition).