



1 21 May 2024
2 EMA/CHMP/518671/2023
3 Committee for Medicinal Products for Human Use (CHMP)

4 **Nilotinib hard capsules 50, 150 and 200 mg product-**
5 **specific bioequivalence guidance**
6 **Draft**

Draft Agreed by Methodology Working Party (MWP)	23 April 2024
Adopted by CHMP for release for consultation	21 May 2024
Start of public consultation	25 June 2024
End of consultation (deadline for comments)	30 September 2024

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Comments should be provided using this EUSurvey [form](#). For any technical issues, please contact the [EUSurvey Support](#).

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Keywords	<i>Bioequivalence, generics, nilotinib</i>
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12 **Nilotinib hard capsules 50, 150 and 200 mg product-specific bioequivalence guidance**

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

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18 Requirements for bioequivalence demonstration (MWP)*

BCS Classification**	BCS Class: <input type="checkbox"/> I <input type="checkbox"/> III <input checked="" type="checkbox"/> Neither of the two Background: Nilotinib hydrochloride monohydrate is considered a low solubility compound
Bioequivalence study design <i>in case a BCS biowaiver is not feasible or applied</i>	single dose
	cross-over
	healthy subjects
	<input checked="" type="checkbox"/> fasting <input type="checkbox"/> fed <input type="checkbox"/> both <input type="checkbox"/> either fasting or fed
	Strength: 200 mg Background: Highest strength for drug with low solubility but dose proportional pharmacokinetics in dose range 50-200 mg.

	In vitro evaluation: Additionally, <i>in vitro</i> studies showing compatibility of the generic nilotinib formulation with applesauce should be conducted.
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: C_{max} , AUC_{0-t}
	90% confidence interval: 80.00– 125.00%

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

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