



1 31 January 2019
2 EMA/CHMP/802679/2018
3 Committee for Medicinal Products for Human Use (CHMP)

4 **Palbociclib hard capsule 75 mg, 100 mg and 125 mg**
5 **product-specific bioequivalence guidance**
6 **Draft**

Draft Agreed by Pharmacokinetics Working Party (PKWP)	October 2018
Adopted by CHMP for release for consultation	31 January 2019
Start of public consultation	8 February 2019
End of consultation (deadline for comments)	30 June 2019

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

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Keywords	<i>Bioequivalence, generics, palbociclib</i>
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12 **Palbociclib hard capsule 75 mg, 100 mg and 125 mg product-specific bioequivalence**
13 **guidance**
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15 *Disclaimer:*

16 *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*
17 *marketing authorisation application complies with the appropriate scientific, regulatory and legal requirements.*
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19 **B. 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: Palbociclib is a low solubility drug.
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: 125 mg Background: Highest strength for drugs with linear pharmacokinetics and low solubility.

	Number of studies: One
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} , C _{max}
	90% confidence interval: 80.00– 125.00%

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

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