



1 22 June 2017
2 EMA/CHMP/356875/2017
3 Committee for Medicinal Products for Human Use (CHMP)

4 **Dronedarone film-coated tablets 400 mg product-specific**
5 **bioequivalence guidance**
6 Draft

Draft Agreed by Pharmacokinetics Working Party (PKWP)	April 2017
Adopted by CHMP for release for consultation	22 June 2017
Start of public consultation	28 July 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 PKWP@ema.europa.eu

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Keywords	<i>Bioequivalence, generics, dronedarone</i>
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10 **Dronedarone film-coated tablets 400 mg product-specific bioequivalence guidance**

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12 Disclaimer:

13 *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*
14 *marketing authorisation application complies with the appropriate scientific, regulatory and legal requirements.*

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16 **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: Dronedarone 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: 400 mg is the only available strength
Number of studies: one single dose study	

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-t} and C _{max}
	90% confidence interval: 80.00–125.00%

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

20 ** 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
21 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
22 case, the BCS classification of the drug substance should be confirmed by the Applicant at the time of submission based on available data (solubility
23 experiments, literature, etc.). However, a BCS-based biowaiver might not be feasible due to product specific characteristics despite the drug substance being
24 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
25 unacceptable differences in the excipient composition).