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EMA/CHMP/474712/2016 Rev. 1* Corr. 1**
Committee for Medicinal Products for Human Use (CHMP)

Abiraterone acetate tablets 250 mg and 500 mg product-specific bioequivalence guidance

Draft agreed by Pharmacokinetics Working Party	June 2016
Adopted by CHMP for release for consultation	21 July 2016
Start of public consultation	1 August 2016
End of consultation (deadline for comments)	31 October 2016
Agreed by Pharmacokinetics Working Party	December 2016
Adopted by CHMP	23 February 2017
Date of coming into effect	1 September 2017
Draft revision agreed by Pharmacokinetics Working Party	May 2020
Adopted by CHMP for release for consultation	28 May 2020
Start of public consultation	15 June 2020
End of consultation (deadline for comments)	30 September 2020
Adopted by CHMP	12 November 2020
Date of coming into effect	1 March 2021

* This revision concerns the availability of a higher (500 mg) strength.

** The product name has been corrected to include the ester and should read "abiraterone acetate" instead of "abiraterone".

Keywords	<i>Bioequivalence, generics, abiraterone</i>
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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)*

<p>BCS Classification**</p>	<p>BCS Class: <input type="checkbox"/> I <input type="checkbox"/> III <input checked="" type="checkbox"/> Neither of the two</p> <p>Background: Abiraterone acetate may be considered a low solubility compound.</p>
<p>Bioequivalence study design</p> <p><i>in case a BCS biowaiver is not feasible or applied</i></p>	<p>single dose</p> <p>cross-over</p>
	<p>healthy volunteers</p>
	<p><input checked="" type="checkbox"/> fasting <input type="checkbox"/> fed <input type="checkbox"/> both <input type="checkbox"/> either fasting or fed</p>
	<p>Strength: 500 mg</p> <p>Background: the highest strength to be used for a drug with linear pharmacokinetics and low solubility.</p>
	<p>Number of studies: one single dose study</p>

Analyte	<input type="checkbox"/> parent <input checked="" type="checkbox"/> metabolite <input type="checkbox"/> both Background: The parent compound, abiraterone acetate, is almost immediately metabolised after administration and therefore it is not reliably measurable in plasma. Bioequivalence should be based on the metabolite, abiraterone.
	<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%

* 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}. If high intra-individual variability (CV_{intra} > 30%) is expected, the applicants might follow respective guideline recommendations.

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