12 November 2020
EMA/CHMP/567816/2020
Committee for Medicinal Products for Human Use (CHMP)

Overview of comments received on 'Abiraterone tablets 250 mg and 500 mg product-specific bioequivalence guidance' (EMA/CHMP/474712/2016 Rev. 1)

Interested parties (organisations or individuals) that commented on the draft document as released for consultation.

Stakeholder no.	Name of organisation or individual
1	Janssen Pharmaceutical Companies of Johnson & Johnson

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1. General comments – overview

Stakeholder no.	General comment (if any)	Outcome (if applicable)
1	Janssen Pharmaceutical Companies of Johnson & Johnson welcomes the opportunity to comment on the draft revised bioequivalence guidance.	

2. Specific comments on text

Line no.	Stakeholder no.	Comment and rationale; proposed changes	Outcome
Table after line 18: Bioequivalence study design	1	**Comments:** It is understood that, per the Guideline on Investigation of Bioequivalence (2010), for products where the SmPC recommends intake of the reference medicinal product on an empty stomach or irrespective of food intake, the bioequivalence study should be conducted under fasting conditions (as this is considered to be the most sensitive condition to detect a potential difference). However, due to the demonstrated, large effect of the meal on abiraterone systemic exposures and the potential for erroneous abiraterone acetate administrations (i.e., less than at least 1 hour before a meal or less than 2 hours after a meal), it is advisable to ensure that the effect of the meal for the test formulation is similar (or not larger) than that of the reference formulation, for which the short-term safety of abiraterone acetate both in fasted and fed states was established (see Section 5.2, Pharmacokinetics), Zytiga SmPC. **Proposed change:** bioequivalence to be demonstrated in both fast and fed conditions.	Not accepted. The fact that the innovator company has shown for the reference product a large bioavailability difference in a certain non-recommended condition of use is not enough reason to require demonstration of equivalence also in those non-recommended conditions. According to the SmPC of Zytiga, "*administration with food significantly increases the absorption of abiraterone acetate. The efficacy and safety when given with food have not been established therefore this medicinal product must not be taken with food*" and "*The tablets should be taken at least one hour before or at least two hours after eating. These should be swallowed whole with water*". Consequently, demonstration of equivalence in conditions of use that are not recommended in the SmPC (i.e. intake of abiraterone acetate with food) cannot be a regulatory requirement, since failure to show equivalence in the non-recommended conditions of use cannot be a reason for rejection of the marketing authorisation application, unless it is shown that the potential misuse is relatively frequent and the consequences are severe. Furthermore, the innovator company has not shown that a different formulation of abiraterone acetate may have a larger food effect. Unless otherwise justified, it is considered that the large food effect is mostly drug-dependent and all formulations will have a similar food

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			effect, unless specifically designed to reduce it. As these issues have not been addressed / supported in the comment, the requirement of a single dose study in fasted state is not modified. A study investigating the food effect would be necessary if the applied product claims not to have food effect, in contrast to the reference medicinal product, and that the intake of the applied product can be irrespective of food.