12 December 2019
EMA/CHMP/582874/2019
Committee for Medicinal Products for Human Use (CHMP)

Overview of comments received on 'Alectinib hard capsule 150 mg product-specific bioequivalence guidance' (EMA/CHMP/790261/2018)

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

Stakeholder no.	Name of organisation or individual
1	F.Hoffmann-La Roche Ltd.

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1. General comments - overview

Stakeholder number	General comment (if any)	Outcome (if applicable)

2. Specific comments on text

Line no.	Stakeholder no.	Comment and rationale; proposed changes	Outcome
17 B. Requirements for bioequivalence demonstration (PKWP)	1	Comment: The study was done under both fasted and fed conditions. Proposed change (if any): Tick the box '***both***' and remove the tick box '~~*fed*~~'.	Not accepted. Since the reference product must be taken with food, a study in the fed state is sufficient according to the Guideline on the investigation of bioequivalence (CPMP/EWP/QWP/1401/98 Rev 1/Corr).
17 B. Requirements for bioequivalence demonstration (PKWP)	1	Comment: For analyte, the originator company (Roche) explored both parent and metabolite. Proposed change (if any): Add tick box '***metabolite***'.	Not accepted. According to the Guideline on the investigation of bioequivalence (CPMP/EWP/QWP/1401/98 Rev 1/Corr), the general recommendation is that bioequivalence should be evaluated based on parent drug since C_{max} of a parent drug is usually more sensitive to detect differences between formulations in absorption rate. Thus, there is no requirement to measure the metabolite.
17. B. Requirements for bioequivalence demonstration (PKWP)	1	Comment: For Bioequivalence assessment, the main pharmacokinetics variables are AUC infinity, AUC last, Cmax. Proposed change (if any): 'Main pharmacokinetic variables: AUC~~*0-72h*~~ ***0-∞, AUC last***, Cmax'.	Not accepted. According to the Guideline on the investigation of bioequivalence (CPMP/EWP/QWP/1401/98 Rev 1/Corr), the main pharmacokinetic variables to be used in the assessment of bioequivalence for an immediate release formulation are AUC_{0-t}, or, when relevant $AUC_{0-72\ h}$, and $C_{max.}$ AUC_{0-72h} may be used as an alternative to AUC_{0-t} for drugs with long half-lives since a sampling period longer than 72 h is not considered necessary for any immediate release

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			formulation irrespective of the half life of the drug.