1 April 2016
EMA/CHMP/206139/2016
Committee for Medicinal Products for Human Use (CHMP)

Overview of comments on 'Ticagrelor film-coated tablets 90mg product specific bioequivalence guidance' (EMA/CHMP/PKWP/151478/2015)

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

Stakeholder no.	Name of organisation or individual
1	AstraZeneca

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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
Page 2 Table 2nd column 4th row BE study design – fed and fasted studies	1	Comment: As Brilique 90mg tablets are currently administered without regard to food, new products will need to exhibit equivalent exposures in both fasted and fed states. It is therefore recommended that both fed and fasted BE studies are conducted for 90mg ticagrelor tablets, unless data already exist showing that the new product is equivalent in both fasted and fed states Proposed change (if any): The box (row 4) located under 2nd column of table should be ticked to indicate both fed and fasted studies are required to demonstrate BE of 90mg ticagrelor tablets.	The comment has been acknowledged. For products where the SmPC recommends intake of the reference medicinal product irrespective of food intake, the bioequivalence study should be conducted under fasting conditions because fasting conditions are considered to be the most sensitive condition to detect a potential difference between formulations (Guideline on the investigation of bioequivalence CPMP/EWP/QWP/1401/98 Rev. 1/ Corr **)." In order to consider the need for studies in the fed and fasted state, the innovator will need to submit data demonstrating that the food effect is depending on the (immediate release) formulation as justification.
Page 3 Table 2nd column 1st row BE study design - Analyte		Comment: Measurement of ticagrelor's active metabolite provides supportive evidence of comparable therapeutic outcome. As such, it should be noted within the guidance that measurement of the active metabolite can provide relevant information with regards to conducting BE studies for ticagrelor 90mg tablets.	Ticagrelor is absorbed and Cmax of the parent compound is more sensitive to detect differences between formulations in absorption rate than Cmax of a metabolite. Therefore, evaluation of bioequivalence should be based on the parent compound. (Guideline on the

Line no.	Stakeholder no.	Comment and rationale; proposed changes	Outcome
		Proposed change (if any): The box in row 1 for metabolite should also be ticked and a comment included to indicate measurement can provide supportive evidence of comparable therapeutic outcome	investigation of bioequivalence CPMP/EWP/QWP/1401/98 Rev. 1/ Corr **)
Page 2 column 2 row 5 BE Study Design-Strength		Comment: It is recommended that additional text is included within the guidance indicating that *in vivo* bioequivalence can be waived for lower strength ticagrelor tablets, providing that tablets meet with the requirements of dose proportionality and *in vitro* dissolution data support this approach. Proposed change (if any): Include additional point to confirm that an *in vivo* bioequivalence waiver may be appropriate for lower strength ticagrelor tablets, based on dose proportionality to 90mg tablets and supporting *in vitro* dissolution data package.	Not accepted. At this moment ticagrelor tablets are only available at the 90 mg strength. If lower strengths would become available, the template will be adjusted to provide recommendations for the strength to be used in the bioequivalence study.