25 January 2018
EMA/CHMP/730771/2017
Committee for Medicinal Products for Human Use (CHMP)

Overview of comments received on 'Rilpivirine film-coated tablets 25 mg product-specific bioequivalence guidance' (EMA/CHMP/356878/2017)

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

Stakeholder no.	Name of organisation or individual
1	Zentiva, k.s., Czech Republic

30 Churchill Place ● Canary Wharf ● London E14 5EU ● United Kingdom
Telephone +44 (0)20 3660 6000 **Facsimile** +44 (0)20 3660 5555
Send a question via our website www.ema.europa.eu/contact

An agency of the European Union

© European Medicines Agency, 2018. Reproduction is authorised provided the source is acknowledged.

1. General comments - overview

Stakeholder no.	General comment (if any)	Outcome (if applicable)

2. Specific comments on text

Line no.	Stakeholder number	Comment and rationale; proposed changes	Outcome
Line 17 Table / Bioequivalence assessment	1	**Comment:** According to the Guideline on the Investigation of Bioequivalence (CPMP/EWP/QWP/1401/98 Rev. 1/ Corr, 20 January 2010): "… AUC truncated at 72 h (AUC(0-72h)) may be used as an alternative to AUC(0-t) for comparison of extent of exposure as the absorption phase has been covered by 72 h for immediate release formulations. A sampling period longer than 72 h is therefore not considered necessary for any immediate release formulation irrespective of the half-life of the drug. … " Rilpivirine with Tmax at 4-5 h and reported elimination half-life of at least 45 h is a good candidate for use of truncated AUC since sampling up to 72 h would not ensure AUC(0-t) covering at least 80% of AUC(0-∞) due to long elimination. Furthermore, the already approved "Emtricitabine/rilpivirine/tenofovir disoproxil film-coated tablets 200 mg/25 mg/245 mg product-specific bioequivalence guidance (EMA/CHMP/805532/2016, 22-June-2017) proposes the use of Cmax and AUC(0-72h) as primary pharmacokinetic (PK) variables for assessment of bioequivalence of rilpivirine. **Proposed change:** Cmax and AUC(0-72h) are the primary PK variables for assessment of bioequivalence of rilpivirine.	Accepted. It is a company's choice to select either $AUC_{(0-72h)}$ or $AUC_{(0-t)}$ as the primary PK variable. To be consistent with "Emtricitabine/rilpivirine/tenofovir disoproxil film-coated tablets 200 mg/25 mg/245 mg product-specific bioequivalence guidance (EMA/CHMP/805532/2016, 22-June-2017), C_{max} and $AUC_{(0-72h)}$ are the primary PK variables for assessment of bioequivalence of rilpivirine.