1 25 June 2015
2 EMA/CHMP/PKWP/269533/2015
3 Committee for Medicinal Products for Human Use (CHMP)

4 Asenapine sublingual tablets 5 and 10 mg product-5 specific bioequivalence guidance

6 Draft

Draft Agreed by Pharmacokinetics Working Party	June 2015
Adoption by CHMP for release for consultation	25 June 2015
Start of public consultation	15 July 2015
End of consultation (deadline for comments)	1 November 2015

7
8

Comments should be provided using this template. The completed comments form should be sent to PKWPsecretariat@ema.europa.eu.

9

Keywords	***Bioequivalence, generics, asenapine***

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

Asenapine sublingual tablets 5 and 10 mg product-specific bioequivalence guidance

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)*

BCS Classification	**BCS Class:** ☐ **I** ☐ **III** ☐ **Neither of the two** **Background:** asenapine may be considered a high solubility compound with limited absorption. However, the active substance reaches the circulation primarily by absorption in the oral cavity, rather than by swallowing and absorption through the gastrointestinal tract. Therefore, in accordance with the guideline on the investigation of bioequivalence, the product cannot be considered for a BCS based biowaiver.
BE Study design *in case a BCS biowaiver is not feasible or applied*	**single dose** **cross-over**
	healthy volunteers or patients in case of intolerability
	☒ **fasting** ☐ **fed** ☐ **both** ☐ **either fasting or fed**
	Strength: 5 mg **Background:** the lower strength would be expected to be more discriminating between formulations. In

	addition dose related adverse effects could cause problems with tolerability of the highest strength.
	Number of studies: one
Analyte	☒ **parent** ☐ **metabolite** ☐ **both**
	☒ **plasma/serum** ☐ **blood** ☐ **urine**
	Enantioselective analytical method: ☐ **yes** ☒ **no**
Bioequivalence assessment	**Main pharmacokinetic variables:** AUC_{0-72h}, 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 (CVintra > 30 %) is expected, the applicants might follow respective guideline recommendations.