EUROPEAN MEDICINES AGENCY
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Committee for Medicinal Products for Human Use (CHMP)

Tadalafil Product-Specific Bioequivalence Guidance

Draft

Draft Agreed by Pharmacokinetics Working Party	**October 2013**
Adoption by CHMP for release for consultation	24 October 2013
Start of public consultation	15 November 2013
End of consultation (deadline for comments)	15 February 2014

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

Keywords	***Bioequivalence, generics, tadalafil***

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Tadalafil 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:** Tadalafil is a low solubility compound.
BE Study design	**single dose** **cross-over**
	healthy volunteers
	☐ fasting ☐ fed ☒ both ☐ either fasting or fed

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	Background: The reference product is considered to have specific formulation characteristics to enhance the rate of absorption of the drug and therefore, it cannot be assumed that the impact of food will be the same regardless of formulation. The product can be taken without regard to food. Thus, both fasted and fed state comparisons of test to reference formulations are required.
	Strength: 20 mg because it is the highest strength **Background:** Linear PK in the dose range 2.5 mg – 20 mg
	Number of studies: two single dose studies (20 mg fasted and 20 mg fed)
Analyte	☒ **parent** ☐ **metabolite** ☐ **both**
	☒ **plasma** ☐ **blood** ☐ **urine**
	Enantioselective analytical method: ☐ **yes** ☒ **no**
Bioequivalence assessment	**Main pharmacokinetic variables:** AUC_{0-72h}, Cmax
	90% confidence interval: 80.00– 125.00

16 * As drug variability has not been reviewed, this guidance is not applicable to highly variables drugs.

17 ** The BCS classification should be confirmed by the Applicant at time of submission based on available data (solubility experiments, literature, etc.). If
18 a drug substance has been classified as BCS class II or IV, no further solubility investigations are needed.