EUROPEAN MEDICINES AGENCY
SCIENCE MEDICINES HEALTH

21 May 2024
EMA/94136/2024
Committee for Medicinal Products for Human Use (CHMP)

Methylphenidate, prolonged-release tablet 18 mg, 27 mg, 36 mg and 54 mg and modified release capsule 5 mg, 10 mg, 20 mg, 30 mg, 40 mg, 50 mg and 60 mg product-specific bioequivalence guidance

Draft

Draft Agreed by Methodology Working Party (MWP)	23 April 2024
Adopted by CHMP for release for consultation	21 May 2024
Start of public consultation	25 June 2024
End of consultation (deadline for comments)	30 September 2024

Comments should be provided using this EUSurvey form. For any technical issues, please contact the EUSurvey Support.

Keywords	***Bioequivalence, generics, methylphenidate***

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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 (MWP)

Bioequivalence study design	**For Single Unit Formulations** **Single dose fasting:** All strengths or bracketing approach, healthy volunteers. **Single dose fed:** The highest/most sensitive strength in healthy subjects may be sufficient provided that, in addition to the usual waiver of strength criteria, the shape of the formulations of the strengths should be similar. **Background:** Single dose fasting and fed studies are required for prolonged-release formulations without accumulation. **For Multiple Unit Formulations** **Single dose fasting:** Highest strength, healthy volunteers. **Single dose fed:** Highest strength, healthy volunteers. **Background:** Single dose fasting and fed studies are required for prolonged-release formulations without accumulation.

	cross-over
Analyte	☒ **parent** ☐ **metabolite** ☐ **both**
	☒ **plasma/serum** ☐ **blood** ☐ **urine**
	Enantioselective analytical method: ☐ **yes** ☒ **no**
Bioequivalence assessment	Main pharmacokinetic variables: Single dose fasting: AUC_{0-t}, AUC_{0-inf}, C_{max}, AUC_{0-3h}, $C_{max0-3h}$, AUC_{3-24h} and $Cmax_{3-24h}$ Single dose fed: AUC_{0-t}, AUC_{0-inf}, C_{max}, AUC_{0-4h}, $C_{max0-4h}$, AUC_{4-24h} and $Cmax_{4-24h}$
	90% confidence interval: 80.00– 125.00%
	To be noted: *In vitro* studies of release in alcohol solutions should also be performed. *In vitro* compatibility with mixing with applesauce should be demonstrated where applicable.