EUROPEAN MEDICINES AGENCY
SCIENCE MEDICINES HEALTH

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Committee for Medicinal Products for Human Use (CHMP)

Enzalutamide soft capsule 40 mg and film-coated tablet 40 mg & 80 mg product-specific bioequivalence guidance

Draft Agreed by Pharmacokinetics Working Party (PKWP)	28 October 2020
Adopted by CHMP for release for consultation	11 November 2021
Start of public consultation	15 December 2021
End of consultation (deadline for comments)	31 March 2022
Agreed by Pharmacokinetics Working Party	
Adopted by CHMP	
Date for coming into effect	

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

Keywords	***Bioequivalence, generics, enzalutamide***

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Enzalutamide soft capsule 40 mg and film-coated tablet 40 & 80 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:** Enzalutamide may be considered a low solubility compound with complete absorption.
Bioequivalence study design *in case a BCS biowaiver is not feasible or applied*	**single dose** **cross-over or parallel**
	healthy male volunteers
	Capsules: ☒ **fasting** ☐ **fed** ☐ **both** ☐ **either fasting or fed** Tablets: ☐ **fasting** ☐ **fed** ☒ **both** ☐ **either fasting or fed** The reference product can be taken with or without food according to the SmPC. Since the specific formulation (solid dispersion) of the tablet is known to be critical to the performance of the formulation in fed conditions, it cannot be assumed that the impact of food will be the same regardless of formulation. Therefore, both fasted and fed state comparisons of test to reference formulations are required for the

	tablet. A waiver for this fed study may be applicable if the products are manufactured using the same technology and if excipients that might affect bioavailability are qualitatively the same and quantitatively similar between test and reference product.
	Strength: 40 mg for the soft capsules and 80 mg for the tablets **Background:** highest strength to be used for a drug with linear pharmacokinetics and low solubility.
	Number of studies: one single dose study for the soft capsule and two single dose studies (fasted and fed) for the tablet, although the fed study might be waived as explained above.
	Other design aspects: A cross-over design is preferable to a parallel study, but a parallel study is also acceptable.
Analyte	☒ **parent** ☐ **metabolite** ☐ **both**
	☒ **plasma/serum** ☐ **blood** ☐ **urine**
	Enantioselective analytical method: ☐ **yes** ☒ **no**
Bioequivalence assessment	**Main pharmacokinetic variables:** AUC_{0-72h} and C_{max}
	90% confidence interval: 80.00–125.00%

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