



EUROPEAN MEDICINES AGENCY
SCIENCE MEDICINES HEALTH

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Committee for Medicinal Products for Human Use (CHMP)

Lanreotide acetate, prolonged-release solution for injection in prefilled syringe 60, 90 and 120 mg product-specific bioequivalence guidance

Draft Agreed by Pharmacokinetics Working Party (PKWP)	21 March 2022
Adopted by CHMP for release for consultation	22 April 2022
Start of public consultation	17 May 2022
End of consultation (deadline for comments)	31 August 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 MWP@ema.europa.eu

Keywords	<i>Bioequivalence, generics, lanreotide acetate</i>
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14 Lanreotide acetate, prolonged-release solution for injection in a prefilled syringe 60, 90
15 and 120 mg product-specific bioequivalence guidance
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17 Disclaimer:

18 *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*
19 *marketing authorisation application complies with the appropriate scientific, regulatory and legal requirements.*

20 Requirements for bioequivalence demonstration (PKWP)*

Bioequivalence study design	Single dose Background: Taking into account the difficulties in performing a multiple dose study (e.g. 28 day dosing interval, multiple indications and limited target populations), as accumulation is not high and the single dose profile is captured over a prolonged period, a multiple dose study may be waived if the single dose PK is well characterised. Further analysis of the single dose data is therefore required to fully capture the pharmacokinetic profile.
	Parallel design Background: Due to the long half-life and for safety reasons the crossover design may not be practically feasible; therefore, a parallel design can be used.
	Healthy volunteers
	Strength: 120 mg Background: highest strength to be used for a drug with linear pharmacokinetics.
	Other design aspects:

	The use of only one gender, e.g. males only or exactly the same number of male and female subjects in each treatment group, is recommended since gender differences are known to contribute to a high inter-subject variability for lanreotide. $C_{\max}$ has been found to be significantly higher in male than in female subjects and the rate of absorption was slower in female subjects.
Analyte	☒ parent ☐ metabolite ☐ both
	☒ plasma/serum ☐ blood ☐ urine
	Enantioselective analytical method: ☐ yes ☒ no
Bioequivalence assessment	Main pharmacokinetic variables: AUC_{0-t} , $AUC_{0-\infty}$, $C_{\max}$, C_{τ} (concentration at the end of the dosing interval, i.e. day 28), AUC_{0-168h} , $AUC_{168-672h}$ and AUC_{672h-t}
	90% confidence interval: 80.00 – 125.00%
Waiver of bioequivalence study	By default, an in vivo bioequivalence study should be carried out; however, a waiver of in vivo bioequivalence studies may be granted, if the test product has the same quantitative composition as the reference product and demonstrates equivalent molecular, structural, and thermodynamic properties as the reference product using a range of orthogonal techniques. These studies could include: • Molecular structure characterisation (peptide sequence): HRMS (High Resolution Mass Spectrometry) and NMR • Molecular scale organisation: FTIR spectroscopy & FT-Raman spectroscopy • Supramolecular scale organisation (peptide folding): Freeze-fracture TEM, Small-Angle X-ray Scattering (SAXS) and Wide Angle X-ray Scattering (WAXS) or similar methods • Thermal stability: temperature-dependent SAXS. • Water behavior: Differential scanning calorimetry (DSC)

	• Rheological property characterisation: Injectability measurements • In vitro dissolution study At least 5 batches of the test and reference product should be included in the comparability studies. <i>More batches may be needed in case of higher variability of the reference product results.</i> The selection of studies, choice of statistical methods and acceptance criteria should be justified.
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21 * As intra-subject variability of the reference product has not been reviewed to elaborate this product-specific bioequivalence guideline, it is not possible to
22 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-
23 individual variability ($CV_{intra} > 30\%$) is expected, the applicants might follow respective guideline recommendations.

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