EUROPEAN MEDICINES AGENCY
SCIENCE MEDICINES HEALTH

31 January 2019
EMA/CHMP/291571/2018
Committee for Medicinal Products for Human Use (CHMP)

Octreotide acetate depot powder and solvent for suspension for injection 10 mg, 20 mg and 30 mg product-specific bioequivalence guidance

Draft Agreed by Pharmacokinetics Working Party (PKWP)	April 2018
Adopted by CHMP for release for consultation	31 May 2018
Start of public consultation	27 June 2018
End of consultation (deadline for comments)	30 September 2018
Agreed by Pharmacokinetics Working Party (PKWP)	December 2018
Adopted by CHMP	31 January 2019
Date of coming into effect	1 August 2019

Keywords	***Bioequivalence, generics, octreotide***

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

Octreotide acetate depot powder and solvent for suspension for injection 10 mg, 20 mg and 30 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)*

Bioequivalence study design	**Single dose:** In healthy volunteers. **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 characterized. 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 the crossover design may not be practically feasible, therefore a parallel design could be used.
	Strength: 30 mg **Background:** Highest strength to be used for a drug with linear pharmacokinetics.

Analyte	☒ **parent** ☐ **metabolite** ☐ **both**
	☒ **plasma/serum** ☐ **blood** ☐ **urine**
	Enantioselective analytical method: ☐ **yes** ☒ **no**
Bioequivalence assessment	**Main pharmacokinetic variables:** $AUC_{(0-28d)}$, $AUC_{(28-56d)}$, $AUC_{(0-t)}$, $AUC_{(0-\infty)}$, C_{max} and C_t (concentration at the end of the dosing interval, i.e. day 28) **Secondary parameters:** $AUC_{(0-24h)}$, t_{lag}, $C_{max\ per\ partial\ AUC}$ and $C_{max\ initial\ release}$
	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}, $C_{T,ss}$ and partial AUC. If high intra-individual variability (CV_{intra} > 30 %) is expected, the applicants might follow respective guideline recommendations.