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Draft Guidance on Octreotide Acetate

August 2026

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Active Ingredient: Octreotide acetate

Dosage Form: Injectable

Route: Injection

Strengths: EQ 10 mg Base/vial | EQ 20 mg Base/vial | EQ 30 mg Base/vial

Reference Listed Drug: NDA 021008

Recommended Study: One in vivo bioequivalence study with pharmacokinetic endpoints

Eligibility: The test product and reference listed drug (RLD) should be qualitatively (Q1)[1] and quantitatively (Q2)[2] the same. To support Q1 sameness of poly(lactide-co-glycolide) (PLGA), provide comparative characterization data of polymer composition (molar ratio between glycolide and lactide), molecular weight and weight distribution, architecture (i.e., linear or branched)[3] of the PLGA polymer extracted from the test product and the RLD.

1. Class of study: Bioequivalence
   Type of study: In vivo bioequivalence study with pharmacokinetic endpoints
   Design: Single-dose, randomized, parallel, in vivo
   Strength: EQ 30 mg Base/vial
   Dose: EQ 30 mg Base

[1] Q1 (Qualitative sameness) means that the test product uses the same inactive ingredient(s) as the RLD.
[2] Q2 (Quantitative sameness) means that concentrations of the inactive ingredient(s) used in the test product are within ±5% of those used in the RLD.
[3] Hadar J, Skidmore S, Garner J, Park H, Park K, Wang Y, Qin B, Jiang X. Characterization of branched poly(lactide-co-glycolide) polymers used in injectable, long-acting formulations. J Control Release. 2019 Jun 28;304:75-89. doi: 10.1016/j.jconrel.2019.04.039.

Subjects: Healthy males and non-pregnant, non-lactating females
Study design recommendation:

- Administer an intramuscular injection intragluteally.

Analyte to measure: Octreotide in plasma

Bioequivalence based on (90% CI): Octreotide

The 90% confidence intervals of the following pharmacokinetic parameters should meet the acceptable limits of [80.00-125.00]: Log-transformed $AUC_{0\text{-}28}$, AUC_t, $AUC_{0\text{-}\infty}$, and C_{max}, where $AUC_{0\text{-}28}$ is the area under the plasma-concentration vs. time curve from 0 to 28 days, AUC_t is the area under the curve from 0 to the last sampling time point, $AUC_{0\text{-}\infty}$ is the area under the curve from 0 to infinity, and Cmax is the maximum plasma concentration.

Bioequivalence of additional strengths: EQ 10 mg Base/vial and EQ 20 mg Base/vial based on (i) an acceptable bioequivalence study on the EQ 30 mg Base/vial strength, (ii) evidence supporting identical formulation composition across all strengths

Studies to support quality assessment:

1. Use a minimum of two lots of the PLGA excipient to prepare the three primary batches of drug product.
2. To support quality assessment of the PLGA excipient, provide the following data:
    - Polymer composition (molar ratio between lactide to glycolide)
    - Molecular weight and weight distribution
    - Architecture (i.e., linear or branched)
    - Inherent viscosity
    - Glass transition temperature
    - Residual monomer contents
3. In vitro release testing method and sampling times: Conduct comparative in vitro drug release testing on 12 dosage units each of all strengths of the test product and RLD and develop appropriate specifications for quality control purpose. An accelerated method may be acceptable when properly developed and validated with sufficient justification.

Device: The RLD is presented as a kit containing a vial of drug, prefilled syringe of diluent, vial adapter, and needle with needle guard. The prefilled syringe, vial adapter, and needle with needle guard are the device constituent parts.
FDA recommends that prospective applicants examine the size and shape, the external critical design attributes, and the external operating principles of the RLD device when designing the test device including:

- Single-use, single-dose injectable kit requiring reconstitution
- Needle gauge and length
- Needle safety feature

User interface assessment: An abbreviated new drug application should include complete comparative analyses so FDA can determine whether any differences in design for the user interface of the proposed generic product, as compared to the RLD, are acceptable and whether the product can be expected to have the same clinical effect and safety profile as the RLD when administered to patients under the conditions specified in the labeling. For additional information, refer to the guidance for industry *Comparative Analyses and Related Comparative Use Human Factors Studies for a Drug-Device Combination Product Submitted in an ANDA*.[a]

Document History: Recommended January 2011; Revised February 2014, August 2026

[a] We update guidances periodically. For the most recent version of a guidance, refer to the FDA guidance webpage at https://www.fda.gov/regulatory-information/search-fda-guidance-documents.