Contains Nonbinding Recommendations

Draft – Not for Implementation

Draft Guidance on Afamelanotide

February 2023

This draft guidance, when finalized, will represent the current thinking of the Food and Drug Administration (FDA, or the Agency) on this topic. It does not establish any rights for any person and is not binding on FDA or the public. You can use an alternative approach if it satisfies the requirements of the applicable statutes and regulations. To discuss an alternative approach, contact the Office of Generic Drugs.

In general, FDA's guidance documents do not establish legally enforceable responsibilities. Instead, guidances describe the Agency's current thinking on a topic and should be viewed only as recommendations, unless specific regulatory or statutory requirements are cited. The use of the word *should* in Agency guidances means that something is suggested or recommended, but not required.

Active Ingredient: Afamelanotide

Dosage Form; Route: Implant; subcutaneous

Strength: 16 mg

Recommended Study: One in vivo bioequivalence study with pharmacokinetic endpoints

1. Type of study: In vivo bioequivalence study with pharmacokinetic endpoints
   Design: Single-dose, randomized, parallel, 14-day in vivo
   Strength: 16 mg
   Subjects: Healthy males and non-pregnant, non-lactating females
   Additional comments: The product should be administered following the instruction per the product labeling.

Analyte to measure: Afamelanotide in plasma

Bioequivalence based on (90% CI): Afamelanotide

The 90% confidence intervals of the following pharmacokinetic parameters should meet the acceptable limits of [80.00-125.00]: Log-transformed $AUC_{0\text{-}96h}$ and C_{max}, where $AUC_{0\text{-}96h}$ is the area under the plasma-concentration vs. time curve from 0 to 96 hours post-dose, and C_{max} is the maximum plasma concentration. $AUC_{0\text{-}14day}$ should be submitted as supportive data.

Waiver request of Additional Strengths: Not applicable

Dissolution test method and sampling times: Conduct comparative dissolution testing on 12 dosage units each of the test and reference products. Specifications will be determined upon review of the Abbreviated New Drug Application (ANDA).

Additional information:

Device
The Reference Listed Drug (RLD) is presented as a sterile solid, single dose implant. The device constituent is the implant.

FDA recommends that prospective applicants examine the size and shape and external critical design attributes of the RLD device when designing the Test (T) device including:

- Sterile, single dose implant
- Compatible with an implantation cannula system that will be identified in product labeling

User interface assessment:
An ANDA for this product 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 most recent version of the FDA guidance for industry on *Comparative Analyses and Related Comparative Use Human Factors Studies for a Drug-Device Combination Product Submitted in an ANDA*.[a]

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[a] For the most recent version of a guidance, check the FDA guidance web page at https://www.fda.gov/regulatory-information/search-fda-guidance-documents.