

Contains Nonbinding Recommendations

Draft – Not for Implementation

Draft Guidance on Setmelanotide Acetate

August 2022

This draft guidance, when finalized, will represent the current thinking of the Food and Drug Administration (FDA, or the Agency) on this topic.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.

This guidance, which interprets the Agency’s regulations on bioequivalence at 21 CFR part 320, provides product-specific recommendations on, among other things, the design of bioequivalence studies to support abbreviated new drug applications (ANDAs) for the referenced drug product. FDA is publishing this guidance to further facilitate generic drug product availability and to assist the generic pharmaceutical industry with identifying the most appropriate methodology for developing drugs and generating evidence needed to support ANDA approval for generic versions of this product.

The contents of this document do not have the force and effect of law and are not meant to bind the public in any way, unless specifically incorporated into a contract. This document is intended only to provide clarity to the public regarding existing requirements under the law. FDA guidance documents, including this guidance, should be viewed only as recommendations, unless specific regulatory or statutory requirements are cited. The use of the word should in FDA guidances means that something is suggested or recommended, but not required.

This is a new draft product-specific guidance for industry on generic setmelanotide acetate.

Active Ingredient: Setmelanotide acetate

Dosage Form; Route: Solution; subcutaneous

Recommended Study: Request for waiver of in vivo bioequivalence study requirements

To qualify for a waiver from submitting an in vivo bioequivalence study on the basis that bioequivalence is self-evident under 21 CFR 320.22(b)(1), a generic setmelanotide acetate injection product must be qualitatively (Q1)¹ and quantitatively (Q2)² the same as the Reference Listed Drug (RLD).

In addition to ensuring active pharmaceutical ingredient (API) sameness (i.e., same primary sequence and physicochemical properties) for the drug substance, it is recommended to conduct

¹ Q1 (Qualitative sameness) means that the test product uses the same inactive ingredient(s) as the reference listed drug.

² Q2 (Quantitative sameness) means that concentrations of the inactive ingredient(s) used in the test product are within $\pm 5\%$ of those used in the reference listed drug.

the following comparative analyses of the proposed generic setmelanotide acetate and the RLD product on no less than three batches of the proposed drug product tested on or near release and at the end of the proposed shelf life and no less than three batches of the RLD aged tested prior to expiry, after aging under conditions consistent with the label storage conditions:

- API-related impurity profile comparison: new impurities found in the proposed generic drug product but not in the RLD and impurities found at a significantly higher level in the proposed generic drug product than in the RLD, should be identified. If upon Agency assessment, an impurity is identified that has the potential to increase the immunogenicity risk, further immunogenicity assessments or studies may be required.
- Oligomer/aggregation states: oligomer/aggregation propensity and the nature of the aggregates formed for the proposed product should be similar to that of the RLD.

Unique Agency Identifier: PSG_213793