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Draft – Not for Implementation

Draft Guidance on Glucagon

November 2021

This draft guidance, when finalized, will represent the current thinking of the Food and Drug Administration (FDA, or the Agency) on this topic.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

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

Active Ingredient: Glucagon

Dosage Form; Route: Solution; subcutaneous

Strength: 0.5 mg/0.1 mL and 1 mg/0.2 mL

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

Waiver:

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

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

[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 reference listed product.

In addition, the following comparative analysis on at least three batches of the proposed generic glucagon and the RLD should be provided.

- API sameness: The proposed drug substance should contain the same primary sequence and biological activities as the RLD.

- Impurity profile comparison: We recommend applicants provide a comparative characterization of impurity profile of the proposed drug product and the RLD on no less than three batches of the proposed drug product tested prior to the end of the proposed shelf life, and no less than three batches of the RLD tested prior to expiry, after aging under conditions consistent with the worst-case label storage conditions. If upon the Agency's 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 profile of the proposed product should be similar to the RLD's in the same condition of use as described in the labeling.

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