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Draft Guidance on Motixafortide Acetate

May 2025

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Active Ingredient:	Motixafortide acetate
Dosage Form:	Powder
Route:	Subcutaneous
Strength:	EQ 62 mg Base/vial
Recommended Studies:	Request for waiver of in vivo bioequivalence study requirements and comparative characterization studies to support active ingredient sameness

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 motixafortide acetate subcutaneous powder product should be qualitatively (Q1)[1] and quantitatively (Q2)[2] the same as the reference listed drug (RLD).

An applicant may seek approval of a drug product that differs from the RLD in preservative, buffer, or antioxidant provided that the applicant identifies and characterizes the differences and provides information demonstrating that the differences do not affect the safety or efficacy of the test product.[3]

[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] 21 CFR 314.94(a)(9)(iii).

Comparative characterization studies to support active ingredient sameness:

In addition to ensuring active ingredient sameness (i.e., same primary sequence and physiochemical properties) for the drug substance, it is recommended to conduct the following comparative analyses of the proposed generic motixafortide acetate subcutaneous powder and the designated reference standard (RS) 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 RS aged prior to expiry, after aging under conditions consistent with the label storage conditions.[4]

1. Oligomer/aggregation states: Oligomer/aggregation propensity and the nature of the aggregates formed for the proposed product should be similar to that of the RS.
2. Active ingredient-related impurity profile comparison: New impurities found in the proposed generic drug product but not in the RS and impurities found at a significantly higher level in the proposed generic drug product than in the RS, should be identified and characterized.

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[4] Samples should be aged under conditions consistent with the worst-case label storage conditions.