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Draft Guidance on Difelikefalin Acetate

May 2023

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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: Difelikefalin acetate

Dosage Form; Route: Solution; Intravenous

Strength: EQ 0.065 mg Base/1.3 mL (EQ 0.05 mg Base/mL)

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

In vivo bioequivalence study may be waived on the basis that bioequivalence is self-evident (21 CFR 320.22(b)), for a generic difelikefalin acetate intravenous solution product that is qualitatively (Q1)[1] and quantitatively (Q2)[2] the same as the reference listed drug (RLD). An applicant may seek approval of a drug product intended for parenteral use that differs from the RLD in preservative, buffer, or antioxidant if the identified differences are characterized and demonstrated to not affect the safety or efficacy of the proposed drug product.[3]

In addition to ensuring active pharmaceutical ingredient sameness, a comparative assessment of peptide-related impurity profile including aggregation profile is recommended with at least three batches of the proposed generic product and the RLD.

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[1] Q1 (Qualitative sameness) means that the test product uses the same inactive ingredient(s) as the reference 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 product.
[3] 21 CFR 314.94(a)(9)(iii)