Contains Nonbinding Recommendations

Draft – Not for Implementation

Draft Guidance on Vasopressin

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This draft guidance, when finalized, will represent the current thinking of the Food and Drug Administration (FDA, or the Agency) on this topic.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

Active Ingredient:	Vasopressin
Dosage Form; Route:	Solution; intravenous
Strength:	20 units/mL (20 units/mL), 20 units/100 mL (0.2 units/mL), 40 units/100 mL (0.4 units/mL), 60 units/100 mL, (0.6 units/mL), and 200 units/10 mL (20 units/mL)
Recommended Study:	Request for waiver of in vivo bioequivalence study requirements

Waiver:

In vivo bioequivalence (BE) study may be waived on the basis that BE is self-evident (21 CFR 320.22(b)), for a generic vasopressin injection solution product that is qualitatively (Q1)[1] and

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

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 if the applicant identifies and characterizes the differences and provides information demonstrating that the differences do not affect the safety or efficacy of the proposed drug product.[3]

In addition to ensuring active pharmaceutical ingredient API sameness (i.e., same primary sequence), the following comparative analyses of the proposed generic vasopressin and the RLD product should be provided on at least three batches each of the proposed generic and the RLD aged under various conditions.[4]

1. API related impurity profile comparison: new impurities found in the proposed generic product but not in the RLD and impurities found at a significantly higher level in the proposed generic product than in the RLD, should be identified[5]
2. Comparative comparison of aggregation profile and any secondary structure

---

Unique Agency Identifier: PSG_204485

[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.
[3] 21 CFR 314.94(a)(9)(iii)
[4] Samples should be aged under conditions consistent with the worst-case label storage conditions.
[5] Immunogenicity assessment may be requested in situations where the comparative impurity or aggregation profile indicates the presence of an unusual new impurity or aggregation state, or a markedly elevated level of an impurity or aggregation state in the proposed generic product relative to the RLD. The need for such an immunogenicity assessment will be determined during ANDA assessment.