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Draft Guidance on Pegcetacoplan

August 2024

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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:	Pegcetacoplan
Dosage Form:	Solution
Route:	Intravitreal
Strength:	15 mg/0.1 mL (15 mg/0.1 mL)
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 pegcetacoplan intravitreal solution 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 intended for parenteral use 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).

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 pegcetacoplan and the designated reference standard (RS) 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 RS product aged prior to expiry, after aging under conditions consistent with the label storage conditions.[4]

1. Secondary structure.
2. 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.
3. Biological activities[5].
4. 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. If upon Agency assessment, an impurity is identified that has the potential to increase the immunogenicity risk, further immunogenicity assessments or studies may be recommended.
5. Comparative study demonstrating comparable innate immune response risk of the test and RS products.

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

[5] Applicant may provide justification for not conducting biological assays as part of the comparative analyses if there is evidence that any secondary and higher order structure of the peptide active ingredient that may be present does not contribute to the functional activity.