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Draft Guidance on Articaine Hydrochloride

May 2026

This draft guidance, when finalized, will represent the current thinking of the Food and Drug Administration (FDA, or the Agency) on this topic.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

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: Articaine hydrochloride

Dosage Form: Solution/drops

Route: Ophthalmic

Strength: EQ 8% Base

Reference Listed Drug: NDA 218643

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

Waiver request of in vivo bioequivalence study: 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 articaine hydrochloride ophthalmic solution 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 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.

An applicant may seek approval of a drug product intended for ophthalmic use that differs from the RLD in preservative, buffer, substance to adjust tonicity, or thickening agent 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 proposed drug product.[3]

1. Class of study: Characterization
   Articaine hydrochloride ophthalmic solution products should have comparable physicochemical properties to the reference standard (RS) such as pH, specific gravity, buffer capacity, osmolality, and viscosity.
   Study design recommendations: Comparative analysis should be performed on three exhibit batches of both test product and RS, if available.[4]

Device: The RLD is presented in a vial with a dropper tip. The vial with dropper tip is the device constituent part. FDA recommends that prospective applicants examine the size and shape, the external critical design attributes, and the external operating principles of the RLD device when designing the test device.

User interface assessment: An abbreviated new drug application (ANDA) for this product should include complete comparative analyses so FDA can determine whether any differences in design for the user interface of the proposed generic product, as compared to the RLD, are acceptable and whether the product can be expected to have the same clinical effect and safety profile as the RLD when administered to patients under the conditions specified in the labeling. For additional information, refer to the guidance for industry *Comparative Analyses and Related Comparative Use Human Factors Studies for a Drug-Device Combination Product Submitted in an ANDA.*[a]

Quality assessment: For quality-related recommendations for supporting drug product development, refer to the guidance for industry *Quality Considerations for Topical Ophthalmic Drug Products.*[a]

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[3] FDA has determined that any qualitative or quantitative deviations from the RLD regarding the inactive ingredients specified in 21 CFR 314.94(a)(9)(iv) require scientific justification. This justification should address the potential impact on bioequivalence of the proposed test product and inform the determination of whether appropriate in vivo bioequivalence studies are necessary. Prospective applicants are advised to submit a pre-ANDA development meeting request to discuss the justification for any such deviations and the intended approach to demonstrate bioequivalence.

[4] It may be acceptable to evaluate fewer than three batches of the RS if a prospective applicant provides adequate justification and supporting evidence demonstrating the unavailability of RS lots. Data from a minimum of three batches of the test product should be submitted in the ANDA.

[a] We update guidances periodically. For the most recent version of a guidance, refer to the FDA guidance webpage at https://www.fda.gov/regulatory-information/search-fda-guidance-documents.