

Contains Nonbinding Recommendations

Draft – Not for Implementation

Draft Guidance on Ketorolac Tromethamine; Phenylephrine Hydrochloride
December 2025

This draft guidance, when finalized, will represent the current thinking of the Food and Drug Administration (FDA, or the Agency) on this topic.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 Ingredients:	Ketorolac tromethamine; Phenylephrine hydrochloride
Dosage Form:	Solution
Route:	Irrigation
Strength:	EQ 0.3% Base; EQ 1% Base
Recommended Studies:	Request for waiver of in vivo bioequivalence study requirements

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 ketorolac tromethamine and phenylephrine hydrochloride irrigation 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

Ketorolac tromethamine; phenylephrine hydrochloride irrigation solution products should have comparable physicochemical properties to the reference standard (RS) including but not limited to pH, specific gravity, osmolality, buffer capacity, and viscosity, if applicable. Comparative analysis should be performed on three exhibit batches, if available, of both test product and RS.

Additional information:

Quality assessment:

For quality-related questions, prospective applicants may consider submitting a controlled correspondence to the quality discipline to obtain guidance on quality-related aspects of this product.

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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) necessitate 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 required. Prospective applicants are advised to submit a pre-abbreviated new drug application (ANDA) development meeting request to discuss the justification for any such deviations and the intended approach to demonstrate bioequivalence.