Contains Nonbinding Recommendations

Draft Guidance on Latanoprost

This draft guidance, when finalized, will represent the current thinking of the Food and Drug Administration (FDA, or the Agency) on this topic.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

Active Ingredient: Latanoprost

Dosage Form; Route: Solution/drops; ophthalmic

Strength: 0.005%

Recommended Studies: Two options: waiver or in vivo study

Additional comments: Latanoprost ophthalmic solution products should have comparable physicochemical properties to the Reference Standard (RS) including but not limited to pH, specific gravity, buffer capacity, osmolality, and viscosity, if applicable. Comparative analysis should be performed on three exhibit batches, if available, of both test and RS products.

I. Waiver option:

To qualify for a waiver of the in vivo bioequivalence (BE) study, a generic latanoprost ophthalmic solution product should be qualitatively (Q1)[1] and quantitatively (Q2)[2] the same as the Reference Listed Drug (RLD).

An in vivo BE study with clinical endpoint is requested for any latanoprost ophthalmic solution product that has a different inactive ingredient from the RLD,[3] a difference of more than 5% in the amount of any inactive ingredient compared to that of the RLD, or differences in comparative physicochemical characterization data.

II. In vivo option:

Recommended studies: One study

Type of study: Bioequivalence study with pharmacokinetic (PK) end points

[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] For ophthalmic drug products, FDA has determined that, as a scientific matter, any qualitative or quantitative deviations from the RLD, even in inactive ingredients listed in 21 CFR 314.94(a)(9)(iv), should be accompanied by an appropriate in vivo BE study or studies. *ANDA Submissions –Refuse-to-Receive Standards: Guidance for Industry.*
https://www.fda.gov/downloads/drugs/guidancecomplianceregulatoryinformation/guidances/ucm370352.pdf

Design: Single-dose, parallel design, in vivo in aqueous humor
Strength: 0.005%
Subjects: Patients undergoing indicated cataract surgery.
Additional comments: Please refer to the Guidance on Loteprednol Etabonate ophthalmic suspension/drops[4] for additional comments regarding the in vivo pharmacokinetic study in aqueous humor.

Analytes to measure (in appropriate biological fluid): Primary active metabolite, acid of latanoprost [(Z)-7-[(1R,2R,3R,5S)-3,5-Dihydroxy-2-[(3R)-3-hydroxy-5-phenylpentyl]cyclopentyl]hept-5-enoic acid], in aqueous humor.

Bioequivalence based on (95% CI): Acid of latanoprost

Dissolution test method and sampling times: Not applicable.

[4] Guidance on Loteprednol Etabonate.
http://www.fda.gov/downloads/Drugs/GuidanceComplianceRegulatoryInformation/Guidances/UCM249244.pdf