Contains Nonbinding Recommendations

Draft Guidance on Tobramycin

This draft guidance, when finalized, will represent the current thinking of the Food and Drug Administration (FDA, or the Agency) on this topic.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

Dosage Form; Route: Ointment; ophthalmic

Recommended Studies: In vitro study

In vitro study:

To qualify for the in vitro option for this drug product all of the following criteria should be met:

i. The test and reference listed drug (RLD) formulations are qualitatively[1] and quantitatively[2] the same (Q1/Q2).

ii. Acceptable comparative physicochemical characterizations of the test and Reference Standard (RS) products. The comparative study should be performed on at least three exhibit batches of both the test and RS products and should include:[3]

- Comparative appearance.
- Comparative acidity and alkalinity of the extracted ointment base.
- Comparative polymorphic form of tobramycin.
- Comparative rheological properties including yield stress and viscosity. The applicant should characterize viscosity over a range of shear rates.
- Comparative drug particle size and size distribution. The particle size distribution should be compared using population bioequivalence (PBE) (95% upper confidence bound) based on D_{50} and SPAN [i.e. $(D_{90}-D_{10})/D_{50}$)]. The applicant should provide no fewer than ten data sets from three different batches of both the test and RS products for PBE analysis. Full profiles of the particle distribution should also be submitted for all samples tested. Please refer to the Guidance on Budesonide inhalation suspension for additional information regarding PBE.

iii. Acceptable comparative in vitro drug release of tobramycin from the test and RS products. The methodology used for in vitro drug release testing should be able to discriminate the effect of process variability in the production of the test formulation.

[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] The manufacturing process for the exhibit batches should be reflective of the manufacturing process to be utilized for commercial batches.