Contains Nonbinding Recommendations

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Draft Guidance on Ganciclovir

May 2024

This draft guidance, when finalized, will represent the current thinking of the Food and Drug Administration (FDA, or the Agency) on this topic.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

Dosage Form: Gel

Route: Ophthalmic

Strength: 0.15%

Recommended Studies: One in vitro bioequivalence study with supportive characterization studies

To demonstrate bioequivalence by this option, the test product should be qualitatively (Q1)[1] and quantitatively (Q2)[2] the same as the reference listed drug (RLD).[3]

One in vitro bioequivalence study:

1. Type of study: Comparative in vitro release testing (IVRT) of ganciclovir
   Design: Should be performed on three batches each of the test and reference standard (RS) products using at least 12 units from each batch
   Strength: 0.15%

[1] Q1 (Qualitative sameness) means that the test product uses the same inactive ingredient(s) as the RLD 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 RLD 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 bioequivalence study or studies. *ANDA Submissions – Refuse-to-Receive Standards: Guidance for Industry*.

Additional comments: The IVRT method study should include information on the method development and validation to detect potential formulation differences and capture the complete release profile of ganciclovir.

Bioequivalence based on: Comparative analysis of release profiles should be established using an appropriate statistical method (e.g., model independent approach using similarity factor (f_2)). For more information on calculation of f_2 factor, refer to the most recent version of the FDA guidance for industry on *Dissolution Testing of Immediate Release Solid Oral Dosage Forms*.[a]

Comparative characterization studies:

Comparative physicochemical characterization of the test and the RS products. The comparative study should be performed on at least three batches each of the test[4] and RS products and should include:

a. Appearance.
b. pH.
c. Specific gravity.
d. Osmolality.
e. Rheological properties including yield stress and viscosity. The applicant should characterize viscosity over a range of shear rates.

Additional information:

Device:
The RLD is presented in a tube with a dropper tip. The tube with a 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 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 most recent version of the FDA guidance for industry on *Comparative Analyses and Related Comparative Use Human Factors Studies for a Drug-Device Combination Product Submitted in an ANDA*.[a]

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

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Unique Agency Identifier: PSG_022211

[a] For the most recent version of a guidance, check the FDA guidance website at https://www.fda.gov/regulatory-information/search-fda-guidance-documents.