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Draft Guidance on Triamcinolone Acetonide

February 2023

This draft guidance, when finalized, will represent the current thinking of the Food and Drug Administration (FDA, or the Agency) on this topic.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

Dosage Form; Route: Suspension; injection

Strength: 40 mg/mL

Recommended Studies: Two in vitro bioequivalence studies with supporting characterization studies

To be eligible for the bioequivalence studies recommended in this guidance, the test product should meet the following criteria:

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

2. Acceptable comparative physicochemical characterization of the test and the reference standard (RS) products. The comparative study should be performed on a minimum of three exhibit batches of the test product[3] and three batches of the RS product and should include:
    a. Polymorphic form of triamcinolone acetonide
    b. Crystalline shape and morphology of triamcinolone acetonide
    c. Appearance, pH, osmolality, specific gravity, soluble fraction of triamcinolone acetonide, sedimentation rate and volume, and viscosity over a range of shear rates

[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.

In vitro bioequivalence study 1:
Drug particle size and size distribution of triamcinolone acetonide

Additional comments: The particle size distribution should be compared using population bioequivalence (PBE) (95% upper confidence bound) based on D50 and SPAN [i.e., (D90-D10)/D50]. 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. Refer to the most recent version of the FDA product-specific guidance on *Budesonide Inhalation Suspension* (NDA 020929)[a] for additional information regarding PBE.

In vitro bioequivalence study 2:
Comparative in vitro drug release of triamcinolone acetonide from the test and RS products

Additional comments: A properly developed and validated method that can detect potential formulation differences and capture the complete release profile of triamcinolone acetonide should be provided. Equivalence in triamcinolone acetonide release should be established using a proper statistical method from at least three batches of Test and RS products. One suggested approach is a model independent similarity (f2) factor. For more information on calculation of f2 factor, refer to the most recent version of the FDA guidance for industry on *Dissolution Testing of Immediate Release Solid Oral Dosage Forms*.[b]

Dissolution test method and sampling times: The dissolution information for this drug product can be found in the FDA's Dissolution Methods database, http://www.accessdata.fda.gov/scripts/cder/dissolution/. Conduct comparative dissolution testing on 12 dosage units each of all strengths of the test and reference products. Specifications will be determined upon review of the Abbreviated New Drug Application (ANDA).

Additional information:

Device:
The RLD is presented as a kit in a sterile tray that includes: one single-dose vial of triamcinolone acetonide injectable suspension 40 mg/mL; one suprachoroidal space (SCS) Microinjector syringe with vial adapter attached, one 30-G x 900-µm needle, and one 30-G x 1100-µm needle. The SCS Microinjector syringe, vial adapter, and needles are the device constituent parts.

FDA recommends that prospective applicants examine the size and shape, the external critical design attributes, and the external operating principles of the RLD devices when designing the Test (T) devices including:

- Microinjector syringe designed for suprachoroidal space injection
- Vial adapter
- Needle gauge and length

User interface assessment:
An 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 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*.[b]

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[a] For the most recent version of a product-specific guidance, check the FDA product-specific guidance web page at https://www.accessdata.fda.gov/scripts/cder/psg/index.cfm.
[b] For the most recent version of a guidance, check the FDA guidance web page at https://www.fda.gov/regulatory-information/search-fda-guidance-documents.