Contains Nonbinding Recommendations

Draft Guidance on Azelastine Hydrochloride

This draft guidance, when finalized, will represent the current thinking of the Food and Drug Administration (FDA, or the Agency) on this topic.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

Dosage Form; Route: Metered spray; nasal

Recommended Studies: In vitro studies

FDA recommends the following in vitro studies to establish bioequivalence (BE) of the test (T) and reference (R) nasal sprays containing azelastine hydrochloride.

In Vitro Studies

FDA recommends that applicants conduct the following in vitro BE studies on samples from each of three or more batches of the T product and three or more batches of the R product, with no fewer than 10 units from each batch. FDA recommends that three primary stability batches be also used to demonstrate in vitro BE, if appropriate. The three batches of the T product should be prepared from three different batches of the same critical device components (e.g., pump and actuator).

1. Single actuation content
2. Droplet size distribution by laser diffraction
3. Drug in small particles/droplets
4. Spray pattern
5. Plume geometry
6. Prime and repriming

Additional Comments: Refer to the product-specific guidance for *Fluticasone Propionate Nasal Spray Metered* [1] for recommendations on design and equivalence criteria for the aforementioned in vitro BE studies, and general recommendations on the conduct of the in vitro BE studies and data submission.

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[1] https://www.fda.gov/downloads/Drugs/GuidanceComplianceRegulatoryInformation/Guidances/UCM461051.pdf

Additional Information

Formulation:

FDA recommends that the T formulation be qualitatively (Q1)[2] and quantitatively (Q2) [3] the same as the R formulation.

Device:

Applicants should refer to the FDA Guidance for Industry entitled, *Comparative Analyses and Related Comparative Use Human Factors Studies for a Drug-Device Combination Product Submitted in an ANDA* (January 2017),[4] which provides the Agency's current thinking on the identification and assessment of any differences in the design of the user interface for a proposed generic drug-device combination product when compared to its RLD.

FDA recommends that applicants consider the following characteristics of the R product in designing the T product:

- External operating principles and external critical design attributes of the R product
- Size and shape of the R product
- Number of doses in the R product

In addition, studies should be conducted to support the functionality, accuracy, and robustness[5] of the proposed T product.

[2] Q_1 (qualitative sameness) means that the T formulation uses the same inactive ingredient(s) as the R formulation.
[3] Q_2 (quantitative sameness) means that concentrations of the inactive ingredient(s) used in the T formulation are within ± 5% of those used in the R formulation.
[4] https://www.fda.gov/downloads/Drugs/GuidanceComplianceRegulatoryInformation/Guidances/UCM536959.pdf
[5] Refer to the FDA Guidance for Industry *Nasal Spray and Inhalation Solution, Suspension, and Spray Drug Products – Chemistry, Manufacturing, and Controls Documentation* (July 2002) for relevant principles regarding studies to support nasal spray devices.