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Draft Guidance on Sumatriptan Succinate

November 2022

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Active Ingredient:	Sumatriptan succinate
Dosage Form; Route:	Injectable; subcutaneous
Strengths:	EQ 4mg base/0.5 mL and EQ 6mg base/0.5 mL
Recommended Studies:	Request for wavier of in vivo bioequivalence study requirements, in vitro bioequivalence studies on delivered volume and extended needle length, and supportive characterization studies on trigger force and ejection time

The Reference Listed Drug (RLD) has two presentations: (1) a single-dose vial, and (2) single-dose, prefilled syringe cartridges that are co-packaged with an autoinjector pen and a carrying case. This guidance provides recommendations for presentation (2), the single-dose, prefilled syringe cartridges that are co-packaged with an autoinjector pen and a carrying case.

Waiver of in vivo bioequivalence study requirements:

In vivo bioequivalence study may be waived on the basis that bioequivalence is self-evident under 21 CFR 320.22(b), for a generic sumatriptan succinate injectable product is qualitatively (Q1)[1] and quantitatively (Q2)[2] the same as the RLD formulation.

[1] Q1 (qualitative sameness) means that the T formulation uses the same inactive ingredient(s) as the R formulation
[2] Q2 (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.

An applicant may seek approval of a drug product that differ from the RLD in preservative, buffer or antioxidant if the applicant identifies and characterizes the differences and provides information demonstrating that the differences do not affect the safety or efficacy of the proposed drug product.[3]

In vitro bioequivalence studies with supportive comparative studies:

For EQ 4 mg base/0.5 mL and EQ 6 mg base/0.5 mL strengths of test (T) and reference (R) product with an autoinjector presentation, the FDA recommends that prospective applicants conduct the following in vitro bioequivalence studies. For each strength, use three or more batches of the T product and three or more batches of R product, with no fewer than 10 units from each batch. The three batches of the T product should be prepared from three different batches of the same critical device components. The T product should consist of the final device constituent part and final drug constituent formulation intended to be marketed. The manufacturing process for the T batches should be reflective of the manufacturing process to be utilized for the commercial batch. T and R products should be studied under the same instrumental conditions. Method validation should be performed using the R product, and the lot number(s) for the R products used for the validation should be provided. Applicants should provide all relevant standard procedures and validation data for each of the in vitro bioequivalence studies listed below.

In vitro bioequivalence studies:

1. Type of study: Delivered volume
   Strength: EQ 4mg base/0.5 mL and EQ 6mg base/0.5 mL
   Design: The delivered volume test should be performed to compare the volume of fluid ejected out of the T and R devices for each strength

   Equivalence based on: Population Bioequivalence (PBE) analysis of delivered volume

2. Type of study: Extended needle length
   Strength: EQ 4mg base/0.5 mL and EQ 6mg base/0.5 mL
   Design: The extended needle length test should be performed to compare the needle length that extends out of the T and R devices after ejection of the volume of fluid for each strength

   Equivalence based on: PBE analysis of extended needle length

Additional comments: Refer to the most recent version of FDA product-specific guidance on *Budesonide Inhalation Suspension* (NDA 020929)[a] for relevant principles regarding PBE analysis procedures.

[3] 21CFR 314.94(a)(9)(iii)

Supportive comparative characterization studies:

1.	Type of study:	Ejection time
	Strength:	EQ 4mg base/0.5 mL and EQ 6mg base/0.5 mL
	Design:	The ejection time test should be performed to compare the time to eject the volume of fluid out of T and R devices for each strength
2.	Type of study:	Trigger force
	Strength:	EQ 4mg base/0.5 mL and EQ 6mg base/0.5 mL
	Design:	The trigger force test should be performed to compare the force required to activate the T and R devices for each strength

Additional information:

Device:
The RLD is presented as single-dose, prefilled syringe cartridges that are co-packaged with an autoinjector pen and a carrying case. The autoinjector pen is the device constituent.

For an autoinjector pen, 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 T device including:

- A single-dose, fixed-dose, autoinjector device capable of delivering the same dose as the RLD product
- Needle gauge and length

User interface assessment:
An Abbreviated New Drug Application (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]

Revision History: Recommended November 2019; Revised November 2022

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[a] For the most recent version of the 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.