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Draft Guidance on Cabotegravir; Rilpivirine

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This draft guidance, when finalized, will represent the current thinking of the Food and Drug Administration (FDA, or the Agency) on this topic.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

Dosage Form; Route: Suspension, extended release; intramuscular

Recommended Study: One in vivo bioequivalence study with pharmacokinetic endpoints

1. Type of study: In vivo bioequivalence study with pharmacokinetic endpoints
   Design: Single-dose, parallel, in vivo
   Strength: Cabotegravir 600 mg/3 mL, rilpivirine 900 mg/3 mL
   Subjects: Male and nonpregnant, non-lactating females, general population.
   Additional comments: Prior to injection of extended-release injectable suspensions, an optional oral lead-in dosing followed by a washout period may be considered to assess the tolerability of cabotegravir and rilpivirine as described in the product label.

Analytes to measure: Cabotegravir in plasma; rilpivirine in plasma

Bioequivalence based on (90% CI): Cabotegravir; rilpivirine

Waiver request of in vivo testing: 400 mg cabotegravir, 600 mg rilpivirine based on (i) acceptable bioequivalence study on the 600 mg cabotegravir, 900 mg rilpivirine strength, (ii) proportional similarity of the formulations across all strengths, and (iii) acceptable in vitro dissolution testing of all strengths.

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 the Test and Reference products. Specifications will be determined upon review of the Abbreviated New Drug Application (ANDA).

Additional information:

Device:
The Reference Listed Drug (RLD) is presented as a kit that consists of one vial of cabotegravir, one vial of rilpivirine, two identical vial adapters, two identical 5-mL syringes, and two identical injection needles with needle guards. The vial adapters, syringes, and injection needles with needle guard are the device constituents.

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:

- Vial adapters
- Needle gauge and length
- Needle guard system

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*.[a]

Unique Agency Identifier: PSG_212888

[a] 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.