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Draft Guidance on Cladribine

February 2022

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This guidance, which interprets the Agency’s regulations on bioequivalence at 21 CFR part 320, provides product-specific recommendations on, among other things, the design of bioequivalence studies to support abbreviated new drug applications (ANDAs) for the referenced drug product. FDA is publishing this guidance to further facilitate generic drug product availability and to assist the generic pharmaceutical industry with identifying the most appropriate methodology for developing drugs and generating evidence needed to support ANDA approval for generic versions of this product.

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This is a new draft product-specific guidance for industry on generic cladribine.

Active Ingredient: Cladribine

Dosage Form; Route: Tablet; oral

Recommended Study: One study

1. Study Design: Single-dose, two-treatment, two-period crossover in vivo
Strength: 10 mg
Subjects: Patients with relapsing forms of multiple sclerosis who plan to receive the first or second treatment course of cladribine
Additional comments:
 - a. Implement screening recommendations and safety monitoring, including complete blood count, during the treatment as recommended in the labeling.
 - b. Exclude patients with expected changes in concomitant medications that can potentially affect the pharmacokinetics of cladribine.
 - c. Exclude pregnant or lactating females.

- d. For subjects of reproductive health:
 - Females should use effective contraception during the study and for at least 6 months after the final dose. Females using systemically acting hormonal contraceptive should add a barrier method during the study and for at least 4 weeks after the last dose.
 - Males with female partners of reproductive potential should use effective contraception during the study and for at least 6 months after the last dose.
- e. Conduct the study on a specific day (e.g., the first day) of each cycle within one treatment course. The same dose (e.g., 10 mg or 20 mg) should be given on the same day in each cycle.
- f. Submission of an Investigational New Drug Application (IND) is required prior to the conduct of a bioequivalence study for a cytotoxic drug product such as cladribine (See 21 C.F.R § 320.31).

Analyte to measure: Cladribine in plasma

Bioequivalence based on (90% CI): Cladribine

Waiver request of in vivo testing: Not applicable

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.

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