Contains Nonbinding Recommendations

Draft – Not for Implementation

Draft Guidance on Brincidofovir

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This draft guidance, when finalized, will represent the current thinking of the Food and Drug Administration (FDA, or the Agency) on this topic.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

Dosage Form; Route: Suspension; Oral

Strength: 10 mg/mL

Recommended Study: One in vivo bioequivalence study with pharmacokinetic endpoints

1. Type of study: Fasting
   Design: Single-dose, two-treatment, two-period crossover in vivo
   Strength: 10 mg/mL
   Subjects: Healthy males not of reproductive potential (i.e., surgically sterile) and females not of reproductive potential
   Additional comments: The bioequivalence study dose should not exceed 100 mg. Exclude subjects with abnormal liver function tests. Monitor liver function tests prior to dosing, one to two weeks post-dosing, and at end of study. Monitor subjects until resolution of adverse events. Ensure an adequate washout period between treatments in the crossover study due to the long elimination half-life of cidofovir-diphosphate.

Analyte to measure: Brincidofovir in plasma

Bioequivalence based on (90% CI): Brincidofovir

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. Note that a dosage unit for a suspension is the labeled strength (1 mL). Specifications will be determined upon review of the abbreviated new drug application.

Product-specific testing conditions for in vitro feeding tube studies: The approved labeling for the reference product states that the product may be administered by a nasogastric (NG) or gastrostomy (G) tube. Conduct the in vitro feeding tube studies, including comparative recovery testing, sedimentation volume and redispersibility testing, and in-use stability in designated dispersion media (i.e., water). For general procedures of in vitro feeding tube studies, refer to the most recent version of the FDA guidance for industry on *Oral Drug Products Administered Via Enteral Feeding Tube: In Vitro Testing and Labeling Recommendations*.[a]

Testing tube: NG tube (6 French) and G tube (12 French)

Three types of tube configurations including different materials and/or different designs. At least one G tube should be tested with an inflated balloon design.

Holding times of 0 and 15 minutes on Day 0 and Day 8

Test Strength: 10 mg/mL

For enteral administration (i.e., feeding tube), draw up suspension with an enteral syringe. Flush with water before and after enteral administration. Report the pH value of the water.

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[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.