Contains Nonbinding Recommendations

Draft – Not for Implementation

Draft Guidance on Letermovir

February 2026

This draft guidance, when finalized, will represent the current thinking of the Food and Drug Administration (FDA, or the Agency) on this topic.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

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Active Ingredient: Letermovir

Dosage Form: Pellets

Route: Oral

Strengths: 20 mg/packet, 120 mg/packet

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: 120 mg/packet at the administered dose of 120 mg
   Subjects: Healthy males and non-pregnant, non-lactating females
   Additional comments:
   - Females of reproductive potential should use effective contraception during the study.
   - Mix pellets with 3 teaspoons (15 mL) of soft food (such as applesauce, yogurt, or pudding) and administer the entire mixture within 10 minutes. Do not crush or chew pellets. Conduct a bioequivalence study using a consistent approach for both test product and reference listed drug (RLD) according to the RLD labeling.

Analyte to measure: Letermovir in plasma

Bioequivalence based on (90% CI): Letermovir

Waiver request of in vivo testing of additional strength: Justification based on (i) an acceptable bioequivalence study on the 120 mg/packet strength, (ii) acceptable comparative in vitro dissolution studies between the 20 mg/packet and the 120 mg/packet strengths using 12 units per strength, and (iii) proportional similarity of the formulations between both strengths

Dissolution: Dissolution test(s) should be included for quality control and to support a waiver request of in vivo testing of additional strengths.

Dissolution test method and sampling times: Provide a dissolution method development report for the test product containing information and data that demonstrate appropriateness of the selected dissolution method[1] and sampling times, such as the discriminating ability to detect changes in critical quality attributes that could potentially impact drug product performance.

Product-specific testing conditions for in vitro enteral tube studies: The approved labeling for the RLD states that the product may be administered by a nasogastric tube (NG tube) or gastrostomy tube (G tube). Conduct the in vitro enteral tube studies listed below. For general procedures of in vitro enteral tube studies, refer to the most recent version of the guidance for industry *Oral Drug Products Administered Via Enteral Feeding Tube: In Vitro Testing and Labeling Recommendations*.[a]

Testing tubes: NG tube (5 French polyurethane), NG tube (6 French polyvinylchloride and silicone) or G tube (12 French)

Testing strength: 120 mg/packet at a dose of 480 mg (4 x 120 mg/packet)

In vitro enteral tube testing:

1. Comparative recovery testing
    - NG tube
        - 5 French NG tubes with polyurethane and
        - 6 French NG tubes with polyvinylchloride and silicone
    - G tube
        - 12 French tubes with 3 different tube materials (e.g., polyvinylchloride, silicone, polyurethane) and/or designs (e.g., various numbers of ports and/or eyes, retention balloons, open or closed distal end)
        - At least one tube should be tested with an inflated balloon design
    - Reporting of the pH value of the water
    - Holding times: 0 and 2 hours
2. Sedimentation volume and redispersibility testing
3. In-use stability in designated dispersion media (i.e., water)
4. Particle size distribution study

[1] Applicant-developed, United States Pharmacopeia drug product monograph or Dissolution Methods database, https://www.accessdata.fda.gov/scripts/cder/dissolution/index.cfm

Dispersion and rinse medium: Pour oral pellets into a medicine cup containing room temperature water, wait 10 minutes, do not shake or swirl the medicine cup. Stir and administer entire mixture right away using the syringe and NG tube or G tube. Rinse the cup with room temperature water, stir and administer entire mixture using the syringe and NG tube or G tube. Flush remaining contents from NG tube or G tube with recommended volume of water after enteral administration.

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[a] For the most recent version of a guidance, refer to the FDA guidance website at https://www.fda.gov/regulatory-information/search-fda-guidance-documents.