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Draft Guidance on Levacetylleucine

December 2025

This draft guidance, when finalized, will represent the current thinking of the Food and Drug Administration (FDA, or the Agency) on this topic.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

Dosage Form: For suspension

Route: Oral

Strength: 1 gm/packet

Recommended Studies: Two in vivo bioequivalence studies with pharmacokinetic endpoints

1. Type of study: Fasting
   Design: Single-dose, two-treatment, two-period crossover in vivo
   Strength: 1 gm/packet
   Subjects: Healthy males and non-pregnant, non-lactating females
   Additional comments: Females of reproductive potential should use effective contraception during the study and for 7 days after the last dose.

2. Type of study: Fed
   Design: Single-dose, two-treatment, two-period crossover in vivo
   Strength: 1 gm/packet
   Subjects: Healthy males and non-pregnant, non-lactating females
   Additional comments: Same comments above.

Analyte to measure: Levacetylleucine in plasma

Bioequivalence based on (90% CI): Levacetylleucine

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 for each of the test product and reference listed drug (RLD).[1] Specifications will be determined upon review of the abbreviated new drug application.

Product-specific testing conditions for in vitro feeding tube studies: Since the approved labeling for the RLD states that the product may be administered by a gastrostomy (G) tube. Conduct the in vitro feeding tube studies listed below. For general procedures of in vitro feeding 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 tube: G tube (12 French)

Dispersion medium: 40 mL water

Holding times: 0 and 15 minutes

Repeated administration

In vitro feeding tube testing:

1. Comparative recovery testing
   Three 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.
2. Sedimentation volume and redispersibility testing
3. In-use stability in designated dispersion media (i.e., water)
4. Particle size distribution study

For enteral administration (i.e., feeding tube), open and empty the entire contents of one packet and constitute into oral suspension with 40mL of water. Draw into a catheter tip syringe and immediately deliver through the testing tube. Flush with 20 mL water. Report the pH value of the water.

Document History: Recommended December 2025

Unique Agency Identifier: PSG_219132

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

[1] If the RLD is not available, refer to the most recent version of the guidance for industry *Referencing Approved Drug Products in ANDA Submissions*.