

*Contains Nonbinding Recommendations*  
*Draft – Not for Implementation*  
**Draft Guidance on Uridine Triacetate**  
**October 2024**

This draft guidance, when finalized, will represent the current thinking of the Food and Drug Administration (FDA, or the Agency) on this topic.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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<b>Active Ingredient:</b>	Uridine triacetate
<b>Dosage Form:</b>	Granule
<b>Route:</b>	Oral
<b>Strengths:</b>	2 gm/packet, 10 gm/packet
<b>Recommended Study:</b>	One in vivo bioequivalence study with pharmacokinetic endpoints

1. Type of study: Fed  
Design: Single-dose, two-treatment, two-period crossover in vivo  
Strength: 6 gm (6 gm measured from one packet of uridine triacetate granules, 10 gm/packet)  
Subjects: Healthy males and non-pregnant, non-lactating females  
Additional comments: For applicants planning to only submit an abbreviated new drug application (ANDA) referencing uridine triacetate granules 2 gm/packet, in vivo bioequivalence study may be conducted using up to three packets of the 2 gm/packet product taking into consideration the baseline uridine concentrations.

**Analyte to measure:** Uridine in plasma

Because the active metabolite uridine is an endogenous substance, the plasma concentrations of uridine should be corrected for baseline endogenous concentrations. Refer to the most recent version of the FDA guidance for industry on *Bioequivalence Studies with Pharmacokinetic Endpoints for Drugs Submitted Under an ANDA*.<sup>a</sup>

**Bioequivalence based on (90% CI):** Baseline-corrected uridine

**Waiver request of in vivo testing:** Note that uridine triacetate granules 2 gm/packet and uridine triacetate granules 10 gm/packet are the subject of two separate reference listed drugs (RLD<sup>1</sup>). If applicants plan to pursue both products, two separate applications must be submitted comparing to the appropriate RLDs. In this case, applicants may request a waiver of in vivo bioequivalence testing for the uridine triacetate granules 2 gm/packet, based on the following: (i) acceptable bioequivalence study on the 6 gm strength (6 gm measured from one packet of 10 gm/packet), (ii) acceptable in vitro dissolution testing of both strengths, and (iii) proportional similarity of the formulations between both 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 for each of the test product and RLD.<sup>1</sup> Specifications will be determined upon review of the ANDA.

**Product-specific testing conditions for in vitro feeding tube studies:** These studies apply only if applicant is planning to submit an ANDA referencing the RLD of uridine triacetate granules, 10 gm/packet. The approved labeling for the RLD states that the product may be administered via a nasogastric (NG) tube or gastrostomy (G) tube when necessary (e.g., severe mucositis or coma). Conduct the in vitro feeding tube studies including comparative recovery testing with four repeated administrations, and sedimentation volume and redispersibility testing. 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*.<sup>a</sup>

Testing tubes: NG tube (8 French) and G tube (12 French)

Testing strength: 10 gm

Dispersion medium: Disperse the crushed drug granules in 4 fluid ounces (about 120 mL) of the reconstituted food starch-based thickening product. After administration of the mixture using a NG tube or G tube, flush the tube with water.

Incubation times: 0 and 15 minutes

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

<sup>1</sup> If the RLD is not available, refer to the most recent version of the FDA guidance for industry on *Referencing Approved Drug Products in ANDA Submissions*.