

## Draft Guidance on Didanosine

This draft guidance, when finalized, will represent the current thinking of the Food and Drug Administration (FDA, or the Agency) on this topic.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

**Active Ingredient:** Didanosine

**Dosage Form; Route:** Delayed release capsules; oral

**Recommended Studies:** Two studies

1. Type of study: Fasting  
Design: Single-dose, two-treatment, two-period crossover in vivo  
Strength: 400 mg  
Subjects: Healthy males and non-pregnant, non-lactating females  
Additional comments: None

---

2. Type of study: Fed  
Design: Single-dose, two-treatment, two-period crossover in vivo  
Strength: 400 mg  
Subjects: Healthy males and non-pregnant, non-lactating females  
Additional comments: Applicants may consider using a reference-scaled average bioequivalence approach. If using this approach, applicant should provide evidence of high variability in the pharmacokinetic parameters area under the plasma concentration time curve and/or peak concentration from the study (i.e., within-subject variability  $\geq 30\%$ ). For the method for statistical analysis using the reference-scaled average bioequivalence approach, refer to the detailed information described in the Product Specific Guidance for Progesterone Capsules.

**Analyte to measure (in appropriate biological fluid):** Didanosine in plasma

**Bioequivalence based on (90% CI):** Didanosine

**Additional strengths:** Bioequivalence of the 125 mg, 200 mg, and 250 mg strengths to the corresponding reference product strengths may be demonstrated based on principles laid out in the FDA guidance on *Bioequivalence Studies with Pharmacokinetic Endpoints for Drugs Submitted Under an ANDA*.

**Dissolution test method and sampling times:**

For modified release drug products, FDA recommends that applicants develop specific discriminating dissolution methods. Applicants may also use the dissolution method set forth in

any related official United States Pharmacopeia (USP) drug product monograph, or in the FDA's database (available at <http://www.accessdata.fda.gov/scripts/cder/dissolution/>), provided that Applicants submit adequate dissolution data supporting the discriminating ability of such a method. If a new dissolution method is developed for the modified release drug product, FDA recommends that the submission includes the dissolution method development and validation report with the complete information/data supporting the proposed method. Conduct comparative dissolution testing on 12 dosage units each of all strengths of the test and reference products. Specifications will be determined upon review of the abbreviated new drug application.