

## Draft Guidance on Budesonide

This draft guidance, once finalized, will represent the Food and Drug Administration's (FDA's) current thinking on this topic. It does not create or confer any rights for or on any person and does not operate to bind FDA or the public. You can use an alternative approach if the approach satisfies the requirements of the applicable statutes and regulations. If you want to discuss an alternative approach, contact the Office of Generic Drugs.

**Active Ingredient:** Budesonide

**Dosage Form; Route:** Capsules; oral

**Recommended Studies:** Three studies

1. Type of study: Fasting  
Design: Single-dose, partially or fully replicated crossover design, in vivo  
Strength: 3 mg  
Subjects: Healthy males and nonpregnant females, general population  
Additional comments: Other study designs are acceptable if appropriate. Specific recommendations are provided below

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2. Type of study: Fed  
Design: Single-dose, partially or fully replicated crossover design, in vivo  
Strength: 3 mg  
Subjects: Healthy males and nonpregnant females, general population  
Additional comments: Other study designs are acceptable if appropriate. Specific recommendations are provided below.

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**Analytes to measure:** Budesonide in plasma

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

**Additional comments regarding the BE study with PK endpoints:**

(1). Applicants may consider using a reference-scaled average bioequivalence (BE) approach for budesonide. If using this approach, the applicant should provide evidence of high variability in the BE parameters (i.e., within-subject variability  $\geq 30\%$ ) for the reference product. For general information on this approach, refer to the progesterone capsule guidance for additional information regarding highly variable drugs.

(2). For the fasting study, the following PK parameters will be evaluated: Log-transformed  $AUC_{0-4}$ ,  $AUC_{4-t}$ ,  $AUC_{0-\infty}$ , and  $C_{max}$ , where  $AUC_{0-4}$  is the area under the plasma concentration vs. time curve from 0 to 4 hours,  $AUC_{4-t}$  is the area under the plasma concentration vs. time curve from 4 to the last measurable time point. Applicants should have extensive sampling points around  $T_{max}$  to have accurate estimation of  $C_{max}$  and  $T_{max}$ , and at least four non-zero measurements of concentration are recommended for

each partial AUC. For the fed study, the following PK parameters will be evaluated: Log-transformed  $AUC_{0-t}$ ,  $AUC_{0-\infty}$ , and  $C_{max}$ . Applicants should submit  $AUC_{0-4}$  and  $AUC_{4-t}$  data as supportive evidence of comparable therapeutic outcome.

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3. Type of study: In vitro comparative dissolution study  
Strength: 3 mg  
Apparatus: U.S. Pharmacopoeia (USP) Apparatus 2 (paddle), with capsule sinker  
Pretreatment stage: 2 hours in 1000 mL 0.1 N HCl at 75 rpm  
Evaluation stage: Each of  
(1) pH 4.5 acetate buffer at 75 rpm  
(2) pH 6.0 phosphate buffer at 75 rpm  
(3) pH 6.5 phosphate buffer at 75 rpm  
(4) pH 6.8 phosphate buffer at 75 rpm  
(5) pH 7.2 phosphate buffer at 75 rpm  
(6) pH 7.5 phosphate buffer at 75 rpm  
Volume: 1000 mL  
Temperature: 37° C  
Sample times: 0.5, 1, 1.5, 2, 2.5, 3, 4, 6, and 8 hours, or as needed for profile comparison  
Additional comments: The applicant should use at least 12 dosage units of both the test and reference products per test
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**Waiver request of in vivo testing:** Not applicable

**Dissolution test method and sampling times:** The dissolution information for this drug product can be found on the FDA-Recommended Dissolution Methods website available to the public at the following location: <http://www.accessdata.fda.gov/scripts/cder/dissolution/>. 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 (ANDA).