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Draft – Not for Implementation

Draft Guidance on Budesonide

November 2025

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Active Ingredient:	Budesonide
Dosage Form:	Suspension
Route:	Oral
Strength:	2 mg/10 mL
Recommended Studies:	Demonstrate comparable physicochemical properties, and two options to demonstrate bioequivalence: (1) one in vitro bioequivalence study (comparative dissolution) and two in vivo bioequivalence studies with pharmacokinetic endpoints or (2) one in vitro bioequivalence study (comparative dissolution) and one in vivo bioequivalence study with pharmacokinetic endpoints

Recommendations for demonstrating comparable physicochemical properties:

The test product should demonstrate comparable physicochemical properties to the reference listed drug (RLD), including drug substance particle size distribution, pH, viscosity, and specific gravity. Comparative analyses should be conducted using at least three lots of the test product and three lots of the RLD. Acceptance criteria should be predefined and scientifically justified based on the characterization of the RLD.

I. Option 1: One in vitro bioequivalence study (comparative dissolution) and two in vivo bioequivalence studies with pharmacokinetic endpoints

1. Type of study: In vitro comparative dissolution study

Comparative dissolution testing should be conducted using 12 dosage units each of the test product and the RLD in multiple media, including three compendial media covering pH 1.2 - 6.8 (pH 1.2, 4.5, and 6.8) and the quality control (QC) medium (unless identical to the compendial media). Provide a dissolution method development report that includes data and information demonstrating appropriateness of the selected dissolution method and sampling times. The dissolution method should be capable of detecting meaningful changes in critical quality attributes that could potentially impact in vivo performance of the drug product.

2. Type of study: Fasting
Design: Single-dose, two-treatment, two-period crossover in vivo
Strength: 2 mg/10 mL at a dose of 2 mg (10 mL)
Subjects: Healthy males and non-pregnant, non-lactating females
Additional comments:
    - Female subjects of reproductive potential should use non-hormonal contraceptives during the study and continue to use effective contraception for one week after the last dose.
    - Applicants may consider using a reference-scaled average bioequivalence approach for budesonide. If using this approach, provide evidence of high variability in the pharmacokinetic parameters (i.e., within-subject variability≥30%) for the RLD.

3. Type of study: Fed
Design: Single-dose, two-treatment, two-period crossover in vivo
Strength: 2 mg/10 mL at a dose of 2 mg (10 mL)
Subjects: Healthy males and non-pregnant, non-lactating females
Additional comments: See above.

II. Option 2: One in vitro bioequivalence study (comparative dissolution) and one in vivo bioequivalence study with pharmacokinetic endpoints

The test product should be qualitatively the same and quantitatively similar to the RLD. A test product is considered quantitatively similar if the sum of absolute differences in percentage composition (w/w) of all excipients between the test product and the RLD is within 10% (w/w).

1. Type of study: In vitro comparative dissolution study

Comparative dissolution testing should be conducted using 12 dosage units each of the test product and the RLD in multiple media, including three compendial media covering pH 1.2 - 6.8 (pH 1.2, 4.5, and 6.8) and the quality control (QC) medium (unless identical to the compendial media). Provide a dissolution method development report that includes data and information demonstrating appropriateness of the selected dissolution method and sampling times. The

dissolution method should be capable of detecting meaningful changes in critical quality attributes that could potentially impact in vivo performance of the drug product.

2. Type of study: Fasting
   Design: Single-dose, two-treatment, two-period crossover in vivo
   Strength: 2 mg/10 mL at a dose of 2 mg (10 mL)
   Subjects: Healthy males and non-pregnant, non-lactating females
   Additional comments:
   - Female subjects of reproductive potential should use effective contraception during the study and for one week after the last dose.
   - Applicants may consider using a reference-scaled average bioequivalence approach for budesonide. If using this approach, provide evidence of high variability in the pharmacokinetic parameters (i.e., within-subject variability≥30%) for the RLD.

Analyte to measure: Budesonide in plasma

Bioequivalence based on (90% CI): Budesonide

Alternative approach:
FDA is supportive of the development of alternative bioequivalence approaches. In order to clarify FDA's expectations for prospective applicants early in product development and to assist applicants to submit an abbreviated new drug application (ANDA), FDA strongly encourages applicants to discuss their development program for an alternative approach to bioequivalence with FDA via the pre-ANDA meeting pathway.

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