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*Draft – Not for Implementation*

**Draft Guidance on Bisoprolol Fumarate; Hydrochlorothiazide**

**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This draft guidance, when finalized, will represent the current thinking of the Food and Drug Administration (FDA, or the Agency) on this topic.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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**Active Ingredients:** Bisoprolol fumarate; Hydrochlorothiazide

**Dosage Form:** Tablet

**Route:** Oral

**Strengths:** 2.5 mg; 6.25mg, 5 mg; 6.25 mg, 10 mg; 6.25 mg

**Recommended Study:** One in vivo bioequivalence study with pharmacokinetic endpoints

1. Type of study: Fasting
   Design: Single-dose, two-treatment, two-period crossover in vivo
   Strength: 10 mg; 6.25 mg
   Subjects: Healthy males and non-pregnant, non-lactating females
   Additional comments: None

**Analytes to measure:** Bisoprolol and hydrochlorothiazide in plasma

**Bioequivalence based on (90% CI):** Bisoprolol and hydrochlorothiazide

**Waiver request of in vivo testing:** 2.5 mg; 6.25 mg and 5 mg; 6.25 mg strengths based on (i) acceptable bioequivalence study on the 10 mg; 6.25 mg strength, (ii) acceptable in vitro dissolution testing of all strengths, and (iii) proportional similarity of the formulations across all 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 all strengths of the test product and reference listed drug (RLD).[1] Specifications will be determined upon review of the abbreviated new drug application.

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**Document History:** Recommended May 2007; Finalized May 2008; Revised October 2024

**Unique Agency Identifier:** PSG_020186

[1] 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*.