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Draft Guidance on Buprenorphine Hydrochloride

November 2025

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Active Ingredient: Buprenorphine hydrochloride

Dosage Form: Film

Route: Buccal

Strengths: EQ 0.075 mg Base; EQ 0.15 mg Base; EQ 0.3 mg Base; EQ 0.45 mg Base; EQ 0.6 mg Base, EQ 0.75 mg Base, EQ 0.9 mg Base

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: EQ 0.9 mg Base
   Subjects: Healthy males and non-pregnant, non-lactating females
   Additional comments:
   - Use an opioid antagonist (e.g., naltrexone) to mitigate safety risks of the opioid (e.g., respiratory depression) in healthy subjects. Administer the opioid antagonist before or at the same time that buprenorphine hydrochloride buccal film is administered. Continue to administer the antagonist as appropriate (e.g., within 12 hours post dose) to adequately block buprenorphine induced pharmacological effects based on the opioid antagonist and buprenorphine's effective duration. Monitor vital signs (e.g., pulse oximetry and continuous respiratory monitoring) during the study and implement standards and practice for detection and management of respiratory depression.
   - Allow the film to dissolve without water.

Analyte to measure: Buprenorphine in plasma

Bioequivalence based on (90% CI): Buprenorphine

Waiver request of in vivo testing: EQ 0.075 mg Base; EQ 0.15 mg Base; EQ 0.3 mg Base; EQ 0.45 mg Base; EQ 0.6 mg Base, EQ 0.75 mg Base strengths based on (i) an acceptable bioequivalence study on the EQ 0.9 mg Base 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 strength of the test product and the reference listed drug (RLD).[1] Specifications will be determined upon review of the abbreviated new drug application.

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[1] If the RLD is not available, refer to the most recent version of the guidance for industry *Referencing Approved Drug Products in ANDA Submissions*.