

Draft Guidance on Buprenorphine Hydrochloride

This draft guidance, when finalized, will represent the current thinking of the Food and Drug Administration (FDA, or the Agency) on this topic.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

Dosage Form; Route: Film; buccal

Recommended Studies: One study

1. Type of study: Fasting
Design: Single-dose, two-treatment, two-period crossover in vivo
Strength: EQ 0.9 mg Base
Subjects: Males and non-pregnant, non-lactating females, general population
Additional comments:
 - A. An opioid antagonist, such as naltrexone hydrochloride oral tablet, 50 mg, may be used to minimize opioid-related adverse events. The opioid antagonist should be administered well in advance of dosing, to achieve adequate blockade of opioid receptors. Consult with a physician who is an expert in the administration of opioids for the appropriate dose and dosing regimen of an opioid antagonist for a single dose of buprenorphine buccal film EQ 0.9 mg base administered to a study subject who has not received any opioid within 14 days of dosing.
 - B. A clear plan for continuous respiratory monitoring from the time of dosing past the time of expected peak effect of the drug (i.e., at least 3 hours after dosing) should be included. Standard operating procedures (SOPs) should be in place for assessing and treating ventilatory depression, and personnel qualified to treat ventilatory emergencies should be immediately available.

Analytes to measure (in appropriate biological fluid): Buprenorphine and its active metabolite, nor-buprenorphine, in plasma.

Submit the metabolite data as supportive evidence of comparable therapeutic outcome. For the metabolite, the following data should be submitted: individual and mean concentrations; individual and mean pharmacokinetic parameters; and geometric means and ratios of means for AUC and C_{max}.

Bioequivalence based on (90% CI): Buprenorphine

Waiver request of in vivo testing: Buprenorphine 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 buccal films based on (i) acceptable BE 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 on the FDA-Recommended Dissolution Methods web site, 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).