Contains Nonbinding Recommendations

Draft Guidance on Nicotine Polacrilex

This draft guidance, when finalized, will represent the current thinking of the Food and Drug Administration (FDA, or the Agency) on this topic.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

Dosage Form; Route: Chewing Gum; buccal

Recommended Studies: One study

1. Type of study: Fasting
   Design: Single-dose, two-way crossover in vivo
   Strength: Eq. 4 mg base
   Subjects: Males and non-pregnant, non-lactating females, general smoking population
   Additional comments: Chew the gum slowly until there is a tingling sensation, then place the chewing gum between your cheek and gum. When the tingle is gone, begin chewing again, until the tingle returns. Repeat this process until most of the tingle is gone (about 30 minutes).

Analytes to measure (in appropriate biological fluid): Nicotine in plasma

Bioequivalence based on (90% CI): Nicotine

Waiver request of in vivo testing: Eq. 2 mg base (regular flavor) based on (i) an acceptable bioequivalence study on the Eq. 4 mg base strength (regular flavor), (ii) acceptable in vitro release testing (dissolution testing) or in vivo release testing (chew-out study) of all strengths, and (iii) proportional similarity in the formulations of all strengths.

Nicotine Polacrilex Gum with an alternate flavor (Eq. 2 mg base and Eq. 4 mg base (mint and orange flavored)) may be eligible for a waiver of the bioequivalence study requirements based on (i) an acceptable bioequivalence study on the Eq. 4 mg base strength(regular flavor), (ii) acceptable in vitro release testing (dissolution testing) or in vivo release testing (chew-out study) of all strengths and flavors, (iii) proportional similarity in the formulations of all strengths and flavors, and (iv) the flavor component is the only difference in the formulation between the flavored and regular gum.

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).

Additional Information

Chew-out study:

A multi-dose, crossover chew-out study comparing Nicotine Polacrilex Gum Regular Flavor, Eq. 2 mg base and Eq. 4 mg base to evaluate the in vivo nicotine release of the generic formulations to the RLD, is requested if the dissolution method cannot be developed. Sampling after chewing the gum is recommended at 5, 10, 20 and 30 minutes.