

Contains Nonbinding Recommendations
Draft Guidance on Nicotine Polacrilex

This draft guidance, once finalized, will represent the Food and Drug Administration's (FDA's) current thinking on this topic. It does not create or confer any rights for or on any person and does not operate to bind FDA or the public. You can use an alternative approach if the approach satisfies the requirements of the applicable statutes and regulations. If you want to discuss an alternative approach, contact the Office of Generic Drugs.

Active ingredient: Nicotine Polacrilex

Form/Route: Chewing Gum/Buccal

Recommended studies: 1 study

1. Type of study: Fasting
Design: Single-dose, two-way crossover in vivo
Strength: Eq. 4 mg base
Subjects: Healthy males and nonpregnant females, general smoking population
Additional Comments: A fed study is not requested. Please refer to the Amantadine Hydrochloride Tablet Draft Guidance for additional information regarding fed study exemption criteria.

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 (regular flavor) based on (i) an acceptable bioequivalence study on the Eq. 4 mg 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. Please refer to the Mirtazapine Tablet Draft Guidance for additional information regarding waivers of in vivo testing.

Nicotine Polacrilex Gum with alternate flavors cannot be filed in the same ANDA as the regular flavor. For each flavor, a separate submission (ANDA) should be submitted.

Nicotine Polacrilex Gum with an alternate flavor (Eq. 2 mg and Eq. 4 mg (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 strength of the 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:

Please note that a **Dissolution Methods Database** is available to the public at the OGD website at <http://www.accessdata.fda.gov/scripts/cder/dissolution/>. Please find the dissolution information

for this product at this website. Please 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 application.

Additional Information

Chew-out study:

A multi-dose, crossover chew-out study comparing Nicotine Polacrilex Gum Regular Flavor, Eq. 2 mg and Eq. 4 mg 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.