Contains Nonbinding Recommendations

Guidance on Nateglinide

This guidance represents 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: Nateglinide

Form/Route: Tablets/Oral

Recommended studies: 2 studies

1. Type of study: Fasting
   Design: Single-dose, two-way crossover *in-vivo*
   Strength: 120 mg
   Subjects: Normal, healthy, males and females, general population
   Additional comments: All subjects should fast overnight for at least 10 hours prior to dosing and for 4 hours after dosing. A single oral dose (120 mg) should be administered with 240 mL of 20% glucose solution. Since, multiple plasma concentration peaks were often observed under fasting conditions, please ensure that the same sampling schedule is followed during the study for both test and reference drug administration.
   Females should not be pregnant or lactating, and if applicable, should practice abstention or contraception during the study.

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2. Type of study: Fed
   Design: Single-dose, two-way crossover *in-vivo*
   Strength: 120 mg
   Subjects: Normal, healthy, males and females, general population
   Additional comments: A single oral dose (120 mg) should be administered with 240 mL of water 30 minutes after start of a standard high-fat FDA breakfast. Subjects should start the recommended meal 30 minutes prior to administration of the drug product. Study subjects should eat this meal in 30 minutes or less; however, the drug product should be administered 30 minutes after start of the meal.
   Females should not be pregnant or lactating, and if applicable, should practice abstention or contraception during the study.

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

Bioequivalence based on (90% CI): Nateglinide

Waiver request of in-vivo testing: 60 mg, based on (i) acceptable bioequivalence studies on the 120 mg strength, (ii) proportionally similar across all strengths, and (iii) acceptable in vitro dissolution testing of all strengths.

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.fda.gov/cder/ogd/index.htm. 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.