Contains Nonbinding Recommendations

Draft Guidance on Nintedanib Esylate

This draft guidance, when finalized, will represent the current thinking of the Food and Drug Administration (FDA, or the Agency) on this topic.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

Dosage Form; Route: Capsule; oral

Recommended Studies: Two in vivo studies

1. Type of study: Fasting
   Design: Single-dose, two-way crossover in vivo
   Strength: 150 mg nintedanib
   Subjects: Healthy males, general population
   Additional comments: Due to the embryofetal toxicity of nintedanib, the study should be conducted in healthy male subjects. See additional warnings and precautions in the approved drug label.

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2. Type of study: Fed
   Design: Single-dose, two-way crossover in vivo
   Strength: 150 mg nintedanib
   Subjects: Healthy males, general population
   Additional comments: Same as comments above

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

Bioequivalence based on (90% CI): Nintedanib

Waiver request of in vivo testing: 100 mg strength based on (i) acceptable bioequivalence studies on the 150 mg strength, (ii) proportional similarity of the formulations between both strengths, and (iii) acceptable in vitro dissolution testing of both 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 both strengths of the test and reference products. Specifications will be determined upon review of the abbreviated new drug application (ANDA).