Contains Nonbinding Recommendations

Draft Guidance on Pirfenidone

This draft guidance, when finalized, will represent the current thinking of the Food and Drug Administration (FDA, or the Agency) on this topic.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

Dosage Form; Route: Tablet; oral

Recommended Studies: Two studies

1. Type of study: Fasting
   Design: Single-dose, two-way, crossover *in-vivo*
   Strength: 801 mg
   Subjects: Healthy males and non-lactating, non-pregnant females

   Additional comments: Sponsors should follow the recommendations indicated in the product's prescribing information. The liver enzymes, including alanine aminotransferase (ALT), alanine transaminase (AST), and bilirubin, should be checked at baseline and monitored during treatment. Adequate precautions should be taken to avoid or minimize the photosensitivity associated with the product's use.

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2. Type of study: Fed
   Design: Single-dose, two-way, crossover in-vivo
   Strength: 801 mg
   Subjects: Healthy males and non-lactating, non-pregnant females

   Additional comments: Same as above.

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

Bioequivalence based on (90% CI): Pirfenidone

Waiver request of in-vivo testing: 267 mg and 534 mg strength tablets based on (i) acceptable bioequivalence studies on the 801 mg strength, (ii) proportionally similar across all strengths, and (iii) acceptable in vitro dissolution testing of all strengths. The 534 mg strength is currently listed as 'discontinued' in the Orange Book and for its approval, the sponsors are requested to petition the FDA to determine if the discontinuation/withdrawal of the strength is not due to Safety and or Efficacy reasons.

Dissolution test method and sampling times: The dissolution information for this drug product can be found on the FDA-Recommended Dissolution Methods website 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).