Contains Nonbinding Recommendations

Draft Guidance on Apalutamide

This draft guidance, when finalized, will represent the current thinking of the Food and Drug Administration (FDA, or the Agency) on this topic.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

Dosage Form; Route: Tablet; oral

Recommended Studies: Two studies

1. Type of study: Fasting
   Design: Single-dose, two-way crossover in-vivo
   Strength: 60 mg
   Subjects: Males, general population
   Additional Comments: Apalutamide can cause fetal harm and potential loss of pregnancy. Male study subjects with female partners of reproductive potential should use effective contraception (e.g. practice abstention or contraception) during and 3 months after in vivo bioequivalence studies.

   Apalutamide has a long terminal elimination half-life. Ensure adequate washout periods between treatments in a crossover study or consider using a parallel study design. For long half-life drug products with low intra-subject variability in distribution and clearance, an AUC truncated to 72 hours may be used in place of AUC_{0-t} or AUC_{0-inf}. For either a crossover or parallel study, sample collection time should be adequate to ensure completion of gastrointestinal transit of the drug product and absorption of the drug substance. Collect sufficient blood samples in the bioequivalence studies to adequately characterize the peak concentration (C_{max}) and time to reach peak concentration (T_{max}).

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2. Type of study: Fed
   Design: Single-dose, two-way crossover in-vivo
   Strength: 60 mg
   Subjects: Males, general population
   Additional Comments: See comments above.

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

Bioequivalence based on (90% CI): Apalutamide

Waiver request of in-vivo testing: Not Applicable

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 the test and reference products. Specifications will be determined upon review of the abbreviated new drug application (ANDA).