Contains Nonbinding Recommendations

Draft – Not for Implementation

Draft Guidance on Apalutamide

August 2024

This draft guidance, when finalized, will represent the current thinking of the Food and Drug Administration (FDA, or the Agency) on this topic.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

In general, FDA's guidance documents do not establish legally enforceable responsibilities. Instead, guidances describe the Agency's current thinking on a topic and should be viewed only as recommendations, unless specific regulatory or statutory requirements are cited. The use of the word *should* in Agency guidances means that something is suggested or recommended, but not required.

Active Ingredient: Apalutamide

Dosage Form: Tablet

Route: Oral

Strengths: 60 mg, 240 mg

Recommended Studies: Two in vivo bioequivalence studies with pharmacokinetic endpoints

1. Type of study: Fasting
   Design: Single-dose, two-treatment, two-period crossover in vivo
   Strength: 240 mg
   Subjects: Healthy males
   Additional comments: Male subjects with female partners of reproductive potential should use effective contraception and should not donate sperm during the study and for 3 months after the last dose. 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.

2. Type of study: Fed
   Design: Single-dose, two-treatment, two-period crossover in vivo
   Strength: 240 mg
   Subjects: Healthy males
   Additional comments: See comments above.

Analyte to measure: Apalutamide in plasma

Bioequivalence based on (90% CI): Apalutamide

Waiver request of in vivo testing: 60 mg strength based on (i) acceptable bioequivalence studies on the 240 mg strength, (ii) acceptable in vitro dissolution testing of both strengths, and (iii) proportional similarity of the formulations between both strengths

Dissolution test method and sampling times: The dissolution information for this drug product can be found in the FDA's Dissolution Methods database, 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.

Product-specific testing conditions for in vitro feeding tube studies: The approved labeling for the RLD states that the 240 mg tablet may be administered through a feeding tube. Conduct the in vitro feeding tube studies, including comparative recovery, sedimentation volume and redispersibility, and in-use stability in designated dispersion media. For general procedures of in vitro feeding tube studies, refer to the most recent version of the FDA guidance for industry on *Oral Drug Products Administered Via Enteral Feeding Tube: In Vitro Testing and Labeling Recommendations*.[a]

Testing tube: Nasogastric tube (8 French) and gastrostomy (G) tube (12 French)

1. Three types of tube configurations including different tube materials (e.g., polyvinyl chloride, silicone, polyurethane) and/or designs (e.g., various numbers of ports and/or eyes, open or closed distal end, retention balloons), with at least one G tube should be tested with an inflated balloon design
2. Holding times of 0 and 15 minutes
3. Reporting of the pH value of the water

Sedimentation volume and redispersibility testing

In-use stability in designated dispersion media (i.e., water)

Document History: Recommended May 2019; Revised August 2024

Unique Agency Identifier: PSG_210951

[a] For the most recent version of a guidance, check the FDA guidance website at https://www.fda.gov/regulatory-information/search-fda-guidance-documents.