Contains Nonbinding Recommendations

Draft Guidance on Enzalutamide

This draft guidance, when finalized, will represent the current thinking of the Food and Drug Administration (FDA, or the Agency) on this topic.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

Dosage Form; Route: Capsule; oral

Recommended Studies: Two studies

1. Type of study: Fasting
   Design: Single-dose, two-way crossover in vivo
   Strength: 40 mg at a dose of 160 mg (4x40mg)
   Subjects: Healthy males, general population
   Additional comments: a. Enzalutamide is contraindicated for use in women who are or may become pregnant. b. Enzalutamide has a long terminal elimination half-life (>24 hrs). Ensure adequate washout periods between treatments in the crossover studies. Also consider using a parallel study design due to enzalutamide's long half-life. For long half-life drug products, an AUC truncated to 72 hours may be used in place of AUC_{0-t} or $AUC_{0-\infty}$. 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 (Cmax) and time to reach peak concentration (tmax).

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2. Type of study: Fed
   Design: Single-dose, two-way crossover in vivo
   Strength: 40 mg at a dose of 160 mg (4x40mg)
   Subjects: Healthy males, general population
   Additional comments: Same as above

Analytes to measure: Enzalutamide in plasma

Bioequivalence based on (90% CI): Enzalutamide

Waiver request of in vivo testing: Not applicable

Dissolution test method and sample 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).