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Draft Guidance on Enzalutamide

November 2024

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Active Ingredients:	Enzalutamide
Dosage Form:	Tablet
Route:	Oral
Strengths:	40 mg, 80 mg, 120 mg ¹ , 160 mg ¹
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: 160 mg
Subjects: Healthy males
Additional comments: Applicants may consider one of the following options:
 - Conduct the study using one enzalutamide tablet (1 × 160 mg) of the test product and two enzalutamide tablets (2 × 80 mg) of the reference standard (RS)².
 - Conduct the study using one enzalutamide tablet (1 × 160 mg) of the test product and one enzalutamide tablet (1 × 160 mg) of the RS³.
 - Conduct a single fasting study for the 160 mg strength if the applicant already has an approved abbreviated new drug application (ANDA) for the 80 mg strength that includes both fasting and fed studies.

¹ The strengths identified are the subject of an approved suitability petition (FDA-2021-P-1296).

² The currently designated RS is the reference listed drug, NDA 213674, enzalutamide tablets, 80 mg.

³ This option can be used when a petitioned abbreviated new drug application for enzalutamide tablets, 160 mg is approved and designated as the RS.

- Exclude subjects with a history of or risk factors for seizure. Subjects with female partners of reproductive potential should use effective contraception during the study and for three months after the last dose. Ensure an adequate washout period between treatments in the crossover study due to the long elimination half-life of enzalutamide. Alternatively, a parallel study design may be considered.

2. Type of study: Fed
Design: Single-dose, two-treatment, two-period crossover in vivo
Strength: 160 mg
Subjects: Healthy males
Additional comments: See comments above.

Analyte to measure: Enzalutamide in plasma

Bioequivalence based on (90% CI): Enzalutamide

Waiver request of in vivo testing: 40 mg, 80 mg, and 120 mg strengths based on (i) acceptable bioequivalence studies on the 160 mg strength, (ii) acceptable in vitro dissolution testing of all strengths, and (iii) proportional similarity of the formulations across all 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 for each of all strengths of the test product and reference listed drug (RLD).⁴ Specifications will be determined upon review of the ANDA.

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Unique Agency Identifier: PSG_213674

⁴ If the RLD is not available, refer to the most recent version of the FDA guidance for industry on *Referencing Approved Drug Products in ANDA Submissions*.