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Draft Guidance on Testosterone Undecanoate

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This draft guidance, when finalized, will represent the current thinking of the Food and Drug Administration (FDA, or the Agency) on this topic.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

Dosage Form: Capsule

Route: Oral

Strengths: 100 mg, 150 mg, 200 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: 200 mg
   Subjects: Asymptomatic hypogonadal males (serum testosterone measurements below 300 ng/dL in the morning on at least two separate days)
   Additional comments: Exclude elderly males. Subjects should not be receiving any treatment for their hypogonadism. Ex vivo conversion of testosterone undecanoate to testosterone may occur during the blood collection and sample handling. This conversion factor should be considered in bioanalytical methodology to ensure accurate measurement of testosterone undecanoate.

2. Type of study: Fed
   Design: Single-dose, two-treatment, two-period crossover in vivo
   Strength: 200 mg
   Subjects: Asymptomatic hypogonadal males (serum testosterone measurements below 300 ng/dL in the morning on at least two separate days)
   Additional comments: See comments above.

Analytes to measure: Testosterone undecanoate and testosterone in plasma

Bioequivalence based on (90% CI): Testosterone undecanoate

Submit the baseline corrected testosterone data as supportive evidence of comparable therapeutic outcome. For the metabolite, the following data should be submitted: individual and mean concentrations, individual and mean pharmacokinetic parameters, and geometric means and ratios of means for AUC and Cmax.

Waiver request of in vivo testing: 100 mg and 150 mg strengths based on (i) acceptable bioequivalence studies on the 200 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 each of all strengths of the test and reference products. Specifications will be determined upon review of the abbreviated new drug application.

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