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Draft Guidance on Testosterone Undecanoate

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This draft guidance, when finalized, will represent the current thinking of the Food and Drug Administration (FDA, or the Agency) on this topic.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

This guidance, which interprets the Agency's regulations on bioequivalence at 21 CFR part 320, provides product-specific recommendations on, among other things, the design of bioequivalence studies to support abbreviated new drug applications (ANDAs) for the referenced drug product. FDA is publishing this guidance to further facilitate generic drug product availability and to assist the generic pharmaceutical industry with identifying the most appropriate methodology for developing drugs and generating evidence needed to support ANDA approval for generic versions of this product.

The contents of this document do not have the force and effect of law and are not meant to bind the public in any way, unless specifically incorporated into a contract. This document is intended only to provide clarity to the public regarding existing requirements under the law. FDA guidance documents, including this guidance, should be viewed only as recommendations, unless specific regulatory or statutory requirements are cited. The use of the word should in FDA guidances means that something is suggested or recommended, but not required.

This is a new draft product-specific guidance for industry on generic testosterone undecanoate.

Active Ingredient: Testosterone undecanoate

Dosage Form; Route: Capsule; oral

Recommended Studies: Two studies

1. Type of study: Fasting
   Design: Single-dose, two-treatment, two-period crossover in vivo
   Strength: 237 mg
   Subjects: Hypogonadal males (serum testosterone measurements below 300 ng/dL in the morning on at least two separate days) who are otherwise healthy
   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 and testosterone.

2. Type of study: Fed
Design: Single-dose, two-treatment, two-period crossover in vivo
Strength: 237 mg
Subjects: Hypogonadal males (serum testosterone measurements below 300 ng/dL in the morning on at least two separate days) who are otherwise healthy
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: 158 mg and 198 mg based on (i) acceptable bioequivalence studies on the 237 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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