

## Guidance on Testosterone

This guidance represents the Food and Drug Administration's (FDA's) current thinking on this topic. It does not create or confer any rights for or on any person and does not operate to bind FDA or the public. You can use an alternative approach if the approach satisfies the requirements of the applicable statutes and regulations. If you want to discuss an alternative approach, contact the Office of Generic Drugs.

**Active ingredient:** Testosterone

**Form/Route:** Extended Release Tablets/Buccal

**Recommended studies:** 2 Studies

1. Type of study: Fasting  
Design: Single-dose, two-way crossover *in-vivo*  
Strength: 30 mg  
Subjects: Testosterone-deficient (hypogonadal) males  
Additional Comments:
  - Subjects should not currently be receiving any treatment for their hypogonadism.
  - The inclusion criterion for testosterone-deficient (hypogonadal) males is serum testosterone levels below 2.5 ng/ml.
  - At least three predose levels will serve as baseline.
  - A 'fed' BE study is not recommended because the product is a buccal adhesive, not to be ingested. This obviates the need for oral dose dumping assessment due to food.

2. Type of study: *In vitro* adhesion comparative performance testing study  
Design: A tensiometry study is recommended to compare the peak detachment force for test and reference products.<sup>1</sup> Water is recommended between the buccal tablets and the base plate of the tensiometer. The loading weight and length of time the loading weight is applied to press the buccal tablet into contact with the base plate should be specified. Following removal of the weight, the rate at which the buccal tablet is pulled away from the base plate should be specified. The peak detachment force should be measured as the force required to detach the buccal tablet from the base plate. The comparative adhesion test should be conducted using 12 individual units of the test and reference products.

Prior to conducting studies for submission to the ANDA, the firm should determine appropriate loading weight, length of time the loading weight is applied to press the buccal tablet into contact with the base plate of the tensiometer, and the rate at which the buccal tablet is pulled away from the base plate.<sup>2</sup> These studies should be conducted to assure the appropriateness of the test conditions to the test and reference products.

<sup>1</sup> HE Junginger et al, Mucoadhesive hydrogels in drug delivery. Encyclopedia Pharm Technol, 2002

<sup>2</sup> SJ Jackson, AC Perkins. In vitro assessment of the mucoadhesion of cholestyramine to porcine and human gastric mucosa. Eur J Pharm Biopharm. 2001;52:121-127

**Analytes to measure (in appropriate biological fluid):** Total testosterone in plasma.

**Bioequivalence based on (90% CI):** Baseline-adjusted testosterone

**Waiver request of in-vivo testing:** Not Applicable

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**Dissolution test method and sampling times:**

Please note that a **Dissolution Methods Database** is available to the public at the OGD website at <http://www.fda.gov/cder/ogd/index.htm>. Please find the dissolution information for this product at this website. Please 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 application.