

NEW DRUG UPDATE

Drug Name:	testosterone
Trade Name (Manufacturer):	Axiron® (Lilly)
Form:	Topical solution
Strength:	30 mg per 1.5 mL pump actuation
FDA Approval:	November 23, 2010
Market Availability:	Anticipated April 2011
FDA Approval Classification:	Standard review
Classification:	Specific Therapeutic Class (HIC3): Androgenic Agents (F1A)

Indication:¹ Testosterone (Axiron) is a topical androgenic preparation indicated for replacement therapy in males with deficiency or absence of endogenous testosterone, as a result of congenital or acquired primary hypogonadism or hypogonadotropic hypogonadism.

Contraindications/Warnings: Axiron should not be used in men with carcinoma of the breast or prostate. Testosterone may cause fetal harm and should not be used by pregnant or breastfeeding women.

Patients with benign prostate hyperplasia should be monitored for worsening of their conditions. Axiron may cause azoospermia. Patients with cardiac, renal, or hepatic disease may develop edema with or without congestive heart failure. Axiron may cause sleep apnea in patients with risk factors. Care should be taken to avoid exposure of the product to women or children. Secondary exposure may result in signs of virilization.

Serum testosterone, prostate specific antigen (PSA), liver function, lipids, hematocrit, and hemoglobin should be monitored in patients using Axiron.

Drug Interactions: Axiron may decrease blood glucose levels, reducing the insulin requirement for patients with diabetes. Changes in anticoagulant activity may also be observed, and more frequent monitoring of prothrombin time (PT) and International Normalized Ratio (INR) are recommended. The concurrent use of Axiron with adrenocorticotropic hormone or corticosteroids may result in fluid retention, particularly in patients with cardiac, renal, or hepatic disease.

Common Adverse Effects: Adverse events occurring in more than four percent of patients include: skin site reaction, increased hematocrit, headache, diarrhea, vomiting, and increased PSA.

Special Populations:

Pediatrics: The safety and efficacy of Axiron have not been evaluated in patients less than 18 years of age. The use of testosterone products in children may result in acceleration of bone growth and premature epiphysis closure.

Pregnancy: Pregnancy Category X.

Geriatrics: Axiron has not been evaluated in a sufficient number of older adults to determine if efficacy and safety in those over age 65 is different from younger patients.

Renal Impairment: Axiron has not been studied in patients with renal impairment.

Hepatic Impairment: Axiron has not been studied in patients with hepatic impairment.

Gender: Axiron is only indicated for use in male patients.

Dosages: Therapy should be initiated at 60 mg every morning, with 30 mg, one pump actuation, being applied to each axilla. The dose may be adjusted down to 30 mg or increased to as high as 120 mg, with dose increases only occurring in 30 mg increments. Dose adjustment should be based on serum testosterone concentration from a single blood draw two to eight hours after application. Dose adjustment should only occur at least 14 days after initiation or dose change.

Patients should be advised to wash their hands with soap and water immediately following application. Patients should cover the application site with clothing after the solution has dried. The application site should be washed thoroughly with soap and water prior to any contact between the application site and another person.

Clinical Trials: A literature search was performed using “testosterone solution”.

The method of administration and monitoring parameters associated with topical testosterone therapy make it difficult to perform blinded studies on these agents. Consequently, many of the studies involving topical testosterone preparations are open-label, increasing the possibility for bias in study findings. Due to lack of alternative evidence, the open-label trial outlined in Axiron’s packing insert is described below.

Axiron was evaluated in an open label trial across 26 centers and including 155 hypogonadal male subjects.² Patients received an Axiron dose of 60 mg on days one through 15, and 76.1 percent of patients achieved an average serum total testosterone level in the normal range, defined as 300 to 1,050 ng/dL. On day 45, doses were adjusted based on their average serum testosterone level, as measured on day 15. Dose adjustment occurred again on day 90, based on the testosterone level taken on day 60. On day 60, 84.8 percent of subjects had a normal average serum testosterone level. The study concluded on day 120, at which point 84.1 percent of patients experienced a normal average serum testosterone level.

Other Drugs Used for Condition:³ Other topical and transdermal testosterone products include: Androderm[®], Androgel[®], Fortesta[™], and Testim[®].

Place in Therapy: The 2002 American Association of Clinical Endocrinologists Medical Guidelines for Clinical Practice for the Evaluation and Treatment of Hypogonadism in Adult Male Patients do not endorse the use of a specific agent or dosage form for testosterone delivery⁴. No data exists to suggest that Axiron is superior to other topical formulations of testosterone. Attention should be given to identifying the product that reduces the risk of abuse and accidental exposure to other individuals with whom the patient may have physical contact.

References

¹ Axiron [package insert]. Indianapolis, IN; Lilly USA; November 2010.

² Axiron [package insert]. Indianapolis, IN; Lilly USA; November 2010.

³ Available at: www.clinicalpharmacology.com. Accessed January 31, 2011.

⁴ American Association of Clinical Endocrinologists. American Association of Clinical Endocrinologists Medical Guidelines for clinical practice for the evaluation and treatment of hypogonadism in adult male patients-2002 update. *Endocr Pract.* 2002; 8(6):440-456.