XYOSTED™ (testosterone enanthate) injection, for subcutaneous use CIII
Initial US approval: 1953
IMPORTANT SAFETY INFORMATION

WARNING: BLOOD PRESSURE INCREASES

- **XYOSTED™ can cause blood pressure increases that can increase the risk for major adverse cardiovascular events (MACE), including non-fatal myocardial infarction, non-fatal stroke and cardiovascular death, with greater risk for MACE in patients with cardiovascular risk factors or established cardiovascular disease.**
- **Before initiating XYOSTED™, consider the patient's baseline cardiovascular risk and ensure blood pressure is adequately controlled.**
- **Starting approximately 6 weeks after initiating therapy, periodically monitor for and treat new-onset hypertension or exacerbations of pre-existing hypertension in patients on XYOSTED™.**
- **Re-evaluate whether the benefits of XYOSTED™ outweigh its risks in patients who develop cardiovascular risk factors or cardiovascular disease while on treatment.**
- **Due to this risk, use XYOSTED™ only for the treatment of men with hypogonadal conditions associated with structural or genetic etiologies.**

XYOSTED™ INDICATIONS AND USAGE

XYOSTED™ (testosterone enanthate) injection is an androgen indicated for testosterone replacement therapy in adult males for conditions associated with a deficiency or absence of endogenous testosterone.

- Primary hypogonadism (congenital or acquired)
- Hypogonadotropic hypogonadism (congenital or acquired)

LIMITATIONS OF USE

- Safety and efficacy of XYOSTED™ in men with "age-related hypogonadism" (also referred to as "late-onset hypogonadism") have not been established
- Safety and efficacy of XYOSTED™ in males less than 18 years old have not been established

CONTRAINDICATIONS

XYOSTED™ is contraindicated in:

- Men with carcinoma of the breast or known or suspected carcinoma of the prostate.
- Women who are pregnant. Testosterone can cause virilization of the female fetus when administered to a pregnant woman.
- Men with known hypersensitivity to XYOSTED™ or any of its ingredients (testosterone enanthate and sesame oil).
- Men with hypogonadal conditions, such as "age-related hypogonadism", that are not associated with structural or genetic etiologies. The efficacy of XYOSTED™ has not been established for these conditions, and XYOSTED™ can increase blood pressure (BP) that can increase the risk of MACE.

WARNINGS AND PRECAUTIONS

Blood Pressure Increases—In clinical trials, XYOSTED™ increased systolic BP in the first 12 weeks of treatment by an average of 4 mmHg based on ambulatory blood pressure monitoring (ABPM) and by an average of 4 mmHg from baseline following 1 year of treatment based on blood pressure cuff measurements. In the 1-year trial, 10% of XYOSTED™-treated patients were started on antihypertensive medications or required changes to their antihypertensive medication regimen.

BP increases can increase the risk of MACE, with greater risk in patients with established cardiovascular disease or risk factors for cardiovascular disease.

In some patients, the increase in BP with XYOSTED™ may be too small to detect, but can still increase the risk for MACE.

Before initiating XYOSTED™, consider the patient's baseline cardiovascular risk and ensure blood pressure is adequately controlled. Check BP approximately 6 weeks after initiating XYOSTED™ and periodically thereafter. Treat new-onset hypertension or exacerbations of pre-existing hypertension. Re-evaluate whether the benefits of continued treatment with XYOSTED™ outweigh its risks in patients who develop cardiovascular risk factors or cardiovascular disease.

Polycythemia—Increases in hematocrit, reflective of increases in red blood cell mass, may require discontinuation of XYOSTED™. Check that hematocrit is not elevated prior to initiating XYOSTED™. Evaluate hematocrit approximately every 3 months while the patient is on XYOSTED™. If hematocrit becomes elevated, stop XYOSTED™ until the hematocrit decreases to an acceptable level. If XYOSTED™ is restarted and again causes hematocrit to become elevated, stop XYOSTED™ permanently. An increase in red blood cell mass may increase the risk of thromboembolic events.

Cardiovascular Risk—Long-term clinical safety trials have not been completed to assess the cardiovascular outcomes of testosterone replacement therapy in adult males. To date, epidemiologic studies and randomized controlled trials have been inconclusive for determining the risk of MACE, such as non-fatal myocardial infarction, non-fatal stroke, and cardiovascular death, with the use of testosterone compared to non-use. Some studies, but not all, have reported an increased risk of MACE in association with use of testosterone replacement therapy in adult males. XYOSTED™ can cause BP increases that can increase the risk of MACE. Patients should be informed of this possible risk when deciding whether to use or to continue to use XYOSTED™.

Worsening of Benign Prostatic Hyperplasia (BPH) and Potential Risk of Prostate Cancer—Patients with BPH treated with androgens are at an increased risk of worsening of signs and symptoms of BPH. Monitor patients with BPH for worsening signs and symptoms. Patients treated with androgens may be at an increased risk for prostate cancer. Evaluate patients for prostate cancer prior to initiating and during treatment with androgens.

Venous Thromboembolism (VTE)—There have been post-marketing reports of venous thromboembolic events, including deep vein thrombosis (DVT) and pulmonary embolism (PE), in patients using testosterone products, such as XYOSTED™. Evaluate patients who report symptoms of pain, edema, warmth and erythema in the lower extremity for DVT and those who present with acute shortness of breath for PE. If a venous thromboembolic event is suspected, discontinue treatment with XYOSTED™ and initiate appropriate workup and management.

Abuse of Testosterone and Monitoring of Serum Testosterone Concentrations—Testosterone has been subject to abuse, typically at doses higher than recommended for the approved indication and in combination with other anabolic androgenic steroids. Anabolic androgenic steroid abuse can lead to serious cardiovascular and psychiatric adverse reactions.

If testosterone abuse is suspected, check serum testosterone concentrations to ensure they are within therapeutic range. However, testosterone levels may be in the normal or subnormal range in men abusing synthetic testosterone derivatives. Counsel patients concerning the serious adverse reactions associated with abuse of testosterone and anabolic androgenic steroids. Conversely, consider the possibility of testosterone