Xyosted™ (testosterone enanthate) – New formulation approval

- On October 1, 2018, Antares Pharma announced the FDA approval of Xyosted (testosterone enanthate), for testosterone replacement therapy in adult males for conditions associated with a deficiency or absence of endogenous testosterone.

    - Primary hypogonadism (congenital or acquired) is characterized by testicular failure due to cryptorchidism, bilateral torsion, orchitis, vanishing testis syndrome, orchiectomy, Klinefelter's syndrome, chemotherapy, or toxic damage from alcohol or heavy metals. These men usually have low serum testosterone concentrations and gonadotropins (follicle-stimulating hormone, luteinizing hormone) above the normal range.
    - Hypogonadotropic hypogonadism (congenital or acquired) is characterized by gonadotropin or luteinizing hormone-releasing hormone deficiency or pituitary-hypothalamic injury from tumors, trauma, or radiation. These men have low testosterone serum concentrations but have gonadotropins in the normal or low range.
    - The safety and efficacy of Xyosted in adult males with “age-related hypogonadism” (also referred to as “late-onset hypogonadism”) have not been established.
    - The safety and efficacy of Xyosted in males less than 18 years old have not been established.

- Hypogonadism, also known as testosterone deficiency, is a condition in which the body does not produce enough testosterone. Symptoms of male hypogonadism can be treated with testosterone replacement therapy.

- Xyosted is the first subcutaneous testosterone autoinjector product.

    - Testosterone enanthate is also available generically as an intramuscular injection.
    - Other intramuscular formulations of testosterone include the generically available testosterone cypionate and branded Aveed® (testosterone undecanoate).

- The efficacy of Xyosted was evaluated in a 52-week, open-label study in 150 adult males with hypogonadism. Xyosted was administered subcutaneously once weekly. The primary endpoint was the percentage of patients with a time-averaged serum total testosterone concentration (C_{avg}) over the 7-day dosing interval (0 to 168 hours) within the normal range at week 12.

    - Overall, 90% (135/150) of patients who received Xyosted had a serum total testosterone concentration $C_{avg(0\text{-}168h)}$ within the normal range at week 12.

- Xyosted carries a boxed warning for blood pressure increases.

- Xyosted is contraindicated in men with carcinoma of the breast or known or suspected carcinoma of the prostate; women who are pregnant; known hypersensitivity to Xyosted or its ingredients (testosterone enanthate and sesame oil); and men with hypogonadal conditions not associated with structural or genetic etiologies.

- Additional warnings and precautions of Xyosted include: polycythemia; cardiovascular risk; worsening of benign prostate hyperplasia; venous thromboembolism; abuse of testosterone and monitoring of serum testosterone concentrations; potential for adverse effects on spermatogenesis; hepatic adverse events; edema; gynecomastia; sleep apnea; lipids; hypercalcemia; decreased thyroxine-binding globulin; and risk of depression and suicide.

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- The most commonly reported adverse reactions (> 5%) with Xyosted use were hematocrit increase, hypertension, prostatic specific antigen increase, injection site bruising, and headache.

- The recommended starting dose of Xyosted is 75 mg, administered subcutaneously in the abdominal region once a week.

    — The dose should be adjusted based upon total testosterone trough concentrations (measured 7 days after most recent dose) obtained following 6 weeks of dosing and periodically thereafter.

- Antares Pharma plans to launch Xyosted by the end of 2018. Xyosted will be available as 0.5 mL of sterile solution in an autoinjector in three strengths: 50 mg/0.5 mL, 75 mg/0.5 mL, and 100 mg/0.5 mL.