Imvexxy™ (estradiol vaginal inserts) – New drug approval

- On May 30, 2018, TherapeuticsMD announced the FDA approval of Imvexxy (estradiol vaginal inserts), for the treatment of moderate to severe dyspareunia, a symptom of vulvar and vaginal atrophy (VVA), due to menopause.

- VVA is a component of genitourinary syndrome of menopause, which may include dryness, burning and irritation, sexual symptoms such as decreased lubrication, discomfort, and pain, and urinary symptoms such as urgency, dysuria, and recurrent urinary tract infections.

    - VVA affects an estimated 32 million postmenopausal women in the U.S.

- The safety and efficacy of Imvexxy were demonstrated in a placebo-controlled study enrolling 574 postmenopausal women randomized to Imvexxy 4 mcg, 10 mcg or placebo for 12 weeks. Co-primary efficacy variables included mean change from baseline to week 12 for the moderate to severe symptom of dyspareunia, percentage of vaginal superficial and percentage of vaginal parabasal cells on a vaginal smear, and vaginal pH.

    - Imvexxy 4 mcg and 10 mcg inserts were statistically superior to placebo in reducing the severity of moderate to severe dyspareunia (mean change from baseline: -1.52 for 4 mcg [$p = 0.0149$ vs. placebo], -1.69 for 10 mcg [$p < 0.0001$ vs. placebo], vs. -1.28 for placebo).
    - A statistically significant increase in the percentage of superficial cells and a statistically significant decrease in the percentage of parabasal cells on a vaginal smear were also demonstrated for Imvexxy 4 and 10 mcg inserts ($p < 0.0001$).
    - The mean reduction in vaginal pH was also statistically significant for Imvexxy 4 and 10 mcg inserts ($p < 0.0001$).

- Imvexxy carries a boxed warning for endometrial cancer, cardiovascular disorders, breast cancer and probable dementia.

- Imvexxy is contraindicated in patients with undiagnosed abnormal genital bleeding; known, suspected, or history of breast cancer; known or suspected estrogen-dependent neoplasia; active deep vein thrombosis, pulmonary embolism, or history of these conditions; active arterial thromboembolic disease (eg, stroke and myocardial infarction), or a history of these conditions; known anaphylactic reaction or angioedema with Imvexxy; known liver impairment or disease; and known protein C, protein S, or antithrombin deficiency, or other known thrombophilic disorders.

- Other warnings and precautions of Imvexxy include risks from systemic absorption, cardiovascular disorders, malignant neoplasms, probable dementia, gallbladder disease, hypercalcemia, visual abnormalities, addition of a progestin when a woman has not had a hysterectomy, elevated blood pressure, hypertriglyceridemia, hepatic impairment and/or past history of cholestatic jaundice, hypothyroidism, fluid retention, hypocalcemia, exacerbation of endometriosis, hereditary angioedema, exacerbation of other conditions, laboratory tests, and drug laboratory test interactions.

- The most common adverse reaction (≥ 3% and greater than placebo) of Imvexxy use was headache.

- The recommended dosage of Imvexxy is one vaginal insert administered intravaginally daily at approximately the same time for 2 weeks, followed by one insert twice weekly, every three to four days (eg, Monday and Thursday).

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- — Generally, women should be started at the 4 mcg dosage strength. Dosage adjustment should be guided by the clinical response.
- — Use of estrogen-alone, or in combination with a progestin, should be with the lowest effective dose and for the shortest duration consistent with treatment goals and risks for the individual woman.
- — Postmenopausal women should be re-evaluated periodically as clinically appropriate to determine if treatment is still necessary.

- TherapeuticsMD plans to launch Imvexxy in July of 2018. Imvexxy will be available as 4 mcg and 10 mcg vaginal inserts.