Oriahnn™ (elagolix/estradiol/norethindrone acetate; elagolix) – New drug approval

- On May 29, 2020, the FDA announced the approval of AbbVie's Oriahnn (elagolix/estradiol/norethindrone acetate; elagolix), for the management of heavy menstrual bleeding associated with uterine leiomyomas (fibroids) in premenopausal women.
    - The use of Oriahnn should be limited to 24 months due to the risk of continued bone loss, which may not be reversible.
- Fibroids are benign muscle tumors of the uterus that can cause heavy menstrual bleeding, pain, bowel or bladder problems and infertility. Some women may not experience any symptoms, but many do, including heavy bleeding with periods. Fibroids can occur at any age but are most common in women 35 to 49 years of age. They typically resolve after menopause but are a leading reason for hysterectomy in the U.S. when they cause severe symptoms.
- Oriahnn is a co-packaged product containing elagolix/estradiol/norethindrone acetate capsules and elagolix capsules.
    - Elagolix is also available as a single-ingredient product (Orilissa®) for the management of moderate to severe pain associated with endometriosis.
- The efficacy of Oriahnn was established in two randomized, double-blind, placebo-controlled studies in 790 premenopausal women with heavy menstrual bleeding associated with uterine fibroids. Patients received Oriahnn or placebo for 6 months. The primary endpoint in both studies was the proportion of responders, defined as women who achieved both 1) menstrual blood loss (MBL) volume less than 80 mL at the final month and 2) 50% or greater reduction in MBL volume from baseline to the final month.
    - In study 1, the proportion of responders was 68.5% with Oriahnn vs. 8.7% with placebo (difference: 59.8; 95% CI: 51.1, 68.5; $p < 0.001$).
    - In study 2, the proportion of responders was 76.5% with Oriahnn vs. 10.5% with placebo (difference: 66.0; 95% CI: 57.1, 75.0; $p < 0.001$).
- Oriahnn carries a boxed warning for thromboembolic disorders and vascular events.
- Oriahnn is contraindicated in women:
    - With a high risk of arterial, venous thrombotic, or thromboembolic disorders
    - Who are pregnant
    - With known osteoporosis because of the risk of further bone loss
    - With current or history of breast cancer or other hormonally-sensitive malignancies, and with increased risk for hormonally-sensitive malignancies
    - With known hepatic impairment or disease
    - With undiagnosed abnormal uterine bleeding
    - With known anaphylactic reaction, angioedema, or hypersensitivity to Oriahnn or any of its components
    - Taking inhibitors of organic anion transporting polypeptide (OATP)1B1 that are known or expected to significantly increase elagolix plasma concentrations.
- Additional warnings and precautions for Oriahnn include bone loss; hormonally-sensitive malignancies; suicidal ideation, suicidal behavior, and exacerbation of mood disorders; hepatic impairment and transaminase elevations; elevated blood pressure; gallbladder disease or history of

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cholestatic jaundice; change in menstrual bleeding pattern and reduced ability to recognize pregnancy; effects on carbohydrate and lipid metabolism; alopecia; effect of other laboratory results; and risk of allergic reactions due to the inactive ingredients (FD&C Yellow No. 5).

- The most common adverse reactions (> 5%) with Oriahnn use were hot flushes, headache, fatigue, and metrorrhagia.

- The recommended oral dose of Oriahnn is one elagolix 300 mg, estradiol 1 mg, and norethindrone acetate 0.5 mg capsule in the morning, and one elagolix 300 mg capsule in the evening.

    — The recommended duration of treatment with Oriahnn is 24 months.
    — Pregnancy should be excluded before starting Oriahnn or Oriahnn should be started within 7 days from the onset of menses.

- AbbVie plans to launch Oriahnn by the end of June 2020. Oriahnn will be available as a co-packaged product containing elagolix 300 mg, estradiol 1 mg, norethindrone acetate 0.5 mg capsules and elagolix 300 mg capsules.