Myfembree® (relugolix/estradiol/norethindrone acetate) – New drug approval

- On May 26, 2021, Myovant Sciences and Pfizer announced the FDA approval of Myfembree (relugolix/estradiol/norethindrone acetate), for the management of heavy menstrual bleeding associated with uterine leiomyomas (fibroids) in premenopausal women.
    - Use of Myfembree should be limited to 24 months due to the risk of continued bone loss which may not be reversible.
- Uterine fibroids are noncancerous tumors that develop in or on the muscular walls of the uterus. While they are benign tumors, uterine fibroids can cause debilitating symptoms such as heavy menstrual bleeding, pain, increased abdominal girth and bloating, urinary frequency or retention, constipation, pregnancy loss, and, in some cases, infertility.

.

    - An estimated 5 million women in the U.S. suffer from symptoms of uterine fibroids.
- Myfembree contains relugolix, which reduces the amount of estrogen (and other hormones) produced by ovaries, estradiol (an estrogen) which may reduce the risk of bone loss, and norethindrone acetate (a progestin) which is necessary when women with a uterus take estrogen.
- The efficacy of Myfembree was established in two replicate, 24-week, randomized, double-blind, placebo-controlled studies in a total of 768 premenopausal women with heavy menstrual bleeding associated with uterine fibroids. Patients were randomized to receive Myfembree for 24 weeks, placebo for 24 weeks, or relugolix monotherapy for 12 weeks followed by Myfembree for 12 weeks. The primary endpoint was the proportion of women in the Myfembree group compared with women in the placebo group, who achieved menstrual blood loss (MBL) volume of < 80 mL and ≥ 50% reduction from baseline MBL volume over the last 35 days of treatment.
    - In study 1, 72.1% of women treated with Myfembree met the primary endpoint vs. 16.8% with placebo (difference of 55.3, 95% CI: 44.2, 65.6; $p < 0.0001$).
    - In study 2, 71.2% of women treated with Myfembree met the primary endpoint vs. 14.7% with placebo (difference of 56.5, 95% CI: 46.6, 66.5; $p < 0.0001$).
- Myfembree carries a boxed warning for thromboembolic disorders and vascular events.
- Myfembree 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 hormone-sensitive malignancies, and with increased risk for hormone-sensitive malignancies
    - With known hepatic impairment or disease
    - With undiagnosed abnormal uterine bleeding
    - With known anaphylactic reaction, angioedema, or hypersensitivity to Myfembree or any of its components.
- Additional warnings and precautions for Myfembree include bone loss; hormone-sensitive malignancies; depression, mood disorders, and suicidal ideation; hepatic impairment and transaminase elevations; gallbladder disease or history of cholestatic jaundice; elevated blood pressure; change in menstrual bleeding pattern and reduced ability to recognize pregnancy; risk of

Continued . . .

early pregnancy loss; uterine fibroid prolapse or expulsion; alopecia; effects on carbohydrate and lipid metabolism; effect on other laboratory results; and hypersensitivity reactions.

- The most common adverse reactions (≥ 3%) with Myfembree use were hot flush, hyperhidrosis or night sweats, uterine bleeding, alopecia, and decreased libido.

- The recommended dose of Myfembree is one tablet orally once daily. Myfembree should be started as early as possible after the onset of menses but no later than seven days after menses has started.

    — The recommended total duration of treatment with Myfembree is 24 months.
    — Prior to initiation of Myfembree, pregnancy should be excluded, and hormonal contraceptives should be discontinued.

- Myovant Sciences and Pfizer plan to launch Myfembree in June 2021. Myfembree will be available as a fixed-dose combination tablet containing relugolix 40 mg, estradiol 1 mg and norethindrone acetate 0.5 mg.