Myfembree® (relugolix/estradiol/norethindrone acetate) – New indication

- On August 5, 2022, Pfizer announced the FDA approval of Myfembree (relugolix/estradiol/norethindrone acetate), for premenopausal women for the management of moderate to severe pain associated with endometriosis.
    - Use of Myfembree should be limited to 24 months due to the risk of continued bone loss which may not be reversible.
- Myfembree is also approved for premenopausal women for the management of heavy menstrual bleeding associated with uterine leiomyomas (fibroids).
- Endometriosis is a condition in which tissue similar to the uterine lining is found outside of the uterine cavity, which often causes disruptive symptoms like painful periods, fatigue, pain in the lower back and abdomen, heavy menstrual bleeding, and even painful or difficult sexual intercourse.
    - In the U.S., there are approximately 7.5 million premenopausal women with endometriosis and approximately 75-80% of them are symptomatic.
- The approval of Myfembree for the new indication was based on a two randomized, double-blind, placebo-controlled studies in pre-menopausal women with moderate to severe pain associated with endometriosis. A total of 829 patients received 24 weeks of once daily Myfembree or placebo. The first co-primary endpoint was a responder analysis where a responder was defined as a woman who achieved a reduction from baseline in dysmenorrhea (DYS) numerical rating scale (NRS) of at least 2.8 points over the last 35 days of treatment, without an increase in analgesic use (nonsteroidal anti-inflammatory drug [NSAID] or opioid). The second co-primary endpoint was a responder analysis where a responder was defined as a woman who achieved a reduction from baseline in non-menstrual pelvic pain (NMPP) NRS score of at least 2.1 points over the last 35 days of treatment, without an increase in analgesic use (NSAID or opioid) for pain associated with endometriosis.
    - In study 1, 74.5% of Myfembree vs. 26.9% of placebo patients were DYS responders (difference from placebo 47.6%; 95% CI: 39.3, 56.0; $p \leq 0.0001$). NMPP responders were seen for 58.5% of Myfembree vs. 39.6% of placebo patients (difference from placebo 18.9%; 95% CI: 9.5, 28.2; $p \leq 0.0001$).
    - In study 2, 75.1% of Myfembree vs. 30.5% of placebo patients were DYS responders (difference from placebo 44.6%; 95% CI: 35.9, 53.3; $p \leq 0.0001$). NMPP responders were seen for 65.9% of Myfembree vs. 42.5% of placebo patients (difference from placebo 23.4%; 95% CI: 13.9, 32.8; $p \leq 0.0001$).
- Myfembree carries a boxed warning for thromboembolic disorders and vascular events.
- The most common adverse reactions (≥ 3%) with Myfembree use for endometriosis were headache, vasomotor symptoms, mood disorders, abnormal uterine bleeding, nausea, toothache, back pain, decreased sexual desire and arousal, arthralgia, fatigue, and dizziness.

- The recommended dose of Myfembree for the treatment of both indications is one tablet orally once daily at approximately the same time, with or without food.
    - 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.