# Can a drug FDA approved for endometriosis become a mainstay for nonsurgical treatment of HMB in women with fibroids?

**Elagolix** is a GnRH antagonist that is approved in a 2-dose schedule for treatment of endometriosis. It is given orally and, as expected and clearly shown by the investigators in two identical, double-blind, randomized, placebo-controlled phase 3 trials, **significantly reduces heavy menstrual bleeding (HMB) in women with fibroids**. Because previous studies showed an increase in vasomotor symptoms and some negative impact on bone metabolism with elagolix, these studies, in addition to a placebo arm, included one arm with elagolix alone and one arm with "add-back therapy" that utilized estradiol and norethindrone acetate. The add-back therapy attenuated the hypoestrogenic effects of elagolix.

**FAST TRACK**

*Elagolix plus add-back therapy will allow for greater patient acceptance of the GnRH antagonist*

*Schlaff WD, Ackerman RT, Al-Hendy A, et al. Elagolix for heavy menstrual bleeding in women with uterine fibroids. N Engl J Med. 2020;382:328-340.*

**EXPERT COMMENTARY**

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Any women's health care provider is extremely aware of how common uterine fibroids (leiomyomas) are in reproductive-aged women. Bleeding associated with such fibroids is a common source of medical morbidity and reduced quality of life for many patients. The mainstay treatment approach for such patients has been surgical, which over time has become minimally invasive. Finding a nonsurgical treatment for patients with fibroid-associated HMB is of huge importance. The recent failure of the selective progesterone receptor modulator ulipristal acetate to be approved by the US Food and Drug Administration (FDA) was a significant setback to finding an excellent option for medical management. A gonadotropin-releasing hormone (GnRH) antagonist like elagolix could become an incredibly important "arrow in the quiver" of women's health clinicians.

*The author reports being an advisory board member for AbbVie Inc.*

## Details about elagolix

As mentioned, elagolix was FDA approved in 2-dose regimens for the treatment of dysmenorrhea, nonmenstrual pelvic pain, and dyspareunia associated with endometriosis. One would expect that such a GnRH antagonist would reduce or eliminate HMB in patients with fibroids, although formal study had never been undertaken. Previous studies of elagolix had shown the most common adverse reaction to be vasomotor symptoms—hot flashes and night sweats. In addition, the drug shows a dose-dependent decrease in bone mineral density (BMD), although its effect on long-term bone health and future fracture risk is unknown.[1]

**Study specifics.** The current study by Schlaff and colleagues was performed including 3 arms: a placebo arm, an elagolix 300 mg twice daily arm, and a third arm that received elagolix 300 mg twice daily and hormonal "add-back" therapy in the form of estradiol 1 mg and norethindrone acetate 0.5 mg daily. The authors actually report on two phase 3 six-month trials that were identical, double-blind, and randomized in nature. Both trials involved approximately 400 women. About 70% of the study participants overall were black, and the average age was approximately 42 years (range, 18 to 51). At baseline, BMD scores were mostly in the normal range. HMB for inclusion was defined as a volume of more than 80 mL per month.

The primary end point was menstrual blood loss volume less than 80 mL in the final month and at least a 50% reduction in menstrual blood loss from baseline to the final month. In the placebo group, only 9% and 10%, respectively, met these criteria.

**Results.** In the first study group, 84% of those receiving elagolix alone achieved the primary end point, while the group that received elagolix plus add-back therapy had 69% success.

### WHAT THIS EVIDENCE MEANS FOR PRACTICE

Elagolix is currently available (albeit not in the dosing regimen used in the current study or with built-in add-back therapy), and these study results offer an encouraging nonsurgical approach to HMB. The addition of add-back therapy to this oral GnRH antagonist will allow greater patient acceptance from a quality-of-life point of view because of diminution of vasomotor symptoms while maintaining BMD.

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In the second study, both the elagolix group and the add-back group showed that 77% of patients met the primary end point criteria.

The incidences of hot flashes in the elagolix-alone groups were 64% and 43%, respectively, while with add-back therapy, they were 20% in both trials. In the placebo groups, 9% and 4% of participants reported hot flashes. At 6 months, the elagolix-only groups in both trials lost more BMD than the placebo groups, while BMD loss in both add-back groups was not statistically significant from the placebo groups.

## Study strengths

Schlaff and colleagues conducted a very well-designed study. The two phase 3 clinical trials in preparation for drug approval were thorough and well reported. The authors are to be commended for including nearly 70% black women as study participants, since this is a racial group known to be affected by HMB resulting from fibroids.

Another strength was the addition of add-back therapy to the doses of elagolix. Concerns about bone loss from a health perspective and vasomotor symptoms from a quality-of-life perspective are not insignificant with elagolix-alone treatment, and proof that add-back therapy significantly diminishes or attenuates the efficacy of this entity is extremely important. ●

**FAST TRACK**

*Add-back therapy reduced the incidences of hot flashes from 64% and 43% to 20% and 20%, respectively*


**Reference**

1. Taylor HS, Giudice LC, Lessey BA, et al. Treatment of endometriosis-associated pain with elagolix, an oral GnRH antagonist. *N Engl J Med.* 2017;377:28-40.