International Journal of Reproduction, Contraception, Obstetrics and Gynecology
Khan F. Int J Reprod Contracept Obstet Gynecol. 2025 Aug;14(8):2836-2839
www.ijrcog.org
pISSN 2320-1770 | eISSN 2320-1789

DOI: https://dx.doi.org/10.18203/2320-1770.ijrcog20252375

New Drug Update

Elagolix - a novel drug for management of endometriosis and uterine fibroids

Farha Khan*

Department of Obstetrics and Gynecology, St. Joseph' s General Hospital, Guntur, Andhra Pradesh, India

Received: 16 June 2025
Accepted: 14 July 2025

***Correspondence:**
Dr. Farha Khan,
E-mail: docfarhakhan@gmail.com

ABSTRACT

Endometriosis and uterine fibroids are two hormone-dependent gynecological disorders that significantly impact women's health impairing their quality of life. Traditional medical therapies used to control symptoms have side effects such as initial symptom flare and hypoestrogenic complications which limit their use. Elagolix is an oral non-peptide gonadotropin releasing hormone receptor (GnRH) antagonist. It is a new therapeutic approach which acts by directly and reversibly suppressing pituitary gonadotropin secretion. It acts by binding competitively to GnRH receptors in pituitary gland which leads to a rapid dose dependent suppression of LH and FSH leading to reduction in production of ovarian sex hormones (estrogen and progesterone). Alternative medications like GnRH agonists cause a transient hormone flare which is complete and long lasting before down regulation. Elagolix immediately inhibits GnRH receptor signaling, avoiding this flare phenomenon. The degree of hormonal suppression can be adjusted by dosing, allowing partial or near-complete suppression of estradiol levels, which is beneficial for tailoring therapy to minimize hypoestrogenic side effects. Elagolix, offers a safe and effective approach in the management of uterine fibroids and endometriosis. Clinical trials have demonstrated that Elagolix significantly reduces fibroid-associated heavy menstrual bleeding and alleviates endometriosis-related pelvic pain. Its rapid onset of action and adjustable dosing regimen allow individualized therapy aimed at balancing efficacy and minimizing hypoestrogenic adverse effects such as bone mineral density loss and vasomotor symptoms.

Keywords: Elagolix, Endometriosis, Fibroid, GnRH antagonist, Estrogen, Progesterone

INTRODUCTION

Endometriosis and uterine fibroids are two hormone-dependent gynecological disorders that significantly impact women's health impairing their quality of life. Traditional medical therapies used to control symptoms have side effects such as initial symptom flare and hypoestrogenic complications which limit their use. Elagolix is an oral nonpeptide gonadotropin releasing hormone receptor (GnRH) antagonist. It is a new therapeutic approach which acts by directly and reversibly suppressing pituitary gonadotropin secretion. It causes reversible suppression of gonadotropins. Elagolix is a medication used primarily for managing conditions associated with hormonal imbalances, particularly those driven by hormone estrogen. It works by suppressing the production of ovarian hormones like estrogen and progesterone.[1] These effects occur within 24 hours after the initiation of treatment and can be readily reversed by discontinuation of the drug, owing to its short half-life.[2]

DRUG

It is a small molecule, second generation GnRH receptor antagonist that is active orally. It acts by binding competitively to GnRH receptors in pituitary gland which leads to a rapid dose dependent suppression of luteinizing hormone (LH) and follicle-stimulating hormone (FSH) leading to reduction in production of ovarian sex hormones (estrogen and progesterone).[3] It is used for the treating hormone dependent proliferative diseases like uterine fibroids and endometriosis.

Elagolix has been approved by the US FDA in July 2018 for managing endometriosis associated moderate to severe pain in dose of 150-200 mg. It is the first oral medication used for managing pain due to endometriosis. It should be used in minimum dose and for minimum duration to decrease bone loss.[4]

MECHANISM OF ACTION

Elagolix competitively binds to GnRH receptors in the pituitary gland. It blocks GnRH signaling thus suppressing FSH, LH and therefore minimizing estrogen and progesterone.[4,5]

Elagolix gets rapidly absorbed in approximately 1-2 hours after oral administration and cleared in 4-6 hours through liver. It facilitates expeditious regulation of drug levels with the goal of attaining the most comparative level of hormone suppression.[6] It is metabolized by cytochrome P450 enzymes.[7]

Alternative medications like GnRH agonists cause a transient hormone flare which is complete and long lasting before down regulation. Elagolix immediately inhibits GnRH receptor signaling, avoiding this flare phenomenon. The degree of hormonal suppression can be adjusted by dosing, allowing partial or near-complete suppression of estradiol levels, which is beneficial for tailoring therapy to minimize hypoestrogenic side effects.[8]

ROLE IN ENDOMETRIOSIS

Endometriosis is a condition where tissues similar to endometrium grow outside the uterus. There is estrogen induced inflammation which leads to severe dysmenorrhea, chronic pelvic pain, infertility, dyspareunia, bowel and bladder symptoms like constipation and painful urination.[9] Endometriosis associated pain can affect a woman's quality of life.

Treatment options are hormonal therapies that suppress ovulation and menstruation, NSAIDS, and surgical suppression. Hormonal suppression is attained by using estrogen progesterone contraceptives, progesterone only medication and GnRH agonists.[9] According to "estrogen threshold hypothesis" absolute suppression of estrogen is not necessary for treatment of endometriosis associated pain. On the contrary, estrogen concentration can be kept at a level that it will not cause pain but decreases hypoestrogenic effects. Injectable GnRH agonists reduce estrogen hormone levels but at the same time they reduce bone mineral density and produce vasomotor symptoms as well, due to which long term use of such agents without hormone replacement is not possible.

Elaris EM-I and EM-II were phase III, randomized, double-blind, placebo-controlled, multicenter clinical trial done over a period of 6 months, for endometriosis associated pain.[10] They concluded that doses of 150 mg once a day and 200 mg twice a day, both dosing regimens significantly reduced dysmenorrhea and pelvic pain vs placebo, with high dose showing stronger effects. Elagolix high-dose is FDA-approved for dysmenorrhea symptoms and non-menstrual pelvic pain in women with endometriosis and moderate to severe endometriosis-associated pain for up to 6 months; low-dose may be used longer (16–24 months) due to milder bone impact.[6,7,10]

It is associated with hypoestrogenic effects such as decreased bone mineral density and vasomotor symptoms when administered alone, that are consistent with its mechanism of action.[5]

ROLE IN FIBROID MANAGEMENT

Uterine fibroids are most common benign tumors of the female reproductive tract. They arise from the smooth muscle layer of uterus. Women when symptomatic have heavy prolonged bleeding leading to anemia, pelvic pain and pressure. Estrogen and progesterone are believed to be causative factors.[11]

Definitive treatment is hysterectomy. Other treatment options are tranexamic acid, NSAIDS, Hormonal medications like combined oral contraceptives, progestins, GnRH agonist, selective progesterone receptor modulators, interventional therapies like uterine-artery embolization and magnetic resonance–guided focused ultrasonography. Injectable GnRH agonists produce long term gonadal suppression leading to hypoestrogenic effects. Therefore, Elagolix, which is safe, effective and produces rapid reversible suppression of ovarian hormones, is a useful alternative.[8]

Elagolix in combination with estradiol and norethindrone acetate, was approved by US FDA in May 2020 for treatment of fibroid related HMB up to 24 months of use.[6]

It is available as two co-packaged capsules: Elagolix 300 mg plus estradiol 1 mg plus norethindrone 0.5 mg to be taken in the morning, and Elagolix 300 mg alone to be taken in evening.

Elagolix along with add back therapy decreased reduction in bone mineral density as compared to Elagolix alone. Combination offers an effective alternative to surgery for many women, particularly those seeking fertility preservation or wishing to avoid invasive procedures.

Phase III randomized, double-blind, placebo-controlled trials (e.g., Elaris UF-1 and UF-2) evaluated elagolix 300 mg twice daily + add-back therapy (estradiol 1 mg + norethindrone acetate 0.5 mg daily) for heavy menstrual bleeding due to uterine fibroids to reduce heavy menstrual bleeding and fibroid volume and found that bleeding was significantly reduced and hemoglobin was improved. This combination offers an effective alternative to surgery for many women, particularly those seeking fertility preservation or wishing to avoid invasive procedures.[1]

BENEFITS

It improves fibroid related HMB, useful for patients with contraindication to add back therapy, achieved primary end point in 77-84% after 6 months and 89% after 13 months of therapy, and fibroid volume reduced by 40-50% after 6 months and an even greater reduction was noted after 12 months of therapy.

ADVERSE EFFECTS

The adverse effects are tabulated in Table 1.[3]

ADD-BACK THERAPY

To reduce side effects, especially bone loss and hot flushes, add-back therapy of low-dose estrogen + progestin is recommended for: use more than 6 months, and high-dose regimens (e.g., 200 mg BID or 300 mg BID for fibroids).

CONTRAINDICATION

Elagolix is generally a well-tolerated drug. The following are the contraindications given in Table 2.

Table 1: Adverse effects.

System and side effect	Cause
Vasomotor	
Hot flushes	Estrogen suppression
Night sweats	
Neurologic	
Headache	Hormonal shifts
Insomnia	Estrogen reduction or mood effect
Psychiatric	
Mood changes, irritability	CNS hormone effects
Depression/suicidal ideation	Rare, monitor high-risk patients
Gastrointestinal	
Nausea	Mild and transient
Reproductive	
Amenorrhea	Suppression of ovulation/endometrial thinning
Irregular bleeding or spotting	Hormonal imbalance
Decreased libido	Estrogen suppression
Musculoskeletal	
Decrease in bone mineral density (BMD)	Dose- and duration-related
Metabolic/lipid	
↑ Total cholesterol, LDL, triglycerides	Mild increases
Hepatic	
Elevated liver enzymes (ALT/AST)	Rare, usually asymptomatic

Table 2: Absolute and relative contraindications.

Condition	Reason
Absolute contraindications	
Pregnancy	Risk of fetal harm due to hormonal suppression
Known or suspected pregnancy	Elagolix suppresses ovulation and is teratogenic in animal studies
Severe hepatic impairment (Child-Pugh C)	Impaired drug metabolism; Elagolix is hepatically metabolized
Concomitant use of strong OATP1B1 inhibitors (e.g., gemfibrozil, cyclosporine)	Can significantly increase Elagolix blood levels, raising toxicity risk
Relative contraindications	
Moderate hepatic impairment	Use lowest effective dose; increased drug exposure
History of severe depression or suicidal ideation	Mood changes are a known side effect of Elagolix
Osteoporosis or low bone mineral density	Elagolix can lead to further BMD loss
Undiagnosed abnormal uterine bleeding	Must rule out malignancy or other causes before starting treatment

PREREQUISITES BEFORE STARTING ELAGOLIX

Prerequisites before starting Elagolix include: it excludes pregnancy, assess liver function, assess bone mineral density (BMD), review of psychiatric history, rule out other causes of abnormal bleeding, check for drug interactions, especially with strong OATP1B1 inhibitors (e.g., gemfibrozil), efficacy of Elagolix may be reduced by estrogen-containing contraceptives, inform patient about possible side effects: hot flushes, mood changes, decreased bone density, and plan for regular monitoring during treatment (liver function, mood, BMD if applicable)

CONCLUSION

Elagolix, offers a safe and effective approach in the management of uterine fibroids and endometriosis. Clinical trials have demonstrated that Elagolix significantly reduces fibroid-associated heavy menstrual bleeding and alleviates endometriosis-related pelvic pain. Its rapid onset of action and adjustable dosing regimen allow individualized therapy aimed at balancing efficacy and minimizing hypoestrogenic adverse effects such as bone mineral density loss and vasomotor symptoms. The introduction of Elagolix has expanded the non-surgical therapeutic landscape. Overall, Elagolix represents a valuable addition to the armamentarium for managing hormone-dependent gynecologic disorders, improving patient outcomes with an oral, reversible mechanism of action.

Funding: No funding sources
Conflict of interest: None declared
Ethical approval: Not required

REFERENCES

1. Schlaff WD, Ackerman RT, Al-Hendy A, Archer DF, Barnhart KT, Bradley LD, et al. Elagolix for heavy menstrual bleeding in women with uterine fibroids. N Engl J Med. 2020;382(4):328-40.
2. Ng J, Chwalisz K, Carter DC, Klein CE. Dose-dependent suppression of gonadotropins and ovarian hormones by Elagolix in healthy premenopausal women. J Clin Endocrinol Metab. 2017;102:1683-91.
3. Lamb YN. Elagolix: First Global Approval. Drugs. 2018;78(14):1501-8.
4. AbbVie Inc. Prescribing information for OrilissaTM (Elagolix) tablets, for oral use. 2018. Available at: http://www.accessdata.fda.gov/. Accessed on 14 April 2025.
5. Struthers RS, Nicholls AJ, Grundy J, Chen T, Jimenez R, Yen SS, et al. Suppression of gonadotropins and estradiol in premenopausal women by oral administration of the nonpeptide gonadotropin-releasing hormone antagonist Elagolix. J Clin Endocrinol Metab. 2009;94(2):545-51.
6. Donnez J, Dolmans MM. Uterine fibroid management: from the present to the future. Hum Reprod Update. 2016;22:665-86.
7. Allaire C, Bedaiwy MA, Yong PJ. Diagnosis and management of endometriosis. CMAJ. 2023;195(10):E363-71.
8. Gurusamy KS, Vaughan J, Fraser IS, Best LM, Richards T. Medical therapies for uterine fibroids — a systematic review and network meta-analysis of randomised controlled trials. PLoS One. 2016;11(2):e0149631.
9. Ali M, Sara AR, Al Hendy A. Elagolix in the treatment of heavy menstrual bleeding associated with uterine fibroids in premenopausal women. Expert Rev Clin Pharmacol. 2021;14(4):427-37.
10. Taylor HS, Giudice LC, Lessey BA, Abrao MS, Kotarski J, Archer DF, et al. Treatment of endometriosis-associated pain with Elagolix, an oral GnRH antagonist. N Engl J Med. 2017;377(1):28-40.
11. Wegienka G, Baird DD, Hertz-Picciotto I, Harlow SD, Steege JF, Hill MC, et al. Self-reported heavy bleeding associated with uterine leiomyomata. Obstet Gynecol. 2003;101:431-7.

Cite this article as: Khan F. Elagolix - a novel drug for management of endometriosis and uterine fibroids. Int J Reprod Contracept Obstet Gynecol 2025;14:2836-9.