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Review Article

Elagolix as an oral substitute for injectable GnRH antagonists in IVF: a review and recent developments

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ABSTRACT

During controlled ovarian stimulation for in vitro fertilization (IVF), a luteinizing hormone (LH) surge can trigger the release of a premature oocyte before scheduled oocyte retrieval. Suppressing this surge is critical in order to achieve a successful round of IVF. Gonadotropin Releasing Hormone (GnRH) antagonists bind to the GnRH receptor in the pituitary gland and prevent endogenous GnRH from stimulating LH release. This is a rapid and reversible blockade used by clinicians to enable successful IVF outcomes. Traditionally, injectable antagonist agents like ganirelix/cetrorelix have been popular but are reported as painful and expensive. Recently, new literature regarding the use of elagolix, an oral non-peptide GnRH antagonist, as a potentially less invasive and cheaper alternative has been published. This review critically appraises the present evidence on elagolix as an oral alternative for LH surge suppression in IVF. A literature search was conducted using PubMed as the primary database, supplemented by Google Scholar to identify additional relevant sources. Search terms included combinations of phrases like “elagolix,” “IVF,” “GnRH antagonist,” “ovarian stimulation,” “ganirelix,” “cetrorelix,” “HPO axis.” Studies were included if they reported original data or reviewed existing evidence on GnRH antagonist use in the context of ovarian stimulation for IVF. Studies examining elagolix’s use in the management of endometriosis-associated pain were also included. Reference lists of identified studies were further reviewed to pull additional relevant information. This search yielded additional studies that met the inclusion criteria. Across the available studies, elagolix demonstrates comparable LH suppression to injectable GnRH antagonists, offering a reduced injection and per-cycle cost burden for IVF patients. However, this evidence is limited to a small number of majorly retrospective and a few prospective cohort studies. No randomized controlled trials have been published to date. Dosage and safety data relevant to elagolix’s use in IVF also remains scarce. According to our analysis, elagolix shows promise, but larger clinical trials and prospective studies are needed to solidify elagolix as a cost-effective and hypoalgesic alternative.

Keywords: Elagolix, Oral GnRH antagonist, In vitro fertilization, LH surge suppression

INTRODUCTION

The success of in vitro fertilization depends on precise control over the timing of ovulation and oocyte retrieval. A premature LH surge can disrupt this process by triggering ovulation, risking oocyte loss and complete cycle cancellation. To prevent this, GnRH antagonists like ganirelix and cetrorelix are used, which require daily subcutaneous injections and are associated with high costs

and pain. More recently, elagolix, an orally administered non-peptide GnRH antagonist originally approved for endometriosis related pain management, has emerged as a potential alternative.

This review evaluates the current literature on elagolix’s safety, efficacy and patient-centered advantages in the context of ovarian stimulation for IVF.

BIOLOGY OF LH URGE AND SUPPRESSION

IVF relies on controlled ovarian stimulation to facilitate the simultaneous growth and development of multiple ovarian follicles. Since each growing follicle produces estradiol (E2), the combined serum E2 levels rise faster and higher than in a natural cycle. Sustained high E2 levels exert positive feedback to the hypothalamus and pituitary gland, triggering an LH surge.^{1,2} This initiates a cascade of intracellular cell-signalling processes within the follicle, which leads to the resumption of meiosis and final oocyte maturation.³ If ovulation takes place before the scheduled retrieval procedure, the oocytes are lost and the IVF cycle may need to be cancelled.⁴ A premature LH surge is associated with significantly lower pregnancy rates (8.4% vs. 28% in cycles without a surge), along with fewer oocytes retrieved and reduced fertilisation rates.⁵

TRADITIONAL APPROACH TO SUPPRESS LH SURGE

To prevent a premature LH surge, clinicians have been using GnRH antagonists which occupy GnRH binding sites on the pituitary gonadotrope cells via competitive inhibition. This mechanism leads to the suppression of pituitary gonadotropin and blocks the LH surge. GnRH antagonists are reversible and their discontinuation leads to rapid revival of the HPO axis.⁶

The most widely used GnRH antagonists, ganirelix and cetrorelix, are typically administered daily via subcutaneous injection. The first therapeutic application of GnRH antagonists in IVF was demonstrated in 1994 when cetrorelix was shown to suppress endogenous LH levels during ovarian stimulation. This marked a shift from longer GnRH agonist-based protocols that had previously been a practice.⁷

Subsequently, ganirelix was established as an effective alternative through a double blind, randomized, dose finding study which determined the optimal dose required to prevent a premature LH surge in women undergoing ovarian stimulation with recombinant Follicle Stimulating Hormone.⁸ Together, ganirelix and cetrorelix became the standard antagonist treatments used in IVF. However, patients and clinicians have raised concerns about these injectables as they can be quite painful and expensive with a per unit average cost between \$125-175.⁹

ELAGOLIX PHARMACOLOGY

In response to these challenges, scientists have explored elagolix, an orally administered non-peptide GnRH antagonist. It is characterized by a half-life of between 4-6 hours and a rapid absorption rate which allows for flexible dosing.

Elagolix was originally approved by the FDA for the management of endometriosis-associated pain in July 2018.¹⁰ The approval was based on two pivotal Phase 3

randomized controlled trials, which established elagolix's efficacy on approved doses of 150 mg once daily or 200 mg twice daily.¹¹ Similar to ganirelix and cetrorelix, elagolix competitively binds to the GnRH receptor to block LH release. However, its non-peptide structure allows oral ingestion, unlike peptide based injectable antagonists.¹²

In a 3-month randomized, dose finding study in 205 healthy ovulatory women, elagolix doses ranging from 100-300 mg showed ovulation suppression in a dose-dependent manner.¹³ However, the 300 mg dose (twice daily) resulted in ovulation in 27% of the women, indicating failure of suppression even at a high dosing. This dose dependent effect largely extends to hormonal suppression, with low doses of elagolix leading to partial estradiol suppression and higher doses achieving greater suppression.¹⁴ Because of its established approval history and an existing human and pharmacokinetic safety profile, elagolix has emerged as a candidate in the IVF context.

CLINICAL EVIDENCE FOR LH SURGE SUPPRESSION

Till date, evidence on elagolix's efficacy in the context of LH suppression during IVF is limited to a small number of retrospective studies and only a few prospective counterparts. No randomized controlled trials have been published as of date.

Mouanness and Merhi conducted a retrospective study on a group of 269 patients undergoing IVF.⁹ 50 mg of oral elagolix administered every other day was compared with daily injections of ganirelix/cetrorelix. LH and estradiol levels were found to be comparable between the two groups with no significant difference. IVF outcomes like the number of retrieved oocytes, matured oocytes, fertilization rate were also similar. A substantial cost difference was noted between the two groups, with elagolix priced at \$19 per pill. Similarly, Soliman et al compared elagolix with ganirelix in a retrospective study of 194 patients struggling with infertility.⁴ Rates for fresh embryo transfers, biochemical pregnancy, implantation and cycle cancellation did not differ significantly. This suggests that elagolix might have similar reproductive outcomes to standard injectable antagonists.

A prospective study by Boniface et al examined 75 oocyte donors, weighing 200 mg elagolix with 250 mcg ganirelix and used historical donors as a control.¹⁵ They reported 4.2 fewer injections per cycle and an average savings of \$289.10 per cycle. Taken together, these studies suggest that elagolix may achieve clinical outcomes comparable to injectable antagonists. However, all available evidence is limited to relatively small sample sizes and an inadequate number of prospective studies. Grisendi et al conducted an editorial review of the use of GnRH antagonists to inhibit LH surge in IVF and similarly concluded that current evidence, while promising, remains preliminary and

specifically noted the absence of large-scale randomized trials evaluating elagolix in this context.¹⁶

BROADER GYNAECOLOGICAL USE

Beyond its emerging role in IVF, elagolix has an established clinical history in the management of pain related to endometriosis. Related trials demonstrated significant improvements in dysmenorrhea and non-menstrual pelvic pain at both the approved doses, 150 mg one daily or 200 mg twice.¹¹ Additionally, elagolix use has been associated with significant dose-dependent improvements in health-related quality of life across domains like social and emotional well-being.¹⁷

Extension studies of these trials concluded that pain relief and safety profile were consistent through 12 months of continued treatment. Long term use however, was associated with bone mineral density loss.¹⁸ Elagolix in combination with estradiol/norethindrone acetate was also approved for the treatment of uterine fibroid related heavy bleeding for up to 24 months.¹⁹

SAFETY AND TOLERABILITY

As noted previously, extended use of elagolix has been associated with dose-dependent bone mineral density loss¹⁸, an important consideration when evaluating the safety profile for IVF cycles. Accordingly, elagolix carries boxed contraindications for use in pregnancy, which can result in osteoporosis and severe hepatic impairment, per its FDA prescribing guidelines.²⁰

The most common reported side effects include increased lipid levels, headaches, hot flashes and nausea as a result of the hypoestrogenic state induced by GnRH antagonists.¹¹ Safety reporting specific to elagolix's use in ovarian stimulation for IVF remains scarce; only one cohort study reported no adverse effects in the elagolix group during the study duration.¹⁵ Other studies have not

specifically reported on side effects and have focused instead on efficacy and cost outcomes.

PATIENT CENTERED ADVANTAGES AND LIMITATIONS

For patients, elagolix offers the advantage of oral administration, eliminating the need for painful daily self-injections, along with lower per-cycle costs compared to injections.⁹

As discussed previously, elagolix, even at the highest dose may fail to suppress ovulation, raising doubts about breakthrough ovulation and potential cycle cancellation.¹³ Furthermore, no optimal dosing for elagolix in the IVF regimen exists. Published studies have tested varying doses, including 50 mg alternatively and 200 mg every night which muddles direct comparison across studies.

WHERE ELAGOLIX FITS AND FUTURE DIRECTIONS

Current evidence suggests that elagolix may achieve LH suppression and clinical outcomes comparable to injectable GnRH antagonists, while offering lower costs and a reduced injection burden to patients undergoing IVF. This review extends these observations by amalgamating the most recent cohort data across parameters like safety, efficacy and cost and highlights the limitations of present literature.

Key gaps remain, including a lack of randomized controlled trials, inconsistent dosing regimens, small population sizes and limited reports on patient safety. Future research should prioritize randomized clinical trials directly comparing elagolix to injectable antagonists, especially focusing on establishing an optimal IVF specific dosing protocol and systematic adverse effects reporting.

Table 1: Tabular representation of elagolix dosage, endpoints and side effects across multiple studies.

Study type	Elagolix dose	No. of patients	Primary endpoint(s) achieved	Secondary endpoints
Retrospective cohort comparing elagolix to injectable GnRH antagonists in IVF⁹	50 mg every other day	269 total (173 elagolix, 96 ganirelix/cetrotide)	Elagolix given at a small dose of 50 mg was as effective as standard dosage of injectable GnRH antagonists.	Similar gonadotropin dose, stimulation period, oocyte yield vs. the injectable group
Prospective cohort study with historical and oocyte donors¹⁵	200 mg daily	150 total (75 oocyte donors and 75 historical donors)	0 cases of premature donors were observed in either group, yielding a similar average of total and mature oocyte counts	Fertilization rate of 79.2% (elagolix) vs 84.6% (ganirelix); blastocyst development rate of 62.9% (elagolix) vs. 57.3% (ganirelix)
Prospective, comparative single center study of elagolix vs.	Not mentioned in abstract	n=220 (110 in elagolix group and 100 receiving subcutaneous	Elagolix group showed significantly lower mean serum LH levels and E2 levels compared to	Oocytes retrieved (17.5±5.3 vs. 18.4±5.0), MII oocytes (13.5±4.5 vs. 14.1±4.2);

Continued.

Study type	Elagolix dose	No. of patients	Primary endpoint(s) achieved	Secondary endpoints
cetrorelix ²¹		cetrorelix)	cetrorelix, P4 was also comparable	fertilization rate (70% vs 72%)
Retrospective cohort study comparing elagolix to ganirelix in a private university affiliated center⁴	200 mg twice daily	n=194	Comparable cycle cancellation rates (7.0% (elagolix) vs. 4.9%); frozen ET biochemical pregnancy rate was significantly higher with elagolix (74.5% vs.55.9%)	Frozen ET: sustained implantation and miscarriage rates similar between both groups. Fresh ET: No significant difference in pregnancy implantation or miscarriage.

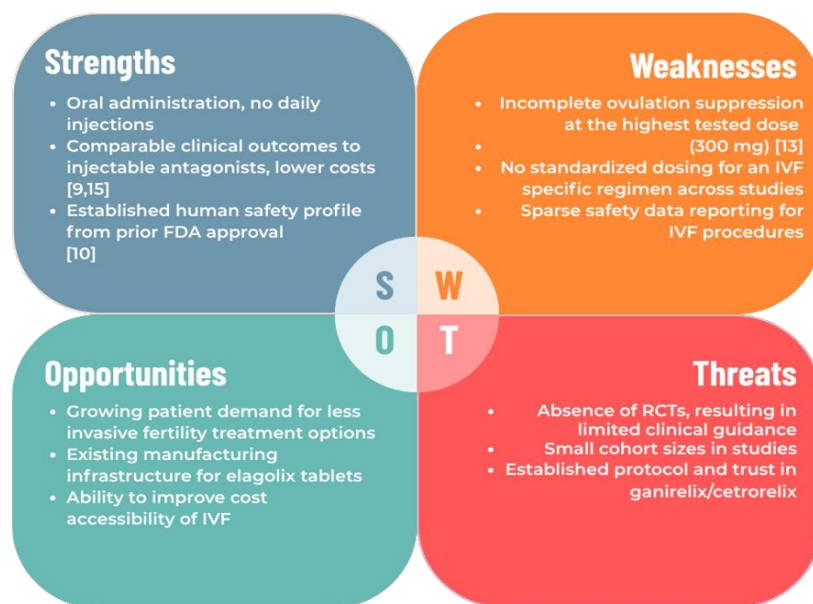


Figure 1: SWOT Analysis of elagolix.

CONCLUSION

All in all, elagolix depicts a promising, though not entirely validated, alternative to GnRH antagonists like ganirelix and cetrorelix for LH surge suppression in IVF.

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REFERENCES

1. Kauffman AS. Neuroendocrine mechanisms underlying estrogen positive feedback and the LH surge. *Front Neurosci.* 2022;16:953252.
2. Christian CA, Moenter SM. The neurobiology of preovulatory and estradiol-induced gonadotropin-releasing hormone surges. *Endocr Rev.* 2010;31(4):544-77.
3. Baldini GM, Baldini D, Lot D, Ferri D, Malvasi A, Fioretti B, et al. The trigger in IVF cycles: molecular pathways and clinical implications. *Int J Mol Sci.* 2025;26(24):11962.
4. Soliman D, Naoom R, Zaid M, Soliman S. The role of elagolix in ovulation suppression during controlled ovarian stimulation: a retrospective cohort study. *F S Rep.* 2024;5(4):356-62.
5. Aldarsooni M, Alfarah M, Albohammod F, Al-Jaroudi D. Effect of premature luteinizing hormone surge on pregnancy outcomes in intracytoplasmic sperm injection or in vitro fertilization cycles. *Front Med (Lausanne).* 2025;11:1429033.
6. Kumar P, Sharma A. Gonadotropin-releasing hormone analogs: understanding advantages and limitations. *J Hum Reprod Sci.* 2014;7(3):170-4.
7. Diedrich K, Diedrich C, Santos E, Zoll C, Al-Hasani S, Reissmann T, et al. Suppression of the endogenous luteinizing hormone surge by the gonadotrophin-releasing hormone antagonist cetrorelix during ovarian stimulation. *Hum Reprod.* 1994;9(5):788-91.
8. The Ganirelix Dose-Finding Study Group. A double-blind, randomized, dose-finding study to assess the efficacy of the gonadotrophin-releasing hormone antagonist ganirelix (Org 37462) to prevent premature luteinizing hormone surges in women undergoing ovarian stimulation with recombinant follicle

- stimulating hormone (Puregon). *Hum Reprod.* 1998;13(11):3023-31.
9. Mouanness M, Merhi Z. Elagolix represents a less invasive and cheaper option than injectable GnRH antagonist for ovulation suppression in IVF. *J Clin Endocrinol Metab.* 2025;110(2):e456-60.
10. Lamb YN. Elagolix: first global approval. *Drugs.* 2018;78(14):1501-8.
11. 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.
12. Ezzati M, Carr BR. Elagolix, a novel, orally bioavailable GnRH antagonist under investigation for the treatment of endometriosis-related pain. *Womens Health (Lond).* 2015;11(1):19-28.
13. Archer DF, Ng J, Chwalisz K, Chiu YL, Feinberg EC, Miller CE, et al. Elagolix suppresses ovulation in a dose-dependent manner: results from a 3-month, randomized study in ovulatory women. *J Clin Endocrinol Metab.* 2020;105(3):821-32.
14. Taylor HS, Dun EC, Chwalisz K. Clinical evaluation of the oral gonadotropin-releasing hormone-antagonist elagolix for the management of endometriosis-associated pain. *Pain Manag.* 2019;9(5):497-515.
15. Boniface C, Schnorr JN, Gray J, McLaughlin J, Cook H, Slowey M, et al. The role of elagolix in the suppression of ovulation in donor oocyte cycles. *F S Rep.* 2023;4(2):179-82.
16. Grisendi V, Grandi G, Capuzzo M, La Marca A. The use of oral GnRH antagonists to inhibit the LH surge in women undergoing ovarian stimulation for in vitro fertilization. *Expert Rev Clin Pharmacol.* 2024;17(12):1089-91.
17. Taylor HS, Soliman AM, Johns B, Pokrzywinski RM, Snabes M, Coyne KS. Health-related quality of life improvements in patients with endometriosis treated with elagolix. *Obstet Gynecol.* 2020;136(3):501-9.
18. Surrey E, Taylor HS, Giudice L, Lessey BA, Abrao MS, Archer DF, et al. Long-term outcomes of elagolix in women with endometriosis: results from two extension studies. *Obstet Gynecol.* 2018;132(1):147-60.
19. 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.
20. US Food and Drug Administration. Orilissa (elagolix) tablets: supplement approval letter. Silver Spring (MD): US Food and Drug Administration; 2023. Available from: https://www.accessdata.fda.gov/drugsatfda_docs/appletter/2023/210450Orig1s009ltr.pdf Accessed on 05 August 2026.

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