NATIONAL INSTITUTE FOR HEALTH AND CARE EXCELLENCE

Health Technology Evaluation

Linzagolix for treating symptoms of endometriosis ID6357

Final Scope

Remit/evaluation objective

To appraise the clinical and cost effectiveness of linzagolix within its marketing authorisation for treating symptoms of endometriosis.

Background

Endometriosis is a common, long-term gynaecological disorder where the tissue that normally lines the womb (endometrium) grows in other places. When this tissue breaks down as part of the normal menstrual cycle it becomes trapped in a person's pelvis. Endometriosis is mainly a disease of the reproductive years and, although its exact cause is unknown, it is hormone mediated and is associated with menstruation. Approximately 1 in 10 women of reproductive age in the UK suffers from endometriosis[1]. Endometriosis can be a chronic condition affecting people throughout their reproductive lives and beyond.

Endometriosis is typically associated with symptoms such as pelvic pain, painful periods and subfertility. People with endometriosis report pain, which can be frequent, chronic and/or severe, as well as tiredness, more sick days, and a significant physical, sexual, psychological and social impact. People with endometriosis typically present with pain but can delay seeking help because of a perception that pelvic pain is normal. Diagnosis can only be made definitively by laparoscopic visualisation of the pelvis, but other, less invasive methods may be useful in assisting diagnosis, including ultrasound.

Management options for endometriosis include pharmacological, non-pharmacological and surgical treatments. NICE guideline 73 (NG73) recommends a short trial of an analgesic such as paracetamol or a non-steroidal anti-inflammatory drug (NSAID) alone or in combination for first-line management of endometriosis-related pain. The use of neuromodulators to treat neuropathic pain should be considered in line with the NICE clinical guideline on neuropathic pain (CG173). As endometriosis is an oestrogen-dependent condition, most drug treatments for endometriosis work by suppressing ovarian function and are contraceptive. Surgical treatment aims to ablate or excise deposits of endometrial tissue. After laparoscopic excision or ablation of endometriosis, combination hormonal treatment to prolong the benefits of surgery and manage symptoms can be considered. The choice of treatment depends on the person's preferences and priorities in terms of pain management and/or fertility.

The technology

Linzagolix (Yselty, Theramex) does not have a marketing authorisation in the UK for treating symptoms of endometriosis. Linzagolix with or without hormone therapy has been compared with placebo in a double-blind phase 3 trial in females aged 18-49 years with moderate to severe endometriosis-associated pain. It has a marketing authorisation for moderate to severe symptoms of uterine fibroids in adults of reproductive age.

Intervention(s)	Linzagolix (with or without hormone-based therapy)
Population(s)	Adults with symptoms of endometriosis
Subgroups	If the evidence allows the following subgroups will be considered: • people having short-term treatment of 6 months or less, with hormone-based therapy • people having short-term treatment of 6 months or less, without hormone-based therapy • people having longer-term treatment, with hormone-based therapy • people having longer-term treatment, without hormone-based therapy
Comparators	**Where hormone-based therapy is suitable** Established clinical management without linzagolix, including: • analgesics or non-steroidal anti-inflammatory drug (NSAID) alone or in combination with each other • neuromodulators • relugolix-estradiol-norethisterone acetate (subject to NICE evaluation) • other hormonal treatment such as combined hormonal contraception (off-label for some combined hormonal contraceptives), oral progestogens, intrauterine system or uterine coil, gonadotropin-releasing hormone (GnRH) agonists • surgery such as excision/ablation with or without hysterectomy. **Where hormone-based therapy is not suitable** Established clinical management without linzagolix, including: • analgesics or non-steroidal anti-inflammatory drug (NSAID) alone or in combination with each other • neuromodulators • surgery such as excision/ablation with or without hysterectomy.
Outcomes	The outcome measures to be considered include: • pain • opioid use • analgesic use • recurrence, progression and regression of endometriosis

	• admission to hospital • subsequent surgical treatment • fertility • adverse effects of treatment • complications of treatment • health-related quality of life.
Economic analysis	The reference case stipulates that the cost effectiveness of treatments should be expressed in terms of incremental cost per quality-adjusted life year. The reference case stipulates that the time horizon for estimating clinical and cost effectiveness should be sufficiently long to reflect any differences in costs or outcomes between the technologies being compared. Costs will be considered from an NHS and Personal Social Services perspective. The availability of any commercial arrangements for the intervention, comparator and subsequent treatment technologies will be taken into account. The availability and cost of biosimilar and generic products should be taken into account.
Other considerations	Guidance will only be issued in accordance with the marketing authorisation. Where the wording of the therapeutic indication does not include specific treatment combinations, guidance will be issued only in the context of the evidence that has underpinned the marketing authorisation granted by the regulator.
Related NICE recommendations	**Related technology appraisals in development:** Relugolix–estradiol–norethisterone acetate for treating symptoms of endometriosis (ID3982). NICE technology appraisal. Publication to be confirmed **Related NICE guidelines:** Endometriosis: diagnosis and management (2017; updated 2024) NICE guideline 73 Fertility problems: assessment and treatment (2013, reviewed 2015) NICE guideline 156 Heavy menstrual bleeding: assessment and management (2018, reviewed 2021) NICE guideline 88 Neuropathic pain in adults: pharmacological management in non-specialist settings (2013; reviewed 2020) NICE clinical guideline 173 **Related interventional procedures:**

	Laparoscopic helium plasma coagulation for the treatment of endometriosis (2006) NICE interventional procedures guidance 171 **Related quality standards:** Endometriosis (2018) NICE quality standard 172
Related National Policy	The NHS Long Term Plan, 2019. NHS Long Term Plan Department for Health and Social Care, 2022. Women's Health Strategy, priority area 11 NHS England (2023/2024) NHS manual for prescribed specialist services (2023/2024). Chapter 58. Highly specialist adult gynaecological surgery and urinary surgery services for females NHS England (2018) NHS Standard contract for complex gynaecology - Severe endometriosis; Schedule 2 The services A. Service specifications (E10/S/a - Complex Gynaecology – Severe Endometriosis)

References

1. Rogers, P. A., D'Hooghe, T. M., Fazleabas, A., Gargett, C. E., Giudice, L. C., Montgomery, G. W., Rombauts, L., Salamonsen, L. A., & Zondervan, K. T. (2009). Priorities for endometriosis research: recommendations from an international consensus workshop. *Reproductive sciences, 16*(4), 335–346. doi.org/10.1177/1933719108330568