NATIONAL INSTITUTE FOR HEALTH AND CARE EXCELLENCE

Single Technology Appraisal

Relugolix–estradiol–norethisterone acetate for treating symptoms of endometriosis [ID3982]

Final scope

Remit/evaluation objective

To appraise the clinical and cost effectiveness of relugolix–estradiol–norethisterone acetate 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[1]. 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[2]. Endometriosis can be a chronic condition affecting people throughout their reproductive lives (and sometimes 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[3]. 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

Relugolix (Ryeqo, Gedeon Richter) does not currently have a marketing authorisation in the UK for the treatment of symptoms associated with endometriosis. It has been studied in clinical trials in combination with oestradiol and norethindrone acetate

compared with placebo in premenopausal women aged 18 to 50 years old with moderate to severe endometriosis-associated pain.

Intervention(s)	Relugolix in combination with oestradiol and norethindrone acetate (also known as norethisterone acetate)
Population(s)	Adults with symptoms of endometriosis
Comparators	Established clinical management without relugolix in combination with oestradiol and norethindrone, including: • analgesics or non-steroidal anti-inflammatory drug (NSAID) alone or in combination with each other • neuromodulators • hormonal treatment such as combined hormonal contraception (off-label for some combined hormonal contraceptives), oral progestogens, gonadotropin-releasing hormone (GnRH) agonists.
Outcomes	The outcome measures to be considered include: • overall pain • opioid use • analgesic use • recurrence 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.

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 NICE Guidelines:** Endometriosis: diagnosis and management (2017) NICE guideline 73 Fertility problems: assessment and treatment (2013, reviewed 2017) 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) 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 NHS England (2018/2019) NHS manual for prescribed specialist services (2018/2019). 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. Health technology briefing note (2021). NIHR Innovation observatory. Accessed August 2022.

2. 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

3. Endometriosis: diagnosis and management (2017) NICE guideline 73

