NATIONAL INSTITUTE FOR HEALTH AND CARE EXCELLENCE

Health Technology Evaluation

Relugolix–estradiol–norethisterone acetate for treating pain associated with endometriosis

Draft scope

Draft remit/evaluation objective

To appraise the clinical and cost effectiveness of relugolix–estradiol–norethisterone acetate within its marketing authorisation for treating pain associated with 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 treatment of pain 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 endometriosis-associated pain.

Intervention(s)	Relugolix in combination with oestradiol and norethindrone acetate (also known as norethisterone acetate)
Population(s)	Adults with endometriosis-associated pain
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) analogues.
Outcomes	The outcome measures to be considered include: • overall pain • opioid use • analgesic use • recurrence of endometriosis • admission to hospital • 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)

Questions for consultation

Which treatments are considered to be established clinical practice in the NHS for treating endometriosis-associated pain?

Have all relevant comparators for **r**elugolix–estradiol–norethisterone acetate been included in the scope?

Are surgical options (endometrial ablation, excision and hysterectomy, with or without oophorectomy) relevant as comparators for **r**elugolix–estradiol–norethisterone acetate?

Where do you expect relugolix–estradiol–norethisterone acetate to fit in the treatment pathway for treating endometriosis-associated pain?

- Will relugolix–estradiol–norethisterone acetate be used as an add-on therapy to analgesics and NSAIDs in clinical practice?
- Will relugolix–estradiol–norethisterone acetate be used as an add-on therapy to neuromodulators in clinical practice?

Are the outcomes listed appropriate?

Are there any subgroups of people in whom **r**elugolix–estradiol–norethisterone acetate is expected to be more clinically effective and cost effective or other groups that should be examined separately?

NICE is committed to promoting equality of opportunity, eliminating unlawful discrimination and fostering good relations between people with particular protected characteristics and others. Please let us know if you think that the proposed remit and scope may need changing in order to meet these aims. In particular, please tell us if the proposed remit and scope:

- could exclude from full consideration any people protected by the equality legislation who fall within the patient population for which **r**elugolix–estradiol–norethisterone acetate will be licensed;
- could lead to recommendations that have a different impact on people protected by the equality legislation than on the wider population, e.g. by making it more difficult in practice for a specific group to access the technology;
- could have any adverse impact on people with a particular disability or disabilities.

Please tell us what evidence should be obtained to enable the Committee to identify and consider such impacts.

Do you consider **r**elugolix–estradiol–norethisterone acetate to be innovative in its potential to make a significant and substantial impact on health-related benefits and how it might improve the way that current need is met (is this a 'step-change' in the management of the condition)?

Do you consider that the use of **r**elugolix–estradiol–norethisterone acetate can result in any potential significant and substantial health-related benefits that are unlikely to be included in the QALY calculation?

Please identify the nature of the data which you understand to be available to enable the Appraisal Committee to take account of these benefits.

To help NICE prioritise topics for additional adoption support, do you consider that there will be any barriers to adoption of this technology into practice? If yes, please describe briefly.

NICE intends to appraise this technology through its Single Technology Appraisal (STA) Process. We welcome comments on the appropriateness of appraising this topic through this process. (Information on the Institute's Technology Appraisal processes is available at http://www.nice.org.uk/article/pmg19/chapter/1-Introduction).

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

