NATIONAL INSTITUTE FOR HEALTH AND CARE EXCELLENCE

Health Technology Evaluation

Linzagolix for treating moderate to severe symptoms of uterine fibroids ID6190

Draft scope

Draft remit/evaluation objective

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

Background

Uterine fibroids are noncancerous growths of the uterus. The exact cause of fibroids is not known, but they have been linked to the hormone oestrogen.[1] Most are asymptomatic, but they can cause significant morbidity. The most common symptom of uterine fibroids is heavier than normal or prolonged menstrual bleeding. Other symptoms include pelvic pressure or pain, frequent urination, constipation and pain or discomfort during sex. In rare cases, complications with fibroids can interfere with pregnancy or cause infertility.[1] The type and severity of symptoms is influenced by the location, size and number of fibroids.[2] Fibroids are generally classified by their location. Intramural fibroids grow within the muscular uterine wall. Submucosal fibroids grow in the muscle layer beneath the uterus's inner lining and grow into the uterine cavity. Subserosal fibroids develop outside of the uterus and grow into the pelvis.

Fibroids usually develop during the reproductive years (from around 16 to 50 years) when oestrogen levels are at their highest.[1] The prevalence of symptomatic fibroids is low in women younger than 30 years but is between 20 to 50% in women older than 30 years.[3] Risk factors for uterine fibroids include race, family history of fibroids, age and obesity.[4]

Oestrogen and progesterone control the proliferation and maintenance of uterine fibroids. Most medical treatments act by interfering with their production or function.[4]

For people with uterine fibroids less than 3 cm in diameter and not causing distortion of the uterine cavity, NICE guideline 88 (NG88) recommends considering a levonorgestrel-releasing intrauterine system (LNG-IUS) for the treatment of heavy menstrual bleeding. If heavy menstrual bleeding worsens or an LNG-IUS is not suitable, pharmacological treatments (such as tranexamic acid and non-steroidal anti-inflammatory drugs) and hormonal treatments (such as combined hormonal contraception, cyclical oral progestogens and gonadotrophin-releasing hormone analogues) are recommended. Surgery (second-generation endometrial ablation or hysterectomy) is recommended as an option if treatment is unsuccessful or declined, or symptoms are severe. For people with submucosal uterine fibroids less than 3 cm in diameter hysteroscopic removal should be

considered. For people with uterine fibroids of 3 cm or more in diameter, the same pharmacological and surgical treatments are recommended as options as well as uterine artery embolisation and myomectomy. Pretreatment with a gonadotrophin-releasing hormone analogue before hysterectomy and myomectomy should be considered if uterine fibroids are causing an enlarged or distorted uterus.

NICE technology appraisal 832 recommends relugolix-estradiol-norethisterone acetate as an option for treating moderate to severe symptoms of uterine fibroids in adults of reproductive age.

The technology

Linzagolix (Yselty, Theramex) has a marketing authorisation in the UK for treatment of moderate to severe symptoms of uterine fibroids in adult women of reproductive age. It has been studied in clinical trials alone and in combination with hormonal add-back therapy compared with placebo in adults with heavy menstrual bleeding associated with uterine fibroids.

Intervention(s)	Linzagolix
Population(s)	People with moderate to severe symptoms associated with uterine fibroid(s)
Comparators	• Relugolix-estradiol-norethisterone acetate Hormonal treatments, including: • levonorgestrel-releasing intrauterine system (LNG-IUS; off-label for some LNG-IUSs) • combined hormonal contraception (off-label for some combined hormonal contraceptives) • cyclical oral progestogens • gonadotrophin-releasing hormone analogues (off-label for some gonadotrophin-releasing hormone analogues)

Outcomes	The outcome measures to be considered include: • change in menstrual blood loss volume • time to menstrual blood loss response • pain • uterine fibroid volume • haemoglobin levels • change in bone mineral density • rates and route of surgery • impact on fertility and pregnancy and teratogenic effects • mortality • adverse effects of treatment, including but not limited to vasomotor symptoms, incontinence and pelvic organ prolapse • 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. If the technology is likely to provide similar or greater health benefits at similar or lower cost than technologies recommended in published NICE technology appraisal guidance for the same indication, a cost comparison may be carried out. 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**: Relugolix–estradiol–norethisterone acetate for treating moderate to severe symptoms of uterine fibroids. (2022) NICE Technology appraisal guidance 832 Fluid-filled thermal balloon and microwave endometrial ablation techniques for heavy menstrual bleeding (2004) NICE Technology Appraisal 78. Guidance on the static list. **Related Interventional Procedures:** Transcervical ultrasound-guided radiofrequency ablation for symptomatic uterine fibroids (2021) NICE interventional procedures guidance 689. Ultrasound-guided high-intensity transcutaneous focused ultrasound for symptomatic uterine fibroids (2019) NICE interventional procedures guidance 657. Hysteroscopic morcellation of uterine leiomyomas (fibroids) (2015) NICE interventional procedures guidance 522. Magnetic resonance image-guided transcutaneous focused ultrasound for uterine fibroids (2011) NICE interventional procedures guidance 413. Uterine artery embolisation for fibroids (2010) NICE interventional procedures guidance 367. Magnetic resonance (MR) image-guided percutaneous laser ablation of uterine fibroids (2003) NICE interventional procedures guidance 30. Laparoscopic laser myomectomy (2003) NICE interventional procedures guidance 23. Laparoscopic morcellation of uterine fibroids (2021) NICE interventional procedures guidance 703. Hysteroscopic removal of uterine fibroids with power morcellation (2021) NICE interventional procedures guidance 704. **Related Guidelines**: Heavy menstrual bleeding: assessment and management (2021) NICE guideline NG88. **Related Quality Standards**: Heavy menstrual bleeding (2020) NICE quality standard 47. **Related NICE Pathways**: Heavy menstrual bleeding (2020) NICE pathway
Related National Policy	The NHS Long Term Plan (2019) NHS Long Term Plan NHS England (2018) NHS manual for prescribed specialist services (2018/2019) Chapters 9 & 58

Questions for consultation

Where do you consider linzagolix will fit into the existing care pathway for the treatment of uterine fibroids?

Would linzagolix be a candidate for managed access?

Do you consider that the use of linzagolix can result in any potential 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 committee to take account of these benefits.

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 linzagolix is 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.

NICE is considering evaluating this technology through its cost comparison evaluation process.
Please provide comments on the appropriateness of appraising this topic through this process.
(Information on NICE's health technology evaluation processes is available at https://www.nice.org.uk/about/what-we-do/our-programmes/nice-guidance/nice-tehnology-appraisal-guidance/changes-to-health-technology-evaluation).

Technologies can be evaluated through the cost-comparison process if they are expected to provide similar or greater health benefits, at a similar or lower cost, compared with technologies that have been previously recommended (as an option) in published NICE guidance for the same indication. Companies can propose cost-comparison topics to NICE at any stage during topic selection and scoping. NICE will route technologies for evaluation through the cost-comparison process if it is agreed during scoping that the process is an appropriate route to establish the clinical and cost effectiveness of the technology.

NICE's health technology evaluations: the manual states the methods to be used where a cost comparison case is made.

- Is the technology likely to be similar in its clinical effectiveness and resource use to any of the comparators? Or in what way is it different to the comparators?

- Will the intervention be used in the same place in the treatment pathway as the comparator(s)? Have there been any major changes to the treatment pathway recently? If so, please describe.
- Will the intervention be used to treat the same population as the comparator(s)?
- Overall is the technology likely to offer similar or improved health benefits compared with the comparators?
- Would it be appropriate to use the cost-comparison methodology for this topic?

References

1. NHS. Fibroids. Accessed January 2023.
2. Mayo Clinic. Uterine fibroids: symptoms and causes. Accessed January 2023.
3. BMJ Best Practice: uterine fibroids. Accessed January 2023.
4. Lumsden M.A.; Fibroids: diagnosis and management; BMJ; 351:h4887; 2015