NATIONAL INSTITUTE FOR HEALTH AND CARE EXCELLENCE

Health Technology Evaluation

Linzagolix for treating moderate to severe symptoms of uterine fibroids [ID6190]

Final scope

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 hormones oestrogen and progesterone.[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, with approximately one third of people with uterine fibroids experiencing heavy menstrual blood loss.[2] 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.[3] The type and severity of symptoms is influenced by the location, size and number of fibroids.[4] 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.[3] The prevalence of symptomatic fibroids is low in people younger than 30 years but is between 20 to 50% in people older than 30 years.[5] Black people have an increased risk of uterine fibroids compared with white people. Other risk factors for uterine fibroids include family history of fibroids, age and obesity.[6]

Oestrogen and progesterone control the proliferation and maintenance of uterine fibroids. Most medical treatments act by interfering with their production or function.[5]

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. Pre-treatment 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 treating moderate to severe symptoms of uterine fibroids in adults 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	Linzagolix (with or without hormone-based therapy)
Population	People of reproductive age with moderate to severe symptoms associated with uterine fibroid(s)
Subgroups	If the evidence allows the following subgroups will be considered: • People having short-term treatment of 6 months or less • People having longer-term treatment, with hormone-based therapy • People having longer-term treatment, without hormone-based therapy
Comparators	• Gonadotropin-releasing hormone analogues (off-label for some gonadotropin-releasing hormones) • Relugolix-estradiol-norethisterone acetate **Where hormone-based therapy is not suitable** • Established clinical management without linzagolix

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. 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

References

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6. Lumsden M.A.; Fibroids: diagnosis and management; BMJ; 351:h4887; 2015