Linzagolix tablets (Yselty® ▼) for treatment of uterine fibroids

Bath and North East Somerset, Swindon and Wiltshire Together

The BSW Area Prescribing Committee recommends the prescribing of LINZAGOLIX 100mg & 200mg tablets (Yselty® ▼) for treating uterine fibroids in accordance with NICE TA996.

AMBER following specialist initiation: 1-month supply

NICE recommendation for use (NICE TA996)[1]

NICE technology appraisal TA996 (14 August 2024) recommends Linzagolix as an option for treating moderate to severe symptoms of uterine fibroids in adults of reproductive age only if:

- it is intended to be used for longer-term treatment (normally for more than 6 months and not for people who need short-term treatment, for example, before planned surgery)
- the following dosage is used:

—with hormonal add-back therapy (ABT): 200 mg once daily

-without hormonal ABT: 200 mg once daily for 6 months, then 100 mg once daily.

N.B. Concomitant hormonal add-back therapy (ABT) as per SPC: **estradiol 1 mg and norethisterone acetate 0.5 mg tablet once daily**

Initial treatment options for symptoms of uterine fibroids include levonorgestrel-releasing intrauterine system or combined hormonal contraception. For treating moderate to severe symptoms of uterine fibroids, injectable gonadotrophin-releasing hormone (GnRH) agonists are often used before surgical options. Linzagolix is a new oral option alongside Relugolix- estradiol-norethisterone acetate (Ryeqo®: BSW guidance for this is found here). All common pharmacological methods to control fibroid-related heavy periods should have been considered before either Linzagolix or relugolix-estradiol-norethisterone acetate are considered.

Costing information[1]

The NHS list price (excluding VAT) of linzagolix (Yselty®) is £80.00 for a 28-pack of 100mg or 200mg tablets. The cost for an 84 pack of estradiol and norethisterone tablets, known as hormonal add-back therapy (ABT), is £13.20. At list price, 12 months of treatment would cost £1,040.00 (without ABT) and £1,097.20 (with ABT).

Clinical Effectiveness[1,2]

Linzagolix is a selective non-peptide GnRH receptor antagonist that inhibits endogenous GnRH signalling by binding competitively to GnRH receptors in the pituitary gland, thereby modulating the hypothalamic-pituitary-gonadal axis. When administered exogenously, linzagolix results in dose-dependent suppression of luteinizing hormone and follicle-stimulating hormone, leading to decreased blood concentrations of estradiol and progesterone. The efficacy of Yselty was evaluated in two phase 3, randomised, double-blind and placebo-controlled studies, PRIMROSE 1 and PRIMROSE 2 (placebo vs active treatment). NICE concluded that the results from PRIMROSE 1 & 2 showed that linzagolix was more effective than placebo at treating moderate to severe symptoms of uterine fibroids.

Adverse effects/contra-indications[2]

Contraindications include hypersensitivity to the active substances or to any of the excipients, pregnancy or breastfeeding, genital bleeding of unknown aetiology, and known osteoporosis.

The most frequent adverse drug reactions in clinical trials were hot flush (≥ 1/10), bone mineral density decreased, hyperhidrosis, vaginal haemorrhage, elevated liver enzymes, nausea/vomiting, headache (≥ 1/100 to < 1/10)

See SPC for full safety data, cautions and interactions.

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Patient factors[2]

Patients with a history of depression should be carefully monitored- see monitoring section below.
Linzagolix should be avoided in women with moderate (eGFR = 30– 59 mL/min), severe renal impairment (eGFR < 30 mL/min) or end-stage renal disease. Prescribers are recommended to monitor for adverse reactions in women who have mild renal impairment (eGFR = 60-89 mL/min) although no dose adjustment is required.
Linzagolix should be avoided in women with severe hepatic impairment (Child-Pugh C). No dose adjustment is necessary in women with mild or moderate hepatic impairment (Child-Pugh A or B).

Prescribing information (see SPC for full information)[2]

- Treatment should only be initiated by a specialist in the management of uterine fibroids. **After a minimum of one month's treatment, the specialist may ask the patient's GP to take over prescribing responsibilities of treatment. The patient will be followed up by secondary care (usually at 6 months although this will be determined on an individual patient basis).** This may be in-person or remotely.
- Prior to initiation or reinstitution, a complete medical history (including family history) will be taken by the specialist. Blood pressure and a physical examination must be performed guided by the contraindications and warnings for use.
- The SPC states that in patients with risk factors for osteoporosis or bone loss, a dual X-ray absorptiometry (DXA) is recommended prior to starting treatment. Treatment should not be initiated if the risk associated with BMD loss exceeds the potential benefit of the treatment. The SPC also states that a DXA scan is recommended after 1 year of treatment for all women to verify that the patient does not have an unwanted degree of BMD loss. Thereafter, depending on the prescribed dose of linzagolix, BMD assessment is recommended annually (Linzagolix 100 mg) or at a frequency determined by the treating physician based on the woman's individual risk and previous BMD assessment (Linzagolix 100 mg or 200mg with concomitant ABT). Local opinion is that patients only need DXA scan if they are not replaced with ABT and this should fall to the responsibility of the consultant to arrange.
- Linzagolix with or without concomitant ABT has not been demonstrated to provide contraception. Women of childbearing potential at risk of pregnancy have to use effective non-hormonal contraception while on treatment with linzagolix.
- Increases in lipid levels were observed with linzagolix treatment. These increases were generally of no clinical relevance. However, in women with pre- existing elevated lipid profiles monitoring of lipid levels is recommended.

Monitoring[2,3]

- Linzagolix can be expected to lead to a reduction in menstrual bleeding and often leads to amenorrhoea.
- Patients with a history of depression should be carefully monitored and advised to seek medical attention in case of mood changes and depressive symptoms, including shortly after initiating the treatment. The benefit of continued therapy should be assessed by the specialist.
- Seek advice from the specialist if sustained clinically significant hypertension develops during treatment with linzagolix, and the benefit of continued therapy can be assessed by the specialist.

References

1. National Institute for Health and Care Excellence. Technology appraisal 996; Linzagolix for treating moderate to severe symptoms of uterine fibroids 14th August 2024
2. Theramex UK Ltd. Summary of Product Characteristics; Yselty 100mg film-coated tablets ▼ 17th October 2024.

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