Healthcare Improvement Scotland | SMC Advice on new medicines

Advice document
SMC2841

linzagolix film-coated tablets (Yselty®)

Theramex

05 September 2025

The Scottish Medicines Consortium (SMC) has completed its assessment of the above product and, following review by the SMC executive, advises NHS Boards and Area Drug and Therapeutics Committees (ADTCs) on its use in NHSScotland. The advice is summarised as follows:

ADVICE: following an abbreviated submission

linzagolix (Yselty®) is accepted for use within NHSScotland.

Indication under review: in adult women of reproductive age for symptomatic treatment of endometriosis in women with a history of previous medical or surgical treatment for their endometriosis

Linzagolix offers an additional treatment choice in the therapeutic class of gonadotrophin-releasing hormone (GnRH) receptor antagonists that is taken with concomitant hormonal add-back therapy (ABT).

Linzagolix has the advantage of allowing flexibility in the choice of concomitant ABT compared with an alternative GnRH antagonist that is available with ABT as a fixed-dose combination therapy. Linzagolix with ABT is more expensive than the alternative but the overall net budget impact is likely to be small.

Chair
Scottish Medicines Consortium

1. Clinical Context

1.1. Medicine background

Linzagolix (as choline salt) is a selective, non-peptide gonadotrophin-releasing hormone (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.

The recommended dose of linzagolix for endometriosis is 200 mg orally once daily taken together with concomitant hormonal add-back therapy (+ ABT).[1, 2] A dual X-ray absorptiometry (DXA) scan is recommended before starting treatment in patients with risk factors for osteoporosis or bone loss, and after 1 year of treatment for all women. Monitoring of bone mineral density (BMD) is recommended to continue for the treatment duration. Refer to the Summary of Product Characteristics (SPC) for details.[1-3]

1.2. Relevant comparator

Relugolix combination therapy (relugolix CT) (Ryeqo®) is a fixed-dose combination tablet containing 40 mg relugolix, 1 mg estradiol (as hemihydrate), and 0.5 mg norethisterone acetate. Relugolix is another GnRH receptor antagonist. The submitting company considered that relugolix CT is the relevant comparator for this submission. Relugolix CT was accepted for use within NHS Scotland by SMC on 13th January 2025 (SMC2666).

2. Summary of Clinical Evidence

2.1. Evidence to support comparable efficacy with relevant comparators

Efficacy and safety data for linzagolix were derived from a randomised, double-blind, placebo-controlled, multicentre, phase III study (EDELWEISS 3), and its randomised, double-blind, extension study (EDELWEISS 6).[3, 4] In EDELWEISS 3, adult women of reproductive age with surgically confirmed endometriosis and moderate to severe endometriosis associated pain (EAP) (n= 484) were randomised to receive a daily dose of 200 mg linzagolix + ABT (consisting of estradiol 1 mg and norethisterone acetate 0.5 mg), 75 mg linzagolix or placebo for 6 months. Patients who completed the 6 month treatment period had the option to enter the extension study (EDELWEISS 6) where they continued to receive linzagolix for 6 months. Those who had previously received placebo in EDELWEISS 3 were randomised to linzagolix 75 mg, or linzagolix 200 mg + ABT.[3, 4] The results suggested that linzagolix + ABT resulted in a clinically meaningful and significant reduction in dysmenorrhea and non-menstrual pelvic pain (NMPP) compared with placebo, with stable or decreased use of analgesics.

In the absence of direct evidence comparing linzagolix + ABT and relugolix CT, an indirect treatment comparison (ITC) was conducted. Using the Bucher method, the submitting company utilised the results from the EDELWEISS 3 study of linzagolix + ABT and from two phase III studies, SPIRIT 1 and SPIRIT 2, of relugolix CT, which were combined through a meta-analysis.[5] Notwithstanding limitations inherent in the indirect comparisons, the results suggested that the efficacy and safety were comparable between linzagolix 200 mg +ABT and relugolix CT.

3. Company Estimate of Eligible Population, Uptake and Budget Impact

3.1. Company's number of patients assumed to be eligible for treatment

SMC is unable to publish the estimated patient numbers as the company considered that these were commercial in confidence.

3.2. Budget Impact assumption

Medicines reviewed under the abbreviated submissions process are estimated to have a limited net budget impact and resource allocation across NHS Scotland.

References

1. Theramex. Linzagolix 100mg/200mg film-coated tablets (Yselty®) Summary of product characteristics. Electronic Medicines Compendium www.medicines.org.uk/emc/ Last updated 08 May 2025.

2. The European Medicines Agency (EMA). European Public Assessment Report. Linzagolix choline (Yselty®). 12/03/2025, EMEA/H/C/005442. www.ema.europa.eu.

3. Donnez J, Becker C, Taylor H, Carmona Herrera F, Donnez O, Horne A*, et al.* Linzagolix therapy versus a placebo in patients with endometriosis-associated pain: a prospective, randomized, double-blind, Phase 3 study (EDELWEISS 3). Hum Reprod. 2024;39(6):1208-21.

4. Dolmans MM, Horne A, Renner S,, Boolell M, and Bestel E. Long term efficacy of Linzagolix in women with endometriosis-associated pain. Presented at ESHRE 2024; 2024. Available from:

https://www.eshre.eu/ESHRE2024/Programme/ESHRE-2024-Searchable-scientific.

5. Giudice LC, As-Sanie S, Arjona Ferreira JC, Becker CM, Abrao MS, Lessey BA*, et al.* Once daily oral relugolix combination therapy versus placebo in patients with endometriosis-associated pain: two replicate phase 3, randomised, double-blind, studies (SPIRIT 1 and 2). Lancet. 2022;399(10343):2267-79.

This assessment is based on data submitted by the applicant company up to and including 24 June 2025.

Medicine prices are those available at the time the papers were issued to SMC for consideration. SMC is aware that for some hospital-only products national or local contracts may be in place for comparator products that can significantly reduce the acquisition cost to Health Boards. These contract prices are commercial in confidence and cannot be put in the public domain, including via the SMC Detailed Advice Document. Area Drug and Therapeutics Committees and NHS Boards are therefore asked to consider contract pricing when reviewing advice on medicines accepted by SMC.

Patient access schemes: A patient access scheme is a scheme proposed by a pharmaceutical company in order to improve the cost-effectiveness of a medicine and enable patients to receive access to cost-effective innovative medicines. A Patient Access Scheme Assessment Group (PASAG), established under the auspices of NHS National Services Scotland reviews and advises NHSScotland on the feasibility of proposed schemes for implementation. The PASAG operates separately from SMC in order to maintain the integrity and independence of the assessment process of the SMC. When SMC accepts a medicine for use in NHSScotland on the basis of a patient access scheme that has been considered feasible by PASAG, a set of guidance notes on the operation of the scheme will be circulated to Area Drug and Therapeutics Committees and NHS Boards prior to publication of SMC advice.

Advice context:

No part of this advice may be used without the whole of the advice being quoted in full.

This advice is based on the estimation of at least similar comparative efficacy and limited net budget impact compared with other medicinal products, within the same therapeutic class, that are in routine use within NHSScotland.

This advice represents the view of the Scottish Medicines Consortium and was arrived at after evaluation of the evidence submitted by the company. It is provided to inform the considerations of Area Drug & Therapeutics Committees and NHS Boards in Scotland in determining medicines for local use or local formulary inclusion. This advice does not override the individual responsibility of health professionals to make decisions in the exercise of their clinical judgement in the circumstances of the individual patient, in consultation with the patient and/or guardian or carer.