

Report Yselyt[®] - linzagolix colina

Product & Mechanism of action	Authorized indications Licensing status	Essential therapeutic features	NHS impact
<p>Substance: linzagolix choline</p> <p>Brand Name: Yselyt</p> <p>Originator/licensee: ObsEva Ireland Ltd</p> <p>Classification: NCE</p> <p>ATC code: G02C</p> <p>Orphan Status: Eu: No Us: -</p> <p>Mechanism of action: linzagolix choline is a selective, non-peptide GnRH receptor antagonist that binds to the GnRH receptors in the pituitary gland, resulting in a dose-dependent reduction of LH and FSH production subsequently leads to a dose-dependent reduction of estrogen levels [1,2].</p>	<p>Authorized Indication: EMA: linzagolix choline is indicated for the treatment of moderate to severe symptoms of UF in adult women of reproductive age[1].</p> <p>Route of administration: OS</p> <p>Licensing status EU CHMP P.O. date: 16/12/2021 FDA M.A. date: -</p> <p>EU Speed Approval Pathway:No</p> <p>-----</p> <p>ABBREVIATIONS: ABT: add-back therapy AE: Adverse Event Als: aromatase inhibitors CHMP: Committee for Medicinal Products for Human Use FSH: follicle-stimulating hormone GnRH: gonadotropin-releasing hormone HMB: heavy menstrual bleeding LGX: linzagolix LH: luteinizing hormone MBL: menstrual blood loss M.A.: Marketing Authorization MRgFUS: magnetic resonance guided focused ultrasound radiofrequency ablation; NSAIDs: Non-steroidal anti-inflammatories p: p-Value P.O.: Positive Opinion pts: patients RFVTA: radiofrequencyvolumetric thermal ablation SPRMs: Selective progesterone receptor modulators UAE: Uterine artery embolization UF: uterine fibroids vs.: versus</p>	<p>Summary of clinical EFFICACY: PRIMROSE 1 (n=526) and PRIMROSE 2 (n=511)are randomized, double-blind, placebo-controlled phase 3 trials, with essentially identical design, investigating the efficacy and safety of two dosing regimens of LGX, 100 mg and 200 mg once daily, alone and in combination with hormonal ABT (estradiol 1mg/ norethisterone 0.5mg) once daily for 52 weeks. Pts were included if they had HMB (defined as >80mL MBL/cycle) due to UF and were excluded if they had significant risk of osteoporosis. Pts were randomized to one of the following five treatments: placebo, LGX 100 mg, LGX 100 mg + ABT, LGX 200 mg, LGX 200 mg + ABT. The primary efficacy endpoint was HMB reduction to ≤ 80 mL MBL at week 24. In PRIMROSE 1 trial responder rates were (in the placebo, 100 mg, 100 mg + ABT, 200 mg and 200 mg + ABT groups, respectively): 35%, 56%, 67%, 71% and 75% (p<0.003for all active treatment groups compared to placebo), while in PRIMROSE 2 trial responder rates were, respectively: 29%, 57%, 77%, 78% and 94% (p<0.001 for all active treatment groups compared to placebo) [2-5].</p> <p>Summary of clinical SAFETY: One drug-related serious AE (hypertension) was observed in the 100 mg group. Most common non-seriousAEs (in PRIMROSE 1 and PRIMROSE 2 treatment arms vs. placebo arm, respectively) were: hot flushes (6.0%; 14.1%; vs. 6.7%; 3.8%), headache (8.0%; 4.0%; vs. 5.8%; 5.7%), and anemia (1.0%; 19.2%; vs. 3.8%;10.5%) [3-4, 6].</p> <p>Ongoing studies: <ul style="list-style-type: none"> • For the same indication:Yes • For other indications:Yes </p> <p>Discontinued studies (for the same indication):No</p> <p>-----</p> <p>References: 1. https://www.ema.europa.eu.translate.goog/en/medicines/human/summaries-opinion/yselyt? x tr sl=en& x tr tl=it& x tr hl=it& x tr pto=op,sc 2. https://adisinsight.springer.com/drugs/800032710 3. https://clinicaltrials.gov/ct2/show/NCT03070899?term=primrose+1&draw=2&rank=1 4. https://clinicaltrials.gov/ct2/show/NCT03070951?term=PRIMROSE+2&draw=2&rank=1 5. Stewart, Elizabeth A. et al. "Efficacy and safety of linzagolix (lgx) for the treatment of heavy menstrual bleeding (HMB) due to uterine fibroids (UF): results from two phase 3 randomized clinical trials". Fertility and Sterility, Volume 114, Issue 3, e527. DOI:https://doi.org/10.1016/j.fertnstert.2020.09.016 6. Bradley, Linda D. et al. "Linzagolix may address the long-term treatment needs of women with uterine fibroids (UF) who have contraindications to hormonal add-back therapy (ABT): results from two phase 3 randomized clinical trials". Fertility and Sterility, Volume 114, Issue 3, e527 DOI:https://doi.org/10.1016/j.fertnstert.2020.09.017 7. Giuliani, Emma et al. "Epidemiology and management of uterine fibroids." International journal of gynaecology and obstetrics: the official organ of the International Federation of Gynaecology and Obstetrics vol. 149,1 (2020): 3-9. doi:10.1002/ijgo.13102 8. https://clinicaltrials.gov/ct2/results?cond=&term=&type=Intr&rslt=&recrs=b&recrs=a&recrs=f&recrs=g&recrs=h&recrs=e&recrs=i&age_v=&gndr=&intr=Linzagolix&titles=&outc=&spons=&lead=&id=&cntry=&state=&city=&dist=&locn=&phase=2&rsb=&strd_s=&strd_e=&prcd_s=&prcd_e=&sfpd_s=&sfpd_e=&rfpd_s=&rfpd_e=&lupd_s=&lupd_e=&sort= 9. https://clinicaltrials.gov/ct2/results?cond=Uterine+Fibroid&term=&type=Intr&rslt=&recrs=b&recrs=a&recrs=f&recrs=d&recrs=g&recrs=h&recrs=e&recrs=i&age_v=&gndr=&intr=Linzagolix&titles=&outc=&spons=&lead=&id=&cntry=&state=&city=&dist=&locn=&phase=2&rsb=&strd_s=&strd_e=&prcd_s=&prcd_e=&sfpd_s=&sfpd_e=&rfpd_s=&rfpd_e=&lupd_s=&lupd_e=&sort=</p>	<p>Cost of therapy: The price of linzagolix choline is not yet available.</p> <p>Epidemiology: UF affect women during their reproductive years and are diagnosed in up to 70% of white women and more than 80% of African women. Most women with fibroids are asymptomatic but 30% of them will present severe symptoms [7].</p> <p>-----</p> <p>POSSIBLE PLACE IN THERAPY The treatment of UF is directed to improve symptomatologyand influenced by the pts's desire for future fertility, desire to retain the uterus, likelihood of achieving treatment goals, and overall health status. A step-up approach is recommended by many international obstetrics and gynecology societies when treating UF, whichbegins with pharmacological and minimally invasive treatmentsbefore moving to surgery Available pharmacological treatments include: -First line non-hormonal treatment:NSAIDs and tranexamic acid, -First line hormonal treatment: combined contraceptives, progestins, -Second line hormonal treatment: SPRMs and anti-progestins, GnRH agonist and antagonist, -Adjuvant therapy with iron supplementation, -Als [7].</p> <p>OTHER INDICATIONS IN DEVELOPMENT: endometriosis [8]</p> <p>SAME INDICATION IN EARLIER LINE(S) OF TREATMENT:-</p> <p>OTHER DRUGS IN DEVELOPMENT for the SAME INDICATION: telapristone acetate, vilaprisan, elagolix, relugolix, asoprisnil[9]</p> <p>*Service reorganization:No *Possible off label use:No</p>