Report ORGOVYX® relugolix

Product & Mechanism of action	Authorized indications Licensing status	Essential therapeutic features	NHS impact
Substance: relugolix **Brand Name:** Orgovyx **Originator/licensee:** Myovant Sciences Ireland Limited. **Classification:** NCE **ATC code:** L02BX04 **Orphan Status:** **Eu:** No **Us:** No **Mechanism of action:** Relugolix is a hormone antagonist that competitively binds to GnRH receptors in the anterior pituitary gland, preventing native GnRH from binding. This reduces the secretion of LH andFSH, causing a reduction in the production of testosterone from the testes [1].	**Authorized Indication:** **EMA** relugolix is indicated for the treatment of adult pts with advanced hormone-sensitive prostate cancer [1]. **FDA**: relugolix is a GnRH receptorantagonist indicated for the treatment of adult pts with advancedprostate cancer [2]. **Route of administration:** OS **Licensing status** **EU CHMP P.O. date:** 24/02/2022 **FDA M.A. date:** 18/12/2020 **EU Speed Approval Pathway:** No **FDA Speed Approval Pathway:** Yes --- **ABBREVIATIONS:** **ADT:** Androgen Deprivation Therapy **AEs:** Adverse events **CHMP**: Committee for Medicinal Product for Human Use **CI**: Confidence Interval **FSH**: follicle-stimulating hormone **GnRH:** Gonadotropin-releasing hormone **LH**: Luteinizing Hormone **MA**: Marketing Authorization **PO**: Positive Opinion **PSA**: Prostate-specific antigen **Pts**: patients **SoC**: Standard of Care **Vs**.: versus	**Summary of clinical EFFICACY:** **HERO (NCT03085095):**is a randomized, multinational, open label, phase III study in adult men with advanced prostate cancer, requiring at least one year of androgen deprivation therapy.Eligible pts could have one of three clinical disease presentations: evidence of biochemical (PSA) or clinical relapse after local primary intervention with curative intent, newly diagnosed hormone-sensitive metastatic disease, or advanced localized disease unlikely to be cured by local primary intervention with curative intent. Pts (n=934) were randomly assigned in a 2:1 ratio to receive either relugolix (n=622; 120 mg once daily after a single oral loading dose of 360 mg) or leuprolide acetate (n=308; 22.5 mg by injection every three months) for 48 weeks. The primary endpoint was the sustained castration rate, defined as the cumulative probability of testosterone suppression to less than 50 ng per deciliter during receipt of trial treatment from day 29 through 48 weeks. Sustained testosterone suppression was achieved in 96.7% of the pts in the relugolix group (95% CI, 94.9 to 97.9).The leuprolide group had a sustained castration rate of 88.8% (95% CI, 84.6 to 91.8)[3]. **Summary of clinical SAFETY:** The overall incidence of AEs was consistent across treatment groups. Hot flash was the most common AE in both groups (54.3% in the relugolix group vs. 51.6% in the leuprolide group). Diarrhea was reported in a higher percentage of pts in the relugolix group (12.2%) than in the leuprolide group (6.8%). All cases of diarrhea were mild or moderate (grade 1 or grade 2), and no pt was withdrawn because of diarrhea. Fatal events were reported for 1.1% of the pts in the relugolix group and 2.9% of those in the leuprolide group. After 48 weeks of treatment, the incidence of major adverse cardiovascular events (defined as nonfatal myocardial infarction, nonfatal stroke, and death from any cause) was 2.9% (exact 95% CI, 1.7 to 4.5) in the relugolix group and 6.2% (exact 95% CI, 3.8 to 9.5) in the leuprolide group[3]. **Ongoing studies:** ● ***For the same indication:*** Yes. ● ***For other indications:*** Yes. **Discontinued studies (for the same indication):** No. **References:** 1. https://www.ema.europa.eu/en/medicines/human/summaries-opinion/orgovyx 2. https://www.accessdata.fda.gov/drugsatfda_docs/label/2020/214621s000lbl.pdf 3. https://www.nejm.org/doi/10.1056/NEJMoa2004325?url_ver=Z39.882003&rfr_id=ori:rid:crossref.org&rfr_dat=cr_pub%20%200pubmed 4. https://www.drugs.com/price-guide/orgovyx 5. https://www.aiom.it/wp-content/uploads/2020/12/2020_LG_AIOM_Carcinoma_Prostata.pdf 6. https://www.annalsofoncology.org/article/S0923-7534(20)39898-7/fulltext 7. https://clinicaltrials.gov/ct2/home	**Cost of therapy:** The US price for 30 tablets of relugolix 120 mg is $2,573.99 [4]. **Epidemiology:** In Italy, prostatic carcinoma is currently the most frequent neoplasm among men and represents more than 20% of all tumors diagnosed around the 50th year of age. The largest proportion of pts has to be found in the North of the country (1,428 cases per 100,000 inhabitants in the Northwest and 1,395 in the Northeast, respectively) compared to the Center (1,015) and the South (588)of Italy[5]. **POSSIBLE PLACE IN THERAPY** The SoC for advanced hormone-dependent prostate cancer is neo-adjuvant ADT for 4-6 months (± neoadjuvant docetaxel), followed by electron beam radiotherapy + ADT and adjuvant ADT for the subsequent two years. The alternative option includes radical prostectomy + pelvic lymphadenectomy[6]. **OTHER INDICATIONS IN DEVELOPMENT:** Yes (Uterine Fibroids, Contraception, Endometriosis) [7]. **SAME INDICATION IN EARLIER LINE(S) OF TREATMENT:**No [7]. **OTHER DRUGS IN DEVELOPMENT for the SAME INDICATION:** Yes (Trabectedin, Darolutamide, HPN424) [7]. *Service reorganization Y/N: No *Possible off label use Y/N: Yes

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