Relugolix tablets (Orgovyx® ▼) for treatment of prostate cancer

Bath and North East Somerset, Swindon and Wiltshire Together

The BSW Area Prescribing Committee recommends the prescribing of RELUGOLIX 120mg tablets (Orgovyx® ▼) for treating adults with advanced hormone-sensitive prostate cancer in accordance with NICE TA995.

AMBER following specialist initiation: 1-month supply

NICE recommendation for use (NICE TA995)[1]

NICE technology appraisal TA995 (14 August 2024) recommends Relugolix as an option for treating prostate cancer in adults:

- with advanced hormone-sensitive prostate cancer
- alongside radiotherapy for high-risk localised or locally advanced hormone sensitive prostate cancer
- as neoadjuvant treatment before radiotherapy for high-risk localised or locally advanced hormone-sensitive prostate cancer.

NICE also noted that because relugolix is an oral treatment, it may be more convenient for some people than injectable androgen deprivation therapy (ADT) drug treatments. Such treatments are also associated with injection site reactions, including infections and swollen and sore injection sites. Relugolix is associated with faster testosterone recovery times after stopping treatment and reduced risk of cardiovascular events, which may be beneficial for some people.

Costing information[1]

The NHS list price (excluding VAT) of relugolix (Orgovyx®) is £87.45 for a 30-pack of 120mg tablets. At list price, 12 months of treatment would cost £1,065.80 (not including loading dose).

Clinical Effectiveness[1,2]

Relugolix is a nonpeptide GnRH receptor antagonist that competitively binds to GnRH receptors in the anterior pituitary gland preventing native GnRH from binding and signalling the secretion of luteinizing hormone (LH) and follicle-stimulating hormone (FSH). Consequently, the production of testosterone from the testes is reduced. In humans, FSH and LH concentrations rapidly decline upon initiating treatment with Orgovyx® and testosterone concentrations are suppressed to below physiologic concentrations. Treatment is not associated with the initial increases in FSH and LH concentrations and subsequently testosterone ("potential symptomatic flare") observed upon initiation of treatment with a GnRH analogue.

The NICE committee concluded that the evidence from the phase 3 multicenter, open-label trial HERO suggested that relugolix is more effective at reaching and maintaining sustained testosterone suppression below 50 ng/dl and reducing the risk of Major Adverse Cardiac Events (MACE) compared with leuprolide.

Adverse effects/contra-indications[2]

Contraindications are hypersensitivity to the active substances or to any of the excipients. The most frequent adverse drug reactions in clinical trials were hot flush, diarrhoea and musculoskeletal pain (≥ 1/10). See SPC for full safety data, cautions and interactions.

Patient factors[2]

- Relugolix (Orgovyx®) has no or negligible influence on the ability to drive and use machines, but **fatigue** (very common) and **dizziness** (common) are adverse reactions that may influence the ability to drive and use machines.
- **Cardiovascular disease** such as myocardial infarction and stroke has been reported in patients with androgen deprivation therapy. Therefore, all cardiovascular risk factors should be taken into account.
- Long-term suppression of testosterone in men who have had orchiectomy or who have been treated with a GnRH receptor agonist or GnRH antagonist is associated with **decreased bone density**. Decreased bone density, in patients with additional risk factors, may lead to osteoporosis and increased risk of bone fracture.
- Use with caution in patients with **severe renal impairment**; exposure to relugolix in patients with severe renal

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impairment may be increased by up to 2-fold. The amount of relugolix removed by haemodialysis is unknown.

- **Hepatic impairment** - patients with known or suspected hepatic disorder were excluded in long term clinical trials. Mild, transient increases in alanine aminotransferase (ALT) and aspartate aminotransferase (AST) have been observed but were not accompanied by an increase in bilirubin or associated with clinical symptoms. LFT monitoring in patients with known or suspected hepatic disorder is advised.
- Androgen deprivation therapy may prolong the **QT interval**. Assess the benefit risk ratio including the potential for Torsade de pointes prior to initiating relugolix in patients with a history of or risk factors for QT prolongation and in patients receiving concomitant medicinal products that might prolong the QT interval.
- **Fertility** - relugolix may impair fertility in males of reproductive potential.
- **Contraception** - it is not known whether relugolix or its metabolites are present in semen. Effective contraception must be used during treatment and for up to 2 weeks after the last dose of this medicine.

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

- Relugolix should be initiated with a loading dose of 360mg (three tablets) on the first day, followed by a 120mg (one tablet) dose taken once daily at approximately the same time each day.
- Because relugolix does not induce an increase in testosterone concentrations, it is not necessary to add an anti-androgen as surge protection at initiation of therapy.
- If treatment with relugolix is interrupted for greater than 7 days, it must be restarted with a loading dose of 360 mg on the first day, followed with a dose of 120 mg once daily.
- Treatment should only be initiated by a specialist in the management of prostate cancer. **After a minimum of one month's treatment, the specialist may ask the patient's GP to take over prescribing responsibilities of treatment after treatment has been assessed as efficacious. Subsequent follow-up arrangements will be determined on an individual patient basis.**
- 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.
- For people who don't have metastatic prostate cancer, the duration of treatment is likely to be between 6 and 36 months. The specialist will advise on the duration of treatment. For people with metastatic disease, it is assumed that they would remain on ADT indefinitely. Current median survival figures from diagnosis of metastatic disease are approximately 5 years.

Safety [2]

The most commonly observed adverse reactions during relugolix therapy are physiological effects of testosterone suppression, including hot flushes (54%), musculoskeletal pain (30%) and fatigue (26%). Other very common adverse reactions include diarrhoea and constipation (12% each).[2] Refer to SPC for full safety information.

Monitoring[2]

The therapeutic effect of relugolix (Orgovyx®) should be monitored by clinical parameters and prostate-specific antigen (PSA) serum levels as advised by the specialist.

References

1. National Institute for Health and Care Excellence. Technology appraisal 995; Relugolix for treating hormone-sensitive prostate cancer 14th August 2024
2. Accord Healthcare S.L.U.. Summary of Product Characteristics; Orgovyx 120mg film-coated tablets ▼ 29th April 2022.