NHS
Cheshire and Merseyside

Relugolix for hormone-sensitive prostate cancer (NICE TA995)

AMBER RETAINED - specialist initiation and stabilisation with occasional input to support non-specialist prescribing

Recommendations

The Cheshire and Merseyside Area Prescribing Group recommend relugolix for hormone-sensitive prostate cancer, in accordance with NICE TA995.

Relugolix is recommended, within its marketing authorisation, 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. [1]

Prescribing 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.

Implementation notes

Treatment with relugolix should be initiated and supervised by specialist physicians experienced in the medical treatment of prostate cancer. [2]

Prescribing should be retained by the specialist until after the first follow-up appointment. All patients receiving relugolix should be reviewed by the specialist and there should be clear documentation of efficacy and ongoing need for treatment documented in communication to the patient's GP.

Once treatment has been assessed as efficacious, prescribing may be transferred to primary care, but the patient should remain under specialist review.

The therapeutic effect of relugolix should be monitored by clinical parameters and prostate specific antigen (PSA) serum levels, which will be undertaken by the specialist. [2]

Patient factors [2]

Renal impairment - use with caution in patients with severe renal impairment. The exposure to relugolix in patients with severe renal 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 have not been included 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. Monitoring of liver function in patients with known or suspected hepatic disorder is advised during treatment. The pharmacokinetics of relugolix in patients with severe hepatic impairment has not been evaluated.

Effect on QT/QTc interval prolongation - androgen deprivation therapy may prolong the QT interval. 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, physicians should assess the benefit risk ratio including the potential for Torsade de pointes prior to initiating this medicine.

Cardiovascular disease - 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.

Changes in bone density - long-term suppression of testosterone in men who have had orchiectomy or who have been treated with a gonadotropin-releasing hormone (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.

Drug interactions - co-administration of relugolix with oral P-glycoprotein (P-gp) inhibitors, combined P-gp and strong CYP3A inducers should be avoided. See SPC for full information.

Contraception - it is not known whether relugolix or its metabolites are present in semen. If a patient engages in sexual intercourse with a woman of childbearing potential, effective contraception must be used during treatment and for up to 2 weeks after the last dose of this medicine.

Pregnancy - there is a limited amount of data from the use of relugolix in pregnant women. Exposure to relugolix in early pregnancy may increase the risk of early pregnancy loss.

Breast-feeding - studies in animals indicate that relugolix is excreted into the milk of lactating rats. No data is available regarding the presence of relugolix or its metabolites in human milk or its effect on the breast-fed infant. An effect on breast-feeding newborns/infants cannot be excluded.

Fertility - relugolix may impair fertility in males of reproductive potential.

Safety

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.

Cost

The NHS list price for relugolix is £87.45 per 30-tablet pack (excluding VAT).[3] The annual treatment cost per patient in year 1 (including loading dose) is £1,070. The annual treatment cost in subsequent years is £1,064.

Drug	Dosage	Annual cost per patient (excluding VAT)
Relugolix oral tablet	360mg on day 1, then 120mg once daily	£1,070 in year 1, £1,064 thereafter
Degarelix injection	240mg initially, then 80mg once monthly	£1,941.81 in year 1, £1,681.81 thereafter
Triptorelin injection	3mg every 4 weeks	£897
Triptorelin injection	11.25mg every 3 months	£839.50
Triptorelin injection	22.5mg every 6 months	£828
Triptorelin depot injection	3.75mg every 4 weeks	£1,061.97
Leuprorelin acetate injection	3.75mg every month	£978.12
	11.25mg every 3 months	£915.42
Goserelin injection	3.6mg every 28 days	£840
	10.8mg injection every 12 weeks	£940

Based on assumptions within the NICE resource impact template for TA995, the estimated cost of implementing this guidance in Cheshire and Merseyside is £33,000 in 2025-26, £54,000 in 2026-27, £42,000 in 2027-28, £73,000 in 2028-29, and £76,000 in 2029-30 when it is assumed that steady state is reached. This is based on drug costs alone.

Effectiveness

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. FSH and LH concentrations rapidly decline upon initiating relugolix 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. Following discontinuation of treatment, pituitary and gonadal hormone concentrations return to physiologic concentrations.[2]

The main source of clinical-effectiveness evidence for relugolix was HERO, a multicentre, open-label, phase 3 trial. HERO included people aged 18 and over with androgen-sensitive (hormone-sensitive) advanced prostate cancer eligible for at least 1 year of continuous androgen deprivation therapy (ADT). The primary outcome of HERO was the ‘sustained castration rate,’ defined as the cumulative probability of testosterone suppression to less than 50 ng/dL.

The key secondary outcomes that informed the economic model were time to PSA progression and adverse events including major adverse cardiovascular events (MACE). People were randomly assigned in a 2:1 ratio to either relugolix (n=624) or leuprolide (n=310). The HERO results showed that 96.7% of people who had relugolix reached and maintained sustained testosterone suppression below 50 ng/dL from week 5 (day 29) to week 49 (day 337; 95% confidence interval [CI] 94.9% to 97.9%). Results also suggested a

54% reduction in the risk of MACE for relugolix compared with leuprolide (hazard ratio [HR)] 0.46; 95% CI 0.24 to 0.88).

The company also presented a post-hoc subgroup analysis of the incidence of MACE in people with or without a self-reported medical history of MACE. The results suggested that for people with a history of MACE, the odds of having a MACE after 48 weeks were 5.8 times greater with leuprolide compared with relugolix (odds ratio [OR] 5.8; 95% CI 1.5 to 23.3). For people without a medical history of MACE there was no statistically significant difference (OR 1.5; 95% CI 0.7 to 3.4). The NICE committee concluded that the evidence suggested that relugolix is more effective at reaching and maintaining sustained testosterone suppression below 50 ng/dL and reducing the risk of MACE compared with leuprolide.[1]

References

1. National Institute for Health and Care Excellence. Technology Appraisal 995; Relugolix for treating hormone-sensitive prostate cancer, published 14 August 2024. Accessed 05 September 2024.
2. Accord-UK Ltd. Summary of Product Characteristics; Relugolix 120 mg film-coated tablets, 04 June 2024. Accessed 05 August 2024.
3. NHS Business Services Authority. Dictionary of medicines and devices (dm+d) browser. Accessed 05 August 2024.

Patients who are not eligible for treatment under this policy may still be considered for treatment on an individual basis where their GP or consultant believes exceptional circumstances exist that warrant deviation from the rule of this policy. Follow the locally defined process.