Hertfordshire and West Essex Integrated Care System

NHS Hertfordshire and West Essex Integrated Care Board

HWEICS Prescribing Support Document
Relugolix for the treatment of hormone sensitive prostate cancer

1. Introduction

The document aims to support prescribing of Relugolix in adult men with hormone sensitive prostate cancer across Herts and West Essex ICS.

HWE ICS approved indications for use:

Relugolix is recommended in line with NICE TA995 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.

and line with the following pathway/prescribing support document

2. Summary

Prostate cancer is defined as a "malignant tumour of the prostate". 95% of prostate cancers are adenocarcinomas, meaning that it affects the glandular cells. It is multifocal, so may be caused by a variety of genetic mutations which influences the growth and metastasis rate. Majority of prostate cancers grow slowly though some may be more aggressive. Prostate cancer can be categorised into three stages; early (confined in the gland), locally advanced (in the surrounding tissue) and metastatic (disease spreading in other parts of the body, most frequently in the bone).

The aetiology is unknown however risk factors such as age, Black/Afro-Caribbean ethnicity, family history, genetics and weight play a role in the development of prostate cancer.

Prognosis is calculated using the prostate specific antigen (PSA) level, grade group and clinical stage, known as the Cambridge prognostic group, ranging from 1-5, with 1 having a 1.9% 10-year risk of death from prostate cancer to 5 having 31.9%.

Complications can include local invasion, causing urinary symptoms such as retention, haematuria and erectile dysfunction. It can also spread to the bones, causing pain, fractures or cauda equina.

Treatment Pathway:

Diagnosis of prostate cancer/ indication for hormonal treatment

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Initiation of hormonal treatment in line with NICE recommendations: choices include relugolix, degarelix, leuprolide, triptorelin, goserelin. The preferred choice will be the hormonal treatment with the lowest cost, locally agreed triptorelin. Specific circumstances where relugolix would be preferred 1st choice would be prior history of major adverse cardiovascular events or high risk of major adverse cardiovascular events.
All hormonal treatments including relugolix will be initiated by the secondary care specialist.

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Patient undergoes pre-treatment assessment and monitoring in line with specialist responsibilities below. Patient initiated on relugolix. Full blood count (FBC), Liver and Bone profile, Renal function, Urea and electrolytes (U+Es) and prostate specific antigen (PSA) taken at baseline and followed up for a minimum of 3 months to understand if the patient tolerates treatment. If the patient is tolerant to treatment, they would be prescribed with a further month of treatment to allow transfer of prescribing responsibility to primary care.

Relugolix for treating hormone-sensitive prostate cancer

Clinical information

Relugolix is a non-peptide gonadotrophin-releasing hormone (GnRH) receptor antagonist that reduces the release of luteinising hormone (LH) and follicle-stimulating hormone (FSH), thereby reducing the production of testosterone.

Relugolix is quickly absorbed when taken orally, with peak plasma concentrations achieved within 30 minutes.

Licensed indications

Relugolix is licensed and recommended by NICE as an option for use in:

- Adult patients with advanced hormone-sensitive prostate cancer'
- High-risk localised and locally advanced hormone dependent prostate cancer in combination with radiotherapy'
- Neo-adjuvant treatment prior to radiotherapy in patients with high-risk localised or locally advanced hormone dependent prostate cancer'.

Relugolix for the treatment of hormone-sensitive prostate cancer

Clinical information

Relugolix is a GnRH agonist. It is within the group of drugs labelled as “androgen deprivation therapy” (ADT). It competitively binds to GnRH receptors in the anterior pituitary gland preventing native GnRH from binding and signalling the secretion of LH and FSH. As a result, the production of testosterone from the testes is reduced.

FSH and LH concentrations rapidly decline upon initiating treatment with relugolix, and testosterone concentrations are suppressed to below physiological levels. Treatment is not associated with the initial increases in FSH and LH concentrations and subsequently testosterone (otherwise known as “treatment flare” seen with other GnRH agonists).

The elimination half- life of relugolix is 61.5 hours. It is excreted mainly in urine.

RAG rating

RAG rating

Relugolix has been assigned an ‘AMBER initiation’ prescribing status whereby initial prescribing, 3months is by the specialist clinicians with a minimum of 1 month of prescribing on transferring to primary care. Monitoring will continue under the care of the specialist team, but the prescribing will be continued by the GPs.

3. Criteria for prescribing in primary care

The following must apply before the GP is asked to accept on-going prescribing responsibility for relugolix.

Relugolix should be initiated by a specialist who has undertaken the necessary testing to confirm a diagnosis of hormone-sensitive prostate cancer.

Relugolix

Areas of responsibility

Specialist responsibilities	
1.	Initiate relugolix in patients with hormone-sensitive prostate cancer in line with NICE TA995 recommended criteria. If a switch to relugolix from another hormone treatment is required, this would be managed by the secondary care team; this would be for patients with a prior history of major adverse cardiovascular events.
2.	Complete pre-treatment monitoring: • Assessment for risk factors or pre-existing conditions that may potentially be exacerbated by GnRH agonist therapy, such as cardiovascular disease, QT prolongation and osteoporosis. It is unlikely that relugolix would be initiated in those with existing cardiac issues. • Baseline full blood count (FBC), Liver and Bone profile, Renal function, Urea and electrolytes (U+Es) and prostate specific antigen (PSA). • Check for any drug-drug or drug-disease interactions with relugolix.
3.	Discuss treatment with relugolix with the patient including • Counselling points; to include but not limited to: • Advise on dosage and frequency. • Advise on common side effects with the patient/ carer and symptoms the patient may experience. • Advise patients of potential side-effects • Ongoing requirement for monitoring/review • Patients or their carers should be advised to seek help if side effects are suspected.
4.	Ensure that patient/carer is informed and made aware of their responsibilities (see 'Patient/carer responsibilities').
5.	Prescribe relugolix prior to transferring prescribing to primary care. (see 'Criteria for prescribing in primary care')
6.	Following treatment initiation, monitoring by the secondary specialist team will take place every 12-26 weeks, including the same blood tests as baseline and a consultation with the patient about overall tolerability and side effects.
7.	At the point of requesting the transfer to primary care, to provide advice to primary care prescribers which includes but is not limited to the following: - Clear diagnosis and information that has been discussed with patient and carer - Dosing regime and duration - Additional monitoring requirements (if different to standard ongoing monitoring detailed in primary care prescriber responsibilities below) - Stopping/escalation (re-referral) criteria - Specialist team contact details for GPs to obtain advice and support

GP/primary care responsibilities	
1.	Review the request from the specialist and consider if sufficient information has been provided to take on the responsibility for prescribing relugolix in adult men, patient is on

	a stabilised dose and indication is according to the agreed licensed/NICE approved indications for use.
2.	Prescribe relugolix at the dose advised by the specialist team.
3.	Check for possible drug interactions when newly prescribing or stopping concurrent medication.
4.	Seek advice from the specialist team when required regarding any concerns, for example: side effects or lack of efficacy.
5.	To deal with general health issues of the patient.
6.	To report any adverse events to MHRA via Yellow card Scheme

Patient/Carer responsibilities	
1.	Report to their GP if they do not have a clear understanding of or have any concerns with their treatment.
2.	Inform the GP of any changes in circumstances that could affect their treatment
3.	Report any adverse effects or worsening of condition to the GP and/or specialist whilst taking relugolix.
4.	Attend review appointments with specialist and primary care as requested.

Further information

For full details, please refer to the current individual drug Summary of Product Characteristics (SPC) and BNF.

The recommended daily dosage for this indication is as follows:

Treatment with relugolix should be initiated with a loading dose of 360 mg (three tablets) on the first day, followed by a 120 mg (one tablet) dose taken once daily at approximately the same time each day.

Contra-indications and cautions:

Contra-indicated with:

Hypersensitivity to the drug's active substance or excipients

Cautions:

Please refer to BNF and SPC for complete and up to date list of cautions

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. Prescribing clinicians should assess the benefit risk ratio including the potential for Torsade de pointes prior to initiation. A thorough QT/QTc study showed that there was no intrinsic effect of relugolix on prolongation of the QTc interval.

Cardiovascular disease

Cardiovascular disease such as myocardial infarction (MI) and stroke has been reported in the medical literature 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 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.

Renal impairment: No dose adjustment in patients with mild, or moderate renal impairment is required. Caution is warranted in patients with severe renal impairment

Hepatic impairment: No dose adjustment in patients with mild or moderate hepatic impairment is required. Monitoring of liver function in patients with known or suspected hepatic disorder is advised during treatment, this will be undertaken by specialist team if required. The pharmacokinetics of relugolix in patients with severe hepatic impairment has not been evaluated.

Side effects:

Please refer to SPC for complete and up to date list of side effects. SPC

Very common side-effects (≥ 1/10): Hot flushes, diarrhoea, constipation, musculoskeletal (MSK) pain, fatigue
Common side effects (≥ 1/100 to < 1/10): Anaemia, gynaecomastia, insomnia, depression, dizziness, headache, hypertension, nausea, hyperhidrosis, rash, decreased libido, weight gain, hyperglycaemia, hypercholesterolemia
Uncommon (≥ 1/1,000 to < 1/100): urticarial, angioedema, osteoporosis/osteopenia, elevated aspartate aminotransferase (AST) and alanine aminotransferase (ALT)

Action and Advice

Review and discontinuation of medication

Adverse Event:	Recommended action
Hot flushes	Physiological effect of testosterone suppression Management as per other ADT. NICE guidance on management of hot flushes in men on ADT for prostate cancer
Diarrhoea and Constipation	Simple standard therapy measures. Stop medication if significant and consult specialist clinician
MSK pain	Physiological effect of testosterone suppression Management as per other ADT.
Fatigue	Physiological effect of testosterone suppression Management as per other ADT.
Reduced libido	Physiological effect of testosterone suppression Management as per other ADT.

Pregnancy, Lactation and Fertility
This medicinal product is not indicated in women of childbearing potential. It is not to be used in women who are, or may be, pregnant or breast-feeding.

Contraception
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 and Breastfeeding
Studies in animals have shown that exposure to relugolix in early pregnancy may increase the risk of early pregnancy loss and is also 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.

Fertility

Relugolix may impair men of childbearing potential.

Drug interactions:

For a full list of interactions, please refer to SPC for complete and up to date list of drug interactions.

P-gp inhibitors Anti-infectives Erythromycin*, azithromycin*, clarithromycin*, gentamicin*, tetracycline* Antifungals Ketoconazole*, itraconazole* Antihypertensives carvedilol, verapamil* Antiarrhythmics Amiodarone*, dronedarone*, propafenone, quinidine Antianginal Ranolazine* Immunosuppressive agent Cyclosporine* HIV/HCV protease inhibitor Ritonavir*, telaprevir	Affects exposure of relugolix. *Relugolix to be taken first, then the P-gp inhibitor 6 hours after. Closely monitor for increased adverse reactions. Relugolix can be interrupted for up to 2 weeks to cater for a short course of P-gp inhibitor, however for treatment breaks >7 days, patient must be re-loaded onto relugolix with a 360mg loading dose followed by 120mg daily.*

References

1. Accord SmPC. Orgovyz® 120mg film-coated tablets, Relugolix 120mg film-coated tablets. Accessed April 2025 via: https://www.accord-healthcare-products.co.uk/document/smpc-orgovyx-120mg-film-coated-tablets/changes?back=orgovyx-tablets

2. British National Formulary. London: British Medical Association and The Royal Pharmaceutical Society of Great Britain. Accessed April 2025 via: https://bnf.nice.org.uk/drugs/relugolix/

3. NICE Guidance [TA995]: Relugolix for treating hormone-sensitive prostate cancer. Accessed April 2025 via: https://www.nice.org.uk/guidance/ta995

4. NICE CKS: Prostate cancer. Accessed April 2025 via: https://cks.nice.org.uk/topics/prostate-cancer/

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