Relugolix Therapy

INDICATIONS FOR USE:

INDICATION	ICD10	Regimen Code	HSE approved reimbursement status*
Treatment of adult patients with advanced hormone-sensitive prostate cancer (HSPC).	C61	00830a	CDS 01/01/2024

*This is for post 2012 indications only

TREATMENT:

The starting dose of the drugs detailed below may be adjusted downward by the prescribing clinician, using their independent medical judgement, to consider each patients individual clinical circumstances.

Relugolix is administered orally, once daily starting with a loading dose of 360 mg orally on day 1, followed by 120 mg once daily thereafter until disease progression or unacceptable toxicity develops.

Day	Drug	Dose	Route	Cycle
1	Relugolix	360mg	PO	Cycle 1, Day 1 only (loading dose)
2 and onwards	Relugolix	120mg	PO	Cycle 1, Day 2 and onwards
Relugolix can be taken with or without food. Tablets should be taken with some liquid as needed and should be swallowed whole.				
Tablets should be taken at approximately the same time each day.				
If a dose is missed, relugolix must be taken as soon as the patient remembers. If the dose was missed by more than 12 hours, the missed dose must not be taken and regular dosing schedule should be resumed the following day. If treatment with relugolix is interrupted for greater than 7 days, relugolix must be restarted with a loading dose of 360mg on the first day, followed with a dose of 120 mg once daily.				

ELIGIBILITY:

- Indications as above
- 18 years or older
- Histologically or cytologically confirmed adenocarcinoma of the prostate
- ECOG status 0-2

EXCLUSIONS:

- Hypersensitivity to relugolix or any of the excipients

PRESCRIPTIVE AUTHORITY:

The treatment plan must be initiated by a Consultant with expertise in the treatment of prostate carcinoma.

TESTS:

Baseline tests:

- FBC, renal and liver profile
- Blood glucose
- Bone profile
- ECG

Regular tests:

- FBC, renal and liver profile
- Blood glucose and bone profile as clinically indicated
- ECG as clinically indicated

Disease monitoring:

Disease monitoring should be in line with the patient's treatment plan and any other test/s as directed by the supervising Consultant.

DOSE MODIFICATIONS:

- Any dose modification should be discussed with a Consultant.
- If treatment with relugolix is interrupted for greater than 7 days, relugolix must be restarted with a loading dose of 360mg on the first day, followed with a dose of 120 mg once daily thereafter.
- The co-administration of relugolix with oral P-glycoprotein (P-gp) inhibitors and combined P-gp and strong CYP3A inducers must be avoided. If co-administration is unavoidable, the following dose modifications are recommended.

Dose modification for use with P-gp inhibitors:

- Relugolix administered first and dosing of the P-gp inhibitor should be separated by at least 6 hours.
- Treatment with relugolix may be interrupted for up to 2 weeks if a short course of treatment with a P-gp inhibitor is required.

Dose modification for use with combined P-gp and strong CYP3A inducers:

- The dose of relugolix must be increased to 240 mg once daily. After discontinuation of the combined P-gp and strong CYP3A inducer, the recommended 120 mg dose of relugolix once daily must be resumed.

Renal and Hepatic Impairment:

Table 1: Dose modification of relugolix in renal and hepatic impairment

Renal Impairment	Hepatic Impairment
No dose adjustment in patients with mild or moderate renal impairment is required. Caution is warranted in patients with severe renal impairment.	No dose adjustment in patients with mild or moderate hepatic impairment is required.

SUPPORTIVE CARE:

EMETOGENIC POTENTIAL: Minimal **(Refer to local policy).**

PREMEDICATIONS: Not usually required

OTHER SUPPORTIVE CARE: Not usually required

ADVERSE EFFECTS / REGIMEN SPECIFIC COMPLICATIONS:

The adverse effects listed are not exhaustive. Please refer to the relevant Summary of Product Characteristics for full details.

This medicinal product is subject to additional monitoring. Healthcare professionals are asked to report any suspected adverse reactions.

- **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 relugolix.
- **Cardiovascular disease**: Cardiovascular disease such as myocardial infarction 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 gonadotropin hormone-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.
- **Hepatic impairment**: Patients with known or suspected hepatic disorder have not been included in long-term clinical trials with relugolix. 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.
- **Severe renal impairment**: The exposure to relugolix in patients with severe renal impairment may be increased by up to 2-fold. Because a lower dose of relugolix is not available, caution in patients with severe renal impairment is warranted upon administration of a 120-mg dose of relugolix once daily. The amount of relugolix removed by haemodialysis is unknown.
- **Prostate-specific antigen (PSA) monitoring**: The effect of relugolix should be monitored by clinical parameters and prostate-specific antigen (PSA) serum levels.

- **Fertility and Embryo-Fetal Toxicity**: Based on findings in animals and mechanism of action, relugolix may impair fertility in males of reproductive potential. It is not known whether relugolix or its metabolites are present in semen, however based on findings in animals and mechanism of action, male patients with female partners of reproductive potential are advised to use effective contraception during treatment and for 2 weeks after the last dose of relugolix.

DRUG INTERACTIONS:

- Relugolix is a P-gp substrate and the use of relugolix in combination with oral P-gp inhibitors has shown to increase the oral bioavailability of relugolix. The co-administration of relugolix with combined P-gp and strong CYP3A inducers has resulted in a decrease in the oral bioavailability of relugolix. Therefore, co-administration of relugolix with oral P-gp inhibitors and combined P-gp and strong CYP3A inducers should be avoided. If co-administration cannot be avoided, please refer to Dose Modifications for management guidelines.
- Since androgen deprivation treatment may prolong the QT interval, the concomitant use of relugolix with medicinal products known to prolong the QT interval or medicinal products able to induce Torsade de pointes such as class IA (e.g. quinidine, disopyramide) or class III (e.g. amiodarone, sotalol, dofetilide, ibutilide) antiarrhythmic medicinal products, should be carefully evaluated.
- Current drug interaction databases should be consulted for more information.

REFERENCES:

1. Shore ND et al; HERO Study Investigators. Oral Relugolix for Androgen-Deprivation Therapy in Advanced Prostate Cancer. N Engl J Med. 2020 Jun 4; 382(23):2187-2196. doi: 10.1056/NEJMoa2004325. Epub 2020 May 29. PMID: 32469183.
2. Relugolix (Orgovyx®) SmPC. Last updated: 21/12/2023. Accessed 29/12/2023. Available at: https://www.ema.europa.eu/en/documents/product-information/orgovyx-epar-product-information_en.pdf

Version	Date	Amendment	Approved By
1	02/01/2024		Prof. Maccon Keane
2	03/04/2024	Updated prescriptive authority.	Prof. Maccon Keane

Comments and feedback welcome at oncologydrugs@cancercontrol.ie.