Enzalutamide Monotherapy

INDICATIONS FOR USE:

INDICATION	ICD10	Regimen Code	HSE approved reimbursement status*
Treatment of adult men with metastatic castration-resistant prostate cancer whose disease has progressed on or after docetaxel therapy.	C61	00233a	CDS
Treatment of adult men with metastatic castration-resistant prostate cancer who are asymptomatic or mildly symptomatic after failure of androgen deprivation therapy in whom chemotherapy is not yet clinically indicated	C61	00233b	CDS
The treatment of adult men with high-risk non-metastatic castration-resistant prostate cancer (nmCRPC)	C61	00233c	N/A

*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.

Enzalutamide is administered as a single oral daily dose until disease progression or unacceptable toxicity develops.

Drug	Dose	Route	Cycle
Enzalutamide	160mg once daily	PO	Continuous
The capsules should not be chewed, dissolved or opened but should be swallowed whole with water, and can be taken with or without food.			
If a dose is missed at the usual time, the prescribed dose should be taken as close as possible to the usual time. If a patient misses a dose for a whole day, treatment should be resumed the following day with the usual daily dose.			
Medical castration with an LHRH analogue should be continued during treatment of patients not surgically castrated.			

ELIGIBILITY:

- Indications as above
- ECOG status
  - Metastatic CRPC: 0-2
  - Non-metastatic CRPC : 0-1

EXCLUSIONS:

- Hypersensitivity to enzalutamide or any of the excipients
- Severe hepatic impairment
- Uncontrolled hypertension
- Patients suffering from fructose intolerance

PRESCRIPTIVE AUTHORITY:

The treatment plan must be initiated by a Consultant Medical Oncologist.

TESTS:

Baseline tests:

- FBC, renal and liver profile.
- Blood pressure, ECG in patients at risk of QT prolongation.
- INR for patients on warfarin.

Regular tests:

- 4 weekly FBC, renal and liver profile as clinically indicated
- Blood pressure as clinically indicated
- ECG, creatinine as clinically indicated
- Weekly INR tests if patient is on warfarin until stable warfarin dose established

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.

Renal and Hepatic Impairment:

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

Renal Impairment		Hepatic Impairment
CrCl (mL/min)	**Dose**	No dose adjustment is needed
≥30	No dose adjustment is needed.	
<30	No need for dose adjustment is expected	
Haemodialysis	No need for dose adjustment is expected	
Renal and hepatic dose modifications taken from Giraud et al 2023		

Management of adverse events:

Table 2: Dose modification of enzalutamide for Adverse Events

Adverse reactions	Recommended dose modification
Intolerable or ≥ Grade 3	Interrupt therapy for 7 days or until symptoms resolved to ≤ grade 2, then treatment may be resumed at the same dose or a reduced dose (120mg or 80mg) if warranted.
Seizures	Discontinue
Severe hypertension	Interrupt therapy until hypertension has been controlled.
Posterior reversible encephalopathy syndrome (PRES)	Discontinue

Concomitant use with strong CYP2C8 inhibitors:

- The concomitant use of strong CYP2C8 inhibitors should be avoided if possible.
- If patients must be co-administered a strong CYP2C8 inhibitor, the dose of enzalutamide should be reduced to 80mg once daily.
- If co-administration of the strong CYP2C8 inhibitor is discontinued, the enzalutamide dose should be returned to the dose used prior to initiation of the strong CYP2C8 inhibitors.

SUPPORTIVE CARE:

EMETOGENIC POTENTIAL

- As outlined in NCCP Classification Document for Systemic AntiCancer Therapy (SACT) Induced Nausea and Vomiting - Available on the NCCP website

Minimal **(Refer to local policy).**

For information:

Within NCIS regimens, antiemetics have been standardised by Medical Oncologists and Haemato-oncologists and information is available in the following documents:

- NCCP Supportive Care Antiemetic Medicines for **Inclusion in NCIS** (Medical Oncology) - Available on the NCCP website
- NCCP Supportive Care Antiemetic Medicines for **Inclusion in NCIS** (Haemato-oncology) - Available on the NCCP website

PREMEDICATIONS: Not usually required

OTHER SUPPORTIVE CARE:

Enzalutamide may have a moderate influence on the ability to drive and use machines as psychiatric and neurologic events including seizures have been reported. Patients with a history of seizures or other predisposing factors should be advised of the risk of driving or operating machines.

ADVERSE EFFECTS:

- Please refer to the relevant Summary of Product Characteristics (SmPC) for details.

DRUG INTERACTIONS:

- Current SmPC and drug interaction databases should be consulted for information.

REFERENCES:

1. Beer TM, Armstrong AJ et al. Enzalutamide in metastatic prostate cancer before chemotherapy. N Engl J Med. 2014;371:424-33
2. Scher HI, Fizazi K et al. Increased survival with Enzalutamide in prostate cancer after chemotherapy. N Engl J Med. 2012; 367:1187-1197.
3. Giraud E L, Lijster B D, et al. Dose recommendations for anticancer drugs in patients with renal or hepatic impairment: an update. Available at: https://pubmed.ncbi.nlm.nih.gov/37269847/
4. Hussain M et al. Enzalutamide in Men with Nonmetastatic, Castration-Resistant Prostate Cancer. N Engl J Med. 2018 Jun 28;378(26):2465-2474. doi: 10.1056/NEJMoa1800536.
5. NCCP Classification Document for Systemic Anti-Cancer Therapy (SACT) Induced Nausea and Vomiting. V5 2023. Available at: https://www.hse.ie/eng/services/list/5/cancer/profinfo/chemoprotocols/nccp-classification-document-for-systemic-anti-cancer-therapy-sact-induced-nausea-and-vomiting.pdf
6. Enzalutamide (Xtandi®) SmPC EMA. Accessed October 2024. Available at: https://www.ema.europa.eu/en/documents/product-information/xtandi-epar-product-information_en.pdf

Version	Date	Amendment	Approved By
1	10/1/2015		Dr Miriam O Connor
2	01/01/2016	Inclusion of second licensed and funded indication 00233b	Dr Ray McDermott
3	28/06/2016	Amended requirement for 4 weekly tests to be done as clinically indicated. Deleted requirement for blood pressure to be checked every 2 weeks for first 12 weeks and then every 4 weeks	Dr Ray McDermott
4	20/06/2018	Updated with new NCCP regimen template Clarified dosing with concomitant use with strong CYP2C8 inhibitors	Prof Maccon Keane
5	04/09/2019	Inclusion of new indication	Prof Maccon Keane
6	28/07/2021	Reviewed. Added to regular tests and Table 2 (PRES). Updated adverse effects (enzymes induction and hypersensitivity)	Prof Maccon Keane
7	27/01/2025	Regimen reviewed. Updated renal and hepatic dose modifications table to align with Giraud et al 2023	Prof Maccon Keane

Comments and feedback welcome at oncologydrugs@cancercontrol.ie.