Indication	Metastatic hormone-relapsed prostate cancer: • In adults whose disease has progressed during or after docetaxel-containing chemotherapy. • In people who have no or mild symptoms after ADT has failed and before chemotherapy is indicated. **NB** In metastatic hormone-relapsed prostate cancer, patients should have not previously received treatment with enzalutamide or darolutamide or apalutamide or abiraterone, unless abiraterone has had to be stopped within 3 months of its start solely as a consequence of dose-limiting toxicity and in the clear absence of disease progression. **and** Newly diagnosed metastatic hormone-sensitive prostate cancer in combination with androgen deprivation therapy (ADT). **NB** In newly diagnosed metastatic hormone-sensitive prostate cancer, patients should have not previously received any androgen receptor targeted therapy unless: • they received apalutamide or abiraterone for newly diagnosed metastatic hormone-sensitive prostate cancer which had to be stopped due to dose-limiting toxicity in the clear absence of disease progression • the patient has progressive disease following treatment with 2 years of ADT plus abiraterone with or without enzalutamide for high risk non-metastatic disease as part of the STAMPEDE trial and did not progress whilst on such treatment. • the patient has received abiraterone or abiraterone plus enzalutamide as part of the STAMPEDE-1 trial and has not progressed whilst on treatment.
Treatment Intent	Palliative
Frequency and number of cycles	Repeat every 28 days, continuously. Continue until disease progression, unacceptable toxicity or patient's choice to stop treatment.
Monitoring Parameters pre-treatment	• **Virology screening:** All new patients referred for systemic anti-cancer treatment should be screened for hepatitis B and C and the result reviewed prior to the start of treatment. Patients not previously tested who are starting a new line of treatment, should also be screened for hepatitis B and C. Further virology screening will be performed following individual risk assessment and clinician discretion. • Monitor FBC, U&Es and LFTs and BP with each cycle for 6 months and then every 3 months thereafter if clinically indicated. • **Hepatic Impairment** • No dose adjustment required in mild or moderate impairment (child-Pugh class A or B). Use with caution in severe hepatic impairment (Child-Pugh Class C). • **Renal Impairment** • No dose adjustment is necessary in mild to moderate renal impairment. Use with caution in severe renal impairment or end-stage renal disease no data available. • **Dose reductions:** • If a patient experiences a >/= Grade 3 toxicity or an intolerable adverse reaction, dosing should be withheld for one week or until symptoms improve to </= Grade 2, then resumed at the same or a reduced dose (120 mg or 80 mg) if warranted.

	• **Drug interactions (for comprehensive list refer to BNF/SPC):** • The concomitant use of strong CYP2C8 inhibitors (e.g. gemfibrozil) should be avoided if possible, or used with caution. If patients must be co-administered a strong CYP2C8 inhibitor, the dose of enzalutamide should be reduced to 80 mg 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 inhibitor. • Enzalutamide is a potent enzyme inducer and increases the synthesis of many enzymes and transporters; therefore, interaction with many common medicinal products that are substrates of enzymes or transporters is expected. In consideration of the long half-life of enzalutamide, effects on enzymes may persist for one month or longer after stopping enzalutamide. (See SPC). For example, medicinal products with a narrow therapeutic range that are substrates for P-gp (e.g. colchicine, dabigatran etexilate, digoxin) should be used with caution when administered concomitantly with enzalutamide. • Co-administration with warfarin and coumarin-like anticoagulants should be avoided; if treatment is clinically unavoidable increased INR monitoring should be conducted. • **Adverse reactions:** • **Posterior Reversible Encephalopathy Syndrome (PRES**) has been rarely reported with enzalutamide. In patients developing PRES, treatment of specific symptoms including control of hypertension is recommended along with discontinuation of enzalutamide. • **Severe cutaneous adverse reactions** (SCARs) have been reported with enzalutamide. Patients should be advised of the signs and symptoms and monitored closely for skin reactions. • **Delayed or missed doses:** • If a patient misses a dose 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. • **Driving and Machinery:** Patient should be advised of the possible risks of driving or operating machinery whilst taking enzalutamide.
References	KMCC protocol URO-022 V6 SPC accessed online 05.03.2025 CDF list accessed online V1.353 05.03.2025

NB For funding information, refer to CDF and NICE Drugs Funding List

Repeat every 28 days.

TTO	Drug	Dose	Route	Directions
Day 1	**ENZALUTAMIDE**	**160mg**	PO	Each day as a single dose continuously for 28 days. Swallow this medicine whole. Do not chew or crush. Can be taken with or without food. (available as 40mg tablets)
	NB: For newly diagnosed metastatic hormone-sensitive prostate cancer ADT must be prescribed.			