Indication	For the treatment of metastatic hormone relapsed (castrate-resistant) prostate cancer in patients who are treatment naïve to androgen receptor inhibitors* where chemotherapy is not yet clinically indicated or appropriate and • abiraterone plus prednisolone is not tolerated Or • there are clinical conditions that preclude the use of abiraterone plus prednisolone (for this indication. NB: Chemotherapy may have been given for hormone-sensitive disease) *unless the patient received androgen receptor inhibitor therapy for hormone-sensitive disease and stopped treatment >12 months prior to this treatment without PSA (prostate-specific antigen) progression or evidence of progressive disease at the time androgen receptor inhibitor therapy was discontinued OR the patient commenced abiraterone (with olaparib) for this indication, which was discontinued due to lack of tolerance and in the absence of disease progression. NB Patients should have not received previous PARP inhibitor therapy, unless the patient commenced olaparib (with abiraterone) in this same indication, and this was discontinued due to lack of tolerance (despite dose reductions being instigated) in the absence of any signs of disease progression.
Treatment Intent	Palliative
Frequency and number of cycles	Repeat every 28 days Until disease progression, unacceptable toxicity or patient choice to discontinue treatment, whichever is the sooner.
Monitoring Parameters	• **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 at baseline then at the beginning of each cycle. • Prior to cycle 1: If Hb >/=100g/L, Neuts >/=1.5 x 10^9 /l and PLTS >/=75 x 10^9 /l proceed with treatment. During treatment see table 2. • **Hepatic impairment:** o **Talazoparib:** No dose adjustment required in mild or moderate impairment. Not recommended for combination treatment with enzalutamide in severe impairment (Child-Pugh classification C). o **Enzalutamide:** 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:** o **Talazoparib:** No dose adjustment in mild renal impairment (CrCl 60-89 mL/min). In moderate impairment (CrCl 30-59 mL/min), the recommended dose is 0.35 mg once daily in combination with enzalutamide orally once daily. In severe renal impairment (CrCl 15-29 mL/min), the recommended dose is 0.25 mg once daily in combination with enzalutamide once daily. Talazoparib has not been studied in patients with CrCL <15 mL/min or patients requiring haemodialysis. o **Enzalutamide:** 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. • **Management of adverse reactions and dose adjustments:** • **Talazoparib:** o Interruption of treatment or dose reduction of talazoparib may be required to manage adverse reactions (see table 1). If required, for patients on full dose, the first dose reduction (DR) should be to 0.35mg, second DR to 0.25mg, and third DR to 0.1mg. o **Myelodysplastic syndrome/Acute Myeloid Leukaemia (MDS/AML**) have been reported in patients who received poly (adenosine diphosphate-ribose) polymerase (PARP) inhibitors, including talazoparib. If MDS/AML is confirmed, talazoparib should be discontinued.

	○ Patients should be monitored for clinical signs and symptoms of **deep venous thrombosis and pulmonary embolism.** • **Enzalutamide:** ○ 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. ○ **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),** including Stevens-Johnsons syndrome have been reported with enzalutamide. Patients should be advised of the signs and symptoms and monitored closely for skin reactions. • **Common drug interactions (for comprehensive list refer to BNF/SPC):** ○ **Talazoparib:** ○ If co-administration of P-gp inhibitors (e.g. amiodarone, carvedilol, clarithromycin, erythromycin, indinavir, itraconazole, ketoconazole, quinidine, and verapamil) cannot be avoided, when talazoparib is given with enzalutamide, the patient should be monitored for potential increased adverse reactions. ○ Co-administration of talazoparib with strong BCRP inhibitors (e.g. cyclosporin) may increase talazoparib exposure and should be avoided. If co-administration of strong BCRP inhibitors cannot be avoided, patient should be monitored for potential increased adverse reactions. ○ **Enzalutamide:** ○ 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. • **Missed dose:** If the patient vomits or misses a dose, an additional dose should not be taken. Patients should take their next normal dose at its scheduled time. • **Pregnancy and contraception:** Male patients with female partners of reproductive potential or pregnant partners should be advised to use effective contraception (even after vasectomy), during treatment with talazoparib and for at least 4 months after the final dose. Females of reproductive potential should use effective contraception during treatment and for at least 7 months after the final dose. • **Driving and machinery:** Patient should be advised to not drive or operate machinery if affected by symptoms to include fatigue/asthenia or dizziness whilst taking enzalutamide and talazoparib. • For oral self-administration: refer to local Trust policy on oral anti-cancer medicines and supply Patient Information Leaflet.
References	SPC accessed online 30.01.2025 CDF list accessed online 30.01.2026

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

Table 1. Dose reduction levels for talazoparib when used in combination with enzalutamide

	Talazoparib dose level
Recommended starting dose	0.5 mg once daily
First dose reduction	0.35 mg once daily
Second dose reduction	0.25 mg once daily
Third dose reduction	0.1 mg once daily

Table 2. Dose adjustments for adverse reactions

	Withhold Talazoparib until levels resolve to	**Resume Talazoparib**
Haemoglobin < 80 g/L	≥ 90 g/L	Resume at next lower dose
Platelet count < 50 000/µL	≥ 75 000/µL	
Neutrophil count < 1 000/µL	≥ 1 500/µL	
Non-haematologic adverse reaction Grade 3 or Grade 4	≤ Grade 1	Consider resuming at next lower dose or discontinue

Repeat every 28 days

TTO	Drug	Dose	Route	Directions
Day 1	**TALAZOPARIB TOSYLATE**	**0.5mg**	PO	OD Capsules should be swallowed whole, not chewed, opened or dissolved. Available as 0.1mg* and 0.25mg Dispense original packs (30 capsules).
	ENZALUTAMIDE	**160mg**	PO	OD as a single dose continuously for 28 days. Swallow this medicine whole with water. Do not chew or crush. Can be taken with or without food. Available as 40mg tablets
	Metoclopramide	10mg	PO	TDS PRN Do not take for more than 5 days continuously. (dispense 28 tablets on cycle 1, then only if specified)
	Loperamide	2-4mg	PO	Take 4mg initially then 2mg after each loose stool when required (max 16mg a day) (dispense 1 x op on cycle 1, then when required)
	Luteinising hormone releasing hormone (LHRH) analogue should be continued during treatment in patients not surgically castrated.			

* 0.1mg should only be used when a dose modification is required