Indication	Darolutamide in combination with androgen deprivation therapy (ADT) for the treatment of **non-metastatic hormone-resistant** (castration-resistant) prostate cancer in patients who are at high risk of developing metastatic disease. Patients must not have received any previous 2nd generation androgen receptor inhibitors (such as enzalutamide, darolutamide, apalutamide) or CYP17 enzyme inhibitors (such as abiraterone) unless the patient received apalutamide for non-metastatic hormone-resistant (castration-resistant) which had to be stopped because of dose-limiting toxicity in the clear absence of disease progression. For the treatment of newly diagnosed **metastatic hormone-sensitive** prostate cancer in patients who are unsuitable for treatment with docetaxel or the patient is fit for upfront docetaxel but after fully informed consent has chosen not to receive upfront docetaxel. Patients must not have previously received any androgen receptor targeted agent unless the patient has either received enzalutamide, apalutamide, or abiraterone, for newly diagnosed metastatic hormone-sensitive prostate cancer which had to be stopped because of dose-limiting toxicity in the clear absence of disease progression or the patient has progressive disease following treatment with 2 years of ADT plus abiraterone with or without enzalutamide for high risk non-metastatic disease for example as part of the STAMPEDE trial (ISRCTN78818544) and did not progress whilst on such treatment.
Treatment Intent	Hormone resistant non-metastatic prostate cancer.
Frequency and number of cycles	Repeat every 28 days continuously. Continue until disease progression, unacceptable toxicity or patient choice. A formal medical review as to how darolutamide is being tolerated and whether treatment with darolutamide should continue or not will be scheduled to occur at least by the start of the third 4-weekly cycle of treatment.
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. • Confirm the patient's serum testosterone level is <1.7nmol/L on gonadotrophin releasing hormone agonist/antagonist therapy or after bilateral orchidectomy before starting treatment. • Patients must be prescribed androgen deprivation therapy (ADT). • 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 in mild hepatic impairment (Child-Pugh class A). In moderate to severe impairment (Child-Pugh classes B and C) the recommended starting dose is 300mg twice daily. Darolutamide has not been studied in patients with severe hepatic impairment treatment is at clinicians discretion. • **Renal impairment:** No dose adjustment in mild to moderate renal impairment (CrCl >30 mL/min). In patients with severe renal impairment (CrCl < 30 mL/min) not receiving haemodialysis the recommended starting dose is 300mg twice a day. • **Dose Modification:** If a patient experiences a >/= Grade 3 toxicity or an intolerable adverse reaction dosing should be withheld or reduced to 300 mg twice daily until

	symptoms improve. Treatment may then be resumed at a dose of 600 mg twice daily. Dose reduction below 300mg twice daily is not recommended. • **Ischemic heart disease:** Patients should be monitored for signs and symptoms of ischaemic heart disease and ischaemic cerebrovascular disorders. Management of risk factors, such as hypertension, diabetes, or dyslipidaemia should be optimised. • **Cardiovascular disease:** There is no data for patients with clinically significant cardiovascular disease within 6 months prior to treatment (including but not limited to stroke, myocardial infarction, stable/unstable angina and symptomatic congestive heart failure), therefore the safety of darolutamide has not been established and it is at the clinician's discretion to proceed in these patients. • **Seizures:** Seizures have been reported in patients receiving darolutamide. Patients should be advised of the risk of developing a seizure and to avoid activities where sudden loss of consciousness could cause harm to themselves or others. Consider discontinuation of darolutamide in patients who develop a seizure during treatment. • **<u>Common drug interactions (for comprehensive list refer to BNF/SPC)</u>:** o Use of strong and moderate CYP3A4 inducers and P-gp inducers (e.g. carbamazepine, phenobarbital, St. John's Wort, phenytoin, and rifampicin) during treatment with darolutamide is not recommended, unless there is no therapeutic alternative. o Concomitant use of darolutamide with a combined P-gp **and** strong CYP3A4 inhibitor may increase the risk of adverse reactions, patients on this combination should be monitored closely for adverse reactions, dose modification of darolutamide may be required. o Medicines that may prolong the QT interval should be prescribed with caution. o Co-administration of rosuvastatin should be avoided. • **Missed Dose:** If a dose is missed it should be taken as soon as the patient remembers, do not take 2 doses together to make up for a missed dose. • **Driving and Machinery:** Patients should be advised to be cautious due the risk of seizures. • For oral self-administration: refer to local Trust policy on oral anti-cancer medicines and supply Patient Information Leaflet.
References	SPC accessed online 25.11.2025 CDF list v1.376 accessed online 07.11.2025

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

<u>Repeat every 28 days</u>

TTO	Drug	Dose	Route	Directions
Day 1	**DAROLUTAMIDE**	**600mg**	PO	BD. Swallow whole with food. Tablets available as 300mg.
	NB ADT must be prescribed.			