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.
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 pre-treatment	• 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. • **<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.

	• For oral self-administration: refer to local Trust policy on oral anti-cancer medicines and supply Patient Information Leaflet.
References	SPC accessed online 14.06.2022 CDF list v1.214 accessed online blueteq form accessed online

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

Repeat every 28 days

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