NHS
Somerset, Wiltshire, Avon and Gloucestershire Cancer Alliance

Darolutamide

Indication
Darolutamide in combination with androgen deprivation therapy (ADT) is recommended for treating hormone-relapsed prostate cancer (i.e. non-metastatic castrate resistant prostate cancer) in adults at high risk of developing metastatic disease.

(NICE TA660)

ICD-10 codes
C61

Regimen details

Drug	Dose	Route
Darolutamide	600mg BD	Oral

Cycle frequency
Continuous

Number of cycles
Continued until disease progression or unacceptable toxicity

Administration
Darolutamide is available as 300mg tablets

Darolutamide should be taken with food. Tablets should be swallowed whole with water and not broken or crushed.

If a dose is missed, the dose should be taken as soon as the patient remembers prior to the next scheduled dose. The patient should not take two doses to make up for a missed dose.

Pre-medication
Nil

Emetogenicity
This regimen has mild emetic potential (no routine antiemetics are required).

Additional supportive medication
Nil

Extravasation
N/A

Investigations – pre first cycle

Investigation	Validity period
FBC	14 days
U&E (including creatinine)	14 days
LFTs	14 days
PSA	14 days
ECG	14 days

Investigations – pre subsequent cycles

Investigation	Validity period
FBC	Monthly, increasing to 2-monthly as appropriate
U&E	Monthly, increasing to 2-monthly as appropriate
LFTs	Monthly, increasing to 2-monthly as appropriate
PSA	Monthly, increasing to 2-monthly as appropriate
ECG	As indicated

Standard limits for administration to go ahead

If blood results not within range, authorisation to administer **must** be given by prescriber/ consultant

Investigation	Limit
Creatinine clearance (CrCl)	>30ml/min
Bilirubin	≤1.5 x ULN
AST/ALT	≤ 5 x ULN
Neutrophils	≥1 x 10^9/L

Dose modifications

- **Haematological toxicity**

Withhold darolutamide if neutrophils < 1 x 10^9/L.

- **Renal impairment**

No dose adjustment is required for patient with mild or moderate renal impairment (≥30ml/min).

For patients with creatinine clearance of 15-29ml/min, not receiving haemodialysis, the recommended starting dose is 300mg BD. There is no data for patients with CrCl < 15ml/min

- **Hepatic impairment**

No dose adjustment is necessary for patients with mild hepatic impairment.
For patients with moderate or severe hepatic impairment (Child-Pugh B or C), the recommended starting dose is 300mg BD.

Child Pugh Classification:

Score	1	2	3
Bilirubin (µmol/L)	<34	34-50	>50
Albumin (g/L)	>35	28-35	<28
PT (s prolonged)	<4	4-6	>6
Encephalopathy	none	mild	marked
Ascites	none	mild	marked

The individual scores are summed and then grouped as:

- <7 = A
- 7-9 = B
- >9 = C

- **Other toxicities**

If patient experiences ≥ Grade 3 toxicity or an intolerable adverse reaction, dosing should be withheld or reduced to 300mg BD until symptoms improve. Treatment may then be resumed at a dose of 600mg BD.

Dose reduction below 300mg BD is not recommended as efficacy has not been established.

Adverse effects - for full details consult product literature/ reference texts

- **Serious side effects**

QT prolongation
Ischaemic heart disease
Heart failure

- **Frequently occurring side effects**

Fatigue
Rash
Deranged LFTs
Neutropenia

Significant drug interactions – for full details consult product literature/ reference texts

Strong and moderate CYP3A4 inducers and P-gp inducers (e.g. carbamazepine, phenobarbital, St John's Wort, phenytoin and rifampicin): reduces darolutamide exposure, consider alternative medicines with no or weak potential to induce CYP3A4 or P-gp

Strong CYP3A4 and P-gp inhibitors (e.g. itraconazole): increases darolutamide exposure, monitor closely for toxicity and dose reduce as needed

BCRP, OATP1B1 and OATP1B3 substrates (e.g. methotrexate, sulfasalazine, fluvastatin, atorvastatin, pitavastatin): darolutamide may increase plasma concentrations of these substrates, monitor closely for toxicity if concomitant use cannot be avoided.

Rosuvastatin: 5-fold increase rosuvastatin exposure via BCRP, OATP1B1 and OATP1B3 inhibition, avoid.

Medicinal products which prolong the QT interval: avoid concomitant use. These can include some antiarrhythmics, methadone, moxifloxacin and antipsychotics

Additional comments

References

- National Institute for Health and Care Excellence (NICE TA660) accessed 7th September 2021 via www.nice.org.uk
- Summary of Product Characteristics – Darolutamide (Bayer) accessed 7th September 2021 via www.medicines.org.uk
- Fizazi, K. *et al*. Darolutamide in Nonmetastatic Castration-Resistant Prostate Cancer. N Eng J Med 2019; 380:1235

Written/reviewed by: Eve Blackmore (Senior Oncology Pharmacist, UHBW NHS Trust), Dr Serena Hilman (Consultant Oncologist, UHBW NHS Trust)

Checked by: Kate Gregory (Lead Pharmacist for SACT protocols, SWAG Cancer Alliance)

Authorised by: Dr Jeremy Braybrooke (Consultant Oncologist, UHBW NHS Trust and SWAG Cancer Alliance)

Date: October 2021