# **Darolutamide**

Indication

Indicated for the treatment of adult men with

- Non-metastatic castration resistant prostate cancer (nmCRPC) who are at high risk of developing metastatic disease
- Metastatic hormone sensitive patients in combination with docetaxel.
- Metastatic hormone-sensitive prostate cancer (mHSPC) in combination with androgen deprivation therapy

### **Regimen details**

The recommended dose is 600 mg darolutamide (two tablets of 300 mg) taken twice daily, equivalent to a total daily dose of 1200 mg

If given in combination with docetaxel, the first dose of docetaxel should be administered within 6 weeks of the start of darolutamide treatment

# **Cycle frequency**

Twice daily to continue

### **Number of cycles**

Until disease progression

#### **Administration**

Take orally with food

# Investigations – pre first cycle

Investigation	Validity period
PSA	28 days
FBC	28 days
U+E (including creatinine)	28 days
LFT (including AST)	28 days

### Investigations -pre subsequent cycles

FBC, U+E (including creatinine), LFT, PSA

# Standard limits for administration to go ahead

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

Investigation	Limit
Neutrophil count	$\geq 1.0 \times 10^9 / L$
Platelet count	≥ 100 x 10 <sup>9</sup> /L
eGFR	≥ 30 mL/min/1.73m <sup>2</sup>
Bilirubin	≤ 1.5 x ULN
AST	< 1.5 x ULN

# **Dose modifications**

#### **Toxicity**

If a patient experiences  $a \ge Grade 3$  toxicity or an intolerable adverse reaction related to darolutamide, 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 300 mg twice daily is not recommended, because efficacy has not been established.

### **Renal impairment**

No dose adjustment is necessary for patients with mild or moderate renal impairment.

For patients with severe renal impairment (eGFR 15-29 mL/min/1.73 m<sup>2</sup>) not receiving haemodialysis, the recommended starting dose is 300 mg twice daily

### **Hepatic impairment**

No dose adjustment is necessary for patients with mild hepatic impairment.

The available data on darolutamide pharmacokinetics in moderate hepatic impairment is limited. Darolutamide has not been studied in patients with severe hepatic impairment.

For patients with moderate and severe hepatic impairment (Child-Pugh Classes B and C), the recommended starting dose is 300 mg twice daily

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

#### Serious side effects

Cardiac side effects (Includes arteriosclerosis coronary artery, coronary artery disease, coronary artery occlusion, coronary artery stenosis, acute coronary syndrome, acute myocardial infarction, angina pectoris, angina unstable, myocardial infarction, myocardial ischaemia)

### Frequently occurring side effects

**Fatigue** 

Rash

Pain in extremity

Musculoskeletal pain

Fractures

### • Other side effects

Neutrophil count decreased Bilirubin increased

**AST** increased

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

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.

# References

Summary of product characteristics, EMC: <a href="https://www.medicines.org.uk/emc/product/11324">https://www.medicines.org.uk/emc/product/11324</a> - accessed 16/1/2023

Fiazzi et al Darolutamide in Nonmetastatic, Castration-Resistant Prostate Cancer. N Engl J Med 2019; 380:1235-1246

Smith et al Darolutamide and Survival in Metastatic, Hormone-Sensitive Prostate Cancer. N Engl J Med 2022; 386:1132-1142

# THIS PROTOCOL HAS BEEN DIRECTED BY DR PARIKH, CLINICIAN FOR PROSTATE CANCER

# RESPONSIBILITY FOR THIS PROTOCOL LIES WITH THE HEAD OF SERVICE

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