Apalutamide

Indication
Non-metastatic castrate resistant prostate cancer (nmCRPC) who are at high risk of developing metastatic disease and metastatic castrate sensitive prostate cancer

Regimen details
Apalutamide 240mg (4 tablets) orally daily

Cycle frequency
Continuous treatment, dispense monthly

Number of cycles
Until disease progression

Administration
Patients should take their assigned oral dose of the drug once daily with or without food. Tablets should be taken whole and should not be broken, crushed or dissolved in water.
If a dose of apalutamide is missed, the patient should take the missed dose as soon as possible on the same day with a return to the normal schedule on the following day. The patient should not take extra tablets if not within the first 24 hours of missing a dose

Pre-medication
n/a

Emetogenicity
n/a

Additional supportive medication
Continue androgen deprivation therapy

Extravasation
n/a

Investigations – pre first cycle

Investigation	Validity period
FBC	14 days
U+E (including creatinine)	14 days
LFT (including AST)	14 days
PSA	Baseline
TFTs	Baseline
Testosterone	Baseline

Contra-indications / warnings:
Severe hepatic impairment
History of seizures
Cardiovascular disease
Uncontrolled hypertension

Investigations –pre subsequent cycles

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

Standard limits for administration to go ahead

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

Bloods should have been reviewed by the consultant in clinic to ensure no indication of biochemical progression.
If any blood tests except PSA are outside reference range for laboratory please discuss with named consultant

Dose modifications

Toxicity (except for rash)	**Dose of Apalutamide**
Grade 1 or 2	Short treatment breaks can be instituted at the discretion of the physician until the severity of the toxicity decreases to Grade 1 or returns to baseline. If toxicity recurs, dose reductions to the next lower dose level. i.e. 180 mg (3 tablets) or 120 mg (2 tablets) can be made at the discretion of the physician. Discontinue if toxicity persists after 2 dose reductions.
≥Grade 3	Hold until returns to Grade 1 or returns to baseline and resume at full dose
Recurrence ≥Grade 3	Hold until returns to Grade 1 or returns to baseline, then reduce dose to 180 mg (3 tablets). If toxicity recurs again, reduce dose to 120 mg (2 tablets). Discontinue if toxicity persists after 2 dose reductions.
First occurrence of seizure	Discontinue

Management of Drug-related Rash

Severity	**Intervention**
Grade 1	Continue apalutamide at current dose Initiate dermatological treatment • Topical steroid cream AND • Oral Antihistamines Monitor for change in severity
Grade 2 (or symptomatic grade 1)	Hold apalutamide for up to 28 days Initiate dermatological treatment • Topical steroid cream AND • Oral Antihistamines Monitor for change in severity If rash or related symptoms improve, reinitiate apalutamide when rash is Grade ≤1 Consider dose reduction at a 1 dose level reduction i.e. 180 mg (3 tablets)
Grade ≥ 3	Hold apalutamide for up to 28 days Initiate dermatological treatment • Topical steroid cream AND • Oral Antihistamines AND • Consider short course of oral steroids Reassess after 2 weeks (by site staff), and if the rash is the same or has worsened, initiate oral steroids (if not already done) and refer the patient to a dermatologist • Reinitiate apalutamide at a 1 dose level reduction (i.e. 180 mg (3 tablets) or 120 mg (2 tablets) when rash is Grade ≤1. • If the dose reduction will lead to a dose less than 120 mg, then apalutamide must be stopped (discontinued) If after 28 days, rash has not resolved to Grade ≤1, contact the sponsor to discuss further management and possible discontinuation of apalutamide

Adverse effects –

for full details consult product literature/ reference texts

Fatigue, hot flushes, skin rash, weight decreased, arthralgia, falls, hypothyroidism, hypercholesterolemia, seizures

Significant drug interactions

– for full details consult product literature/ reference texts

Concomitant drugs known to lower seizure threshold e.g. antipsychotics, antidepressants – check with pharmacy
Avoid strong CYP3A4 inducers where possible
Apalutamide is a strong inducer of CYP3A4 and CYP2C19 and a weak inducer of CYP2C9
Concomitant use of substrates of UGT may result in decreased exposure of these medicines
Apalutamide is a weak inducer of P-gp and OATP1B1

Additional comments

References

Erleada SPC - https://www.medicines.org.uk/emc/product/9832

THIS PROTOCOL HAS BEEN DIRECTED BY DR BIRTLE, DESIGNATED LEAD CLINICIAN FOR PROSTATE CANCER

RESPONSIBILITY FOR THIS PROTOCOL LIES WITH THE HEAD OF SERVICE

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