Enzalutamide

Indication
Castrate resistant metastatic prostate cancer
Newly diagnosed metastatic hormone-sensitive prostate cancer (COVID-19 guidance)

Regimen details
Enzalutamide 160mg orally daily

Cycle frequency
Continuous treatment, dispense every 1-3 months

Number of cycles
Until disease progression

Administration
Available as 40mg tablets
Tablets should be swallowed whole, with water and can be taken with or without food

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
LDH	14 days
Testosterone	14 days
PSA	14 days

Investigations –pre subsequent cycles
FBC – monthly initially, increasing to up to every 3 months,
LDH
LFTs and U&Es – monthly initially, increasing to up to every 3 months
PSA
Patient should be reviewed by clinician or designated specialist nurse 4-6 weekly

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	≥ 0.5 x 10^9/L
Platelet count	≥ 25 x 10^9/L
Bilirubin	≤ 2 x ULN
AST	< 3 x ULN

Dose modifications

If ≥ grade 3 toxicity, treatment should be withheld until symptoms resolve. Resume at same or reduced dose (120mg or 80mg)

Consider dose reduction if Grade 1 fatigue or greater to 120 mg od, or if persistent fatigue to 80mg od.

If toxicity occurs within 90 days of commencing treatment then treatment can be switched to abiraterone acetate

Hepatic Impairment

No dose adjustment is necessary for patients with pre-existing mild hepatic impairment (Child-Pugh Class A). Caution is required in patients with moderate hepatic impairment (Child-Pugh Class B) and enzalutamide is not recommended in patients with severe hepatic impairment (Child-Pugh Class C)

Adverse effects –

for full details consult product literature/ reference texts

- **Serious side effects**

Seizures
Posterior reversible encephalopathy syndrome
QT interval prolongation

- **Frequently occurring side effects**

Headache
Fatigue
Hypertension

- **Other side effects**

Flushes
Anxiety
Amnesia
Dry skin

Significant drug interactions

– for full details consult product literature/ reference texts

Enzalutamide is a strong inducer of CYP3A4 and a moderate inducer of CYP2C9 and may therefore cause interactions with drugs with a narrow therapeutic index

Strong CYP2C8 inhibitors (e.g. gemfibrozil) may reduce metabolism and increase toxicity of enzalutaomide, avoid concomitant use. If co-administration is deemed essential, reduce dose to 80mg OD during this period

CYP2C8 inducers (e.g. rifampicin) – may increase enzalutamide metabolism leading to therapeutic failure, avoid concomitant use

Since androgen deprivation treatment may prolong the QT interval, the concomitant use of enzalutamide with medicinal products known to prolong the QT interval or medicinal products able to induce Torsade de pointes such as class IA (e.g. quinidine, disopyramide) or class III (e.g. amiodarone, sotalol, dofetilide, ibutilide) antiarrhythmic medicinal products, methadone, moxifloxacin, antipsychotics, etc. should be carefully evaluated

Additional comments

References

Xtandi SPC - https://www.medicines.org.uk/emc/product/10318/smpc

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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