Enzalutamide

Indication

Treatment of metastatic hormone-relapsed prostate cancer for patients who have progressed on, or after, a docetaxel containing chemotherapy regimen.
(NICE TA316)

Treatment of metastatic hormone-relapsed prostate cancer for patients who are asymptomatic or mildly symptomatic after failure of androgen deprivation therapy (ADT) for whom chemotherapy is not yet clinically indicated.
(NICE TA377)

Treatment of hormone-sensitive metastatic prostate cancer in combination with androgen deprivation therapy.
(NICE TA712)

ICD-10 codes

Codes with a prefix C61

Regimen details

Drug	Dose	Route
Enzalutamide	160mg OD	PO

Cycle frequency

Continued until disease progression or unacceptable toxicity.

Number of cycles

As above

Administration

Enzalutamide is available as 40mg capsules.

Capsules should be swallowed whole with water, either with or without food.

In the event of a missed dose, treatment should be taken as close as possible to the usual time. If a whole day is missed, treatment should continue the next day at the usual 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** (or as per local policy)
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** (or as per local policy)
FBC	Monthly or 2 monthly as indicated
U+E (including creatinine)	Monthly or 2 monthly as indicated
LFTs	Monthly or 2 monthly as indicated
PSA	Monthly or 2 monthly as indicated
ECG	If clinically 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	≤ ULN
AST/ALT	≤ 5 x ULN

Dose modifications

- **Haematological toxicity**

Enzalutamide is not myelosuppressive and so treatment may continue in the presence of myelosuppression.

- **Renal impairment**

CrCl (mL/min)	**Enzalutamide dose**
≥ 30	100%
< 30	No data in patients with CrCl < 30mL/min – use with caution

- **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).

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**

For any ≥ grade 3 toxicity, withhold treatment for one week, or until symptoms improve to ≤ grade 2. Resume treatment at same dose or consider dose reduction to 120mg or 80mg, depending on clinical situation (consultant decision).

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 CYP3A4 inducer and so interactions with medicinal products eliminated via this enzyme are expected (e.g. **fentanyl, tramadol, clarithromycin, warfarin, corticosteroids, levothyroxine, statins, antiepileptics, digoxin, beta blockers, calcium channel blockers**). It may take up to one month for enzyme induction to reach full potential. Avoid concomitant use due to risk of therapeutic failure, or use with caution and close monitoring. Avoid co-administration with **warfarin**.

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

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

Medicinal products which prolong the QT interval: avoid concomitant use.

Additional comments

References

- National Institute for Health and Clinical Excellence. NICE Technology Appraisal Guidance 316 accessed 6 May 2015 via www.nice.org.uk
- Cabot, R et al; NEJM 2012; 367: 1187 – 1197
- Beer, T et al; NEJM 2014; 371: 424 - 433
- Summary of Product Characteristics - Enzalutamide (Astellas) accessed 6 May 2015 via www.medicines.org.uk

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