ENZALUTAMIDE (Xtandi)

INDICATION (ICD10) C61

Check the most recent Blueteq eligibility criteria before prescribing. Blueteq registration required (www.england.nhs.uk/publication/national-cancer-drugs-fund-list/)

Enzalutamide for the treatment of patients with hormone-relapsed (castrate-resistant) metastatic prostate cancer before chemotherapy is indicated where all the following criteria are met (TA377):

2. Either has a proven histological or cytological diagnosis of adenocarcinoma of the prostate OR has presented with a clinical picture consistent with metastatic prostate cancer with both widespread bone metastases radiologically typical of prostate cancer AND a serum PSA of ≥50ng/ml.
3. Has hormone-relapsed (castrate-resistant) metastatic prostate cancer.
4. Has no or only mild symptoms after androgen deprivation therapy has failed.
5. Chemotherapy is not yet indicated.
6. One of the following applies to this patient as regards any previous use of 2nd generation receptor inhibitors (such as enzalutamide, darolutamide or apalutamide) or CYP17 enzyme inhibitors (such as abiraterone).
- has not been previously received any treatment with enzalutamide or darolutamide or apalutamide or abiraterone OR
- has previously received abiraterone for this same pre-chemotherapy indication in hormone-relapsed (castrate-resistant) prostate cancer but it was stopped within 3 months of it starting due to dose-limiting toxicity and in the clear absence of disease progression.
7. ECOG performance status (PS) of 0 or 1 or 2.
8. Enzalutamide is to be continued until disease progression or unacceptable toxicity or patient choice to stop treatment.
9. A formal medical review as to how enzalutamide is being tolerated and whether treatment with enzalutamide should continue or not will be scheduled to occur at least by the start of the third 4-weekly cycle of treatment.
10. Where a treatment break of more than 6 weeks beyond the expected 4-weekly cycle length is needed, I will complete a treatment break approval form to restart treatment, including indicating as appropriate if the patient had an extended break because of COVID 19.
11. Enzalutamide is to be otherwise used as set out in its Summary of Product Characteristics.

Enzalutamide for the treatment of patients with hormone-relapsed (castrate-resistant) metastatic prostate cancer with disease progression during or following treatment with docetaxel-containing chemotherapy where all the following criteria are met (TA316):

2. Either has a proven histological or cytological diagnosis of adenocarcinoma of the prostate OR has presented with a clinical picture consistent with metastatic prostate cancer with both widespread bone metastases radiologically typical of prostate cancer AND a serum PSA of ≥50ng/mL.
3. Has hormone-relapsed (castration-resistant) metastatic prostate cancer.
4. Has been treated with docetaxel-containing chemotherapy and has progressed during or following treatment.
5. One of the following applies to this patient as regards any previous use of 2nd generation receptor inhibitors (such as enzalutamide, darolutamide or apalutamide) or CYP17 enzyme inhibitors (such as abiraterone).
- has not been previously received any treatment with enzalutamide or darolutamide or apalutamide or abiraterone OR
- has previously received abiraterone for this same pre-chemotherapy indication in hormone-relapsed (castrate-resistant) prostate cancer but it was stopped within 3 months of it starting due to dose-limiting toxicity and in the clear absence of disease progression.
6. ECOG performance status (PS) of 0 or 1 or 2.
7. Enzalutamide is to be continued until disease progression or unacceptable toxicity or patient choice to stop treatment.

8. A formal medical review as to how enzalutamide is being tolerated and whether treatment with enzalutamide should continue or not will be scheduled to occur at least by the start of the third 4-weekly cycle of treatment.
9. Where a treatment break of more than 6 weeks beyond the expected 4-weekly cycle length is needed, I will complete a treatment break approval form to restart treatment, including indicating as appropriate if the patient had an extended break because of COVID 19.
10. Enzalutamide is to be otherwise used as set out in its Summary of Product Characteristics.

Enzalutamide in combination with androgen deprivation therapy (ADT) for the treatment of patients with newly diagnosed metastatic hormone-sensitive prostate cancer where all the following criteria are met:
2. Either has a proven histological or cytological diagnosis of adenocarcinoma of the prostate or has presented with a clinical picture consistent with metastatic prostate cancer with both widespread bone metastases radiologically typical of prostate cancer and a serum PSA of ≥50ng/mL.
3. Has newly diagnosed metastatic prostate cancer that is hormone sensitive and has either not been treated with docetaxel and has currently received androgen deprivation therapy (ADT) for no longer than 3 months or has been treated with docetaxel and has received ADT for no more than 9 months.
4. ECOG performance status (PS) of 0 or 1 or 2.
5. Assessed this patient's status as regards receiving upfront docetaxel and have concluded that the patient completed planned docetaxel therapy or discontinued docetaxel before completion of planned treatment duration or should not have been treated with docetaxel or chose not to be treated with docetaxel.
- the patient was treated with docetaxel and completed a planned treatment duration of 6 cycles of docetaxel
- the patient commenced docetaxel and discontinued docetaxel prior to completion of 6 cycles on account of excessive toxicity (i.e. the patient COULD NOT complete planned treatment duration with docetaxel)
- the patient had significant comorbidities which precluded treatment with docetaxel (i.e. the patient SHOULD NOT be treated with docetaxel) and this has been fully discussed with the patient. It is recommended that validated systems of scoring clinical frailty are used as part of the oncology assessment as to explaining the benefits and risks of the treatment options of chemotherapy and enzalutamide
- the patient has been fully consented regarding all of the following: the advantages and disadvantages of upfront docetaxel chemotherapy vs upfront enzalutamide; that the use of upfront enzalutamide would result in there being no further possible treatment with any androgen receptor targeted agents when the patient's disease progresses; and that the patient may not be fit enough to receive docetaxel when the patient's disease progresses. After such informed consent, I confirm that the patient has chosen to receive upfront enzalutamide (i.e. the patient is fit for chemotherapy with docetaxel and has CHOSEN NOT to be treated with docetaxel).
6. Enzalutamide is being given only in combination with ADT.
7.
Has not previously received any androgen receptor targeted agent unless the patient has either received apalutamide for newly diagnosed metastatic hormone-sensitive prostate cancer which had to be stopped because of dose limiting toxicity in the clear absence of disease progression and the patient meets all the other criteria listed on this form or the patient has progressive disease following treatment with 2 years of ADT plus abiraterone with or without enzalutamide for high risk non-metastatic disease as part of the STAMPEDE trial (ISRCTN78818544) and did not progress whilst on such treatment and the patient meets all the other criteria listed on this form.
which of these 2 clinical scenarios applies to this patient:
- the patient has not previously received any androgen receptor targeted agent
- the patient commenced apalutamide which had to be stopped because of dose-limiting toxicity in the clear absence of disease progression and the patient meets all the other criteria listed here

- the patient was treated with 2 years of ADT plus abiraterone with or without enzalutamide for high risk non-metastatic disease as part of the STAMPEDE trial and did not progress whilst on such treatment and the patients meets all the other
criteria listed here.
8. Enzalutamide is to be continued until disease progression or unacceptable toxicity or patient choice to stop treatment.
9. A formal medical review as to how enzalutamide is being tolerated and whether treatment with enzalutamide should continue or not will be scheduled to occur at least by the start of the third 4-weekly of treatment.
10. Where a treatment break of more than 6 weeks beyond the expected 4-weekly cycle length is needed, I will complete a treatment break approval form to restart treatment, including indicating as appropriate if the patient had an extended break because of COVID 19.
11. Enzalutamide is to be otherwise used as set out in its Summary of Product Characteristics

REGIMEN
Days 1 to 28 ENZALUTAMIDE 160mg orally once daily

CYCLE FREQUENCY AND NUMBER OF CYCLES
Until disease progression.

ADMINISTRATION
Available as 40mg tablets
Swallowed whole with water, with or without food.

ANTI-EMETICS
Minimal risk

CONCURRENT MEDICATION REQUIRED

Enzalutamide	-

EXTRAVASATION AND TYPE OF LINE / FILTERS
Not applicable

INVESTIGATIONS
Blood results required before SACT administration
FBC, U&E and LFTs, PSA every cycle, increasing to every 3 cycles
Neutrophils x 10^9/L ≥1.5
Platelets x 10^9/L ≥100
Creatinine every cycle
Blood pressure monthly initially then 3 monthly
Baseline weight and every cycle

MAIN TOXICITES AND ADVERSE REACTIONS

Enzalutamide	Fatigue Hot flush Headache Hypertension Risk of seizures (<1%)

INTERACTIONS WHICH MAY REQUIRE DOSE MODIFICATIONS
(not exhaustive list check SPC/BNF/Stockleys)

Enzalutamide	Enzalutamide is a strong CYP3A4 enzyme inducer therefore there are a large number of interactions, check interactions carefully. Strong CYP2C8 inhibitors should be avoided.

DOSE MODIFICATIONS
Non-haematological
If a patient experiences a ≥grade 3 toxicity or an intolerable adverse reaction, treatment should be withheld for one week or until symptoms improve to ≤grade 2. Resume treatment at the same dose, or a reduced dose (120 mg or 80 mg) if appropriate.

Hepatic impairment
Enzalutamide
No dose adjustment is necessary for patients with mild hepatic impairment (Child Pugh Class A). Caution is advised in patients with moderate hepatic impairment (Child Pugh Class B). It is not recommended in patients with severe hepatic impairment (Child-Pugh Class C).

Renal impairment
Enzalutamide
Caution advised in patients with severe renal impairment (CrCl <30ml/min).

REFERENCES
1. Cabot, R et al; NEJM 2012; 367: 1187–1197
2. Beer, T et al; NEJM 2014; 371: 424-433