APALUTAMIDE (Erleada)

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/)

For the treatment of non-metastatic hormone-resistant (castration-resistant) prostate cancer (in combination with androgen deprivation therapy (ADT)) in patients who are at high risk of developing metastatic disease where the following criteria have been met:

2. A proven histological or cytological diagnosis of adenocarcinoma of the prostate without neuroendocrine differentiation or features of a small cell carcinoma.
3. Non-metastatic prostate cancer as defined by recent imaging with conventional imaging with both a whole body isotope bone scan and a CT/MR scan of the chest, abdomen and pelvis.Note: patients with the sole abnormality of pelvic lymph nodes measuring <2cm in short axis diameter and which are below the aortic bifurcation are eligible for apalutamide in this indication.
4. Hormone-resistant (castrate-resistant) disease as defined by 3 rising PSA levels (after the nadir PSA level) and taken at least 1 week apart during androgen deprivation therapy.
5. Serum testosterone level is <1.7nmol/L on gonadotrophin releasing hormone agonist/antagonist therapy or after bilateral orchidectomy.
6. The current PSA level is ≥2ng/ml.
7. Is at high risk of developing metastatic disease as defined by a PSA doubling time of ≤10 months during continuous ADT.
8. ECOG performance status of either 0 or 1 or 2.
9. Has not received any previous 2nd generation androgen receptor inhibitors (such as enzalutamide, darolutamide, apalutamide) or CYP17 enzyme inhibitors (such as abiraterone) unless apalutamide has been accessed via a company early access scheme for this specific indication and the patient meets all the other criteria listed in this form.
10. Apalutamide is being given only in combination with androgen deprivation therapy.
11. Apalutamide is to be continued until disease progression or unacceptable toxicity or patient choice to stop treatment.
12. A formal medical review as to how apalutamide is being tolerated and whether treatment with apalutamide should continue or not will be scheduled to occur at least by the start of the third 4-weekly cycle of treatment.
13. Where a treatment break of more than 6 weeks beyond the expected 4-week 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.
14. Apalutamide is to be otherwise used as set out in its Summary of Product Characteristics

For the treatment of patients with newly diagnosed metastatic hormone-sensitive prostate cancer (in combination with androgen deprivation therapy (ADT)) who are ineligible for chemotherapy with docetaxel where the following criteria have been 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. Newly diagnosed metastatic prostate cancer that is hormone sensitive and has currently received androgen deprivation therapy (ADT) for no longer than 3 months.
4. Has not received any upfront docetaxel chemotherapy for metastatic hormone sensitive prostate cancer.
5. ECOG performance status (PS) of 0 or 1 or 2.
6. The prescribing clinician has assessed this patient's status as regards receiving upfront docetaxel and have concluded that the patient is ineligible for docetaxel on the grounds of either having significant comorbidities (i.e. the patient should not be treated with docetaxel) or the patient is fit for upfront docetaxel but after fully informed consent has chosen not to receive upfront docetaxel. the patient has significant comorbidities which preclude 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 apalutamide
- the patient has been fully consented regarding all of the following: the advantages and disadvantages of upfront docetaxel chemotherapy vs upfront apalutamide; that the use of upfront apalutamide 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 apalutamide (i.e. the patient is fit for chemotherapy with docetaxel and has CHOSEN NOT to be treated with docetaxel)
7. Apalutamide is being given only in combination with ADT.
8. The patient has not previously received any androgen receptor targeted agent unless the patient has either received enzalutamide 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 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.
which of these 2 clinical scenarios applies to this patient:
- the patient has not previously received any androgen receptor targeted agent
- the patient commenced enzalutamide 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.
9. Apalutamide is to be continued until disease progression or unacceptable toxicity or patient choice to stop treatment.
10. A formal medical review as to how apalutamide is being tolerated and whether treatment with apalutamide should continue or not will be scheduled to occur at least by the start of the third 4-weekly cycle of treatment.
11. 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.
12. Apalutamide is to be otherwise used as set out in its Summary of Product Characteristics.

REGIMEN
APALUTAMIDE 240mg orally once daily continuously
Androgen deprivation therapy (ADT)

CYCLE FREQUENCY AND NUMBER OF CYCLES
Until disease progression

ADMINISTRATION
Available as 60mg tablets
Swallow whole

ANTI-EMETICS
Minimal risk all days

CONCURRENT MEDICATION REQUIRED

Apalutamide	Androgen deprivation therapy (ADT)

EXTRAVASATION AND TYPE OF LINE / FILTERS

Not applicable

INVESTIGATIONS

Blood results required before SACT administration
FBC, U&E and LFTs monthly
Neutrophils x 10^9/L ≥1.5
Platelets x 10^9/L ≥100
PSA every month

MAIN TOXICITES AND ADVERSE REACTIONS

Apalutamide	Arthralgia Hypercholestoraemia Hypertrigylceridaemia Hypertension Hypothyroidism Ischaemic heart disease Rash Fracture risk – consider bisphosphonate Increased seizure risk

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

Apalutamide	Lots of interactions check carefully Dose reductions based on tolerability should be considered when apalutamide is used with strong inhibitors of CYP2C8 (eg clopidogrel) or CYP3A4 (eg clarithromycin).

DOSE MODIFICATIONS

Apalutamide
If a ≥grade 3 toxicity or an intolerable adverse reaction is experienced by the patient, dosing should be held rather than permanently discontinuing treatment until symptoms improve to ≤grade 1 or original grade, then should be resumed at the same dose or a reduced dose (180mg or 120mg), if warranted.

Hepatic impairment

Apalutamide
Not recommended in patients with severe hepatic impairment.

Renal impairment

Apalutamide
Caution in patients with severe renal impairment

REFERENCES

1. CDF