ABIRATERONE (Zytiga) Prednisolone

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/)

Abiraterone 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 (TA259):

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 ≥50 ng/mL.
3. Has hormone-relapsed (castrate-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).
- the patient has not previously received any treatment with enzalutamide or darolutamide or apalutamide or abiraterone
- the patient has previously received enzalutamide for this same post-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. Abiraterone is to be given in combination with prednisolone
7. ECOG performance status (PS) of 0 or 1 or 2.
8. Abiraterone is to be continued until disease progression or unacceptable toxicity or patient choice to stop treatment.
9. A formal medical review as to how abiraterone is being tolerated and whether treatment with abiraterone 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. Abiraterone is to be otherwise used as set out in its Summary of Product Characteristics.

Abiraterone for the treatment of patients with hormone-relapsed (castrate-resistant) metastatic prostate cancer before chemotherapy is indicated where all the following criteria are met (TA387)

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 ≥50 ng/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).
- the patient has not been previously received any treatment with enzalutamide or darolutamide or apalutamide or abiraterone OR
- the patient has previously received enzalutamide 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. Abiraterone is to be given in combination with prednisolone

8. ECOG performance status (PS) of 0 or 1 or 2.
9. Abiraterone is to be continued until disease progression or unacceptable toxicity or patient choice to stop treatment.
10. A formal medical review as to how abiraterone is being tolerated and whether treatment with abiraterone 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. Abiraterone is to be otherwise used as set out in its Summary of Product Characteristics.
For either indication, no previous treatment with enzalutamide, unless enzalutamide has had to be stopped within 3 months of its start solely as a consequence of dose-limiting toxicity and in the clear absence of disease progression

REGIMEN

Days 1 to 28	ABIRATERONE	1000mg orally once daily
	Prednisolone	5mg orally twice daily

CYCLE FREQUENCY AND NUMBER OF CYCLES
Until disease progression.

ADMINISTRATION
Available as 500mg tablets
Swallowed whole with water, taken at least one hour before or at least two hours after eating.

ANTI-EMETICS
Minimal risk

CONCURRENT MEDICATION REQUIRED

Abiraterone	Prednisolone 5mg orally twice daily (must be used in combination with prednisolone, not approved for use in combination with dexamethasone)

EXTRAVASATION AND TYPE OF LINE / FILTERS
Not applicable

INVESTIGATIONS
Blood results required before SACT administration
FBC, U&E and LFTs every 2 weeks for 3 cycles then every cycle
Neutrophils x 10^9/L ≥1.5
Platelets x 10^9/L ≥100
Creatinine every cycle
Blood pressure weekly initially, once monthly when stable
PSA every cycle initially then every 3 cycles
Baseline weight and every cycle

MAIN TOXICITES AND ADVERSE REACTIONS

Abiraterone	Hypertension, hypokalaemia and fluid retention use with caution Adrenocortical insufficiency Hepatotoxicity

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

Abiraterone	Strong inducers of CYP3A4 (eg phenytoin, carbamazepine, rifampicin, rifabutin, rifapentine, phenobarbital, St John's wort) during treatment are to be avoided. Strong inhibitors of CYP3A4 (eg itraconazole, clarithromycin, voriconazole) may be used with caution

DOSE MODIFICATIONS
Non-haematological
In patients with pre-existing hypokalaemia or those that develop hypokalaemia whilst being treated with abiraterone, consider maintaining the patient's potassium level at ≥4.0mM.
For patients who develop grade ≥3 toxicities including hypertension, hypokalaemia, oedema and other non-mineralocorticoid toxicities, treatment should be withheld and appropriate medical management should be instituted. Treatment with abiraterone should not be reinitiated until symptoms of the toxicity have resolved to grade 1 or baseline.

Hepatic impairment
Abiraterone
No dose adjustment is required in pre-existing mild hepatic impairment.
Abiraterone should be avoided in severe hepatic impairment.

ALT or AST >5-19xULN	Withhold abiraterone treatment until ALT or AST recovered to the patient's baseline. Re-treatment may then be considered at a reduced dose of 500mg once daily. For patients being re-treated, serum transaminases should be monitored at a minimum of every two weeks for three months and monthly thereafter. If hepatotoxicity recurs at the reduced dose of 500mg daily, treatment should be discontinued.
ALT or AST ≥20xULN	Discontinue permanently

Renal impairment
Abiraterone
Caution advised in patients with severe renal impairment.

REFERENCES
1. de Bono, JS et al; N Engl J Med 2011; 364: 1995-2005
2. Ryan, CJ et al; NEJM 2013; 368: 138-148