ABIRATERONE AND PREDNISOLONE

A treatment option for men with hormone-refractory metastatic prostate cancer :
whose disease has progressed on or after docetaxel (NICE approved 2012)
or
who have no or mild symptoms after ADT has failed, and before chemotherapy is indicated (NICE approved 2016)

Blueteq registration is required before treatment may start

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

Individual consent is not necessary for this drug

Drugs / Dosage:	Abiraterone	1000mg	PO	once daily throughout treatment
	Prednisolone	5mg bd	PO	throughout treatment

Administration: Abiraterone is available as 500 mg tablets, which should be swallowed whole on an empty stomach i.e. at least one hour before food and at least two hours after any previous food. (Taking the tablets with food can dramatically increase the absorption of abiraterone, dependent on the fat content of the food)

Frequency: continuous treatment until disease progression or unacceptable toxicity.
When abiraterone is discontinued, prednisolone dose should be tapered slowly, and monitoring for adrenocortical insufficiency should occur.

Main Toxicities: fluid retention; hypertension; hypokalaemia; hepatotoxicity; UTIs

Anti-emetics: mildly emetogenic (no anti-emetic routinely required)

Regular Investigations:	FBC	monthly (every 2 months in stable patients)
	LFTs, U&Es, including K^+	} every 2 weeks for the first 3 months*, then every month,
	Blood pressure	} then every 2 months in long-term, stable patients
	PSA	monthly (every 2 months in long-term, stable patients)
	Echo for LVEF	baseline if concerned (there is no safety data for patients with LVEF < 50%)

*If patient's LFTs, K^+ and blood pressure all remain completely within normal limits without any interventions at baseline, 2 week check and 4 week appointment, then it has been agreed locally that monitoring of LFTs, b.p and K^+ may revert to monthly thereafter.
For all other patients, 2-weekly monitoring should continue for 3 months.

Interactions: Abiraterone is a substrate of CYP3A4.
Strong CYP3A4 inducers (e.g. phenytoin, carbamazepine, rifampicin, rifabutin) should be avoided, as this may result in therapeutic failure.
Strong inhibitors of CYP3A4 (e.g., itraconazole, clarithromycin, voriconazole) may be used with caution – in a pharmacokinetic study, the co-administration of ketoconazole had no clinically meaningful effect on the pharmacokinetics of abiraterone.

It is possible that abiraterone may cause increased levels of drugs which are metabolised via CYP2D6 e.g metoprolol, propranolol, haloperidol, flecainide, venlafaxine, desipramine.

Reason for Update: switching from 250mg tablets to 500mg tablets	Approved by Consultant: Dr S Khaksar
Version: 5	Approved by Lead Chemotherapy Nurse: P Deery
Supersedes: Version 4	Date: 13.3.17
Prepared by: S Taylor	Checked by: C Tucker

Codeine, oxycodone and tramadol are all activated via CYP2D6 to their active metabolites, and so initiation or discontinuation of abiraterone may have an effect on analgesic requirements for patients on these agents.

Dose Modifications

Haematological Toxicity: Abiraterone is not myelosuppressive and treatment may continue in the presence of myelosuppression.

Hypertension: Pre-existing hypertension should be controlled (usually via the GP) before treatment with abiraterone starts.
Baseline blood pressure should be < 150/100mmHg.

Blood pressure after abiraterone initiated	Management
Diastolic increase > 20mmHg above baseline or blood pressure rises to > 150/100mmHg	Antihypertensive therapy* may be required (or adjusted, if already on antihypertensives). Abiraterone may continue.
Blood pressure > 180/110mmHg	Abiraterone therapy should be withheld until blood pressure controlled*

* Manage hypertension according to current NICE guidelines:
for previously untreated patients > 55 years, use a calcium channel blocker first-line.
Monitoring of b.p., and management until stabilised, may require GP involvement.

Hypokalaemia: Pre-existing hypokalaemia should be corrected before abiraterone treatment starts.
For any hypokalaemia (K^+ < 3.5mmol/l) which develops while on abiraterone, manage according to local guidelines.
If K^+ < 3.5 – 3.0 mmol/l, abiraterone may continue.
If K^+ < 3.0 mmol/l, withhold abiraterone until K^+ has recovered to normal limits.

Hepatic Impairment: Note that a raised ALP in isolation is usually indicative of bone metastases, and in those circumstances is not an indication for a dose reduction.

No dose adjustment is required for patients with pre-existing mild hepatic impairment. There are no data for patients with pre-existing moderate or severe hepatic impairment (Child-Pugh B or C) and abiraterone is not recommended in these patients.

Hepatotoxicity: If after treatment has started, transaminase levels rise, manage as follows:

ALT	Management
> 5 x ULN - 19 x ULN	Withhold abiraterone treatment until ALT recovered to the patient's baseline. Re-treatment may then be considered at a reduced dose of 500 mg 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 500 mg daily, treatment should be discontinued.
≥ 20 x ULN	Discontinue abiraterone permanently

Renal Impairment: It is not expected that a dose reduction is required for patients with renal impairment. However, there is no clinical experience in patients with prostate cancer and severe renal impairment.

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