Abiraterone (Zytiga®) for
Metastatic Castrate-Resistant Prostate Cancer

DRUG ADMINISTRATION SCHEDULE

<table>
<thead>
<tr>
<th>Day</th>
<th>Cycle length</th>
<th>Drug</th>
<th>Daily Dose</th>
<th>Route</th>
<th>Schedule</th>
</tr>
</thead>
<tbody>
<tr>
<td>Days 1 to 28</td>
<td>4 weeks</td>
<td>Abiraterone</td>
<td>1000mg</td>
<td>Oral</td>
<td>ONCE daily</td>
</tr>
<tr>
<td>Days 1 to 28</td>
<td>4 weeks</td>
<td>Prednisolone</td>
<td>10mg</td>
<td>Oral</td>
<td>ONCE daily</td>
</tr>
</tbody>
</table>

*Abiraterone presented as 500mg tablets since formulation switch in 2017
*Must not be taken with food (see administration notes)

NUMBER OF DAYS PER CYCLE
The recommended dose is 1000 mg abiraterone once daily continuously. One cycle equals four weeks of treatment. Treatment should continue as long as clinical benefit is observed (see below) or until unacceptable toxicity occurs.

APPROVED INDICATIONS

NICE TA387: Pre Chemo
Abiraterone in combination with prednisolone is recommended, within its marketing authorisation, as an option for treating metastatic hormone-relapsed prostate cancer in people who have no or mild symptoms after androgen deprivation therapy has failed, and before chemotherapy.

NICE TA259: Pre Chemo
Abiraterone in combination with prednisolone is recommended as an option for the treatment of castration-resistant metastatic prostate cancer in adults, only if their disease has progressed on or after one Docetaxel containing chemotherapy regimen,

ELIGIBILITY CRITERIA
- Eastern Cooperative Oncology Group (ECOG) performance status of 0, 1 or 2

EXCLUSION CRITERIA
- Uncontrolled hypertension
- History of pituitary or adrenal dysfunction
- Clinically significant heart disease
- Patients previously treated with ketoconazole may theoretically have a lower response rate to abiraterone.
- Patients should continue on androgen deprivation therapy (ADT)

ASSESSMENT OF RESPONSE
Clinical review every 2 weeks for first 3 months after starting, then every 4 weeks. Treatment should continue until:
- Clinical Disease Progression OR
- Any 1 of the following (OR ≥ 2 of the following if clinical benefit):
  - PSA progression (>50% rise confirmed on 2 samples over baseline or nadir)
  - Bone scan new lesions (definite)
  - CT evidence of progression
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ANTI-EMETICS AND SUPPORTIVE MEDICINES
Anti-emetics are not routinely required

PREMEDICATION
All patients should be receiving 10 mg prednisolone daily. Prednisolone is thought to reduce mineralocorticoid side effects of abiraterone such as hypertension, hypokalaemia and fluid retention.

INVESTIGATIONS / MONITORING REQUIRED
- Baseline assessment of BP and cardiac function for patients with cardiac risk factors or history of coronary artery disease
- FBC, U&Es, LFTs & PSA as appropriate prior to each cycle
- Transaminases fortnightly during the first 3 months.
- BP monthly
- Review patient monthly for evidence of fluid retention

REVIEW BY CLINICIAN
Day 28 of each cycle as appropriate

NURSE / PHARMACIST LED REVIEW
Each cycle as applicable according to local protocols

ADMINISTRATION NOTES
- It is acknowledged that abiraterone is not cytotoxic, however abiraterone should be prescribed and dispensed in accordance to NECN oral SACT guidelines.
- In the event of a missed daily dose of either abiraterone, or prednisolone, treatment should be resumed the following day with the usual daily dose.
- Patients with increased stress (e.g. admission to hospital) will require additional steroid supplementation.
- Abiraterone should be taken at least two hours after eating and no food should be eaten for at least one hour after taking the tablets. Taking abiraterone with food can increase absorption by up to 10 times and therefore increase toxicity.
- Abiraterone should be swallowed whole with water.
- If ALT > 5 x ULN at any time treatment should be suspended (see dose modification)
- Steroids should be tapered off slowly when treatment is withdrawn.
- Abiraterone may increase exposure of other medication metabolised by CYP2D6 which include metoprolol, propranolol, venlafaxine, haloperidol, risperidone, propafenone, flecainide, codeine, oxycodone and tramadol (the latter three products requiring CYP2D6 to form their active analgesic metabolites).
- Abiraterone is also an inhibitor of CYP2C8 so patients should be monitored for toxicity of interacting medication (such as pioglitazone).
- Strong CYP3A4 inducers (such as phenytoin, carbamazepine, rifampicin, rifabutin, phenobarbital, St John's wort) should be avoided as they are expected to reduce abiraterone effectiveness.

EXTRAVASATION  Not Applicable
TOXICITIES
- Reduced bone mineral density
- Peripheral oedema
- Hypokalaemia
- Hypertension
- Urinary Tract Infection
- Hepatotoxicity

DOSE MODIFICATION

<table>
<thead>
<tr>
<th>ALT / AST</th>
<th>Action</th>
<th>Reduce dose</th>
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</thead>
<tbody>
<tr>
<td>&lt; 5 x ULN</td>
<td>Continue</td>
<td>1000mg daily</td>
</tr>
<tr>
<td>5 – 20 x ULN</td>
<td>Stop treatment, restart at reduced dose when ALT &lt; 5x ULN, then monitor two-weekly for three months</td>
<td>500mg daily</td>
</tr>
<tr>
<td>20 x ULN</td>
<td>Stop treatment</td>
<td>Stop</td>
</tr>
</tbody>
</table>

TREATMENT LOCATION
Cancer Centre or Cancer Unit where there is an Oncologist with a specialisation in urology patients as appropriate.

REFERENCES: