ABIRATERONE (ZYTIGA ®) PROTOCOL

Abiraterone (Zytiga ®) for 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>5mg twice daily</td>
<td>Oral</td>
<td></td>
</tr>
</tbody>
</table>

- Presented as 250mg tablets
- 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 for use on the National Cancer Drug Fund List for patients who meet the following criteria:
1. Application made by and first cycle of systemic anti-cancer therapy to be prescribed by a consultant specialist specifically trained and accredited in the use of systemic anti-cancer therapy
2. Castrate-resistant metastatic prostate cancer
3. Chemotherapy naïve for metastatic disease
4. PS 0 or 1
5. Asymptomatic or mildly symptomatic patients
6. Chemotherapy not yet indicated

**PREMEDICATION**

All patients should be receiving at least 5mg prednisolone daily and ideally 10mg. Prednisolone is thought to reduce mineral-corticoid side effects of abiraterone.

**INVESTIGATIONS / MONITORING REQUIRED**

- Baseline assessment of BP and cardiac function for patients with cardiac risk factors or history of coronary artery disease
- FBC, U&E, LFT's & PSA as appropriate prior to each cycle
- Transaminases fortnightly during the first 3 months.
- BP monthly
- Review patient monthly for evidence of fluid retention
ELIGIBILITY CRITERIA

- Eastern Cooperative Oncology Group (ECOG) performance status of 0, 1 or 2
- ALT or AST < 2.5x ULN (or < 5 x ULN if known liver mets)
- No Uncontrolled hypertension
- No History of pituitary or adrenal dysfunction
- No Clinically significant heart disease
- No previous treatment with Ketoconazole
- Patients should continue on androgen deprivation therapy

Stopping Criteria:

- Clinical Disease Progression
- OR 1 of the following:
  - PSA progression (>50% rise confirmed on 2 samples over baseline or nadir)
  - Bone scan new lesions (definite)
  - CT evidence of progression
- OR ≥ 2 of the following if clinical benefit
  - PSA progression (>25% rise confirmed on 2 samples over baseline or nadir)
  - Bone scan new lesions
  - CT evidence of progression

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 tapers off slowly when treatment is withdrawn.
- Abiraterone may increase exposure of other medication metabolised by CYP2D6 which include metoprolol, propranolol, desipramine, venlafaxine, haloperidol, risperidone, propafenone, flecaidine, codeine, oxycodone and tramadol (the latter three products requiring CYP2D6 to form their active analgesic metabolites).
- The effect of CYP3A4 inhibitors/inducers (such as ketoconazole, voriconazole, Phenytoin and carbamazepine) are unclear but theoretically may interact.
EXTRAVASATION  Not Applicable

TOXICITIES

- Reduced bone mineral density
- Peripheral oedema
- Hypokalaemia
- Hypertension
- Urinary Tract Infection
- Hepatotoxicity

DOSE MODIFICATION

Hepatotoxicity -

<table>
<thead>
<tr>
<th>ALT / AST</th>
<th>Action</th>
<th>Reduce dose</th>
</tr>
</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; 5xULN</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: