Abiraterone and Prednisolone Therapy

**INDICATIONS FOR USE:**

<table>
<thead>
<tr>
<th>INDICATION</th>
<th>ICD10</th>
<th>Regimen Code</th>
<th>*Reimbursement Status</th>
</tr>
</thead>
<tbody>
<tr>
<td>Abiraterone is indicated in combination with prednisone or prednisolone for the treatment of metastatic castration resistant prostate cancer in adult men whose disease has progressed on or after a docetaxel-based chemotherapy regimen.</td>
<td>C61</td>
<td>00103a</td>
<td>CDS</td>
</tr>
<tr>
<td>Treatment of metastatic castration resistant prostate cancer in adult men who are asymptomatic or mildly symptomatic after failure of androgen deprivation therapy in whom chemotherapy is not yet clinically indicated</td>
<td>C61</td>
<td>00103b</td>
<td>CDS</td>
</tr>
</tbody>
</table>

*If the reimbursement status is not defined, the indication has yet to be assessed through the formal HSE reimbursement process.

**TREATMENT:**

*The starting dose of the drugs detailed below may be adjusted downward by the prescribing clinician, using their independent medical judgement, to consider each patient's individual clinical circumstances.*

Abiraterone is administered as a single oral daily dose until disease progression or unacceptable toxicity develops (1 cycle = 28 days).

Androgen ablative therapy (e.g. LHRH agonist, LHRH antagonist) should be maintained.

<table>
<thead>
<tr>
<th>Drug</th>
<th>Dose</th>
<th>Route</th>
<th>Cycle</th>
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</thead>
<tbody>
<tr>
<td>Abiraterone</td>
<td>1000mg daily</td>
<td>PO without food at the same day. Tablets should be swallowed whole with water.</td>
<td>Continuous therapy</td>
</tr>
<tr>
<td>Prednisone or Prednisolone</td>
<td>10mg daily or 5mg BD</td>
<td>PO with food</td>
<td>Continuous therapy</td>
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</table>

In the event of a missed daily dose of either abiraterone, prednisone or prednisolone, treatment should be resumed the following day with the usual daily dose.

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.

**ELIGIBILITY:**

- Indications as above
- ECOG status 0-2
- Life expectancy > 3 months
- Bilirubin < 1.5 x ULN, AST/ALT < 2.5 x ULN, Alkaline Phosphatase < 6 x ULN
- Creatinine < 1.5 x ULN
- Serum potassium > 3.5mmol/L
EXCLUSIONS:
- Hypersensitivity to abiraterone or any of the excipients
- Uncontrolled hypertension (systolic blood pressure >160mmHg or diastolic > 95mmHg)
- Severe hepatic impairment
- Active or symptomatic viral hepatitis
- Clinically significant heart disease (LVEF < 50% at baseline)
- History of adrenal dysfunction
- Patients with visceral metastases
- Patients who have received > 7days of ketoconazole

PRESCRIPTIVE AUTHORITY:
The treatment plan must be initiated by a Consultant Medical Oncologist

TESTS:
Baseline tests:
- FBC, renal and liver profile
- Glucose, blood pressure
- ECG if clinically indicated or if history of cardiac problems

Regular tests:
- FBC, renal and liver profile, glucose and blood pressure every 2 weeks for cycles 1-3 and every 4 weeks thereafter
- ECG if clinically indicated or if history of cardiac problems

Disease monitoring:
Disease monitoring should be in line with the patient’s treatment plan and any other test/s as directed by the supervising Consultant.

DOSE MODIFICATIONS:
- Any dose modification should be discussed with a Consultant.
Renal and Hepatic Impairment:

### Table 1: Dose modification of abiraterone in renal and hepatic impairment

<table>
<thead>
<tr>
<th>Renal Impairment</th>
<th>Hepatic Impairment</th>
</tr>
</thead>
<tbody>
<tr>
<td>No dose modification is necessary in patients with renal impairment. However there is no clinical experience in patients with prostate cancer and severe renal impairment. Caution is advised in these patients.</td>
<td>Bilirubin</td>
</tr>
<tr>
<td></td>
<td>1.5 – 3 x ULN</td>
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<tr>
<td></td>
<td>&gt; 3 x ULN</td>
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Management of adverse events:

**Hypokalemia Management:**

Hypokalemia has been observed and should be aggressively managed. Serum potassium should be monitored closely in patients who develop hypokalemia.

<table>
<thead>
<tr>
<th>Serum K+ (mmol/L)</th>
<th>Grade of Hypokalemia</th>
<th>Action</th>
<th>Further Action or Maintenance</th>
</tr>
</thead>
<tbody>
<tr>
<td>Low K+ or History of hypokalemia</td>
<td></td>
<td>Weekly (or more frequent) laboratory electrolyte evaluations.</td>
<td>Titrate dose to maintain potassium &gt; 3.5 mmol/L and &lt; 5.0 mmol/L (&gt; 4.0 mmol/L recommended).</td>
</tr>
<tr>
<td>&lt; 3.5 – 3.0</td>
<td>Grade 1</td>
<td>Initiate oral or IV potassium supplementation. Consider monitoring magnesium and replacement if needed.</td>
<td></td>
</tr>
<tr>
<td>&lt; 3.5 – 3.0 Symptomatic</td>
<td>Grade 2</td>
<td>Withhold abiraterone until potassium corrected. Initiate oral or IV potassium supplementation. Consider monitoring magnesium and replacement if needed.</td>
<td></td>
</tr>
<tr>
<td>&lt; 3.0 – 2.5</td>
<td>Grade 3</td>
<td>Withhold abiraterone until potassium corrected. Initiate oral or IV potassium and consider cardiac monitoring in appropriate patients. Consider monitoring magnesium and replacement if needed.</td>
<td></td>
</tr>
<tr>
<td>&lt; 2.5</td>
<td>Grade 4</td>
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</table>

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SUPPORTIVE CARE:

EMETOGENIC POTENTIAL: Minimal (Refer to local policy).

PREMEDICATIONS:
Not usually required

OTHER SUPPORTIVE CARE:
Patients who stop abiraterone may require a gradual withdrawal of the prednisolone.

ADVERSE EFFECTS / REGIMEN SPECIFIC COMPLICATIONS
The adverse effects listed are not exhaustive. Please refer to the relevant Summary of Product Characteristics for full details.

- **Fluid retention**: Fluid retention can occur due to mineralocorticoid excess caused by compensatory adrenocorticotropic hormone (ACTH) drive. The administration of prednisolone will help reduce incidence and severity of fluid retention.

- **Hypertension**: Patients with hypertension should exercise caution while on abiraterone. Rigorous treatment of blood pressure is necessary, since abiraterone can cause a rapid onset of high blood pressure. Blood pressure will need to be monitored once every 2 weeks for the first three months of abiraterone therapy.

- 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.

- **Cardiac Function**: Abiraterone should be used with caution in patients with a history of cardiovascular disease. QT prolongation has been observed in patients experiencing hypokalaemia in association with abiraterone treatment. Cardiac function should be assessed as clinically indicated and the discontinuation of abiraterone treatment considered if there is a clinically significant decrease in cardiac function.

- **Hepatic Dysfunction**: Abiraterone undergoes hepatic metabolism. Hepatic dysfunction (particularly elevated AST and ALT) may occur during the first 3 months after starting treatment so a more frequent monitoring of liver function tests is required (every 2 weeks in the first three months and monthly thereafter). There have been rare post-marketing reports of acute liver failure and hepatitis fulminant, some with fatal outcome.

- **Bone density**: Decreased bone density may occur in men with metastatic advanced prostate cancer. The use of abiraterone in combination with a glucocorticoid could increase this effect.

- **Hyperglycaemia**: The use of glucocorticoids could increase hyperglycaemia, therefore blood sugar should be measured frequently in diabetic patients.

DRUG INTERACTIONS:

- The clearance of drugs metabolized by CYP2D6 may be decreased as abiraterone is a strong inhibitor of CYP2D6. Dose reduction should be considered especially for drugs with a narrow therapeutic index.

- Risk of drug interactions causing decreased concentrations of abiraterone with CYP3A4 inducers.
Since androgen deprivation treatment may prolong the QT interval, caution is advised when administering abiraterone with medicinal products known to prolong the QT interval or medicinal products able to induce Torsade de pointes such as class IA (e.g. quinidine, disopyramide) or class III (e.g. amiodarone, sotalol, dofetilide, ibutilide) antiarrhythmic medicinal products, methadone, moxifloxacin, antipsychotics, etc.

Current drug interaction databases should be consulted for more information.

**ATC CODE:**
Abiraterone – L02BX03

**REFERENCES:**

**Version Date** | **Amendment** | **Approved By**
--- | --- | ---
1 | 20/12/2014 | Updated Tests Dr Ray McDermott
2 | 3/3/2015 | Addition of new indication Dr Derek Power, Dr Maccon Keane
3 | 26/3/2015 | Updated with new Regimen Template and updated Adverse Events Prof Maccon Keane
4 | 01/10/2015 | Updated Adverse Effects and Drug Interactions Dr Maccon Keane
5 | 13/4/2016 | Updated dosing in hepatic impairment and hepatic dysfunction under Adverse Events Dr Maccon Keane
6 | 18/04/2018 | Updated Tests Dr Ray McDermott

Comments and feedback welcome at oncologydrugs@cancercontrol.ie.
### NCCP Regimen: Abiraterone and Prednisone/Prednisolone Therapy

**Tumour Group:** Genitourinary  
**NCCP Regimen Code:** 00103  
**Published:** 20/12/2014  
**Review:** 18/04/2020  
**Version number:** 6  

<table>
<thead>
<tr>
<th>ISMO Contributor: Dr Derek Power, Prof Maccon Keane</th>
<th>Page 6 of 6</th>
</tr>
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