Abiraterone 1000mg and Prednisolone 5mg 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 with prednisone or prednisolone for: the treatment of newly diagnosed high risk metastatic hormone sensitive prostate cancer (mHSPC) in adult men in combination with androgen deprivation therapy (ADT)</td>
<td>C61</td>
<td>00577a</td>
<td>Reimbursement not approved</td>
</tr>
</tbody>
</table>

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 during treatment in patients not surgically castrated.

<table>
<thead>
<tr>
<th>Drug</th>
<th>Dose</th>
<th>Route</th>
<th>Cycle</th>
</tr>
</thead>
<tbody>
<tr>
<td>Abiraterone</td>
<td>1000mg daily</td>
<td>PO without food at the same time each day¹. Tablets should be swallowed whole with water.</td>
<td>Continuous therapy</td>
</tr>
<tr>
<td>Prednisone</td>
<td>5mg daily</td>
<td>PO with food</td>
<td>Continuous therapy</td>
</tr>
</tbody>
</table>

¹Abiraterone should be taken at least one hour before or at least two hours after eating.

ELIGIBILTY:

- Indication as above
- ECOG 0–2
- Patients are required to have at least two of the three following high-risk factors associated with poor prognosis:
  - Gleason score ≥8
  - ≥Three bone lesions
  - Presence of measurable visceral metastasis. (RECIST 1.1)
- Adequate hematologic, hepatic, and renal function
EXCLUSIONS:
- Hypersensitivity to abiraterone or any of the excipients
- Known brain metastasis
- Uncontrolled hypertension (systolic blood pressure >160mmHg or diastolic > 95mmHg)
- Active or symptomatic viral hepatitis or chronic liver disease
- Severe hepatic impairment
- History of adrenal dysfunction
- Clinically significant heart disease (LVEF <50% at baseline)
- Abiraterone with prednisone or prednisolone is contraindicated in combination with Ra-223

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>
<th>Dose</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 1.5 – 3 x ULN and AST and/or ALT 2.5 – 5 x ULN</td>
<td>100% Monitor liver tests at least weekly until grade 1 (Bilirubin &lt; 1.5 x ULN, AST/ALT &lt; 2.5 x ULN).</td>
</tr>
<tr>
<td>&gt; 3 x ULN or &gt; 5 x ULN</td>
<td>Hold abiraterone. Treatment following return of liver</td>
<td></td>
</tr>
</tbody>
</table>

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Management of adverse events:

Table 2: Dose Modification of Abiraterone for Adverse Events

<table>
<thead>
<tr>
<th>Adverse reactions</th>
<th>Recommended dose modification</th>
</tr>
</thead>
<tbody>
<tr>
<td>Grade ≥ 3 toxicities including hypertension, hypokalaemia, oedema and other non-mineralocorticoid toxicities</td>
<td>Withhold treatment 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</td>
</tr>
</tbody>
</table>

Hypokalemia Management:

Patients with pre-existing hypokalaemia or those that develop hypokalaemia while treated with abiraterone, consider maintaining the patient’s potassium level at ≥4.0mM.

**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.
- **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.
- **Anaemia**: may occur in men with metastatic prostate cancer including those undergoing treatment with abiraterone.
- **Sexual dysfunction**: may occur in men with metastatic prostate cancer including those undergoing treatment with abiraterone.
- **Skeletal muscle effects**: Cases of myopathy and rhabdomyolysis have been reported in patients treated with abiraterone. Most cases developed within the first 6 months of treatment and recovered after abiraterone withdrawal. Caution is recommended in patients concomitantly treated with medicinal products known to be associated with myopathy/rhabdomyolysis.
- **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.

**DRUG INTERACTIONS:**

- Abiraterone is an inhibitor of the hepatic drug-metabolising enzymes CYP2D6 and CYP2C8. Caution is advised when administering with medicinal products activated by or metabolised by CYP2D6 or CYP2C8, particularly with medicinal products that have a narrow therapeutic index.
- 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 torsades 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.

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- Spironolactone binds to the androgen receptor and may increase prostate specific antigen (PSA) levels. Use with abiraterone is not recommended.
- Strong inducers of CYP3A4 (e.g., phenytoin, carbamazepine, rifampicin, rifabutin, rifapentine, phenobarbital, St John's wort [Hypericum perforatum]) during treatment are to be avoided, unless there is no therapeutic alternative
- Current drug interaction databases should be consulted for more information.

**ATC CODE:**
Abiraterone – L02BX03

**REFERENCES:**


<table>
<thead>
<tr>
<th>Version</th>
<th>Date</th>
<th>Amendment</th>
<th>Approved By</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>08/01/2020</td>
<td></td>
<td>Prof Maccon Keane</td>
</tr>
</tbody>
</table>

Comments and feedback welcome at oncologydrugs@cancercontrol.ie.

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\(^1\) Post 2012 indication. Not reimbursed through the ODMS or Community Drug Schemes (including the High Tech arrangements of the PCRS community drug schemes). Please check https://www.hse.ie/eng/services/list/5/cancer/proinfo/medonc/cdmp/new.html for the most up to date reimbursement approvals.

ODMS – Oncology Drug Management System
CDS – Community Drug Schemes (CDS) including the High Tech arrangements of the PCRS community drug schemes

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