BNSSG Health Community's Traffic Light System
Shared Care Guidance

Section 1: Heading

Trust: North Bristol NHS and UHB NHS Trust

Specialty / Department: Urology

Drug: Cyproterone Acetate

For the treatment / management of: Prostate cancer (see treatment schedule)

Section 2: Treatment schedule

Cyproterone acetate is available as the following preparations;

1. 50mg tablets
2. 100mg tablets

Appropriate for shared care;

- In the palliative treatment of advanced prostate cancer where LHRHa or surgery are contraindicated, not tolerated or where oral therapy is preferred; cyproterone acetate 300mg a day in 2-3 divided doses after meals.
- In the treatment of hot flushes in patients receiving LHRHa or who have had orchidectomy; 50mg daily adjusted to 50-150mg daily in 1-3 divided doses after meals according to response.

Other indications not requiring shared care;

- To reduce the risk of tumour flare when initiating a LHRHa, 100mg twice daily starting 5-7 days prior to LHRHa initiation and continued for 3-4 weeks after.

There is limited information on the use of cyproterone acetate in patients with renal impairment. No data supports dose reduction in this patient group.

Cyproterone acetate is contraindicated in patients with hepatic impairment.

Section 3: Monitoring

- Baseline PSA, LFTs and FBC.
- Repeat PSA, FBC and U&Es every 3 months.
- LFTs every month for the first 12 months thereafter at the same time as PSA measurements. If signs or symptoms of hepatotoxicity assess LFTs promptly and proceed according to results.
- Hospital review and follow up as clinically indicated.

Direct hepatic toxicity, including jaundice, hepatitis and hepatic failure, which has been fatal in some cases, has been reported in patients treated with 200-300 mg cyproterone acetate. Most reported cases are in men with prostatic cancer. Toxicity is dose-related and develops, usually, several months after treatment has begun. LFTs should be performed pre-treatment, regularly during treatment and whenever any symptoms or signs suggestive of hepatotoxicity occur. If hepatotoxicity is confirmed, cyproterone acetate should normally be withdrawn, unless the hepatotoxicity can be explained by another cause, e.g. metastatic disease, in which case cyproterone acetate should be continued only if the perceived benefit outweighs the risk.

During treatment with high doses of cyproterone acetate (300mg daily) adrenocortical function may be suppressed. Adrenocortical function should be assessed if this is suspected.

Section 4: Side-effects

Refer to SPC for full details http://www.medicines.org.uk/

Cyproterone acetate no longer has black triangle (▼) status. Serious suspected reactions (even if well recognised or causal link uncertain) should be reported to the CSM.

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Very-common (> 1 in 10) side-effects include; Decreased libido, erectile dysfunction, reduced sexual drive and inhibition of gonadal function (these changes are reversible after discontinuation of therapy),

Common (≥ 1/100 to ≤ 1/10) side-effects include; gynaecomastia, hot flushes, sweating, fatigue, lassitude, changes in body weight (mainly due to fluid retention), dyspnoea (This may be due to the stimulatory effect of progesterone and synthetic progestogens on breathing, which is accompanied by hypocapnia and compensatory alkalosis, and which is not considered to require treatment).

The occurrence of (multiple) meningioma has been reported in association with longer term use (years) of cyproterone acetate at doses of 25 mg/day and above. If a patient treated with cyproterone acetate is diagnosed with meningioma, treatment must be stopped.
Some patients with severe chronic depression deteriorate whilst receiving cyproterone acetate. Such patients should be closely monitored for signs of deterioration and warned to contact their doctor immediately if their depression worsens.

Section 5: Drug interactions

- Requirements for oral antidiabetic agents (particularly **thiazolidinediones** such as **pioglitazone** and **rosiglitazone**) and insulin can change when cyproterone acetate is initiated. In diabetic patients consider reviewing requirements in first few weeks of treatment.
- Cyproterone acetate is metabolised by CYP3A4, it is expected that;
  - **Ketoconazole**, **itraconazole**, **ritonavir** and other strong inhibitors of CYP3A4 inhibit the metabolism of cyproterone acetate,
  - Inducers of CYP3A4 such as **rifampicin**, **phenytoin** and products containing **St. John's wort** may reduce the levels of cyproterone acetate.
  - Based on *in vitro* inhibition studies, an inhibition of the cytochrome P450 enzymes CYP2C8, 2C9, 2C19, 3A4 and 2D6 is possible at high cyproterone acetate doses of 100 mg three times per day.
  - The risk of statin-associated myopathy or rhabdomyolysis may be increased when those HMG-CoA inhibitors (**statins**) which are primarily metabolised by CYP3A4 are co-administered with high therapeutic cyproterone acetate doses, since they share the same metabolic pathway.

Section 6: Cautions and special recommendations

- By virtue of its indication cyproterone acetate should not be used in female patients or children.

Cyproterone acetate is also contraindicated in patients;
- with known hypersensitivity to the active substance or any of the excipients,
- with liver disease,
- current or previous, history of liver tumours (unless these are metastases from carcinoma of the prostate,
- existing thromboembolic processes*,
- wasting diseases (with the exception of inoperable carcinoma of the prostate),
- meningioma or a history of meningioma,
- Dubin-Johnson syndrome, Rotor syndrome,
- with Lapp lactase deficiency or glucose-galactose malabsorption.

Caution is required when using cyproterone acetate in patients;
- with a history of severe chronic depression (see Section 4: side-effects, above),
- at risk of thromboembolic events*.

* The occurrence of thromboembolic events has been reported in patients using cyproterone acetate, although a causal relationship has not been established. Patients with previous arterial or venous thrombotic / thromboembolic events (e.g. deep vein thrombosis, pulmonary embolism, myocardial infarction), with a history of cerebrovascular accidents or with advanced malignancies are at increased

risk of further thromboembolic events, and may be at risk of recurrence of the disease during cyproterone acetate therapy.
In patients with a history of thromboembolic processes or suffering from sickle-cell anaemia or severe diabetes with vascular changes, the risk: benefit ratio must be considered in each individual case before cyproterone acetate is prescribed.

Section 7: Advice to the patient

Patients should be advised of common possible side-effects, including; mood changes, breast tenderness, hot flushes, pruritis, risk of blood clots (thrombosis), lowered sex drive (libido) and erectile difficulties (impotence).

Diabetic patients should be advised of the possible effects on blood sugars and how this will be managed.

Report any adverse effects that may be associated with cyproterone acetate use to their specialist or GP.
Patients should be advised of the signs and symptoms of hepatotoxicity and instructed to report these to their GP should they occur.

Section 8: Responsibilities for Secondary Care

1. Assess the patient and establish need for cyproterone acetate.
2. Discuss anticipated benefits and possible side-effects with the patient.
3. Initiate treatment and decide if the patient is suitable to continue treatment.
4. Baseline blood tests, including; LFT's and PSA.
5. Advise Primary care if LFT and / or PSA monitoring required in Primary care setting and if so on frequency of monitoring.
6. Prompt communication with Primary care regarding any changes in treatment.
7. Provide supplies of cyproterone acetate until shared care is agreed with the GP.

Section 9: Responsibilities for Primary Care

1. Continue prescribing cyproterone acetate once treatment has been established by Secondary care.
2. Monitoring for adverse drug reactions and, if appropriate, reporting to the CSM.
3. Monitor LFTs and / or PSA if agreed with the specialist to do so.
4. Seek specialist advice if LFTs rise, or if signs/symptoms of hepatic changes occur.
5. Assessment of continued well-being of patient and seek specialist advice if signs of disease progression (such as bone pain and / or increasing urinary symptoms.
6. Seek specialist advice if intolerable side-effects (e.g. gynaecomastia).

Section 10: Contact details

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Section 11: Document details

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Section 12: Collaboration

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Section 13: References

SPC for cyproterone acetate 100mg tablets (Bayer plc) [last updated 19/08/2010]
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