AWTTC
All Wales Therapeutics & Toxicology Centre
Canolfan Therapiwteg a Thocsicoleg Cymru Gyfan

# Abiraterone acetate for the treatment of non-metastatic and locally advanced, high-risk, hormone-sensitive prostate cancer (OW20)

## November 2022

## ONE WALES INTERIM DECISION

**Abiraterone acetate for the treatment of non-metastatic and locally advanced, high-risk, hormone-sensitive prostate cancer**

**Date of advice: November 2022**

**The following One Wales Medicines Assessment Group (OWMAG) recommendation has been endorsed by health board Chief Executives.**

Using the agreed starting and stopping criteria, abiraterone in combination with prednisolone can be made available within NHS Wales for the treatment of non-metastatic and locally advanced, high-risk, hormone-sensitive prostate cancer. High risk is defined as at least 2 of the following: tumour stage T3 or T4, a Gleason score of 8 to 10, and a PSA level of ≥ 40 ng/ml.

Abiraterone acetate should be prescribed on the basis of lowest acquisition cost.

The risks and benefits of the off-label use of abiraterone for this indication should be clearly stated and discussed with the patient to allow informed consent.
Providers should consult the relevant guidelines on prescribing unlicensed medicines before any off-label medicines are prescribed.

**Clinician responsibility**
Clinicians will be obliged to collect and monitor patient outcomes. Evidence of clinical outcomes will be taken into consideration when reviewing the One Wales Medicines Assessment Group decision.

**Health board responsibility**
Health boards will take responsibility for implementing One Wales Medicines Assessment Group decisions and ensuring that a process is in place for monitoring clinical outcomes.

This advice will be reviewed after 12 months or earlier if new evidence becomes available.

**One Wales advice promotes consistency of access across NHS Wales.**

## Starting and stopping criteria for abiraterone acetate for the treatment of non-metastatic and locally advanced, high-risk, hormone-sensitive prostate cancer

**Starting criteria:**
Patients with newly diagnosed non-metastatic and locally advanced, high-risk, hormone-sensitive prostate cancer including pelvic node positive patients (N1). This advice excludes patients who have metastatic disease i.e. M1 disease in whom the cancer has spread to a different part of the body[1] and appropriate Health Technology assessment advice should be followed for this patient group. Patients for whom this decision does apply, should receive radical radiotherapy unless there is a contraindication. Patients will routinely receive androgen deprivation therapy (ADT) for up to 3 years.
High risk is defined, as per STAMPEDE[2], as at least 2 of the following:

- tumour stage T3 or T4
- a Gleason sum score of 8 to 10
- a prostate-specific antigen (PSA) level of ≥ 40 ng/ml

The recommended treatment dose regimen for adult males is 1,000 mg (two 500 mg tablets) of abiraterone acetate taken as a single daily dose, in combination with 5 mg prednisolone daily. Treatment will start within 12 weeks of commencement of ADT and be continued for up to two years after radiotherapy (maximum treatment course of 2.5 years). The abiraterone acetate product available at the lowest acquisition cost should be prescribed.

**Continuing and stopping criteria:**

Monitoring is recommended in accordance with the Summary of Product Characteristics (SmPC)[3].
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 acetate should not be reinitiated until symptoms of the toxicity have resolved to Grade 1 or baseline[3].
For patients who develop hepatotoxicity during treatment (alanine aminotransferase [ALT] increases or aspartate aminotransferase [AST] increases above 5 times the upper limit of normal [ULN]), treatment should be withheld immediately. Re-treatment following return of liver function tests to the patient's baseline may be given at a reduced dose of 500 mg (1 tablet) once daily, in accordance with the SmPC[3].

**Failure to respond to abiraterone acetate:**

- biochemical failure, or
- radiological progression, or
- clinical progression

In the above situation, abiraterone should be stopped and alternative treatments should be instigated in accordance with NICE guidance or health technology assessment (HTA) advice.

**Stopping criteria:**

- Treatment failure/ disease progression
- Toxicity from treatment (that cannot or does not respond to temporary treatment interruption)
- Treatment has reached 2.5 years
- Patient request

Only one course of treatment may be issued in accordance with this advice.
Requests for repeat courses or continuing treatment beyond 2.5 years should be explored through funding mechanisms such as the individual patient funding request process.
For patients who progress following the full treatment course, subsequent management including novel androgen receptor-targeting agents should be used in accordance with current HTA advice.

**References:**


(1) James D. Brierley, Mary K. Gospodarowicz, Christian Wittekind, eds (2016). TNM Classification of Malignant Tumours, 8th Edition. Chichester, West Sussex, UK: Wiley-Blackwell. ISBN 978-1-4443-3241-4.

(2) James ND, de Bono JS, Spears MR et al. Abiraterone for prostate cancer not previously treated with hormone therapy. New England Journal of Medicine. 2017;377:338-351.

(3) Janssen-Cilag Ltd. ZYTIGA® 500 mg film-coated tablets. Summary of Product Characteristics. Sept 2022 Available at: https://www.medicines.org.uk/emc/product/2381. Accessed Oct 2022.

**One Wales Medicine Assessment Group summary of decision rationale**

Medicine: **abiraterone**
Indication: **abiraterone acetate in combination with prednisolone for the treatment of non-metastatic and locally advanced, high-risk, hormone-sensitive prostate cancer**
Meeting date: **26th September 2022**

| Criteria | OWMAG opinion |
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| Clinical effectiveness | OWMAG notes that the main clinical effectiveness evidence is from three stages of the STAMPEDE multi-platform randomised control trial. All studies concluded that abiraterone plus prednisolone in combination with androgen deprivation therapy (ADT) improved failure-free survival and overall survival compared with treatment with ADT alone. The evidence comparing abiraterone with treatment with docetaxel demonstrated similar efficacy.<br>OWMAG note the differing definitions for high risk disease in NICE and ESMO guidelines, the group consider that for the purposes of this assessment the criteria defined in the STAMPEDE study should apply.<br>OWMAG considers that the evidence provided demonstrated clinical effectiveness. |
| Cost-effectiveness | OWMAG notes the cost effectiveness analysis comparing abiraterone plus prednisolone with ADT to ADT alone. This included a fairly robust model. The analysis had several limitations as list prices were used and there was no comparison with docetaxel which is a treatment option for patients in NHS Wales. The group noted the price reductions required for abiraterone to be considered cost effective or dominant when compared to treatment with ADT alone.<br>OWMAG considers that the evidence provided demonstrated cost effectiveness only at the confidential contract price provided. |
| Budget impact | OWMAG considers that the clinical estimate of patient numbers reported is reasonably accurate. OWMAG acknowledges that budget impact estimates are subject to uncertainty and in the first year is likely to be cost saving. There is particular uncertainty around the patient numbers and the uptake of the comparator treatment, docetaxel. The group note that adverse event costs have not been included in the budget impact and that costs for treatment of docetaxel-related neutropenic sepsis may be significant. Also no ongoing treatments have been considered due to the complexity of the analyses.<br>OWMAG consider that the base case provided in the report is a reasonable estimate of the associated cost to NHS Wales. |

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| Other factors | OWMAG considers that the patient group should be defined as non-metastatic and locally advanced, high-risk, hormone-sensitive prostate cancer where high risk is defined as per the stricter STAMPEDE criteria. |
| Final recommendation | OWMAG recommends that the use of abiraterone is made available for treatment of non-metastatic and locally advanced, high-risk, hormone-sensitive prostate cancer. This recommendation is subject to the development of appropriate start/stop criteria. |
| Summary of rationale | There is evidence to suggest that abiraterone improves failure free survival and overall survival in patients with non-metastatic and locally advanced, high-risk, hormone-sensitive prostate cancer when compared with treatment with ADT alone. When compared to docetaxel, abiraterone improves failure free survival and overall survival is similar. The adverse effect profile of abiraterone is superior to that of docetaxel. It would appear to offer reasonable value for money and cost effectiveness if provided at the contract price. |



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