

## New drugs



Some of the views expressed in the following notes on newly approved products should be regarded as tentative, as there may be limited published data and little experience in Australia of their safety or efficacy. However, the Editorial Executive Committee believes that comments made in good faith at an early stage may still be of value. As a result of fuller experience, initial comments may need to be modified. The Committee is prepared to do this. Before new drugs are prescribed, the Committee believes it is important that full information is obtained from the manufacturer's approved product information, a drug information centre or some other appropriate source.

*Aust Prescr 2012;35:128-35*

### Abiraterone acetate

#### Approved indication: metastatic prostate cancer

#### Zytiga (Janssen-Cilag)

#### 250 mg tablets

#### Australian Medicines Handbook section 14.3.1

Androgens have an important role in the progression of prostate cancer. While castration can reduce progression, the cancer eventually becomes castration resistant and requires chemotherapy with drugs such as docetaxel. As androgen activity is increased at this late stage of the disease, anti-androgen treatments have been researched.

Abiraterone is an inhibitor of cytochrome P450 (CYP) C17. This enzyme is involved in androgen synthesis, so inhibiting it decreases the concentrations of testosterone and other androgens. When given alone abiraterone can cause secondary hyperaldosteronism. To reduce this problem it should be given with prednisone or prednisolone.

This combination was used in a phase II trial to treat 58 men with metastatic prostate cancer which had failed to respond to docetaxel. The response to therapy was assessed by changes in the men's concentrations of prostate specific antigen (PSA). This declined by at least half in 36% of the men. The median time to PSA progression was 169 days.<sup>1</sup>

The same daily dose of abiraterone (1 g orally) was then used in a placebo-controlled phase III trial in 1195 men who had been previously treated with docetaxel. These patients also took prednisone 5 mg twice daily. The median follow-up was 12.8 months. There was a decrease of 50% or more in the PSA concentration in 29% of the men who took abiraterone and in 6% of the placebo group. The time to PSA progression was 10.2 months with abiraterone and 6.6 months with placebo. In the abiraterone group, 42% of the patients died compared with 55% of the placebo group. Overall survival was 14.8 months with abiraterone and 10.9 months with placebo.<sup>2</sup>

In the phase III trial the most common adverse events were fatigue, nausea and back pain, but they occurred at a similar frequency in the placebo group. Hypokalaemia, oedema and fluid retention were more frequent with abiraterone. Less frequent adverse events which occurred more often with abiraterone than placebo included urinary tract infections, hypertension and cardiac disorders, such as arrhythmias and heart failure. Patients with clinically

significant heart disease or uncontrolled hypertension were excluded from the trial.<sup>2</sup>

Abiraterone can increase liver enzymes, so liver function must be monitored frequently. Treatment may need to be reduced or stopped depending on liver function. If prednisolone is stopped abruptly there is a risk of adrenocortical insufficiency. Abiraterone is metabolised by CYP3A4, but interactions with strong inducers and inhibitors of the enzyme have not been evaluated. CYP1A2 and CYP2D6 are inhibited by abiraterone so there is a potential for interactions with drugs which are metabolised by these enzymes. These include codeine, oxycodone and tramadol. Only 5% of the dose is excreted in the urine and there is no recommendation for a reduced dose in renal disease. Abiraterone must not be taken with meals because food alters absorption.

The options for treating metastatic prostate cancer have increased, but the prognosis is still poor. Patients may prefer oral abiraterone to intravenous cabazitaxel, with its cytotoxic adverse effects, but the drugs' effectiveness has not yet been compared. The use of abiraterone in earlier stages of prostate cancer is being investigated. A trial involving men with metastatic castration-resistant prostate cancer was recently unblinded so patients in the placebo group could be switched to active treatment because of the emerging benefit of abiraterone.

**T** manufacturer provided the product information

#### REFERENCES \*†

1. Danila DC, Morris MJ, de Bono JS, Ryan CJ, Denmeade SR, Smith MR, et al. Phase II multicenter study of abiraterone acetate plus prednisone therapy in patients with docetaxel-treated castration-resistant prostate cancer. *J Clin Oncol* 2010;28:1496-501.
2. De Bono JS, Logothetis CJ, Molina A, Fizazi K, North S, Chu L, et al. Abiraterone and increased survival in metastatic prostate cancer. *N Engl J Med* 2011;364:1995-2005.

*First published online 16 May 2012*

The T-score (**T**) is explained in 'New drugs: T-score for transparency', *Aust Prescr* 2011;34:26-7.

\* At the time the comment was prepared, information about this drug was available on the website of the Food and Drug Administration in the USA ([www.fda.gov](http://www.fda.gov)).

† At the time the comment was prepared, a scientific discussion about this drug was available on the website of the European Medicines Agency ([www.ema.europa.eu](http://www.ema.europa.eu)).