3.01 ABIRATERONE,
Tablet containing abiraterone acetate 250 mg,
Tablet containing abiraterone acetate 500 mg,
Zytiga®,
Janssen-Cilag Pty Ltd

ENZALUTAMIDE,
Capsule 40 mg,
Xtandi®,
Astellas Pharma Australia Pty Ltd

1 Purpose of item

1.1 To consider sponsor responses to the PBAC's March 2021 request for comment on amending the existing abiraterone and enzalutamide listings for metastatic castration resistant prostate cancer (mCRPC) to be silent on the 'metastatic' requirement in the indication.

2 Background

Registration status

2.1 Abiraterone is registered for use in combination with prednisone or prednisolone for the treatment of patients with:

- newly diagnosed high-risk metastatic hormone sensitive prostate cancer in combination with androgen deprivation therapy (ADT);
- mCRPC who are asymptomatic or mildly symptomatic after failure of ADT; and
- mCRPC who have received prior chemotherapy containing a taxane.

2.2 Enzalutamide is registered for the treatment of patients with:

- non-metastatic castration-resistant prostate cancer (m0CRPC);
- mCRPC following failure of ADT in whom chemotherapy is not yet indicated; and
- mCRPC who have previously received docetaxel.

Previous PBAC consideration

2.3 At the March 2021 PBAC meeting, the PBAC recommended amending the listings of abiraterone and enzalutamide to allow their use in patients with mCRPC prior to receiving docetaxel. The PBAC considered that removal of the requirement for patients to have either received prior docetaxel or to have a predicted intolerance to

docetaxel would better align the restrictions for abiraterone and enzalutamide with how these drugs are being used in clinical practice and with their TGA indications (paragraph 5.1, abiraterone and enzalutamide Public Summary Document (PSD), March 2021).

2.4 At the March 2021 PBAC meeting, the Committee also noted that the availability of more sensitive screening, such as prostate-specific membrane antigen (PSMA) PET scans, had resulted in patients previously classified as having m0CRPC on conventional imaging being classified as having metastatic disease. Hence, these patients are eligible to receive abiraterone or enzalutamide through the PBS. The PBAC further considered that if sensitive screening tests are used, the majority of patients with a rapidly rising prostate-specific antigen (PSA) are likely to be diagnosed with, or will soon progress to, mCRPC. Given this, the PBAC foreshadowed that it would like to consider revising the abiraterone and enzalutamide listings further, such that the requirement for the disease to be classified as metastatic was removed. The PBAC considered that the one novel hormonal agent (NHA) treatment per patient per lifetime requirement should remain. The PBAC noted that this change to the listing was likely to result in patients being treated earlier, as well as increase the number of patients treated. The PBAC requested that the Department seek comment from the sponsors regarding this proposed listing change (the removal of the word 'metastatic' from the PBS indication) and the associated financial impact for consideration at the July 2021 PBAC meeting (paragraph 5.8, abiraterone and enzalutamide PSD, March 2021).

For more detail on PBAC's view, see section 5 PBAC outcome.

3 Proposed PBS listing changes

3.1 In line with the March 2021 PBAC meeting PSD, the Secretariat proposed amending the March 2021 PBAC recommended abiraterone and enzalutamide listings (where the PBAC recommended removal of prior docetaxel treatment for each drug), without any price change to the existing price and subject to sponsor agreement, as follows:

MEDICINAL PRODUCT medicinal product pack	PBS item code	Max. qty packs	Max. qty units	№.of Rpts	Available brands
ABIRATERONE					
abiraterone acetate 500 mg tablet, 60	11206T	1	60	2	Zytiga
abiraterone acetate 250 mg tablet, 120	2698B	1	120	2	Zytiga
Category/Program: GENERAL – General Schedule (GE) **Prescriber type:** ☒ Medical Practitioners **Restriction type:** ☒ Authority Required (telephone/online PBS Authorities system)					
Severity: Castration resistant ~~metastatic~~ **Condition:** Carcinoma of the prostate **PBS indication:** Castration resistant ~~metastatic~~ carcinoma of the prostate					
Clinical criteria: The treatment must be used in combination with a corticosteroid **AND** The treatment must not be used in combination with chemotherapy **AND** ~~Patient must have failed treatment with docetaxel due to resistance or intolerance; or~~ ~~Patient must be unsuitable for docetaxel treatment on the basis of predicted intolerance to docetaxel~~ **AND** Patient must have a WHO performance status of 2 or less **AND** Patient must not receive PBS-subsidised treatment abiraterone if progressive disease develops while on abiraterone **AND** Patient must not have received prior treatment with enzalutamide; or Patient must have developed intolerance to enzalutamide of a severity necessitating permanent treatment withdrawal.					
NOTEs: not displayed					

MEDICINAL PRODUCT medicinal product pack	PBS item code	Max. qty packs	Max. qty units	№.of Rpts	Available brands
ENZALUTAMIDE					
enzalutamide 40 mg capsule, 112	10174L	1	112	2	Xtandi
Category/Program: GENERAL – General Schedule (GE) **Prescriber type:** ☒ Medical Practitioners **Restriction type:** ☒ Authority Required (telephone/online PBS Authorities system)					
Severity: Castration resistant ~~metastatic~~ **Condition:** Carcinoma of the prostate **PBS indication:** Castration resistant ~~metastatic~~ carcinoma of the prostate					

Clinical criteria: The treatment must not be used in combination with chemotherapy **AND** ~~Patient must have failed treatment with docetaxel due to resistance or intolerance; or~~ ~~Patient must be unsuitable for docetaxel treatment on the basis of predicted intolerance to docetaxel~~ **AND** Patient must have a WHO performance status of 2 or less **AND** Patient must not receive PBS-subsidised treatment with this drug if progressive disease develops while on this drug **AND** Patient must not have received prior treatment with abiraterone; or Patient must have developed intolerance to abiraterone of a severity necessitating permanent treatment withdrawal.
NOTEs: not displayed here

3.2 The sponsor for abiraterone stated in its pre-PBAC response that it was not supportive of the proposal to remove the word 'metastatic' from the current PBS restriction for abiraterone as:

- abiraterone is not TGA approved for use in patients with non-metastatic disease;
- abiraterone is used in combination with prednisone and use earlier in the disease management algorithm would potentially result in patients being on prednisone for longer periods of time. The sponsor indicated that this might be a concern for clinicians given the longer-term safety profile of prednisone; and
- the restriction change could result in inappropriate treatment practices which are not evidence-based, including the use of NHAs in patients with low risk m0CRPC (i.e. PSA doubling time of greater than 10 months) and in patients experiencing biological relapse.

For more detail on PBAC's view, see section 5 PBAC outcome.

4 Consideration of the evidence

Estimated PBS utilisation and financial implications

4.1 The PBAC noted that neither sponsor provided information on the financial impact of broadening the current restrictions for abiraterone and enzalutamide to include patients with m0CRPC.

For more detail on PBAC's view, see section 5 PBAC outcome.

5 PBAC Outcome

5.1 The PBAC did not recommend amending the existing abiraterone and enzalutamide restrictions for castration resistant prostate cancer (CRPC) to remove the criteria that the disease be metastatic.

5.2 The PBAC noted that abiraterone is not TGA registered for use in CRPC patients without metastatic disease. The PBAC noted the sponsor's comments that:

i. abiraterone is used in combination with prednisone and that use earlier in the treatment algorithm may result in patients being treated with prednisone for longer periods of time, and there are potential safety concerns with the longer-term use prednisone; and

ii. there is no clinical trial evidence to support the use of novel hormonal agents (NHAs) in patients with low risk non-metastatic castration resistant prostate cancer (m0CRPC), i.e. those with a prostate-specific antigen (PSA) doubling time of greater than 10 months or patients experiencing biochemical relapse.

5.3 The PBAC noted that enzalutamide is TGA registered for use in the non-metastatic setting; however, considered it would be complex to craft a restriction which appropriately targeted patients at high risk of progressing based on metastases and/or PSA levels.

5.4 The PBAC noted that neither sponsor provided an estimate of the financial implications for revising the listings.

Outcome:
Not recommended

6 Context for Decision

The PBAC helps decide whether and, if so, how medicines should be subsidised through the Pharmaceutical Benefits Scheme (PBS) in Australia. It considers applications regarding the listing of medicines on the PBS and provides advice about other matters relating to the operation of the PBS in this context. A PBAC decision in relation to PBS listings does not necessarily represent a final PBAC view about the merits of the medicine or the circumstances in which it should be made available through the PBS. The PBAC welcomes applications containing new information at any time.

7 Sponsor's Comment

Janssen is supportive of this outcome as it consistent with the clinical evidence available for abiraterone and will continue to ensure its appropriate use.