

5.5 ENZALUTAMIDE, CAPSULE, 40 MG, XTANDI[®], ASTELLAS PHARMA AUSTRALIA PTY LTD,

1 Purpose of Application

- 1.1 Authority required (Streamlined) listing for enzalutamide for treatment of metastatic prostate cancer after treatment failure with docetaxel.

2 Requested listing

- 2.1 The submission sought the following listing:

Name, Restriction, Manner of administration and form	Max. Qty	No. of Rpts	Proprietary Name and Manufacturer	
Enzalutamide Capsules, 40mg, 112	1	2	Xtandi [®]	Astellas

Severity:	Patients with metastatic castration resistant prostate cancer.
Condition:	Castration resistant metastatic carcinoma of the prostate
Restriction:	Authority required (STREAMLINED)
Clinical criteria:	<p>The treatment must not be used in combination with chemotherapy</p> <p>AND</p> <p>Patient must have failed treatment with docetaxel due to resistance or intolerance</p> <p>AND</p> <p>Patient must have a WHO performance status of 2 or less</p> <p>AND</p> <p>Patient must not receive PBS-subsidised enzalutamide if progressive disease develops while on enzalutamide.</p>

- 2.2 The PSCR (p5) agreed with the recommendation in the Commentary that a non-streamlined Authority listing for enzalutamide is appropriate. This would be consistent with the listing for abiraterone. The ESC noted that the cost-offset for prescription processing claimed for enzalutamide will need to be removed from the financial estimates.

- 2.3 Given the draft PI states that the efficacy of enzalutamide in patients who have previously received abiraterone has not been studied, the Commentary suggests the PBAC consider including Prescriber Instructions in the restriction to prevent subsidised use of enzalutamide in patients who have experienced disease progression following treatment with PBS-subsidised abiraterone. The PSCR (p5) strongly disagreed with the suggestion of restricting sequential use of these agents as “[t]his presupposes that prescribers can identify in which patients each medication is most likely to be effective, no such criteria exist and such a restriction would be unusual, cruel and manifestly unjust in an end-stage disease”. The PSCR (p3) further

highlighted evidence that was presented in Section B.8.3 of the submission, about the efficacy of these agents when the other has failed. The ESC noted that this evidence is based on small observational studies which do not provide reliable clinical or economic evidence for using these agents in a sequential or concomitant fashion.

For more detail on PBAC's view, see section 7 "PBAC outcome"

3 Background

- 3.1 The submission was made under TGA/PBAC Parallel Process. At the time of PBAC consideration, a positive TGA Delegate's report was received.
- 3.2 Enzalutamide has not previously been considered by the PBAC. Cabazitaxel and abiraterone were listed on the PBS for the treatment of patients with mCRPC whose disease had progressed following treatment with docetaxel, following positive recommendation at the March and November 2012 PBAC meetings, respectively.

4 Clinical place for the proposed therapy

- 4.1 Metastatic castrate resistant prostate cancer (mCRPC) is advanced cancer of the prostate gland that has spread to the lymph nodes, bones or other organs of the body and is no longer sensitive to hormonal castration (surgical or medical). The first-line of treatment for mCRPC is docetaxel provided chemotherapy is suitable, followed by abiraterone or cabazitaxel after failure with docetaxel therapies. Enzalutamide is an androgen receptor inhibitor that acts on different steps in the androgen receptor signaling pathway. Enzalutamide has been shown to competitively inhibit androgen binding to androgen receptors, and inhibit androgen receptor nuclear translocation and interaction with DNA.
- 4.2 Enzalutamide is a proposed third treatment option for mCRPC after failure with docetaxel. The PBAC noted the recent publication of the PREVAIL trial in the New England Journal of Medicine (1 June 2014) which evaluated the effectiveness of enzalutamide in the pre-docetaxel setting vs placebo.

For more detail on PBAC's view, see section 7 "PBAC outcome"

5 Comparator

- 5.1 The submission nominated abiraterone as the comparator.
- 5.2 The ESC accepted the comparator on the basis of the intended place in therapy of enzalutamide. However, the ESC noted that there is potential for use of enzalutamide beyond the requested restriction in earlier disease, where it may replace other anti-androgens (bicalutamide, flutamide and nilutamide).

For more detail on PBAC's view, see section 7 "PBAC outcome"

6 Consideration of the evidence

Sponsor hearing

6.1 There was no hearing for this item.

Consumer comments

6.2 The PBAC noted and welcomed the input from an organisation (1) via the Consumer Comments facility on the PBS website. The comments described a range of benefits of treatment with enzalutamide including improvement in survival and quality of life.

For more detail on PBAC’s view, see section 7 “PBAC outcome”

Clinical trials

6.3 The submission was based on:

- one direct randomised trial comparing enzalutamide ± prednisone/prednisolone with placebo ± prednisone/prednisolone (AFFIRM, n=1199); and
- one direct randomised trial comparing abiraterone + prednisone/prednisolone with placebo + prednisone/prednisolone (Trial 301, n=1195).The abiraterone data from Trial 301 are the same as those considered by the PBAC for the abiraterone submissions i.e., pre-cross-over analysis in which the constant proportional hazards assumptions are satisfied.

Although there are differences in the common reference between the two trials (placebo with optional (AFFIRM) or mandatory (Trial 301) prednisone/prednisolone), the indirect comparison of the ITT populations is considered to be appropriate. The submission also presents post-hoc sub-group analyses of patients in AFFIRM who did and did not use concomitant corticosteroids. These analyses are considered to not be as relevant as those reported for the ITT populations, because the population who use concomitant corticosteroids in the AFFIRM trial are likely to be more sick and have a poorer prognosis. The PSCR (p3) argued that the sub-group analyses are valuable in demonstrating that enzalutamide not only remains effective even in the more difficult to treat population but by providing the option to not co-administer prednisolone which may avoid activating the mutated androgen-receptor causing disease progression. The ESC did not agree with the response and considered that the ITT population is most appropriate for evaluating clinical efficacy given the sub-group analyses was post-hoc and the requested restriction is not limited to patients with more or less difficult to treat disease in the post-docetaxel setting.

For more detail on PBAC’s view, see section 7 “PBAC outcome”

6.4 Details of the trials presented in the submission are provided in the table below.

Trials and associated reports presented in the submission

Trial ID	Protocol title/ Publication title	Publication citation
Direct randomised trials		
AFFIRM	AFFIRM: A Multinational Phase 3, Randomised, Double-Blind, Placebo-Controlled Efficacy and Safety Study of Oral MDV3100 in Patients with Progressive Castration-Resistant Prostate Cancer Previously Treated with Docetaxel-Based Chemotherapy.	CRPC2; Version 1.0 FINAL – 24 APR 2012
	Scher, H.I., et al. Increased survival with enzalutamide in prostate cancer after chemotherapy.	The New England Journal of Medicine 2012; 367(13): 1187-1197.
	Miller, K., et al. Effect of enzalutamide on health-related quality of life (hrqol) in men with metastatic castration-resistant prostate cancer (mcrpc) following docetaxel-based therapy: Results from	Journal of Clinical Oncology 2013; 31(6_suppl):17

	the affirm study.	
	Sternberg, C.N., et al. Improved outcomes in elderly patients with metastatic castration-resistant prostate cancer treated with the androgen receptor inhibitor enzalutamide: Results from the phase III affirm trial.	Annals of Oncology 2014; 25(2): 429-434.
Trial 301	De Bono, J., et al. Abiraterone and increased survival in metastatic prostate cancer.	The New England Journal of Medicine 2011; 364(21): 1995-2005.
	Fizazi, K., et al. Abiraterone acetate for treatment of metastatic castration-resistant prostate cancer: Final overall survival analysis of the cou-ABI-301 randomised, double-blind, placebo-controlled phase 3 study.	The Lancet Oncology 2012; 13: 983-992.
	Montgomery RB, et al. Effect of corticosteroid (CS) use at baseline (CUB) on overall survival (OS) in patients (pts) receiving abiraterone acetate (ABI): Results from a randomised study (COU-AA-301) in metastatic castration-resistant prostate cancer (mCRPC) post docetaxel (D) (abstract).	Journal of Clinical Oncology 2013; 31(15_suppl (May 20 Supplement)): 5014.
	Ryan, C., et al. Serum androgens as prognostic biomarkers in castration-resistant prostate cancer: Results from an analysis of a randomised phase III trial.	Journal of Clinical Oncology 2013; 31(27): 2791-2798.
	Azad, A.A., et al. Outcomes with abiraterone acetate in metastatic castration-resistant prostate cancer patients who have poor performance status.	European Urology. 2014 Jan 31; [epub] DOI:10.1016/j.eururo.2014.01.030
	Logothetis, C., et al. Effect of abiraterone acetate and prednisone compared with placebo and prednisone on pain control and skeletal-related events in patients with metastatic castration-resistant prostate cancer: Exploratory analysis of data from the COU-AA-301 randomised trial.	Lancet Oncology 2012; 13(12): 1210-1217.
	Sternberg, C., et al. Effect of abiraterone acetate on fatigue in patients with metastatic castration-resistant prostate cancer after docetaxel chemotherapy.	Annals of Oncology 2013; 24(4): 1017-1015.
	Harland, S., et al. Effect of abiraterone acetate treatment on the quality of life of patients with metastatic castration-resistant prostate cancer after failure of docetaxel chemotherapy.	European Journal of Cancer 2013; 49: 3648-3657
	Abiraterone Acetate in Castration-Resistant Prostate Cancer Previously Treated With Docetaxel-Based Chemotherapy	ClinicalTrials.gov Identifier: NCT00638690
	An Extended Study of Abiraterone Acetate in Patients With Advanced Prostate Cancer Who Have Failed Androgen Deprivation and Docetaxel-Based Chemotherapy and Completed Clinical Study COU-ABI-003.	ClinicalTrials.gov Identifier: NCT01798615:
	FDA New Drug Application for abiraterone: Clinical Review	Centre for drug evaluation and research. Application number: 202379Orig1s00 http://www.accessdata.fda.gov/drugsatfda_docs/nda/2011/202379Orig1s000PharmR.pdf
FDA New Drug Application for abiraterone: Statistical Review	Centre for drug evaluation and research. Application number: 202379Orig1s00 http://www.accessdata.fda.gov/drugsatfda_docs/nda/2011/202379Orig1s000StatR.pdf	

6.5 The key features of the direct randomised trials are summarised in the table below.

Key features of the included evidence

Trial	N	Design/ duration	Risk of bias	Patient population	Outcome(s)	Indirect comparison
Enzalutamide versus common reference						
AFFIRM	1199	R, DB, 14.4 months	Low	mCRPC post-	OS, PFS, FACT-	OS, PFS, FACT-P

Trial	N	Design/ duration	Risk of bias	Patient population	Outcome(s)	Indirect comparison
		(median follow up)		docetaxel	P	
Abiraterone versus common reference						
Trial 301	1195	R, DB, 12.8 months (median follow up)	Low	mCRPC post-docetaxel	OS, PFS, FACT-P	OS, PFS, FACT-P

DB=double blind; OS=overall survival; PFS=progression-free survival; R=randomised.

Source: compiled during the evaluation

6.6 Whilst both trial designs generally have a low risk of bias, patients randomised to the placebo arms in both trials were crossed-over to the active therapy before trial completion:

- In Trial 301, the cross-over was planned in the protocol following 67% of the planned 797 deaths;
- In AFFIRM, the cross-over occurred following review by an independent Data Monitoring Committee, performed after 80% of the planned 650 deaths.

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For more detail on PBAC's view, see section 7 "PBAC outcome"

Comparative effectiveness

6.7 Results of overall survival across the direct randomised trials

Results of overall survival across the direct randomised trials

	Trial 301		AFFIRM					
	ITT population (abiraterone + pred)		ITT population (enzalutamide ± pred)		post-hoc Subgroup 1 (enzalutamide + pred)		post-hoc Subgroup 2 (enzalutamide only)	
	AB +PRED (N=797)	PLA +PRED (N=398)	EN ±PRED (N=800)	PLA ±PRED (N=399)	EN +PRED (N=382)	PLA +PRED (N=182)	EN only (N=418)	PLA only (N=217)
Event	333 (42%)	219 (55%)	308 (38.5%)	212 (53.1%)				
Censored								
Median survival (months)	14.8 (NR)	10.9 (NR)	18.4 (17.3, NE)	13.6 (11.3, 15.8)				
Abs. difference								
HR (95%CI)	0.65 (0.54, 0.77)		0.63# (0.53, 0.75)					
Indirect HR (95%CI)								
Treatment interaction								

Abbreviations: AB=abiraterone; ENZ=enzalutamide; PLA = placebo;

FDA analysis

*estimated during the evaluation

For more detail on PBAC's view, see section 7 "PBAC outcome"

Comparative harms

6.8 A similar incidence of adverse events was reported in both arms of AFFIRM. Grade three and higher adverse events were reported more frequently in the placebo arm of

both the AFFIRM trial and Trial 301. The most common adverse events reported more frequently in the enzalutamide arm include: fatigue, diarrhoea, hot flush, musculoskeletal pain, headache, insomnia, paraesthesia, haematuria anxiety and hypertension. The risk of seizures was slightly elevated in the enzalutamide group with a frequency of 0.9% versus 0%.

Benefits/harms

6.9 A summary of the comparative benefits and harms for enzalutamide versus abiraterone is presented in the table below. A comparison of specific adverse events of any grade could not be performed because of limited available safety data for Trial 301.

Summary of comparative benefits and harms for enzalutamide-abiraterone and comparator/PBO

Benefits: Overall survival								
		enzalutamide	placebo	abiraterone	Difference	HR (95% CI)	Ind. difference	Ind. HR (95% CI)
Trial 301	Survival	-	219/398 (55%)	333/797 (42%)	■	■	■	■
	Median-(mths)	-	10.9	14.8			■	■
AFFIRM	Survival	308/800 (39%)	212/399 (53%)	-	■	■	■	■
	Median (mths)	18.4	13.6	-				
Harms								
		enzalutamide	placebo	abiraterone	RR (95% CI)	Ind. RR (95% CI)		
AEs	Trial 301	-	390/394 (99%)	782/791 (99%)	■	■	■	
	AFFIRM	785/800 (98%)	390/399 (98%)	-	■	■	■	
SAEs	Trial 301	-	163/394 (41%)	297/791 (38%)	■	■	■	
	AFFIRM	268/800 (34%)	154/399 (39%)	-	■	■	■	
■	Trial 301	■	■	■	■	■	■	
	AFFIRM	227/800 (28%)	134/399 (34%)	-	■	■	■	

6.10 On the basis of indirect evidence presented by the submission, the comparison of enzalutamide and abiraterone suggested a similar benefit in overall survival. However, the ESC noted that the magnitude of the incremental benefit of enzalutamide compared with abiraterone is uncertain as the overall survival reported in the enzalutamide trial is confounded by the subsequent use of other effective treatments which were not approved for use when the abiraterone trial was conducted.

6.11 On the basis of indirect evidence presented by the submission, enzalutamide is well tolerated and appears to have a similar safety profile to abiraterone, but does not require monitoring of liver function and blood pressure, which is required with abiraterone.

For more detail on PBAC’s view, see section 7 “PBAC outcome”

Clinical claim

- 6.12 The submission claimed enzalutamide as non-inferior in terms of comparative effectiveness and non-inferior in terms of comparative safety over abiraterone. This claim is adequately supported in terms of safety. However the claim regarding effectiveness requires some consideration in light of the potential for differences in the subsequent treatments undertaken by patients in the AFFIRM and Trial 301 trials. Given enzalutamide and cabazitaxel were not approved when Trial 301 was conducted, but abiraterone and cabazitaxel were approved when AFFIRM was conducted and used by a relatively high proportion of patients as subsequent treatment, this may have affected the results of overall survival. This discrepancy may partly explain the observed differences in the median survival in the control arms of the trials (i.e., 13.6 months and 10.9 months in AFFIRM and Trial 301, respectively) given the PBAC has previously accepted that both abiraterone and cabazitaxel offer survival benefits. Thus, the magnitude of the incremental benefit of enzalutamide is uncertain as the overall survival reported in AFFIRM is confounded by the use of other effective treatments.
- 6.13 The PSCR disagreed with the potential effect of subsequent therapies on overall survival and argued that the overall survival indirect comparison is based on incremental differences in results. Further, the PSCR claimed that the available data does not favour enzalutamide given:
- A higher rate of usage of other therapies in the placebo arm of AFFIRM using the ITT population
 - Similar use of abiraterone and cabazitaxel between both enzalutamide and placebo arms using the ITT population as the denominator
 - Earlier start and longer duration of abiraterone and cabazitaxel in the placebo arm.
- 6.14 The ESC considered the difference in OS between the common reference arms suggested there may be an effect of post-discontinuation therapies.

For more detail on PBAC's view, see section 7 "PBAC outcome"

Economic analysis

- 6.15 The equi-effective doses are estimated as enzalutamide 160mg and abiraterone 1000mg, based on the indirect comparison.
- 6.16 The requested DPMQ of enzalutamide (\$ [REDACTED]) is based on the published DPMQ of abiraterone (\$ [REDACTED]) and cost-offsets of liver function tests and prednisolone use. The submission does not incorporate the cost of concomitant prednisolone associated with enzalutamide. The PSCR argued that the cost calculations should not incorporate costs of prednisolone as it is unrelated to the use of enzalutamide. The ESC agreed with the sponsor response.

Cost-minimisation analysis of enzalutamide compared with abiraterone

Product	Category	Units	Cost per unit		Cost per 30 days	Cost per 28 days
			PBS	MBS		
Abiraterone	Abiraterone 250mg tabs	1 box (120 tablets)	\$ [REDACTED]	[REDACTED]	\$ [REDACTED]	\$ [REDACTED]
	Prednisolone 5mg tabs	1 bottle (60 tablets)	\$ [REDACTED]	[REDACTED]		
	Liver function testing	1.54 tests	[REDACTED]	\$ [REDACTED]		
Enzalutamide	Enzalutamide 40mg caps	1 box (112 capsules)	\$ [REDACTED]	[REDACTED]	[REDACTED]	[REDACTED]

Ex-manufacturer price for item abiraterone [REDACTED]
 ^ Ex-manufacturer price for prednisolone [REDACTED]
^a Requested ex-man price for enzalutamide [REDACTED]
 Note: the prices in the table reflect published prices of abiraterone [REDACTED]

For more detail on PBAC’s view, see section 7 “PBAC outcome”

Drug cost/patient:

6.17 The drug cost is \$ [REDACTED] per patient (\$ [REDACTED] months). This compares to \$ [REDACTED] per patient with abiraterone (\$ [REDACTED] months). These estimates are based on the published (not effective) prices and the assumption patients will only receive [REDACTED] months of each treatment.

Estimated PBS usage & financial implications

6.18 This submission was considered by the DUSC. The main issues noted by DUSC include the following:

- The base case estimates assume that use of enzalutamide will be entirely offset by a reduction in the use of abiraterone and cabazitaxel. This may underestimate the financial implications to the government upon listing enzalutamide due to:
 - The potential for enzalutamide to be used subsequent to, rather than only as a substitute for abiraterone (and cabazitaxel) (i.e. an increased market in the post-docetaxel setting);
 - The potential for concomitant use of enzalutamide and abiraterone, rather than only as a substitute for abiraterone, (nb: currently possible under the proposed restriction);
 - The extent of the population with an “unmet clinical need”, i.e. those unable to take abiraterone or cabazitaxel or prednisone/prednisolone (which is required for treatment with abiraterone or cabazitaxel). This has been neither quantified nor accounted for in the current estimates.
- Using an epidemiological approach, the prevalent patient population has been estimated from the modelled incidence rate (derived from answers provided in a commissioned survey) and using a mortality rate that may or may not be relevant to the Australian context nor accounts for factors that may drive prevalence (e.g. age, improved diagnosis, effective therapies). This may over or underestimate the potential number of patients eligible for treatment.
- The potential for use beyond the restriction: (i) use in ‘sicker’ patients (i.e. WHO >2); (ii) use beyond disease progression; and (iii) use in earlier stages of disease (i.e. replacing other anti-androgens) and in light of the Phase 3 PREVAIL study.

6.19 The estimated PBS usage and financial implications are presented in the table below.

Estimated use and financial implications

	2015	2016	2017	2018	2019
Estimation of use and costs of the proposed drug					
Eligible patients	2,432	2,541	2,645	2,752	2,864
ENZ scripts	[REDACTED]	[REDACTED]	[REDACTED]	[REDACTED]	[REDACTED]
ENZ cost to PBS/RPBS (net)	[REDACTED]	[REDACTED]	[REDACTED]	[REDACTED]	[REDACTED]

co-payment)					
Estimation of changes in use and costs of other drugs					
'Current' cost to PBS/RPBS (net co-payment)	██████	██████	██████	██████	██████
Change in 'current' cost to PBS/RPBS (net co-payment)	██████	██████	██████	██████	██████
Net Cost to PBS/RPBS	██████	██████	██████	██████	██████

Estimated financial implications for government health budgets					
Net cost to the MBS	██████	██████	██████	██████	██████
Net cost to health budgets	██████	██████	██████	██████	██████

Source: modified from pp43-44 of the commentary.

- 6.20 The Sponsor acknowledged enzalutamide would join the current risk-sharing agreements with abiraterone and cabazitaxel, but is concerned the current risk-share agreements may significantly underestimate the likely number of patients eligible for treatment. The Sponsor therefore requested the PBAC and DUSC re-assess the likely patient population and the likely number of scripts these patients are expected to require.
- 6.21 The submission stated (pF-5) that leakage of enzalutamide into the pre-docetaxel setting is possible, however this represented limited financial risk to the government should the listing of enzalutamide join the current risk-sharing agreements with abiraterone and cabazitaxel. Other sources of leakage include the use in 'sicker' patients (WHO >2) and use beyond progression, given enzalutamide appears to be a relatively well-tolerated oral therapy. Although comparable leakage is possible with abiraterone and cabazitaxel, the total risk is increased with the listing of enzalutamide due to additional sequential and/or concurrent use of treatments. Additional use beyond the restriction in earlier stage disease may also occur (substituting for other anti-androgens).
- 6.22 The PBAC considered enzalutamide should join the same risk share arrangements as abiraterone.

For more detail on PBAC's view, see section 7 "PBAC outcome"

7 PBAC Outcome

- 7.1 The PBAC recommended an Authority required listing for enzalutamide for the treatment of metastatic prostate cancer after treatment failure with docetaxel, on a cost-minimisation basis with abiraterone. The equi-effective doses are enzalutamide 160 mg and abiraterone 1000 mg.
- 7.2 The PBAC accepted that abiraterone was the appropriate comparator given the intended place of enzalutamide in the current treatment of metastatic prostate. The PBAC noted that there are now a number of new effective agents for metastatic prostate cancer and therefore the treatment algorithm for may continue to evolve over the short-medium term.

- 7.3 The PBAC acknowledged that radium-223 injection was assessed by MSAC at the 61st meeting (for more information, refer to www.msac.gov.au) for the treatment of patients with symptomatic castrate resistant prostate cancer with skeletal metastases. Should radium-223 be MBS listed this therapy would also become a relevant comparator.
- 7.4 The PBAC further considered that given the lack of evidence of efficacy of enzalutamide in patients who have previously received abiraterone, a note should be included in the restrictions to prevent subsidised use in this patient population.
- 7.5 Regarding the clinical trials, the PBAC agreed with the ESC that the ITT population is considered to be most appropriate for determining clinical efficacy and the post-hoc sub-group analyses of patients who did and did not use concomitant corticosteroids were not as relevant. The Pre-PBAC response agreed with the use of the ITT population.
- 7.6 The PBAC accepted that enzalutamide is non-inferior to abiraterone in terms of comparative effectiveness, although the differences in the results of the common reference arms between AFFIRM and Trial 301 undermine the validity of the indirect comparison.
- 7.7 The PBAC considered that the claim of non-inferior comparative safety was reasonable. The PBAC noted the adverse event profile of enzalutamide is different to abiraterone and that enzalutamide does not require liver function monitoring.
- 7.8 The cost-minimisation analysis of enzalutamide allowed for cost offsets for prednisolone use and liver function tests. The PBAC considered this to be reasonable.
- 7.9 The PBAC noted the submission and pre-PBAC response expressed concerns that the current risk share arrangement for cabazitaxel and abiraterone underestimates the patient pool in the post-docetaxel setting. The PBAC did not consider that the submission had provided evidence to support this claim, and recommended that enzalutamide join the same risk share as abiraterone.
- 7.10 Advice to the Minister under Section 101 3BA of the National Health Act:
The PBAC advised the Minister that under Section 101 3BA of the National Health Act, enzalutamide should not be treated as interchangeable with any other drugs.
- 7.11 The PBAC advised that enzalutamide is not suitable for prescribing by nurse practitioners.
- 7.12 The PBAC recommended that the Safety Net 20 Day Rule should apply.

Outcome:

Recommended

8 Recommended listing

- 8.1 Add new item:

Name, Restriction, Manner of administration and form	Max Qty	No. of Rpts	Proprietary Name and Manufacturer	
ENZALUTAMIDE enzalutamide 40 mg capsule, 112	1	2	Xtandi	Astellas

Category/Program:	GENERAL- General Schedule (GE)
Episodicity:	
Severity:	Castration resistant metastatic
Condition:	carcinoma of the prostate
Clinical criteria:	<p>The treatment must not be used in combination with chemotherapy</p> <p>AND</p> <p>Patient must have failed treatment with docetaxel due to resistance or intolerance</p> <p>AND</p> <p>Patient must have a WHO performance status of 2 or less</p> <p>AND</p> <p>Patient must not receive PBS-subsidised treatment with this drug if progressive disease develops while on this drug</p> <p>AND</p> <p>Patient must not have received prior treatment with abiraterone</p> <p>OR</p> <p>Patient must have developed intolerance to abiraterone of a severity necessitating permanent treatment withdrawal.</p>
Administrative Advice	<p>Note: Special Pricing Arrangements apply.</p> <p>Note: No increase in the maximum quantity or number of units may be authorised.</p> <p>Note: No increase in the maximum number of repeats may be authorised</p>

9 Context for Decision

The PBAC helps decide whether and, if so, how medicines should be subsidised in Australia. It considers submissions in this context. A PBAC decision not to recommend listing or not to recommend changing a listing does not represent a final

PBAC view about the merits of the medicine. A company can resubmit to the PBAC or seek independent review of the PBAC decision.

10 Sponsor's Comment

The sponsor is pleased that enzalutamide will be available to patients with mCRPC. The sponsor is not in agreement with the reporting of some of the data as presented in the PSD and is currently in the process of rectifying data errors with the PBAC.