

7.01 ABIRATERONE AND METHYLPREDNISOLONE, Pack containing 120 tablets abiraterone (as acetate) 125 mg and 60 tablets methylprednisolone 4 mg, Yonsa[®] MPRED[™], Sun Pharma ANZ Pty Ltd.

1 Purpose of submission

- 1.1 The Standard re-entry submission requested an Authority Required listing for a composite pack (co-pack) comprising abiraterone acetate tablets in a fine particle formulation (SAA) and oral methylprednisolone (MPRED) tablets for the treatment of patients with metastatic castration resistant prostate cancer (mCRPC).
- 1.2 Listing was requested on a cost-minimisation basis versus the currently PBS-listed formulation of abiraterone acetate (described as originator abiraterone acetate (OAA)) administered with the glucocorticoid prednisone.

Table 1: Key components of the clinical issue addressed by the resubmission

| Component | Description |
|----------------|--|
| Population | Patients aged ≥ 18 years with mCRPC |
| Intervention | SAA 500 mg once daily with concomitant MPRED 4 mg bid |
| Comparator | OAA 1000 mg once daily with concomitant PRED 5 mg bid |
| Outcomes | Bioequivalence between SAA 500 mg and OAA 1000 mg Post-treatment testosterone and PSA levels |
| Clinical claim | SAA 500 mg is bioequivalent to OAA 1000 mg based on pharmacokinetics SAA 500 mg is clinically bioequivalent to OAA 1000 mg with respect to changes in testosterone and PSA levels SAA 500 mg has noninferior safety to OAA 1000 mg |

Blue shading indicates data previously seen by the PBAC.

Source: Table 1.1, p2 of the March 2022 submission.

Abbreviations: bid = twice daily; mCRPC = metastatic castration resistant prostate cancer; MPRED = methylprednisolone; OAA = originator abiraterone acetate; PRED = prednisone; PSA = prostate specific antigen; SAA = SoluMatrix[™] abiraterone acetate

2 Background

Registration status

- 2.1 Abiraterone and methylprednisolone (Yonsa[®] MRPED) was TGA registered on 29 March 2022 for the treatment of patients with: newly diagnosed high-risk metastatic hormone sensitive prostate cancer (mHSPC) in combination with androgen deprivation therapy (ADT), or; patients with metastatic advanced prostate cancer (castration resistant prostate cancer, mCRPC) who are asymptomatic or mildly symptomatic after failure of androgen deprivation therapy (ADT) or; patients with mCRPC who have received prior chemotherapy containing a taxane.

Previous PBAC consideration

2.2 In March 2022, the PBAC did not recommend the listing of Yonsa® MPRED on the PBS. The PBAC raised concerns regarding the quality use of the co-pack in practice, noting there would be a risk of confusion among patients due to differences in dosing of SAA and MPRED compared to the currently listed form of abiraterone (OAA) and prednisone. The PBAC had also noted concern that SAA risked unnecessary proliferation of products and dose forms. The PBAC had considered further information from the sponsor would be required to clarify how these risks would be mitigated (paragraphs 7.1 and 7.4, abiraterone and methylprednisolone Public Summary Document (PSD), March 2022 PBAC meeting).

Table 2: Summary of key matters of concern

| Component | Matter of concern | How the resubmission addresses it |
|--------------------------|---|---|
| Quality Use of Medicines | <p>The PBAC discussed there were significant concerns regarding the quality use of SAA and MPRED in clinical practice. The PBAC considered the following were of high risk:</p> <ul style="list-style-type: none"> • Patient confusion between SAA and OAA given both products are called abiraterone but have different daily doses of 500 mg and 1000 mg, respectively • Confusion regarding timing of oral prednisone (typically given 10 mg daily as per EviQ), contrasting with methylprednisolone 4 mg twice daily <p>The PBAC considered further information from the sponsor would be required to clarify how these risks would be mitigated (Para 6.25, abiraterone and methylprednisolone PSD, March 2022 PBAC meeting)</p> | <p>Addressed</p> <p>The resubmission provided further information regarding how the PBAC's concerns would be mitigated. This included how prescribers would manage the risk associated with patient confusion, as well as updated education materials.</p> <p>For more detail see section 6 Quality Use of Medicines.</p> |

3 Requested listing

3.1 Suggestions and additions proposed by the Secretariat are added in italics and suggested deletions are crossed out with strikethrough.

| MEDICINAL PRODUCT medicinal product pack | Dispensed Price for Max. Qty | Max. qty packs | Max. qty units | №.of Rpts | Available brands |
|--|---------------------------------|-------------------|-------------------|--------------|------------------|
| ABIRATERONE (&) METHYLPREDNISOLONE | | | | | |
| abiraterone acetate 125 mg tablet [120] (&) methylprednisolone 4 mg tablet [60], 1 pack | \$3,444.85 (published) | 1 | 180 | 2 | Yonsa MPRED |
| Category / Program: GENERAL – General Schedule (Code GE) | | | | | |
| Prescriber type: <input checked="" type="checkbox"/> Medical Practitioners | | | | | |
| Restriction type: <input checked="" type="checkbox"/> Authority Required (telephone/online PBS Authorities system) | | | | | |
| Caution The bioavailability on a mg to mg basis of abiraterone combination product and abiraterone single drug product is not equivalent. When changing between abiraterone products, exercise caution in explaining correct dosing directions to the patient. | | | | | |
| Indication: Castration resistant metastatic carcinoma of the prostate | | | | | |

| |
|---|
| Clinical criteria: |
| The treatment must not be used in combination with chemotherapy |
| AND |
| Clinical criteria: |
| Patient must have a WHO performance status of 2 or less |
| AND |
| Clinical criteria: |
| The treatment must cease as not be a PBS benefit where further disease progression occurs whilst being treated with this product any of: (i) a combination treatment containing the individual drugs in one pharmaceutical benefit, (ii) the individual drugs obtained as separate pharmaceutical benefits |
| AND |
| Clinical criteria: |
| Patient must only receive treatment with one novel hormonal drug per lifetime; or |
| Patient must only receive treatment with a subsequent novel hormonal drug where there has been a severe intolerance to another novel hormonal drug leading to permanent treatment cessation |
| Administrative Advice: |
| Applications for authorisation under this restriction may be made in real time using the Online PBS Authorities system (see www.servicesaustralia.gov.au/HPOS) or by telephone by contacting Services Australia on 1800 888 333. |
| Administrative Advice: |
| Where the term 'novel hormonal drug' appears in this restriction, it refers to: (i) abiraterone, (ii) apalutamide, (ii) darolutamide, (iv) enzalutamide. |
| Administrative Advice: Special Pricing Arrangements apply. |

Blue shading indicates data previously seen by the PBAC, although the requested published DPMQ had a minor update from the March 2022 submission due to differences in fees and markups.

- 3.2 The sponsor accepted the proposed restriction amendments made by the PBAC at its March 2022 meeting (Section 3, abiraterone and methylprednisolone PSD, March 2022 PBAC meeting). The resubmission noted the sponsor is amenable to restricting SAA+MPRED to patients who newly initiate abiraterone unless the patient is intolerant to OAA to address quality use of medicines concerns. The PBAC considered that switching between combination and individual components would be acceptable.
- 3.3 The Secretariat proposed further edits to exclude sequential use of the combination product following disease progression on the individual drugs obtained as separate PBS benefits. The Secretariat proposed that the same updated criterion should replace the relevant criterion (regarding ceasing therapy if progressive disease develops) in the abiraterone restriction, in order to exclude a second treatment attempt with abiraterone. The PBAC considered the addition of clinical criterion to prevent sequential use was appropriate.
- 3.4 Abiraterone on the PBS is currently prescribed by medical practitioners only, while methylprednisolone injections can be prescribed by medical practitioners and nurse practitioners. Given the differences in dosage of SAA+MPRED to OAA and prednisone, the PBAC advised that Yonsa MPRED should be prescribed by medical practitioners only.
- 3.5 The resubmission reiterated that because of the difference in administration between SAA and OAA, the products should not be considered interchangeable on an individual

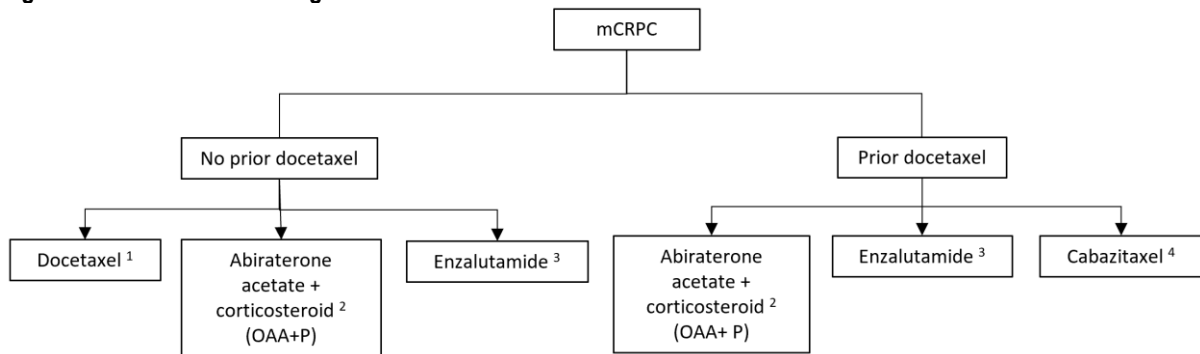
patient basis under Section 101 (3BA) of the *National Health Act 1953*. The PBAC had considered this to be appropriate previously (para 3.5, abiraterone and methylprednisolone PSD, March 2022 PBAC meeting). Brand substitution is not a relevant consideration as the listed pharmaceutical item (medicinal product) is unique.

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

4 Population and disease

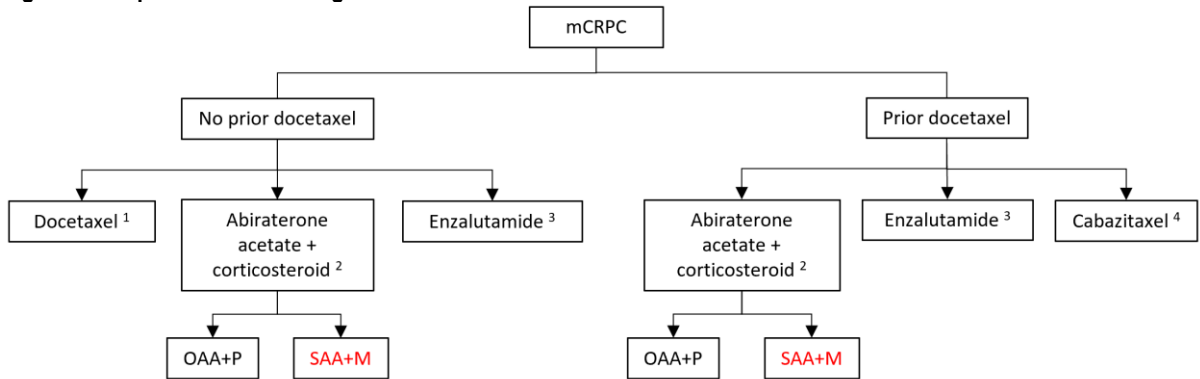
- 4.1 The resubmission provided no further information regarding the population and disease. The following information was seen by the PBAC at its March 2022 meeting.
- 4.2 Prostate cancer is the most commonly diagnosed cancer and the second leading cause of cancer death in Australian males. Due to the introduction of prostate specific antigen (PSA) testing, the majority of patients with prostate cancer are diagnosed at early stages with localised disease. Survival is high in patients with localised disease, with the 5-year survival reported to be 95.2% during 2011-2015. However, metastatic disease has a much poorer prognosis with the median survival for patients with mCRPC at 13 months.
- 4.3 The proposed PBS population for this submission was the same as the PBS patient population for which abiraterone is currently listed, i.e. patients with castration-resistant metastatic carcinoma of the prostate. The definition of mCRPC in the clinical trial informing the submission (STAAR) was defined as disease progression despite serum testosterone levels < 50 ng/dL with ongoing therapy with gonadotropin releasing hormone (GnRH) agonist/antagonist.
- 4.4 The submission proposed that the co-pack of SAA and MPRED would be an alternative to the currently listed abiraterone product given with prednisone. The current and proposed treatment algorithms are shown below, based on current treatment guidelines and the existing PBS listings for products for treatment of metastatic prostate cancer.

Figure 1: Current treatment algorithm



Source: Figure 1.2.1, p 16 of the submission. Abbreviations: mCRPC = metastatic castration resistant prostate cancer; OAA+P = originator abiraterone acetate 1000 mg once daily + prednisone 5 mg twice daily. 1 Unrestricted listing. 2 Must not have received prior enzalutamide treatment OR must have developed intolerance to enzalutamide of a severity necessitating permanent withdrawal. 3 Must not have received prior abiraterone treatment OR must have developed intolerance to abiraterone of a severity necessitating permanent withdrawal. 4 Must have failed treatment with docetaxel due to resistance or intolerance

Figure 2: Proposed treatment algorithm



Source: Figure 1.2.2, p 16 of the submission. Abbreviations: mCRPC = metastatic castration resistant prostate cancer; OAA+P = originator abiraterone acetate 1000 mg once daily + prednisone 5 mg twice daily; SAA+M = SoluMatrix™ abiraterone acetate 500 mg once daily + methylprednisolone 4 mg twice daily. 1 Unrestricted listing. 2 Must not have received prior enzalutamide treatment OR must have developed intolerance to enzalutamide of a severity necessitating permanent withdrawal. 3 Must not have received prior abiraterone treatment OR must have developed intolerance to abiraterone of a severity necessitating permanent withdrawal. 4 Must have failed treatment with docetaxel due to resistance or intolerance.

4.5 Abiraterone is an irreversible inhibitor of CYP17 that reduces production of androgens. Methylprednisolone (MPRED) is a glucocorticoid. The submission stated that MPRED 4 mg is considered to have equivalent glucocorticoid effects to prednisone 5 mg.

5 Comparator

5.1 The resubmission nominated the previously accepted comparator from the March 2022 submission. The comparator was the PBS-listed tablet formulation of abiraterone acetate (referred to as OAA; Zytiga®), which must be administered with a corticosteroid. The PBAC considered ‘...the nominated comparator OAA given with prednisone 5 mg tablets was acceptable given these would likely be replaced by SAA+MPRED in practice, although considered that enzalutamide was also a relevant comparator’ (para 7.3, abiraterone and methylprednisolone PSD, March 2022 PBAC meeting).

- 5.2 In its July 2014 consideration, 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. The cost-minimisation analysis of enzalutamide allowed for cost offsets for prednisolone use and liver function tests (para 7.1 and 7.8, enzalutamide PSD, July 2014 PBAC meeting).

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 Input was received from an individual from a prostate cancer awareness support group (1) via the Consumer Comments facility on the PBS website.

Clinical evaluation

- 6.3 The clinical evidence was unchanged from that presented in the March 2022 submission.
- 6.4 In its March 2022 consideration, the PBAC had noted the STAAR study was the most appropriate evidence as it was a direct comparative trial of SAA with OAA which also included the population proposed for PBS listing. However, the PBAC noted the study had limitations including that the trial was based on surrogate endpoints (serum testosterone and PSA levels), which do not translate to improved overall survival (para 7.5, abiraterone and methylprednisolone PSD, March 2022 PBAC meeting).
- 6.5 Additionally, the PBAC had noted that the TGA Delegate's Overview stated that the STAAR study provided supportive evidence of efficacy only. Therefore, although the data for SAA appeared to be comparable to OAA, the PBAC had considered that it was not possible to exclude potentially significant differences in terms of safety (para 7.5, abiraterone and methylprednisolone PSD, March 2022 PBAC meeting).

Clinical claim

- 6.6 In its March 2022 consideration, the PBAC had noted the TGA Delegate's Overview accepted the claim of bioequivalence for SAA and MPRED to OAA and prednisone, respectively, which was consistent with the submission's claim of noninferior comparative effectiveness and safety (para 6.17, abiraterone and methylprednisolone PSD, March 2022 PBAC meeting). The PBAC's previous concerns regarding patient safety were addressed by the resubmission and discussion is included in the 'Quality Use of Medicines' section below.

6.7 The PBAC considered that the claim of noninferior comparative effectiveness and safety was reasonable.

Economic analysis

6.8 The cost-minimisation economic evaluation is unchanged from that presented in the March 2022 submission. The key assumptions and components of the cost-minimisation approach are summarised in Table 3 below.

Table 3: Key components and assumptions of the cost-minimisation approach

| Component | Claim or assumption |
|----------------------------------|---|
| Therapeutic claim: effectiveness | SAA 500 mg qd in combination with methylprednisolone 4 mg bid is noninferior to OAA 1,000 mg qd in combination with prednisone 5 mg bid in terms of efficacy. |
| Therapeutic claim: safety | SAA 500 mg qd in combination with methylprednisolone 4 mg bid is noninferior to OAA 1,000 mg qd in combination with prednisone 5 mg bid in terms of safety. |
| Evidence base | Direct comparison of a pharmacokinetic studies (Study 102 and Study 104) as well as a randomised controlled trial investigating the comparative efficacy and safety of SAA+M versus OAA+P (STAAR) |
| Equi-effective doses | SAA 500 mg qd in combination with methylprednisolone 4 mg bid ≡ OAA 1,000 mg qd in combination with prednisone 5 mg bid |
| Direct medicine costs | The cost of treatment with SAA 500 mg qd in combination with methylprednisolone 4 mg bid and OAA 1,000 mg qd in combination with prednisone 5 mg bid. |
| Other costs or cost offsets | No other costs or cost offsets resulting from differences in prescribing, administration, medicine-specific monitoring, or management of adverse events were considered in the CMA |

Blue shading indicates data previously seen by the PBAC.

Source: Table 2.8.1, p 87 of the submission. Abbreviations: SAA = abiraterone acetate in fine particle formulation; OAA = originator abiraterone acetate; qd = once daily; bid = twice daily

6.9 The cost-minimisation approach was based on the published price of OAA as a special pricing arrangement (SPA) applies to OAA and the effective indication-specific AEMP for OAA is not known to the sponsor.

6.10 The resubmission again requested an SPA comprising of a published approved ex-manufacturer price (AEMP) of \$3,283.57 and a confidential (effective) AEMP (based on the effective price/s of the relevant comparator). This is in line with the SPA that exists for the currently listed abiraterone formulation for which the published price is \$3,280.86 (AEMP). The sponsor included the October 2021 price of prednisone 5 mg tablets in the calculation of the price for the co-pack and no other costs or cost-offsets. The resubmission agreed with the PBAC that the proposed price of SAA+MPRED should be no higher than the lowest cost comparator for metastatic prostate cancer.

Table 4: Results of the cost-minimisation analysis (published AEMP)

| | SAA+M | OAA | Prednisone |
|---------------------------------|-------------------------------|-------------------------------------|-------------------------|
| AEMP for Max Qty | \$3,283.57 | \$3,280.86 | \$2.71 |
| Treatment days for Max Qty | 30 [120/4; 60/2] | 30 [120/4; 60/2] | 30 [60/2] |
| Total medicine cost per day | \$109.45 [\$3,283.57/30] | \$109.36 [\$3,280.86/30] | \$0.09 [\$2.71/30] |
| Cost of treatment | \$3,283.57 [\$109.45 x 30] | \$3,280.86 [\$109.36 x 30] | \$2.71 [\$0.09 x 30] |
| Total cost of treatment | \$3,283.57 | \$3,283.57 [\$3,280.86 + \$2.71] | |
| Difference in cost of treatment | \$0 | | |

Blue shading indicates data previously seen by the PBAC. PBS prices as at October 2021.

Source: Table 8, abiraterone and methylprednisolone PSD, March 2022. Abbreviations: SAA = abiraterone acetate in fine particle formulation; OAA = originator abiraterone acetate; max = maximum; qty = quantity, AEMP = approved ex-manufacturer price

Estimated PBS usage & financial implications

- 6.11 The estimated PBS usage was unchanged from that presented in the March 2022 submission. The resubmission was not considered by DUSC.
- 6.12 The market share approach previously considered appropriate by PBAC is presented below.

Table 5: Data sources and parameter values applied in the utilisation and financial estimates

| | Value | Source |
|---|--|---|
| Prescriptions | | |
| Predicted prescriptions for OAA | <u>Prescriptions</u> 2022: ██████ ¹ 2023: ██████ ¹ 2024: ██████ ² 2025: ██████ ² 2026: ██████ ² 2027: ██████ ² | Observed data: Services Australia PBS statistics for item numbers 2698B (250 mg, 120 tablets) and 11206T (500 mg, 60 tablets). The evaluation noted it is unclear whether these projected data from before August 2021 remain applicable, but it is likely the impact would be small. Extrapolation: Linear trend analysis using the MS Excel build-in trend line function |
| Changes in utilisation | | |
| Uptake of SAA+M (%) | <u>Uptake</u> 2022: ██████% 2023: ██████% 2024: ██████% 2025: ██████% 2026: ██████% 2027: ██████% | Sponsor assumption |
| Cost of medicines | | |
| SAA+M combination pack SAA 125 mg, 120 tablets + M 4 mg x 60 tablets | Published AEMP: \$3,283.57 | Sponsor proposed |
| <u>OAA</u> 500 mg, 60 tablets 250 mg, 120 tablets | Published AEMP: \$3,280.86 Published AEMP: \$3,280.86 | Schedule of Pharmaceutical Benefits [PBS items 2698B and 11206T; October 2021] |
| <u>Prednisone</u> 5mg, 60 tablets | Effective AEMP: \$2.71 | Schedule of Pharmaceutical Benefits [PBS item 1935W; October 2021] |
| Patient co-payments | | |
| Beneficiary type distribution | General ordinary: 2% General safety net: 3% Concessional ordinary: 63% Concessional safety net: 32% RPBS ordinary: 65% RPBS safety net: 35% | Utilisation of OAA + prednisone [PBS items: 2698B, 11206T, 1935W] |
| Patient co-payments | General ordinary: \$41.30 General safety net: \$6.60 Concessional ordinary: \$6.60 RPBS ordinary: \$6.60 | PBS website |

Blue shading indicates data previously seen by the PBAC.

Source: Table 9, abiraterone and methylprednisolone PSD, March 2022. Abbreviations: PBS = Pharmaceutical Benefits Scheme, AEMP = Approved Ex-Manufacturer Price, M = methylprednisolone, SAA = abiraterone acetate in fine particle formulation, OAA = originator abiraterone acetate

The redacted values correspond to the following ranges:

¹ 10,000 to < 20,000

² 20,000 to < 30,000

6.13 The estimated use and financial implications are shown below. The predicted number of prescriptions in each year was based on the estimated annual percent change from

the trendline analysis. As noted in the previous evaluation, the overall market for abiraterone is unlikely to expand substantially due to the listing of SAA+MPRED.

- 6.14 The resubmission calculated the financial impact based on a published DMPQ of \$3,444.85. This was slightly higher than the March 2022 submission which used a published DMPQ of \$3,444.79. The difference was due to the fees and markups changes implemented from 1 July 2022.
- 6.15 The evaluation also noted the submission calculated its financial impact using outdated copayment amounts from 2021. The table below was updated using the copayments from 1 January 2022.

Table 6: Estimated use and financial implications (published prices)

| | Year 1 | Year 2 | Year 3 | Year 4 | Year 5 | Year 6 |
|---|----------------|----------------|----------------|----------------|----------------|-----------------|
| Estimated extent of use | | | | | | |
| Number of OAA scripts dispensed | █ ¹ | █ ¹ | █ ² | █ ² | █ ² | █ ² |
| Number of prednisone scripts dispensed | █ ¹ | █ ¹ | █ ² | █ ² | █ ² | █ ² |
| SAA+M market share | █% | █% | █% | █% | █% | █% |
| Number of SAA+M scripts dispensed ^a | █ ³ | █ ³ | █ ⁴ | █ ⁴ | █ ⁴ | █ ¹ |
| Estimated financial implications of SAA + MPRED | | | | | | |
| Cost to the PBS/RPBS (\$) | █ ⁵ | █ ⁶ | █ ⁷ | █ ⁷ | █ ⁸ | █ ⁸ |
| Patient co-payments (\$) | █ ⁵ | █ ⁵ | █ ⁵ | █ ⁵ | █ ⁵ | █ ⁵ |
| Total cost to PBS/RPBS (\$) | █ ⁵ | █ ⁶ | █ ⁷ | █ ⁷ | █ ⁸ | █ ⁸ |
| Estimated financial implications of OAA + prednisone | | | | | | |
| Cost to the PBS/RPBS (\$) | █ ⁵ | █ ⁶ | █ ⁷ | █ ⁷ | █ ⁸ | █ ¹⁰ |
| Patient co-payments (\$) | █ ⁵ | █ ⁵ | █ ⁵ | █ ⁵ | █ ⁵ | █ ⁵ |
| Total cost to PBS/RPBS (\$) | █ ⁵ | █ ⁶ | █ ⁷ | █ ⁷ | █ ⁸ | █ ¹⁰ |
| Net financial implications | | | | | | |
| Cost to the PBS/RPBS (\$) | █ ⁹ | █ ⁹ | █ ⁹ | █ ⁹ | █ ⁹ | █ ⁹ |
| Patient co-payments (\$) | █ ⁹ | █ ⁹ | █ ⁹ | █ ⁹ | █ ⁹ | █ ⁹ |
| Total cost to PBS/RPBS (\$) | █ ⁹ | █ ⁹ | █ ⁹ | █ ⁹ | █ ⁹ | █ ⁹ |

Financial estimates adjusted for correct PBS copayments applied from 1 January 2022 during evaluation.

Source: Utilisation + Cost Model workbook - abiraterone and methylprednisolone PSD, November 2022. Abbreviations: PBS = Pharmaceutical Benefits Scheme; RPBS = Repatriation Pharmaceutical Benefits Scheme; OAA = originator abiraterone acetate; SAA+MPRED = abiraterone acetate in fine particle formulation in combination with methylprednisolone

^a Assumes 12.18 scripts per year

The redacted values correspond to the following ranges:

¹ 10,000 < 20,000

² 20,000 to < 30,000

³ 500 to < 5,000

⁴ 5,000 to < 10,000

⁵ \$0 to < \$10 million

⁶ \$10 million to < \$20 million

⁷ \$20 million to < \$30 million

⁸ \$30 million to < \$40 million

⁹ net cost saving

¹⁰ \$40 million to < \$50 million

6.16 The total cost to the PBS/RPBS of listing SAA+MPRED as presented in the resubmission, and adjusted to the correct copayments, was estimated to be \$30 million to < \$40 million in Year 6, and a total of \$100 million to < \$200 million in the first 6 years of listing. The total net savings to the PBS/RPBS of listing SAA+MPRED

as presented in the resubmission was estimated to be a net cost saving in Year 6, and a total net saving of a net cost saving in the first 6 years of listing. The March 2022 submission noted the savings were due to the changes to copayments (para 6.23, abiraterone and methylprednisolone PSD, March 2022).

Quality Use of Medicines

- 6.17 At its March 2022 meeting the PBAC had raised concerns regarding the quality use of SAA and MPRED in clinical practice.
- 6.18 The PBAC had considered that there was a high risk of patient confusion between SAA and OAA given both products are called abiraterone but have different daily doses of 500 mg and 1000 mg, respectively. To address these concerns, the resubmission stated that clinicians are unlikely to prescribe the wrong formulation of abiraterone by accident since the co-pack (SAA+MPRED) and OAA will have separate PBS codes, and the medicines will have different brand names (i.e., YONSA MPRED and Zytiga) and clinicians prescribing OAA will need to write a separate prescription for a corticosteroid as a concomitant medication. The resubmission also noted clinicians are unlikely to switch patients between the SAA+MPRED and OAA after they have started treatment with abiraterone. As described in paragraph 3.5, the PBAC noted SAA+MPRED is not eligible for brand substitution with OAA and switching between brands is therefore not possible at the pharmacy level.
- 6.19 The PBAC had further considered there would be high risk of confusion regarding the timing of taking oral prednisone (typically given 10 mg daily per EviQ), contrasting with methylprednisolone 4 mg twice daily. The resubmission stated that pharmacists will provide the patient with the corresponding consumer medicine information (CMI). The CMI for SAA+MPRED clearly outlines that the co-pack contains two different medicines and describes the recommended dosing instructions for each individual medicine. The resubmission reiterated that SAA can be taken with or without food whereas OAA must be taken in the fasted state either at least one hour before food or two hours after food. The resubmission stated that ability to take medication at the same time, such as is the case with SAA and MPRED, has been shown to increase adherence, reduce self-administration errors, as well as reduced disruption to the activities of daily living for the patient.
- 6.20 The resubmission noted the sponsor's commitment to amend the CMI and to provide education to both prescribers and pharmacists at the launch of SAA+MPRED to create an awareness of the new product, the PBS listing details, and the differences in the dosing instructions compared with OAA. The new educational materials include:
- Amended CMI that includes a pictorial of the tablet of each medicine
 - Detailed prescribing guide
 - Dose comparison charts
 - Labelling recommendation reminders
 - Patient education booklet.

The PBAC advised that further review of the educational material may still be required by the relevant authorities as the information, particularly the pictorials in the drafts, may still be confusing for patients such as the differences in the number of tablets to be taken for the co-pack versus OAA and prednisone.

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

7 PBAC Outcome

- 7.1 The PBAC recommended the General Schedule Authority Required listing of the composite pack (co-pack) comprising abiraterone acetate tablets in a fine particle formulation (SAA) and oral methylprednisolone (MPRED) tablets (Yonsa® MPRED) for the treatment of patients with metastatic castration resistant prostate cancer (mCRPC).
- 7.2 The PBAC considered the claim of noninferior effectiveness and safety of Yonsa MPRED to OAA and prednisone was reasonable. However, the PBAC considered for the purposes of satisfying Section 101(3B) of the *National Health Act 1953*, any treatments for mCRPC are relevant alternative therapies. The PBAC's recommendation for listing was therefore based on, among other matters, its assessment that the cost effectiveness for Yonsa MPRED would be acceptable if it was cost-minimised against the least costly alternative therapy for mCRPC.
- 7.3 The PBAC recalled its March 2022 consideration that the nominated comparator, originator abiraterone acetate (OAA) given with prednisone, was acceptable given these would likely be replaced by Yonsa MPRED in practice, although considered that enzalutamide was also a relevant comparator.
- 7.4 The equi-effective doses are SAA 500 mg + MPRED 8 mg is equivalent to OOA 1000 mg + prednisone 10 mg.
- 7.5 The PBAC noted that the clinical evidence remained unchanged from that presented in the March 2022 submission. The resubmission was based on the STAAR study which was a direct comparative trial of SAA with OAA, which also looked at the population proposed for PBS listing. The PBAC also noted the resubmission's clinical claim was consistent with the TGA Delegate's Overview which accepted the claim of bioequivalence for SAA and MPRED to OAA and prednisone, respectively. Therefore, the PBAC considered that the claim of noninferior comparative effectiveness and safety was reasonable.
- 7.6 The PBAC considered the economic analysis and utilisation estimates were reasonable, although noted that the 1% market share assumption was likely overestimated and may not be realised in practice.
- 7.7 The PBAC discussed that most of the quality use of medicine concerns from the March 2022 consideration were addressed in this resubmission. The PBAC advised that further review of the educational material may still be required by the relevant authorities to ensure patients know the differences in dosage between the co-pack

versus OAA and prednisone.

- 7.8 The PBAC recommended additional updates to the restrictions previously accepted by the PBAC in its March 2022 consideration including:
- A new clinical criterion advising that the switching between the co-pack and individual components is not allowable if disease progression has occurred during treatment
 - flow-on restriction changes to PBS listed abiraterone (Zytiga - PBS item codes 11206T and 2698B) to include the caution regarding exercising caution in explaining correct dosing directions to the patients when changing between abiraterone products.
- 7.9 The PBAC recommended that abiraterone and methylprednisolone should not be treated as interchangeable with any other drugs.
- 7.10 The PBAC advised that abiraterone and methylprednisolone is not suitable for prescribing by nurse practitioners.
- 7.11 The PBAC recommended that the Early Supply Rule should not apply.
- 7.12 The PBAC noted that its recommendation was on a cost-minimisation basis and advised that, because Yonsa MPRED is not expected to provide a substantial and clinically relevant improvement in efficacy, or reduction of toxicity, over OAA and prednisone, or not expected to address a high and urgent unmet clinical need given the presence of an alternative therapy, the criteria prescribed by the *National Health (Pharmaceuticals and Vaccines – Cost Recovery) Regulations 2022* for Pricing Pathway A were not met.
- 7.13 The PBAC noted that this submission is not eligible for an Independent Review as it received a positive recommendation.

Outcome:

Recommended

8 Recommended listing

- 8.1 Add new medicinal product as follows:

| MEDICINAL PRODUCT medicinal product pack | PBS item code | Max. qty packs | Max. qty units | No. of Rpts | Available brands |
|---|------------------|-------------------|-------------------|----------------|---------------------|
| ABIRATERONE (&) METHYLPREDNISOLONE | | | | | |
| abiraterone acetate 125 mg tablet [120] (& methylprednisolone 4 mg tablet [60], 1 pack | New | 1 | 1 | 2 | Yonsa MPRED |
| Restriction Summary New 1 / Treatment of Concept: New 2 | | | | | |
| Category / Program: GENERAL – General Schedule (Code GE) | | | | | |
| Prescriber type: <input checked="" type="checkbox"/> Medical Practitioners | | | | | |
| Restriction type: <input checked="" type="checkbox"/> Authority Required (telephone/online PBS Authorities system) | | | | | |

| | |
|--|---|
| | |
| | Indication: Castration resistant metastatic carcinoma of the prostate |
| | Clinical criteria: |
| | The treatment must not be used in combination with chemotherapy |
| | AND |
| | Clinical criteria: |
| | Patient must have a WHO performance status of 2 or less |
| | AND |
| | Clinical criteria: |
| | The treatment must not be a PBS benefit where disease progression occurs whilst being treated with any of: (i) a combination treatment containing the individual drugs in one pharmaceutical benefit, (ii) the individual drugs obtained as separate pharmaceutical benefits |
| | AND |
| | Clinical criteria: |
| | Patient must only receive subsidy for one novel hormonal drug per lifetime for prostate cancer (regardless of whether a drug was subsidised under a metastatic/non-metastatic indication); or |
| | Patient must only receive treatment with a subsequent novel hormonal drug where there has been a severe intolerance to another novel hormonal drug leading to permanent treatment cessation |
| | Caution The bioavailability on a mg to mg basis of abiraterone combination product and abiraterone single drug product is not equivalent. When changing between abiraterone products, exercise caution in explaining correct dosing directions to the patient. |
| | Administrative Advice: Special Pricing Arrangements apply. |
| | Administrative Advice: Applications for authorisation under this restriction may be made in real time using the Online PBS Authorities system (see www.servicesaustralia.gov.au/HPOS) or by telephone by contacting Services Australia on 1800 888 333. |
| | Administrative Advice: Where the term 'novel hormonal drug' appears in this restriction, it refers to: (i) abiraterone, (ii) apalutamide, (iii) darolutamide, (iv) enzalutamide. |

8.2 Flow on changes

Amend the current abiraterone listing to add the Caution and Clinical Criteria recommended above as follows:

| | |
|---|--|
| PBS item code / medicinal product pack | |
| 2698B / abiraterone acetate 250 mg tablet, 120 | |
| 11206T / abiraterone acetate 500 mg tablet, 60 | |
| Restriction Summary 12699 / ToC: 12700: Authority Required (current as at 1 November 2022) | |
| | |
| | Indication: Castration resistant metastatic carcinoma of the prostate |
| | Clinical criteria: |
| | The treatment must be used in combination with a corticosteroid |
| | AND |
| | Clinical criteria: |
| | The treatment must not be used in combination with chemotherapy |
| | AND |
| | Clinical criteria: |
| | Patient must have a WHO performance status of 2 or less |
| | AND |

| | |
|--|---|
| | Clinical criteria: |
| | Patient must not receive PBS-subsidised treatment with this drug if progressive disease develops while on this drug |
| | <i>The treatment must not be a PBS benefit where disease progression occurs whilst being treated with any of: (i) a combination treatment containing the individual drugs in one pharmaceutical benefit, (ii) the individual drugs obtained as separate pharmaceutical benefits</i> |
| | AND |
| | Clinical criteria: |
| | Patient must only receive subsidy for one novel hormonal drug per lifetime for prostate cancer (regardless of whether a drug was subsidised under a metastatic/non-metastatic indication); or |
| | Patient must only receive subsidy for a subsequent novel hormonal drug where there has been a severe intolerance to another novel hormonal drug leading to permanent treatment cessation |
| | Caution <i>The bioavailability on a mg to mg basis of abiraterone combination product and abiraterone single drug product is not equivalent. When changing between abiraterone products, exercise caution in explaining correct dosing directions to the patient.</i> |
| | Administrative Advice: Special Pricing Arrangements apply. |
| | Administrative Advice: Applications for authorisation under this restriction may be made in real time using the Online PBS Authorities system (see www.servicesaustralia.gov.au/HPOS) or by telephone by contacting Services Australia on 1800 888 333. |
| | Administrative Advice: Where the term 'novel hormonal drug' appears in this restriction, it refers to: (i) abiraterone, (ii) apalutamide, (iii) darolutamide, (iv) enzalutamide. |

These restrictions may be subject to further review. Should there be any changes made to the restriction the sponsor will be informed.

9 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.

10 Sponsor's Comment

The sponsor had no comment.