

**5.18 ESTRADIOL,  
Transdermal gel 500 micrograms (as hemihydrate) in  
0.5 g sachet, 28  
Sandrena<sup>®</sup>,  
ORION PHARMA (AUS) PTY LIMITED**

**1 Purpose of Submission**

- 1.1 The Category 4 submission requested to list estradiol 500 microgram in 0.5 gram gel sachet (Sandrena<sup>®</sup>) as a General Schedule (Unrestricted Benefit) listing with a corresponding 60-day maximum dispensed quantities (MDQ) General Schedule (Restricted Benefit) listing which is consistent with the existing Pharmaceutical Benefits Scheme (PBS) listings for Sandrena 1 mg in 1 gram gel sachet.

**2 Background**

- 2.1 Sandrena 1 mg in 1 gram gel sachet is currently listed on the PBS as a General Schedule Unrestricted Benefit listing (maximum quantity of 1 pack of 28 sachets and 5 repeats) and a General Schedule Restricted Benefit listing (maximum quantity of 2 packs of 28 sachets and 5 repeats – 60-day MDQ).
- 2.2 The submission claimed that the listing of the additional strength of Sandrena gel sachets on the PBS allows for more precise dosing and results in less wastage, with the recommended dose being 0.5 mg – 1.5 mg estradiol daily (Sandrena Product Information). Patients requiring the 500 microgram strength will be able to use one 0.5 gram sachet, instead of half of a 1 gram sachet and discarding the remainder of the gel.

***Registration status***

- 2.3 Sandrena 1 mg in 1 gram gel sachets was first Therapeutic Goods Administration (TGA) registered on 31 August 1998. A new formulation of Sandrena 0.1% gel (0.5 gram and 1 gram sachets) was TGA registered on 8 April 2003.
- 2.4 Sandrena 1 mg/g (0.5 gram and 1 gram gel sachets) are indicated for short-term treatment of climacteric symptoms after natural or surgical menopause. The Product Information notes that wherever possible, the lowest effective dose should be used, and the need for continuation of treatment should be reviewed after 6 months. Sandrena should only be continued for as long as the benefit outweighs the risk.

***Previous PBAC consideration***

- 2.5 Sandrena 500 microgram in 0.5 gram gel sachet has not been considered by the PBAC previously.

- 2.6 Sandrena 1 mg in 1 gram gel sachets was recommended by the PBAC at its June 1998 meeting as a Restricted Benefit listing for use for post-menopausal symptoms where a trial of peri- or post-menopausal low-dose oestrogen therapy has demonstrated intolerance to low-dose oestrogens. At its July 2009 meeting, the PBAC recommended changing the Restricted Benefit listings for the transdermal patch and gel forms of hormone replacement therapy (HRT) to Unrestricted Benefit listings. The PBS listing for Sandrena 1 mg in 1 gram gel sachets was subsequently changed to an Unrestricted listing.

### 3 Requested listing

- 3.1 The submission requested the following new listing:

Add new medicinal product pack as follows:

MEDICINAL PRODUCT medicinal product pack	PBS item code	Max. qty packs	Max. qty units	No. of Rpts	Available brands
ESTRADIOL					
Estradiol 0.1% (1 mg/g) gel, 28 x 500 mg sachets	NEW	1	1	5	Sandrena
<b>Restriction Summary [new] / Treatment of Concept: [new]</b>					
<b>Concept ID</b> (for internal Dept. use)	<b>Category / Program:</b> GENERAL – General Schedule (Code GE)				
	<b>Prescriber type:</b> <input checked="" type="checkbox"/> Medical Practitioners <input checked="" type="checkbox"/> Nurse practitioners				
	<b>Restriction type:</b> <input checked="" type="checkbox"/> Unrestricted benefit				
	<b>Administrative Advice:</b> Estradiol should be used in conjunction with an oral progestogen in women with an intact uterus.				
	<b>Administrative Advice:</b> Continuing Therapy Only:  For prescribing by nurse practitioners as continuing therapy only, where the treatment of, and prescribing of medicine for, a patient has been initiated by a medical practitioner. Further information can be found in the Explanatory Notes for Nurse Practitioners.				
MEDICINAL PRODUCT medicinal product pack	PBS item code	Max. qty packs	Max. qty units	No. of Rpts	Available brands
ESTRADIOL					
Estradiol 0.1% (1 mg/g) gel, 28 x 500 mg sachets	NEW	2	2	5	Sandrena
<b>Restriction Summary [new] / Treatment of Concept: [new]</b>					
<b>Concept ID</b> (for internal Dept. use)	<b>Category / Program:</b> GENERAL – General Schedule (Code GE)				
	<b>Prescriber type:</b> <input checked="" type="checkbox"/> Medical Practitioners <input checked="" type="checkbox"/> Nurse practitioners				
	<b>Restriction type:</b> <input checked="" type="checkbox"/> Restricted benefit				
	<b>Indication:</b> The condition must be stable for the prescriber to consider the listed maximum quantity of this medicine suitable for this patient.				
	<b>Administrative advice:</b> Estradiol should be used in conjunction with an oral progestogen in women with an intact uterus.				

<p><b>Administrative Advice:</b> Continuing Therapy Only:</p> <p>For prescribing by nurse practitioners as continuing therapy only, where the treatment of, and prescribing of medicine for, a patient has been initiated by a medical practitioner. Further information can be found in the Explanatory Notes for Nurse Practitioners.</p>
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- 3.2 As part of its December 2022 consideration, the PBAC recommended Sandrena 1 mg in 1 gram gel sachets as suitable for listing on the PBS with increased MDQ (implemented on 1 April 2024).
- 3.3 The submission requested Sandrena 500 microgram in 0.5 gram gel sachets be included in increased MDQ to align with the Sandrena 1 mg in 1 gram gel sachets MDQ listing.
- 3.4 The guidance for exclusion of a medicine/medicine group from the increased MDQ for chronic conditions, which was accepted by the PBAC at its December 2022 meeting, states that ‘Medicines must be PBS listed for 5 or more years, or generics of medicines which have been listed for 5 or more years, as severe but rare adverse effects frequently become evident during this period.’
- 3.5 The Sandrena Product Information states ‘In patients with an intact uterus, it is necessary to combine Sandrena with an adequate dose of progestogen for adequate duration, at least 12–14 consecutive days per month/28 day cycle to oppose estrogen-stimulated hyperplasia of the endometrium.’ The current Administrative Advice for Sandrena 1 mg in 1 gram gel sachets states that an oral progestogen specifically must be used in women with an intact uterus: ‘Estradiol should be used in conjunction with an oral progestogen in women with an intact uterus.’

## 4 Comparator

- 4.1 The submission proposed a new strength of estradiol gel (500 microgram in 0.5 gram gel sachet), and compared this to the currently listed 1 mg in 1 gram gel sachet of the same drug.

## 5 Consideration of the evidence

### *Sponsor hearing*

- 5.1 There was no hearing for this item.

### *Consumer comments*

- 5.2 The PBAC noted that no consumer comments were received for this item.

### *Clinical claim*

- 5.3 The submission claimed non-inferior comparative effectiveness and non-inferior comparative safety of Sandrena 500 microgram in 0.5 gram gel sachets compared with Sandrena 1 mg in 1 gram gel sachets.

- 5.4 The submission claimed that Sandrena 500 microgram in 0.5 gram gel sachet is bioequivalent to Sandrena 1 mg in 1 gram gel sachet on a 1 mg to 1 mg basis, with the only difference being the volume of gel in the sachet. No bioequivalence statement was provided, however the approval letter from the TGA in 2003 approves ‘the registration of Sandrena 0.1% gel containing oestradiol 1.0 mg per gram of gel’ for both 0.5 gram and 1.0 gram sachets (2003 TGA Approval letter).
- 5.5 The PBAC considered that the claims of non-inferior comparative effectiveness and non-inferior comparative safety were reasonable.

### **Pricing considerations**

- 5.6 The submission referred to the ‘Fact Sheet – Setting an approved ex-manufacturer price for new or extended listings’<sup>1</sup> on the PBS website, which states that ‘for new strengths of already listed drugs, as a general rule, the pricing of half strength formulations is at two-thirds to 70% of the full strength.’ The fact sheet also states ‘These guidelines do not apply in all cases, for example if there is ‘flat’ pricing or for expensive drugs where history indicates pricing of the different strengths is based on the same price per unit (or mg or gram).’
- 5.7 The submission requested an approved ex-manufacturer price (AEMP) for Sandrena 500 microgram in 0.5 gram gel sachets of \$7.92, which is 70% of the AEMP of Sandrena 1 mg in 1 gram gel sachets (AEMP of \$11.32, which came into effect in April 2024 as a result of a price increase request).

### **Drug cost/patient/year: \$279.63**

- 5.8 The estimated drug cost/patient per year would be \$279.63, based on a dispensed price for maximum quantity (DPMQ) of \$21.51 and 13 prescriptions per year.

### **Estimated PBS usage and financial implications**

- 5.9 The requested price was based on 70% of the AEMP of Sandrena 1 mg estradiol in 1 gram gel sachets, as outlined in paragraphs 5.6 and 5.7.
- 5.10 The submission used a market-share approach to estimate the use and financial implications to the PBS/RPBS of the requested listing.
- 5.11 The submission estimated a [REDACTED] % substitution rate from Sandrena 1 mg in 1 gram gel sachets to Sandrena 500 micrograms in 0.5 gram gel sachets, as patients requiring a dose of 500 micrograms of estradiol will switch to the lower strength. The estimate of the extent of substitution was not justified in the submission. Increasing the substitution rate to [REDACTED] % per year increases the total 6 year net saving to the PBS to net

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<sup>1</sup> The Pharmaceutical Benefits Scheme, (2017), ‘Fact sheet - Setting an approved ex-manufacturer price for new or extended listings’, [www.pbs.gov.au/info/industry/pricing/pbs-items/fact-sheet-setting-an-approved-ex-manufacturer-price](http://www.pbs.gov.au/info/industry/pricing/pbs-items/fact-sheet-setting-an-approved-ex-manufacturer-price)

cost saving compared to net cost saving, assuming a █% substitution rate per year.<sup>2</sup> The submission assumed 1:1 script equivalence.

- 5.12 Refer to Table 1 which presents the estimated extent of use, cost of Sandrena 500 micrograms in 0.5 gram gel sachets to the PBS/RPBS and the net financial implications to the PBS/RPBS. The financial impact to Services Australia will be determined by that agency as part of the post PBAC process.
- 5.13 The submission stated that the estimated net financial impact to the PBS/RPBS for the listing of Sandrena 500 microgram in 0.5 gram gel sachet is net cost saving over six years (Year 1 net cost saving to Year 6 net cost saving).
- 5.14 The financial estimates do not account for situations where patients may have an Authority prescription for Sandrena 1 mg in 1 gram gel sachets at an increased quantity where they are using >1 sachet daily. If these patients change to having one prescription dispensed for the 1 mg in 1 gram sachet strength and one prescription dispensed for the 500 microgram in 0.5 gram sachet strength (if recommended by the PBAC), there will be an increase in patient co-payments which are not included in the financial estimates.
- 5.15 The financial estimates do not account for the introduction of the MDQ listing of Sandrena 1 mg in 1 gram gel sachets. While this item is only recently listed, the modelling of future use will also need to account for portion of the market in both proposed and affected medicine calculations.

**Table 1: Estimated use and financial implications**

	Year 1	Year 2	Year 3	Year 4	Year 5	Year 6
<b>Estimated extent of use</b>						
Number of scripts dispensed	█ <sup>1</sup>	█ <sup>1</sup>	█ <sup>1</sup>	█ <sup>1</sup>	█ <sup>1</sup>	█ <sup>1</sup>
<b>Estimated financial implications of Sandrena 500 micrograms in 500 mg gel sachet</b>						
Cost to PBS/RPBS less co-payment	█ <sup>2</sup>	█ <sup>2</sup>	█ <sup>2</sup>	█ <sup>2</sup>	█ <sup>2</sup>	█ <sup>2</sup>
<b>Estimated financial implications of Sandrena 1 mg in 1 gram gel sachet</b>						
Cost to PBS/RPBS less co-payment	█ <sup>3</sup>	█ <sup>3</sup>	█ <sup>3</sup>	█ <sup>3</sup>	█ <sup>3</sup>	█ <sup>3</sup>
<b>Net financial implications</b>						
Net cost to PBS/RPBS	█ <sup>3</sup>	█ <sup>3</sup>	█ <sup>3</sup>	█ <sup>3</sup>	█ <sup>3</sup>	█ <sup>3</sup>

Abbreviations: PBS = Pharmaceutical Benefits Scheme; RPBS = Repatriation Pharmaceutical Benefits Scheme.

Source: Sandrena (estradiol) – UCM workbook

The redacted values correspond to the following ranges:

1 10,000 to < 20,000

2 \$0 to < \$10 million

3 net cost saving

<sup>2</sup> Net saving derived by changing the values in cells E107 to J107 from █% to █% in sheet '2e. Scripts – market', Updated UCM - Sandrena (estradiol) - 05 mg estradiol per 05 g gel - UCM - DoH Request.xlsx'.

## 6 PBAC Outcome

- 6.1 The PBAC recommended the listing of estradiol 500 microgram in 0.5 gram gel sachet (Sandrena) as a General Schedule (Unrestricted Benefit) listing and a corresponding 60-day MDQ General Schedule (Restricted Benefit) listing, consistent with the PBS listings for Sandrena 1 mg in 1 gram gel sachet.
- 6.2 The PBAC considered that the option to prescribe a lower strength estradiol gel sachet would allow greater flexibility in dosing, improve ability to titrate doses to individual requirements and reduce product wastage. The PBAC further noted that clinical guidelines recommend trialling a lower dose of hormone replacement therapy as patients continue with treatment and considered the availability of a lower strength estradiol gel sachet on the PBS will support this in practice.
- 6.3 The PBAC considered the approach used to calculate the proposed price for Sandrena 500 micrograms in 0.5 gram gel sachets to be reasonable.
- 6.4 The PBAC considered the submission's estimated substitution rate of █████% from Sandrena 1 mg gel sachets to Sandrena 500 micrograms gel sachets to be reasonable, and noted the estimated net saving to the PBS from patients switching to the Sandrena 500 micrograms gel sachets.
- 6.5 The PBAC recommended the following Administrative Advice for Sandrena 500 microgram in 0.5 gram gel sachets: 'Estradiol should be used in conjunction with progestogen in women with an intact uterus'. The PBAC recommended that this Administrative Advice be flowed on to the Sandrena 1 mg in 1 gram gel sachets (8286D and 14026F), as well as the following estradiol products listed on the PBS: estradiol 100 microgram/24 hours patch, 8 (8312L, 8765H), estradiol 25 microgram/24 hours patch, 8 (8311K, 8761D), estradiol 37.5 microgram/24 hours patch, 8 (8762E), estradiol 50 microgram/24 hours patch, 8 (8140K, 8763F), estradiol 75 microgram/24 hours patch, 8 (8764G), and that it replace the current Administrative Advice about use in conjunction with an oral progestogen for these listings.
- 6.6 The PBAC found that the criteria prescribed by the *National Health (Pharmaceuticals and Vaccines – Cost Recovery) Regulations 2022* for Pricing Pathway A were not met. Specifically the PBAC found that in the circumstances of its recommendation for Sandrena 500 microgram in 0.5 gram gel sachets:
- a. The treatment is not expected to provide a substantial and clinically relevant improvement in efficacy, or reduction of toxicity, over alternative therapies.
  - b. The treatment is not expected to address a high and urgent unmet clinical need because an alternative estradiol gel sachet product is already PBS listed.
- 6.7 The PBAC noted that this submission is not eligible for an Independent Review as it received a positive recommendation.

**Outcome:**

Recommended

## 7 Recommended listing

### 7.1 Add new item:

MEDICINAL PRODUCT medicinal product pack	PBS item code	Max. qty packs	Max. qty units	No.of Rpts	Available brands
ESTRADIOL					
Estradiol 0.1% (1 mg/g) gel, 28 x 500 mg sachets	NEW	1	1	5	Sandrena
<b>Restriction Summary [new] / Treatment of Concept: [new]</b>					
<b>Concept ID</b> (for internal Dept. use)	<b>Category / Program:</b> GENERAL – General Schedule (Code GE)				
	<b>Prescriber type:</b> <input checked="" type="checkbox"/> Medical Practitioners <input checked="" type="checkbox"/> Nurse practitioners				
	<b>Restriction type:</b> <input checked="" type="checkbox"/> Unrestricted benefit				
	<b>Administrative Advice:</b> Estradiol should be used in conjunction with progestogen in women with an intact uterus.				
	<b>Administrative Advice:</b> Continuing Therapy Only:  For prescribing by nurse practitioners as continuing therapy only, where the treatment of, and prescribing of medicine for, a patient has been initiated by a medical practitioner. Further information can be found in the Explanatory Notes for Nurse Practitioners.				
<b>Restriction Summary [new] / Treatment of Concept: [new]</b>					
<b>Restriction Summary [new] / Treatment of Concept: [new]</b>					
MEDICINAL PRODUCT medicinal product pack	PBS item code	Max. qty packs	Max. qty units	No.of Rpts	Available brands
ESTRADIOL					
Estradiol 0.1% (1 mg/g) gel, 28 x 500 mg sachets	NEW	2	2	5	Sandrena
<b>Restriction Summary [new] / Treatment of Concept: [new]</b>					
<b>Concept ID</b> (for internal Dept. use)	<b>Category / Program:</b> GENERAL – General Schedule (Code GE)				
	<b>Prescriber type:</b> <input checked="" type="checkbox"/> Medical Practitioners <input checked="" type="checkbox"/> Nurse practitioners				
	<b>Restriction type:</b> <input checked="" type="checkbox"/> Restricted benefit				
	<b>Indication:</b> The condition must be stable for the prescriber to consider the listed maximum quantity of this medicine suitable for this patient.				
	<b>Administrative advice:</b> Estradiol should be used in conjunction with progestogen in women with an intact uterus.				
	<b>Administrative Advice:</b> Continuing Therapy Only:  For prescribing by nurse practitioners as continuing therapy only, where the treatment of, and prescribing of medicine for, a patient has been initiated by a medical practitioner. Further information can be found in the Explanatory Notes for Nurse Practitioners.				

### 7.2 Flow-on changes to current PBS listings for Sandrena 1 mg in 1 gram gel sachets (PBS item codes 8286D and 14026F):

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MEDICINAL PRODUCT medicinal product pack	PBS item code	Max. qty packs	Max. qty units	No. of Rpts	Available brands
ESTRADIOL					
Estradiol 0.1% (1 mg/g) gel, 28 x 1 g sachets	8286D	1	1	5	Sandrena
<b>Restriction Summary 36703 / Treatment of Concept: 36703: Unrestricted</b>					
<b>Concept ID</b> (for internal Dept. use)	<b>Category / Program:</b> GENERAL – General Schedule (Code GE)				
	<b>Prescriber type:</b> <input checked="" type="checkbox"/> Medical Practitioners <input checked="" type="checkbox"/> Nurse practitioners				
	<b>Restriction type:</b> <input checked="" type="checkbox"/> Unrestricted benefit				
	<b>Administrative Advice:</b> Estradiol should be used in conjunction with an oral progestogen in women with an intact uterus.				
	<b>Administrative Advice:</b> Continuing Therapy Only:  For prescribing by nurse practitioners as continuing therapy only, where the treatment of, and prescribing of medicine for, a patient has been initiated by a medical practitioner. Further information can be found in the Explanatory Notes for Nurse Practitioners.				
MEDICINAL PRODUCT medicinal product pack	PBS item code	Max. qty packs	Max. qty units	No. of Rpts	Available brands
ESTRADIOL					
Estradiol 0.1% (1 mg/g) gel, 28 x 1 g sachets	14026F	2	2	5	Sandrena
<b>Restriction Summary 14238 / Treatment of Concept: 14238: Restricted</b>					
<b>Concept ID</b> (for internal Dept. use)	<b>Category / Program:</b> GENERAL – General Schedule (Code GE)				
	<b>Prescriber type:</b> <input checked="" type="checkbox"/> Medical Practitioners <input checked="" type="checkbox"/> Nurse practitioners				
	<b>Restriction type:</b> <input checked="" type="checkbox"/> Restricted benefit				
	<b>Indication:</b> The condition must be stable for the prescriber to consider the listed maximum quantity of this medicine suitable for this patient.				
	<b>Administrative advice:</b> Estradiol should be used in conjunction with an oral progestogen in women with an intact uterus.				
	<b>Administrative Advice:</b> Continuing Therapy Only:  For prescribing by nurse practitioners as continuing therapy only, where the treatment of, and prescribing of medicine for, a patient has been initiated by a medical practitioner. Further information can be found in the Explanatory Notes for Nurse Practitioners.				

7.3 Administrative Advice to flow on to the following existing PBS listings for estradiol patches:

PBS number	MPP Preferred Term	Program	Maximum Quantity Packs	Maximum Quantity units	No. of repeats
	estradiol 100 microgram/24 hours patch, 8	GE	1	1	5
	estradiol 100 microgram/24 hours patch, 8	GE	1	1	5

	estradiol 25 microgram/24 hours patch, 8	GE	1	1	5
	estradiol 25 microgram/24 hours patch, 8	GE	1	1	5
	estradiol 37.5 microgram/24 hours patch, 8	GE	1	1	5
	estradiol 50 microgram/24 hours patch, 8	GE	1	1	5
	estradiol 50 microgram/24 hours patch, 8	GE	1	1	5
	estradiol 75 microgram/24 hours patch, 8	GE	1	1	5

***This restriction may be subject to further review. Should there be any changes made to the restriction the Sponsor will be informed.***

## **8 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.

## **9 Sponsor's Comment**

The sponsor had no comment.