6.17 TESTOSTERONE, Transdermal cream 50 mg per mL, 50 mL, AndroForte 5®, Lawley Pharmaceuticals Pty Ltd

1 Purpose of Application

1.1 The minor submission requested that the PBAC reconsider the equi-effective dosing for testosterone transdermal cream 50 mg per mL, 50 mL (referred to as AndroForte 5 from herein) following changes to approved application sites that reduce the recommended dose from 100 mg (2 mL) to 25 mg (0.5 mL) and increase the number of treatments per tube from 25 to 100.

1.2 AndroForte 5 is currently available as an Authority Required listing with a maximum number of six repeats and an AEMP of $49.98. The submission requested a [redacted]% increase in AEMP for this brand, and a new prescribing rule with two repeats.

2 Background

Registration status

2.1 AndroForte 5 was registered by the TGA on 11 July 2014 and is approved for the following indication:

"Use as testosterone replacement therapy for male hypogonadism when testosterone deficiency has been confirmed by clinical features and biochemical tests".

3 Requested listing

3.1 AndroForte 5 is currently registered and listed on the PBS (item code 10378F) as an Authority Required listing for androgen deficiency, micropenis, pubertal induction and the constitutional delay of growth or onset of puberty.

3.2 The submission requested the addition of nurse practitioner as a prescriber type to the existing restriction.

3.3 The submission also requested an additional prescribing rule with a maximum of two repeats, reflecting a reduction in the recommended dose from 100 mg (2 mL) daily to 25 mg (0.5 mL) daily for scrotal application that increases the number of treatments per tube from 25 to 100.

Nurse Practitioner Prescribing

3.4 The PBAC is requested to consider if AndroForte 5 is suitable for inclusion in the PBS medicines for prescribing by nurse practitioner for the continuing treatment phase.

3.5 In March 2015, the PBAC advised that AndroForte 5 is not suitable for prescribing by nurse practitioners. The sponsor has not provided any evidence to support prescribing by nurse practitioners.

3.6 In its pre-PBAC response the sponsor stated it does not wish to pursue prescribing by nurse practitioners.

For more detail on PBAC's view, see section 6 PBAC outcome

4 Comparator

4.1 The submission considered by the PBAC in March 2015 nominated testosterone 1% gel 50 mg (testosterone 1% gel from herein) as a relevant comparator. This was based on the TGA delegate's determination that 'AndroForte and Testogel are therapeutically equivalent for all practical purposes'. This remained unchanged.

4.2 The sponsor acknowledged that AndroForte 5 was listed on a cost-minimisation basis to testosterone 1% gel and that the PBAC considered the equi-effective doses are testosterone 5% cream 100 mg daily and testosterone 1% gel 50 mg daily.

4.3 The minor submission presented a cost-minimisation analysis of scrotal application with new equi-effective doses estimated as scrotal application 25 mg daily and upper body application 100 mg daily.

Table 1 - Cost-minimisation of Androforte 5 with scrotal application versus the existing Androforte 5 cost-minimisation with torso application

	ANDROFORTE® 5 (scrotal application) Proposed	ANDROFORTE® 5 (torso application) Current
Item code	TBC	10378F
DPMQ	$263.04	$65.22
Units	50 mL	50 mL
Strength per unit (mg)	50	50
Strength per pack (mg)	2500	2500
Average dose (mg)	25	100
Cost per dose	$2.61	$2.61
No. days' supply per pack	100	25
Repeats	2	6
Total days' supply + repeats	300	175
Cost per day	$2.63	$2.63
Packs per year	3.7	14.6
Cost per year	$960.75	$960.75

Source: table 3.4, p37 of the submission main body.

4.4 The sponsor requested a price increase based on reductions to the cost per day for AndroForte 5 following scrotal application, assuming all patients will switch to scrotal application. The sponsor anticipates that upper body application will continue due to variable uptake rates and prescribing behaviour.

For more detail on PBAC's view, see section 6 PBAC outcome

5 PBAC consideration of the evidence

Clinical claim

5.1 On 17 November 2020 the TGA updated the PI to include a new site of application, scrotum, for AndroForte 5.

5.2 The PI for AndroForte 5 recommends a dose of 25 to 50 mg (0.5 – 1 mL) applied to the scrotum daily. This compares with a recommended dose of 100 – 200 mg (2 - 4 mL) to the upper body. The submission claims that this change in dose reduces the cost per day of AndroForte 5.

5.3 The submission also claims that scrotal application reduces the risk of accidental exposure of the patient's partner and/or children via passive transfer, which could lead to adverse effects in those exposed with repeated contact. The submission adds that currently there are no other testosterone preparations registered in Australia that can be administered via transdermal scrotal application.

5.4 The sponsor has not submitted clinical evidence to indicate what proportion of patients will be maintained on the 25 mg daily dose, what proportion will need a 50 mg daily dose.

5.5 In its pre-PBAC response the sponsor advised direct feedback from prescribing physicians suggests a 25 mg scrotal dose will achieve mid-eugonadal range (the range

in which the sponsor claims the vast majority of patients experience resolution of symptoms) in 70% of hypogonadal men. The sponsor also submitted that approximately 20% will require an increase to 50 mg and 10% will require a reduction to 12.5 mg.

5.6 Furthermore, the PI maintains upper body as an application site and the sponsor estimates a variable uptake rate of the new application site of 70% in year one, increasing to 90% in year 3 for existing AndroForte 5 users.

Pricing considerations

5.7 The proposed price for AndroForte 5 is shown in table 2.

Table 2 – Current and proposed price for AndroForte 5

AndroForte 5	AEMP	Price to pharmacy	DPMQ
Current price	$49.98	$53.74	$65.76
Requested price	$[redacted] (an increase of [redacted]% per dose)	$[redacted]	$[redacted]

Source: table 3.3, p36 of the submission main body.

5.8 The sponsor claimed that the current AEMP for AndroForte 5 is below the cost of goods, and is therefore unviable. The sponsor did not provide any additional information on the cost of goods for Androforte 5.

5.9 The submission requested a [redacted]% increase in the AEMP for AndroForte 5 claiming that changes to the recommended dose for scrotal application required reconsideration of the equi-effective doses.

5.10 There is insufficient evidence presented to confirm that 100% of the market will switch to using a 25 mg daily dose, which is the basis of the submission's cost minimisation analysis. A conservative approach that patients will be switching to a 50 mg daily dose may be adapted, which would also minimise the impact of patients who will continue to apply AndroForte 5 to the upper body, requiring up to 200 mg daily.

5.11 In its pre-PBAC response the sponsor commented that a comparison of a higher dose with the lowest dose is inappropriate. The sponsor reiterated that a price increase of [redacted]% was requested, not a 4-fold price increase. The sponsor also submitted the requested price increase will be cost-neutral if only 50% of patients switch to scrotal administration.

For more detail on PBAC's view, see section 6 PBAC outcome.

Estimated PBS usage & financial implications

5.12 The minor submission estimated a save to the PBS in Year 6 of listing, with a total net save to the PBS of $0 to <$10 million over the first 6 years of listing. This is summarised in table 3.

Table 3: Estimated use and financial implications

	Year 1	Year 2	Year 3	Year 4	Year 5	Year 6
Estimated extent of use (prescriptions per year)						
Torso application (current)	[redacted][1]	[redacted][1]	[redacted][1]	[redacted][1]	[redacted][1]	[redacted][1]
Scrotal application (proposed)[a]	[redacted][2]	[redacted][2]	[redacted][2]	[redacted][2]	[redacted][2]	[redacted][2]
Estimated financial implications of scrotal application						
Cost to PBS/RPBS	$[redacted][3]	$[redacted][3]	$[redacted][3]	$[redacted][3]	$[redacted][3]	$[redacted][3]
Copayments	-$[redacted][3]	-$[redacted][3]	-$[redacted][3]	-$[redacted][3]	-$[redacted][3]	-$[redacted][3]
Cost to PBS/RPBS less copayments	$[redacted][3]	$[redacted][3]	$[redacted][3]	$[redacted][3]	$[redacted][3]	$[redacted][3]
Net financial implications						
Net cost to PBS/RPBS	-$[redacted][4]	-$[redacted][4]	-$[redacted][4]	-$[redacted][4]	-$[redacted][4]	-$[redacted][4]

[a] Assuming 4 scripts per patient per year as estimated by the submission.
Source: table 4.9, p51 of the submission main body.
The redacted values correspond to the following ranges:
[1]5,000 to <10,000
[2]500 to <5,000
[3]$0 to <$10 million
[4]net cost saving

5.13 This estimate assumes graduated uptake to allow time for clinician education, with 70% Year 1 to 90% from Year 3 onwards.

5.14 A DUSC review undertaken in February 2020 noted that the number of patients initiating on testosterone has stabilised. Based on this, the sponsor applied only general population growth over the forward estimates of 1.7%.

5.15 Notably, the submission forecasts that the introduction of the new application site will cause market displacement of other testosterone products, indicating that the market share for AndroForte 5 is expected to rise. The sponsor considers that scrotal application provides safety and efficacy advantages over other products from the administration of a smaller volume of product, enhanced absorption, and less risk of accidental exposure of the patient's partner and/or children via passive transfer.

Table 4 – Estimated changes to the testosterone market

PBS utilisation	2021	2022	2023	2024	2025	2026
Estimated market displacement						
ANDROFORTE® 5 (current DPMQ)	100%	100%	100%	100%	100%	100%
Reandron 1000	15%	20%	25%	30%	35%	40%
Testogel (all brands), Testavan, Androderm (all brands)	30%	50%	60%	70%	75%	75%
Displaced prescriptions						
All testosterone comparator scripts	[redacted][1]	[redacted][2]	[redacted][3]	[redacted][4]	[redacted][5]	[redacted][5]
Script equivalence (substitution rate = 0.25)	[redacted][6]	[redacted][7]	[redacted][7]	[redacted][8]	[redacted][8]	[redacted][8]
ANDROFORTE® 5 scripts adjusted for variable uptake rate of existing users (proposed DPMQ)	[redacted][7]	[redacted][7]	[redacted][7]	[redacted][8]	[redacted][8]	[redacted][8]

Source: Table 4.5, p46 of the submission main body.

The redacted values correspond to the following ranges:

[1] *30,000 to <40,000*
[2] *50,000 to <60,000*
[3] *60,000 to <70,000*
[4] *80,000 to <90,000*
[5] *90,000 to <100,000*
[6] *5,000 to <10,000*
[7] *10,000 to <20,000*
[8] *20,000 to <30,000*

5.16 Based on historical PBS prescription data, the Department estimated an average annual growth rate of 1.04% between January 2021 and December 2025.

5.17 As this is a minor submission, the financial estimates have not been independently evaluated.

For more detail on PBAC's view, see section 6 PBAC outcome

6 PBAC Outcome

6.1 The PBAC recommended the administrative advice for the restriction be amended to specify scrotal application and that the maximum number of repeats be reduced to 1.

6.2 The PBAC considered that the evidence presented did not support a reconsideration of the equi-effective dose of testosterone. The PBAC considered that there was considerable variation between the dose applied to upper body (100 mg) and scrotum (25 mg), and considered, based on the evidence provided, the proportion of patients that will achieve a clinical benefit with a 25 mg daily dose is uncertain. The PBAC therefore advised that if a single restriction is maintained with one repeat for scrotal application, the premium amount requested above the current unit price of Androforte 5 is appropriate.

6.3 The PBAC noted the sponsor's claim that the requested price increase would be cost neutral to the PBS. The PBAC considered that it was appropriate that the requested

price increase and change in the restriction to reduce the number of repeats to 1 and specify the application site as scrotal, should not result in any additional cost to the PBS.

6.4 The PBAC noted that, consistent with section 84 of the *National Health Act 1953*, the AEMP is the appropriate maximum price of the brand of the pharmaceutical item made up of the drug, form and manner of administration. The PBAC therefore noted, given the same pharmaceutical item could be applied to both the torso and scrotum, it would not be possible to have different AEMPs for different sites of application.

6.5 The PBAC reiterated its previous advice that Androforte 5 is not suitable for prescribing by nurse practitioners.

6.6 The PBAC reiterated its previous advice that the Early Supply Rule should not apply to AndroForte 5.

6.7 The PBAC considered that AndroForte 5 does not meet the criteria prescribed for Pricing Pathway A.

6.8 The PBAC noted that this submission is not eligible for an Independent Review because it received a positive recommendation.

Outcome:
Recommended

7 Recommended listing

Amend existing listing for PBS item 10378F as follows:

Number of repeats changed from 6 to 1

Requested listing

MEDICINAL PRODUCT Medicinal Product Pack	Max. qty packs	Max. qty units	№.of Rpts	Available brands
TESTOSTERONE testosterone 5% (50 mg/mL) cream, 50 mL	1	1	*1*	ANDROFORTE 5®

Add a clinical criterion stating 'Treatment must be applied to the scrotum area' to the following restriction summaries:
Restriction Summary 6910 / ToC: 6910
Restriction Summary 6324 / ToC: 6324
Restriction Summary 6933 / ToC: 6933
Restriction Summary 6919 / ToC: 6919
Restriction Summary 6934 / ToC: 6934

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.