

# Testosterone

## Drug utilisation sub-committee (DUSC)

*February 2020*

### **Abstract**

#### ***Purpose***

DUSC requested to review the use of testosterone two years after a change to the restriction wording allowing general paediatricians to prescribe testosterone for androgen deficiency with established pituitary or testicular disorders. This change was recommended by the PBAC after a stakeholder request in response to the DUSC report in September 2016. DUSC considered it now timely to review the use of testosterone in relation to the previous report and also to assess the impact of restriction changes that have occurred since April 2015.

#### ***Date of listing on the Pharmaceutical Benefits Scheme (PBS)***

There are a variety of listings and forms of testosterone on the PBS. The first was listed prior to 1966.

#### ***Data Source / methodology***

Data were extracted from the Department of Human Services (DHS) prescription database from the earliest available data and continuing to September 2019.

#### ***Key Findings***

- In 2018:
  - 33,615 patients were supplied testosterone; of whom 4,276 received their first testosterone supply in that year.
  - 156,259 subsidised testosterone prescriptions were supplied.
  - expenditure for testosterone supplied through the PBS was \$13,079,019.
- The number of initiating patients stabilised at around 5,000 per year from 2016 onwards, after the restriction change for the androgen deficiency listing in April 2015.
- The restriction changes that have occurred since August 2015 have not affected the overall trend in testosterone use.
- Females accounted for more first initiations of testosterone in 2018 than males in the 15-19, 20-24 and 25-29 year age groups.

## **Purpose of analysis**

DUSC requested to review the use of testosterone two years after a change to the restriction wording allowing general paediatricians to prescribe testosterone for androgen deficiency with established pituitary or testicular disorders. This change was recommended by the PBAC in November 2016 after a stakeholder request in response to the DUSC report in September 2016. The PBAC requested that DUSC conduct a further review of testosterone. DUSC considered it now timely to review the use of testosterone in relation to the previous report and also to assess the impact of restriction changes that have occurred since April 2015.

## **Background**

### **Previous reviews by the DUSC**

#### ***October 2012***

At its June 2012 meeting, the DUSC noted a recently published research article highlighted an increase in PBS-subsidised testosterone prescribing. The DUSC considered it timely to review the utilisation of testosterone and requested a report be prepared for consideration at its October 2012 meeting. The key findings of the report were:

- Utilisation of PBS-subsidised testosterone had doubled over the years 2007 to 2011.
- The listing of two products, testosterone transdermal gel and intramuscular injection 1000 mg, had driven the growth in the market.
- There was a trend towards more GPs initiating therapy than specialists.
- In 2011, Government expenditure for testosterone preparations was \$14.6 million, up from \$5.6 million in 2005. This was a growth of 260% over 5 years.
- Most initiations were for patients aged 40-79 years.

With regard to the testosterone PBS restrictions, the DUSC was concerned that a high degree of variability had been observed in measurement of testosterone levels depending on the assay methodology adopted. The DUSC suggested that the PBAC should review the testosterone restrictions and consider input from the various stakeholders.

#### ***September 2016***

At its September 2016 meeting, DUSC considered a 12 month utilisation analysis of testosterone to assess the impact of restriction changes that occurred on 1 April 2015. The changes included involving a specialist in the treatment for all patients. For males with androgen deficiency who do not have an established pituitary or testicular disorder, the serum testosterone threshold was amended and patients with low serum testosterone due primarily to age, obesity, cardiovascular diseases, infertility or drugs were no longer eligible for PBS treatment. The key findings of the report were:

- The restriction change to testosterone on 1 April 2015 reduced the use of R/PBS subsidised testosterone.
- In the year after the restriction change compared to the year before:
  - The number of patients initiating testosterone therapy was 60% lower.
  - There was an 86% reduction in patients initiating testosterone under the non-established androgen deficiency restriction.
  - There was a reduction in the rate of people 40 years and over starting testosterone.
  - The number of prevalent patients was 20% lower.
  - The number of initiating patients where the first prescription was written by a GP reduced by 80%.
- In 2015, the total number of supplied R/PBS-subsidised testosterone prescriptions was 17% less than in 2014. In 2015, Government expenditure in 2015 was \$16.2 million, down 20% from 2014.

Data obtained from MedicineInsight suggested that there had been a shift to the private market. However, considering both the PBS and private markets, the net result of the restriction changes was a reduction in the number of patients supplied testosterone.

A number of groups responded to the report debating the evidence of testosterone use in adult patients with and without established androgen deficiency. These concerns related to various clinical criteria in the restriction.

DUSC suggested that the effects of the restriction change to remove the word 'male' that occurred 1 October 2015 be monitored and considered for review at a later date.

DUSC requested that the PBAC consider whether to recommend the removal of specialist involvement, or to include general paediatricians, to the restriction for patients under 18 years of age with androgen deficiency due to established pituitary or testicular disorders. At its November 2016 meeting, the PBAC recommended to include specialist general paediatricians in the restriction and the changes were implemented on 1 June 2017.

For details of the DUSC consideration of testosterone, refer to the [Public Release Document](#) from the October 2012 DUSC meeting and the [Public Release Document](#) from the September 2016 DUSC meeting.

## PBS listing details (as at December 2019)

**Table 1: PBS listing of testosterone**

Item	Name, form & strength, pack size	Max. quant.	Rpts	DPMQ	Brand name and manufacturer
10205D	Testosterone undecanoate 1 g/4 mL injection, 4 mL vial	1	1	\$115.59	Reandron® Bayer Australia Ltd
2115H	Testosterone undecanoate 40 mg capsule, 60	1	5	\$33.45	Andriol Testocaps® Merck Sharp & Dohme Pty Ltd
10380H	Testosterone 1% (12.5 mg/actuation) gel, 2 x 60 actuations	1	4	\$76.98	Testogel® Besins Healthcare Australia Pty Ltd
8830R	Testosterone 1% (50 mg/5 g) gel, 30 x 5 g sachets	1	5	\$76.98	Testogel® Besins Healthcare Australia Pty Ltd
11740X	Testosterone 2% (23 mg/actuation) gel, 56 actuations	1	5	\$82.43	Testavan® Ferring Pharmaceuticals Pty Limited
10378F	Testosterone 5% (50 mg/mL) cream, 50 mL	1	6	\$65.22	Androforte 5® Lawley Pharmaceuticals Pty Ltd
8460G	Testosterone 2.5 mg/24 hours patch, 60	1	5	\$77.51	Androderm® Teva Pharma Australia Pty Limited
8619P	Testosterone 5 mg/24 hours patch, 30	1	5	\$77.51	Androderm® Teva Pharma Australia Pty Limited

Source: the [PBS website](#).

All testosterone products were subject to a 15% anniversary price reduction in June 2018.

Testosterone 2% solution was delisted 1 January 2018 and testosterone enanthate injection was delisted 1 February 2018.

### **Restriction**

All testosterone items have Authority Required listings. All the testosterone items in Table 1 are PBS-listed for androgen deficiency, micropenis, pubertal induction and the constitutional delay of growth or onset of puberty. A list of restriction codes is in Appendix A.

**Table 2: Testosterone Restrictions (as at December 2019)**

Micropenis	<p>Population criteria: * Patient must be under 18 years of age.</p> <p>Treatment criteria:</p>
Pubertal induction	<p>* Must be treated by a specialist general paediatrician, specialist paediatric endocrinologist, specialist urologist, specialist endocrinologist or a Fellow of the Australasian Chapter of Sexual Health Medicine; or in consultation with</p>
Constitutional delay of growth or puberty	<p>one of these specialists; or have an appointment to be assessed by one of these specialists. The name of the specialist must be included in the authority application.</p>
Androgen deficiency	<p>Clinical criteria: * Patient must have an established pituitary or testicular disorder.</p> <p>Treatment criteria: * Must be treated by a specialist general paediatrician, specialist paediatric endocrinologist, specialist urologist, specialist endocrinologist or a Fellow of the Australasian Chapter of Sexual Health Medicine; or in consultation with one of these specialists; or have an appointment to be assessed by one of these specialists. The name of the specialist must be included in the authority application.</p>
	<p>Clinical criteria: * Patient must not have an established pituitary or testicular disorder, AND * The condition must not be due to age, obesity, cardiovascular diseases, infertility or drugs.</p> <p>Population criteria: * Patient must be aged 40 years or older.</p> <p>Treatment criteria: * Must be treated by a specialist urologist, specialist endocrinologist or a Fellow of the Australasian Chapter of Sexual Health Medicine; or in consultation with one of these specialists; or have an appointment to be assessed by one of these specialists.</p> <p>Androgen deficiency is defined as:</p> <ul style="list-style-type: none"> <li>(i) testosterone level of less than 6 nmol per litre; OR</li> <li>(ii) testosterone level between 6 and 15 nmol per litre with high luteinising hormone (LH) (greater than 1.5 times the upper limit of the eugonadal reference range for young men, or greater than 14 IU per litre, whichever is higher).</li> </ul> <p>Androgen deficiency must be confirmed by at least two morning blood samples taken on different mornings. The dates and levels of the qualifying testosterone and LH measurements must be, or must have been provided in the authority application when treatment with this drug is or was initiated. The name of the specialist must be included in the authority application.</p>

For details of the current PBS-listing refer to the [PBS website](#).

### **Date of listing on PBS**

- Testosterone esters injection (delisted January 2012): pre-1966
- Testosterone enantate (enanthate) injection (delisted February 2018): pre-1974
- Testosterone undecanoate capsule: April 1990
- Testosterone subcutaneous implant: November 1996
- Testosterone transdermal patch: November 2000
- Testosterone transdermal gel: August 2005
- Testosterone undecanoate injection: August 2006
- Testosterone transdermal solution (delisted January 2018): March 2013
- Testosterone transdermal cream: August 2015

### **Changes to listing**

**Table 3: changes to listing since August 2015**

<b>Date</b>	<b>Change to listing</b>
1 August 2015	Addition of two items for all current restrictions: cream and 1% gel
1 October 2015	Removed population criterion "patient must be male"
1 August 2016	Restriction wording change from "registered member" of the Australasian Chapter of Sexual Health Medicine, to "Fellow" of the Australasian Chapter of Sexual Health Medicine
1 June 2017	Added specialist general paediatricians to the restriction for patients under 18 years of age with androgen deficiency due to established pituitary or testicular disorders
1 January 2018	Testosterone 2% solution delisted Alteration item description: testosterone enanthate changed to enantate
1 February 2018	Testosterone enantate injection delisted
1 August 2019	Addition of 2% gel item for all current restrictions

Current PBS listing details are available from the [PBS website](#).

### **Clinical situation**

Hypogonadism is a disorder that results in the testes being unable to produce both physiological levels of testosterone (androgen deficiency) and adequate numbers of functional sperm for paternity (male infertility). Most often, hypogonadism is due to congenital or acquired defects of the testes (primary testicular failure). Constitutional delay in growth or onset of puberty, micropenis and pubertal induction are examples of primary testicular failure (classical early onset testosterone deficiencies).<sup>1</sup>

There are a variety of Australian and international position and consensus statements regarding testosterone treatment. In 2016, the Endocrine Society of Australia (ESA)

published a position statement<sup>1</sup> including indications for testosterone therapy. The position statement recommended testosterone treatment for androgen-deficient men with proven pathological hypogonadism, regardless of age. The position statement also noted that there are limited data from high-quality randomised controlled trials with clinically meaningful outcomes to justify testosterone treatment in older men without hypothalamic, pituitary or testicular disease.

## Therapeutic Goods Administration (TGA) approved indications

In 2017, the TGA published advice following a review of testosterone in relation to the risk of arterial thromboembolism/venous thromboembolism. As part of its review, the TGA sought advice from the Advisory Committee on the Safety of Medicines (ACSOM). At its 2 September 2016 meeting, ACSOM found that there was evidence of a weak signal of increased cardiovascular risks with use of testosterone medications in general (but not for specific events). The TGA noted this advice, but given there is only a weak signal, determined that it is not necessary to update the Product Information documents for testosterone medicines at this time.

## Dosage and administration

A wide range of products are registered in Australia for use as testosterone replacement therapy. Gel, cream, liquid and patch formulations are generally applied daily; capsules are usually taken twice daily; shorter acting intramuscular (IM) injections given every 2-3 weeks; and longer acting IM injections every 10-14 weeks. Appendix B contains further information regarding dosage and administration of PBS-listed testosterone products.

The current Product Information (PI) and Consumer Medicine Information (CMI) are available from [the TGA \(Product Information\)](#) and [the TGA \(Consumer Medicines Information\)](#).

## Methods

The analyses used data from the DHS supplied prescriptions database for dates of supply up to and including 30 September 2019; extracted November 2019. The DHS supplied prescriptions database includes data submitted to DHS for payment of a PBS or RPBS subsidy by the Government by all approved pharmacies in Australia. This dataset contains de-identified information that includes a unique patient identification number (PIN), dates and quantities of supply of all PBS listed drugs, prescriber and pharmacy information.

Analyses in the report include:

- Prescriptions supplied over time, noting restriction changes ([Figure 1](#) and [Table 4](#))
- Prescriptions by form ([Figure 2](#))
- New and prevalent patient counts ([Figure 3](#))

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<sup>1</sup> Yeap et al. Endocrine Society of Australia position statement on male hypogonadism (part 1): assessment and indications for testosterone therapy. Med J Aust 2016; 205(4): 173-179. DOI: 10.5694/mja16.00393.

- New patients by restriction ([Figure 4](#))
- Prevalent patients by restriction ([Figure 5](#))
- Initiating patients in 2018 by restriction and age ([Figure 6](#))
- Initiating patients over time by sex ([Figure 7](#))
- Initiating patients in 2018 by age and sex ([Figure 8](#))
- Prescriber type ([Figure 9](#))

A patient was defined as an initiator (or 'new patient') based on the date of first supply of PBS subsidised testosterone therapy from April 2003. Age was assigned based on the first supply in the time period.

The number of initiating patients in each age bracket was determined from the DHS supplied prescriptions database. These were then standardised by the Australian population according to the Australian Bureau of Statistics (ABS) Australian Demographic Statistics, March 2019.<sup>2</sup> The rates of patients initiating on testosterone were calculated as the number of initiating patients divided by the ABS Estimated Residential Population (ERP) population in the specific year (as at 30 June), by age or sex as required. The rates were expressed as the number of incident patients per 100,000. The age adjusted rates were derived using the Direct Method.<sup>3</sup>

Prescriber type was attributed to the de-identified approval number of the prescriber by the DHS and was based on the major field of specialty, derived from the combination of the current registered specialty and the most Medicare services provided per quarter. Prescribers can work in several different specialties but are allocated by DHS to one major field of specialty per quarter. The prescriber type attributed to initial testosterone prescriptions was used for this analysis.

Data manipulation was undertaken using SAS.

As all the above described analyses are based on date of supply, there may be small differences compared with publicly available date of processing data on the Medicare Australia Statistics website.<sup>4</sup> In addition, medicines supplied to general patients costing less than the general patient contribution do not receive a PBS benefit (i.e. under co-payment prescriptions) and are not included in Medicare Australia Statistics website data. The DHS Medicare data used in this report includes under co-payment prescriptions from 1 April 2012.

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<sup>2</sup> ABS 3101.0 Australian Demographic Statistics, March 2019; released 19 September 2019  
<<https://www.abs.gov.au/Population>>

<sup>3</sup> [Principles on the use of direct age-standardisation in administrative data collections](#), September 2011, AIHW

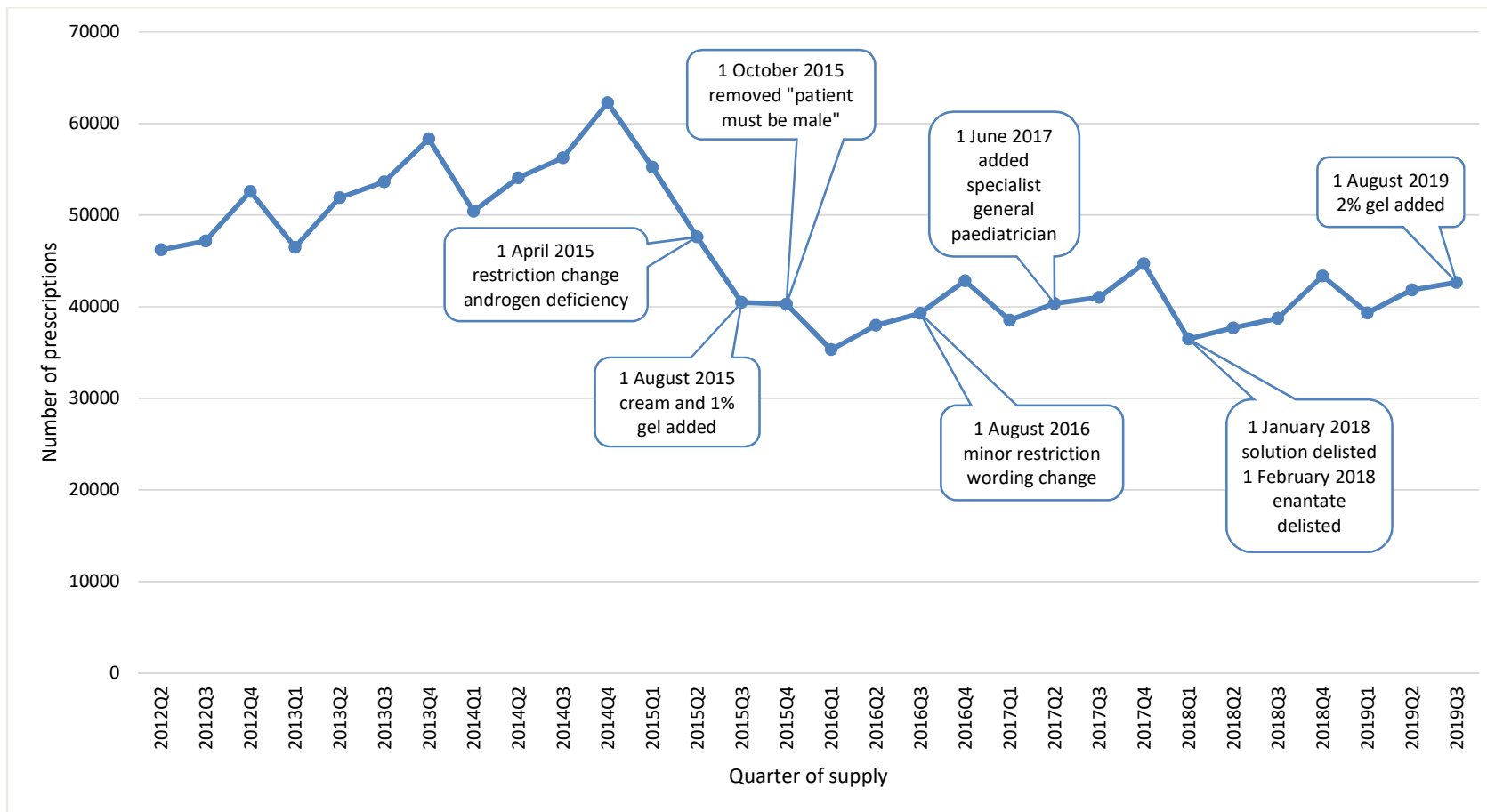
<sup>4</sup> PBS statistics. Australian Government Department of Human Services Medicare. Canberra. Available from  
<[http://medicarestatistics.humanservices.gov.au/statistics/pbs\\_item.jsp](http://medicarestatistics.humanservices.gov.au/statistics/pbs_item.jsp)>.

## **Results**

### **Analysis of drug utilisation**

#### ***Overall utilisation***

Figure 1 depicts the number of testosterone prescriptions supplied from April 2012 to September 2019.



**Figure 1: Testosterone prescriptions supplied per quarter from April 2012 to September 2019.**

Prescriptions by date of supply. Source: DHS supplied prescriptions database; accessed November 2019.

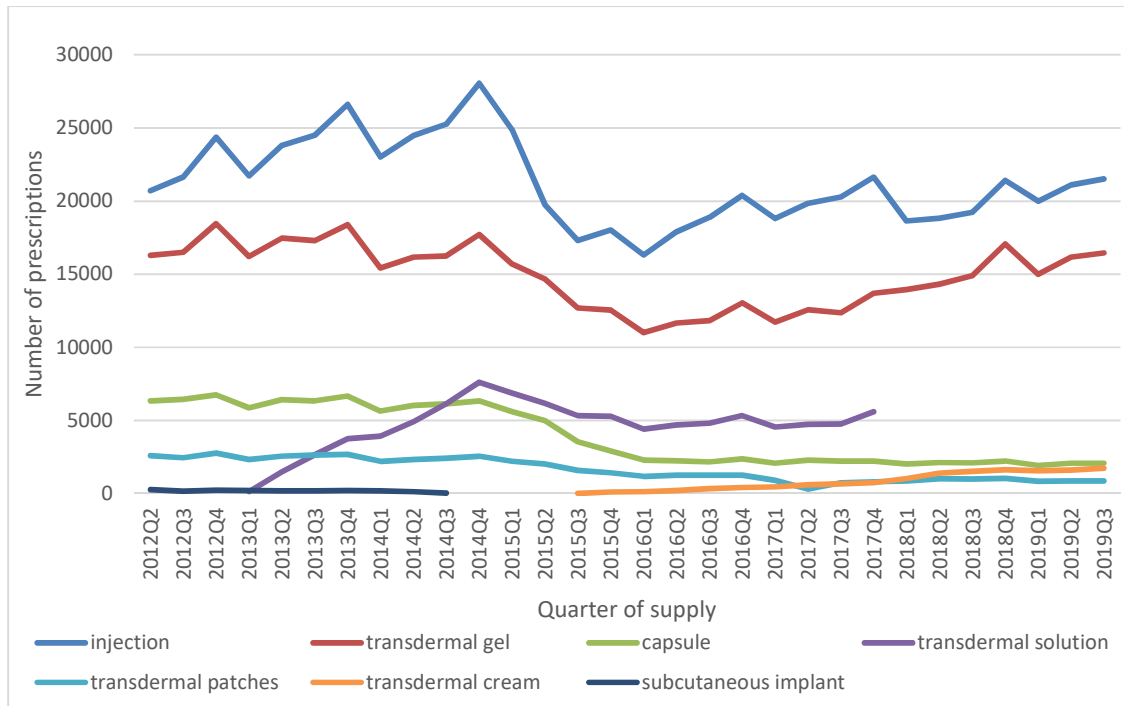
As reported in the September 2016 DUSC report, there was a downwards trend in the number of testosterone prescriptions supplied after the change to the restriction for androgen deficiency on 1 April 2015. However, at that stage, data were available until 30 June 2016, therefore it was unclear whether the market would plateau in the coming years. Figure 1 shows that the use of testosterone has remained steady since the April 2015 restriction change. The restriction changes that have occurred since then have not affected the overall trend in testosterone use.

**Table 4: Testosterone prescriptions supplied by calendar year**

Year	Number of prescriptions supplied	Annual growth
2013	210,300	N/A
2014	222,996	6%
2015	183,573	-18%
2016	155,384	-15%
2017	164,597	6%
2018	156,259	-5%

Prescriptions by date of supply. Source: DHS supplied prescriptions database; accessed November 2019.

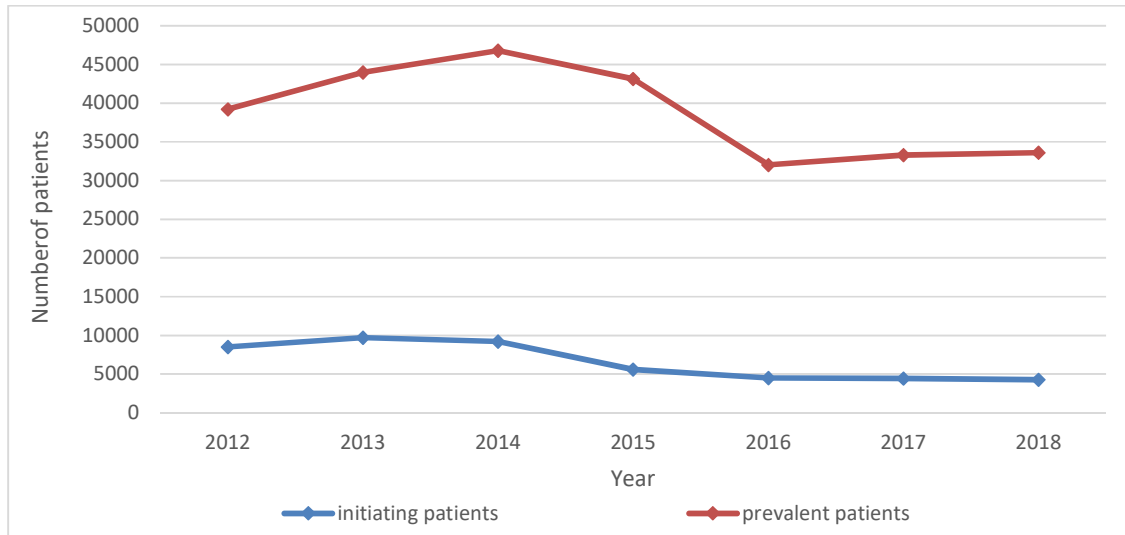
In 2018, government expenditure for testosterone supplied through the PBS was \$13,079,019.



**Figure 2: Testosterone prescriptions supplied per quarter by form from Apr 2012 to Sep 2019.**

Prescriptions by date of supply. Source: DHS supplied prescriptions database; accessed November 2019.

Transdermal gel and injection remained the two most used forms of testosterone (Figure 2).



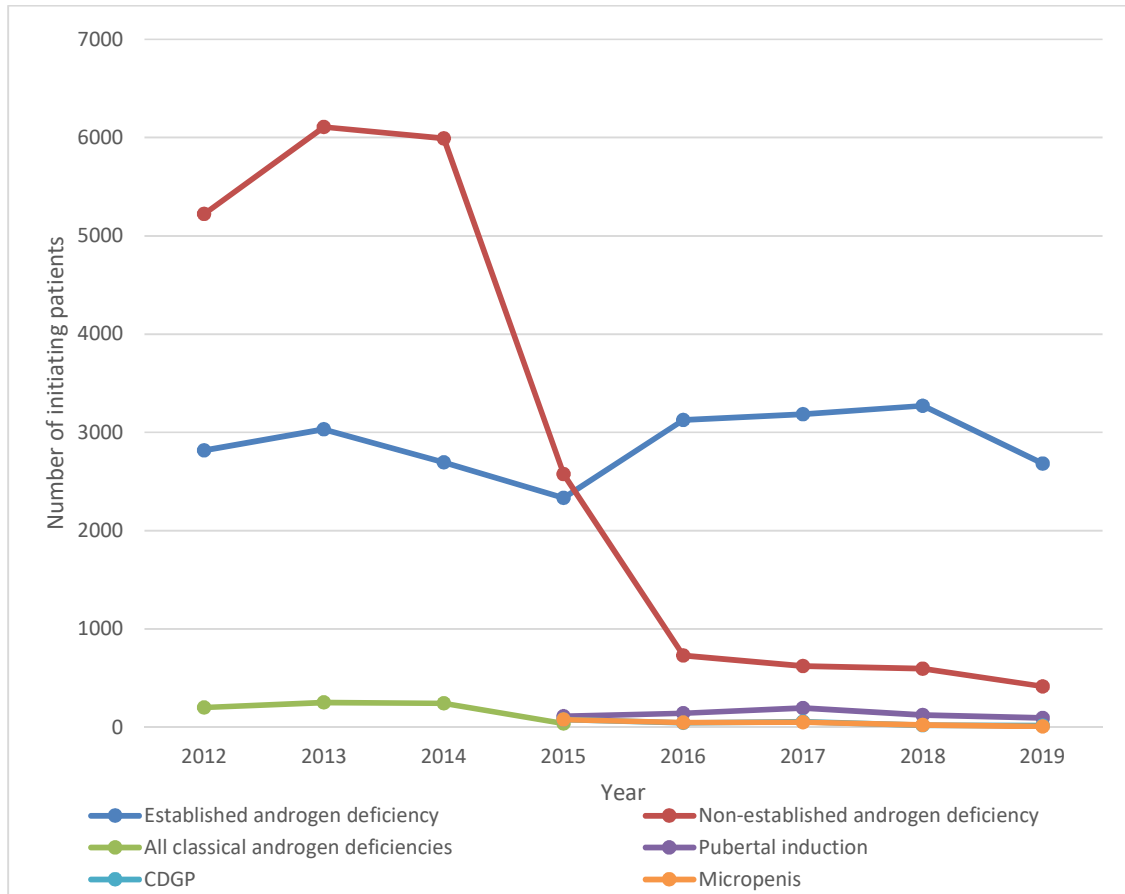
**Figure 3: Number of patients initiating and prevalent to testosterone by calendar year**

Initiation defined as first supply of testosterone since April 2003.

Source: DHS supplied prescriptions database; accessed November 2019.

In 2018, there were 33,615 patients supplied testosterone; of whom 4,276 received their first testosterone supply in that year. The number of initiating patients stabilised at around 5,000 per year from 2016 onwards, after the restriction change for the androgen deficiency listing (Figure 3).

### Patients initiating testosterone therapy by restriction



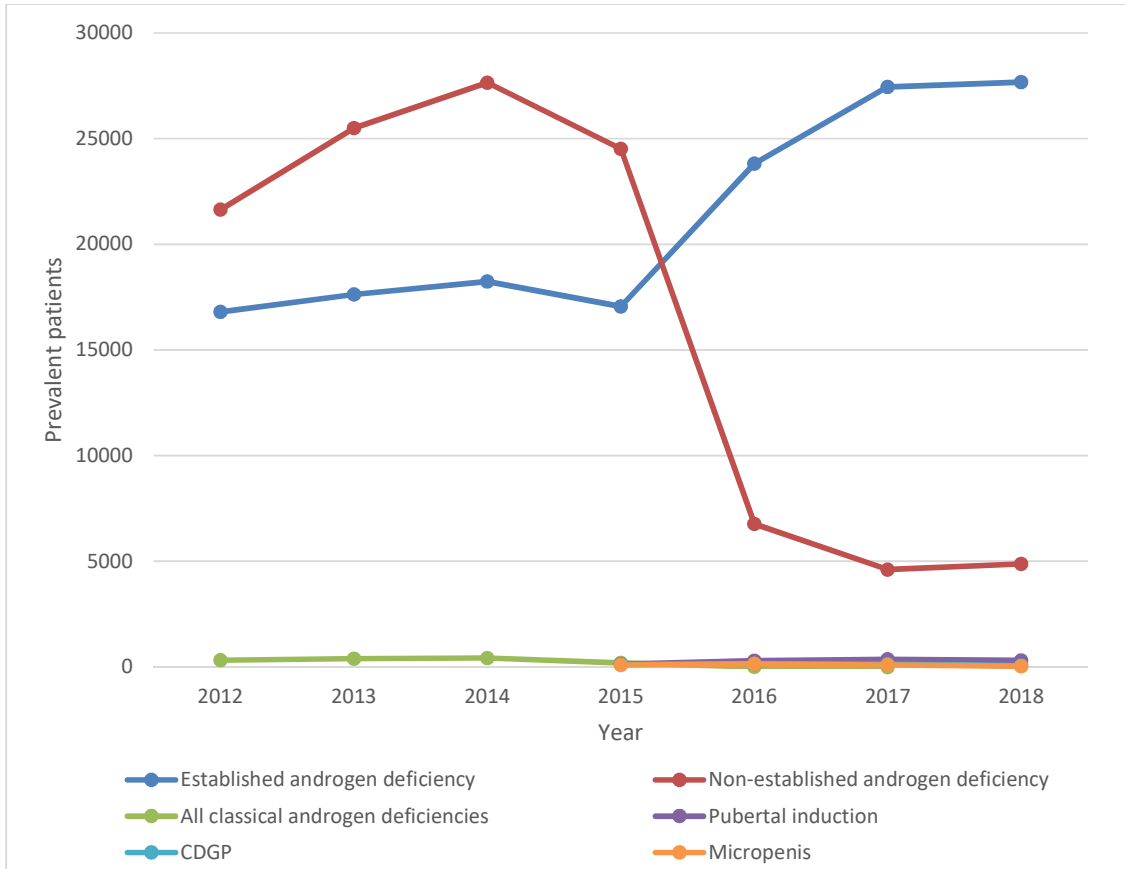
**Figure 4: Initiating patients by restriction**

CDGP: constitutional delay of growth and puberty

Classical androgen deficiencies: pubertal induction, micropenis and constitutional delay of growth/puberty

Initiation defined as first supply of testosterone since April 2003. In the presented period, there were 2,355 initiating patients with an unknown or invalid restriction (not shown). Source: DHS supplied prescriptions database; accessed November 2019.

As noted in the September 2016 report, the number of patients initiating testosterone for non-established androgen deficiency fell 86% in the year after the restriction change. In the same time period, the number of patients initiating testosterone treatment for classical androgen deficiency did not decline. The updated data (Figure 4) show that the number of patients initiating testosterone under each of the restriction codes remained stable since 2016 (noting that 2019 is part year to September).



**Figure 5: Prevalent patients by restriction**

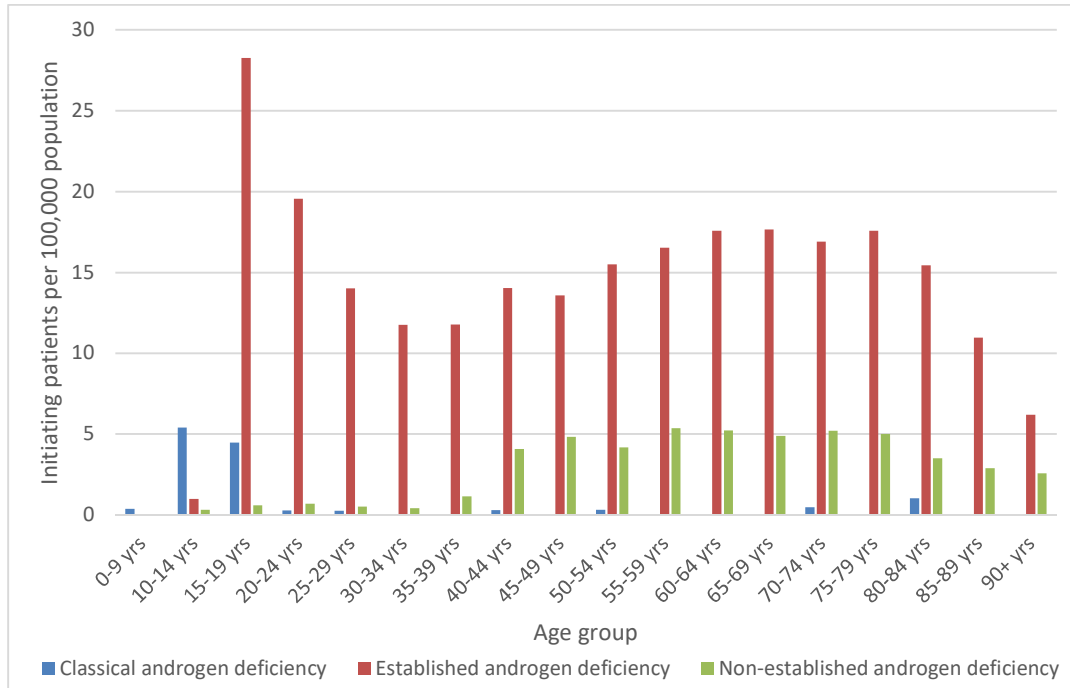
CDGP: constitutional delay of growth and puberty

Classical androgen deficiencies: pubertal induction, micropenis and constitutional delay of growth/puberty

In the presented period, there were, on average, 644 patients per year with an unknown or invalid restriction (not shown). Source: DHS supplied prescriptions database; accessed November 2019.

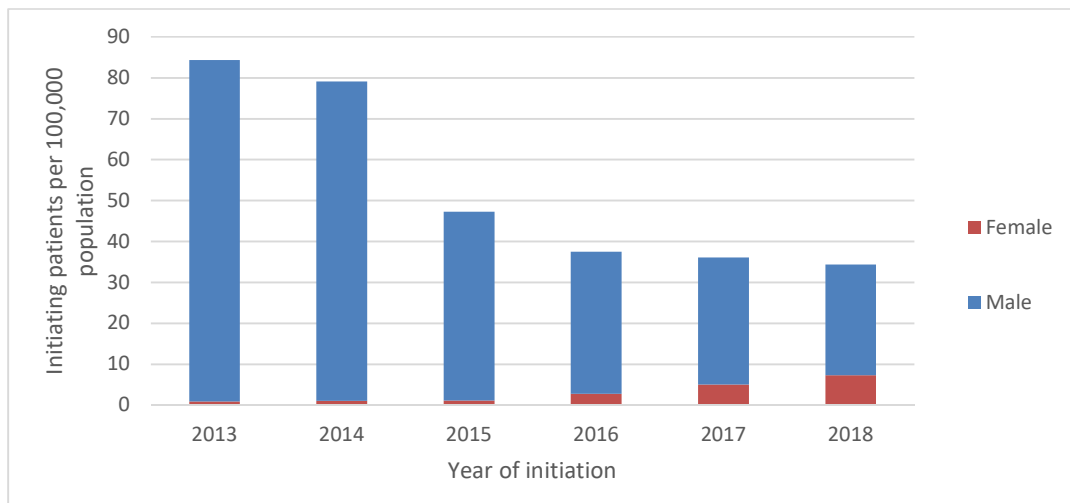
Figure 5 shows that after the restriction change in 2015, the number of prevalent patients treated under the non-established androgen deficiency code decreased, while there was an increase in patients supplied testosterone under the established androgen deficiency code. This increase was not as substantial as the decrease in people supplied under the non-androgen deficiency code. However, the increase in patients supplied under the established androgen deficiency code cannot be accounted for by new patients (which did not increase, per Figure 4).

**Utilisation by age and sex**



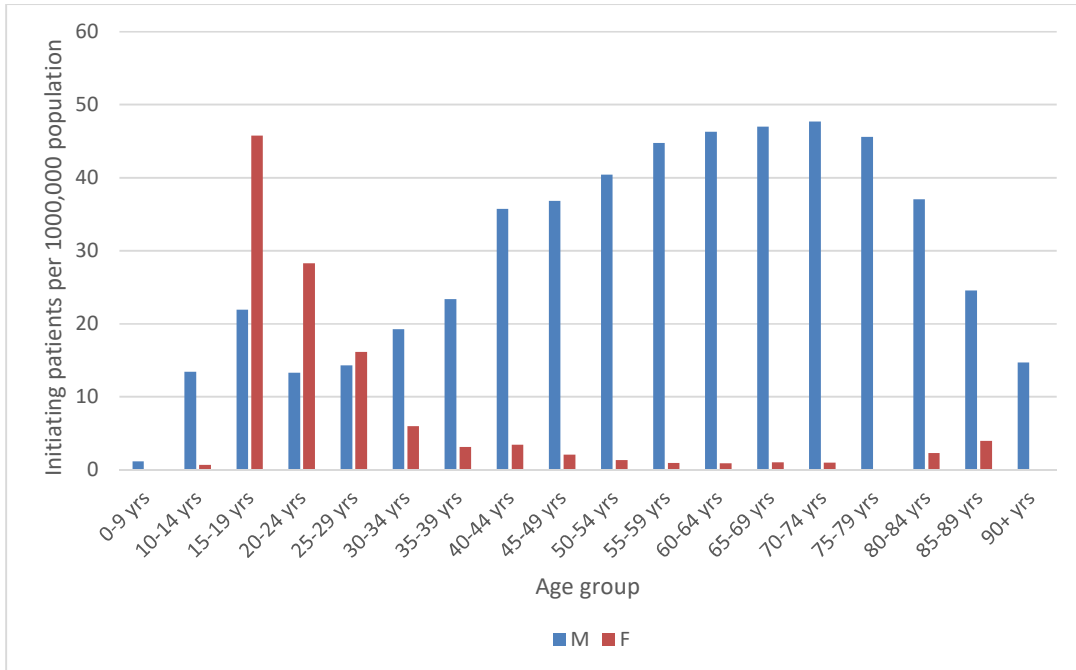
**Figure 6: Patients initiating testosterone in 2018 by restriction and age (adjusted)**

Classical androgen deficiency: pubertal induction, micropenis and constitutional delay of growth/puberty  
 Age adjusted by estimated resident population (ERP) 30 June 2018. Patient numbers ≤5 were amended to equal 5 before age adjustment. Initiation defined as first supply of testosterone since April 2003. In the presented period, there were 239 initiating patients with an unknown or invalid restriction (not shown).  
 Sources: DHS supplied prescriptions database, accessed November 2019; ABS Australian Demographic Statistics Mar 2019, Table 8 ERP by age and sex at 30 June 2018.



**Figure 7: Patients initiating testosterone by year and sex (adjusted)**

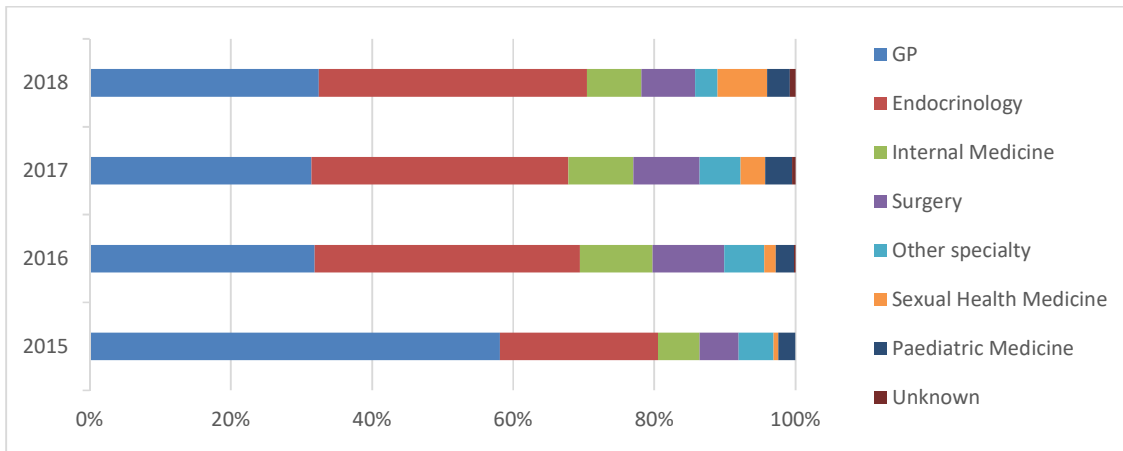
Age adjusted by estimated resident population (ERP) at 30 Jun per year. Sources: DHS supplied prescriptions database, accessed November 2019; ABS 3101.0 Australian Demographic Statistics, Table 59. ERP.



**Figure 8: Patients initiating testosterone in 2018 by age and sex (adjusted)**

Age adjusted by estimated resident population (ERP) 30 June 2018. Patient numbers ≤5 were amended to equal 5 before age adjustment. Initiation defined as first supply of testosterone since April 2003. Sources: DHS supplied prescriptions database, accessed November 2019; ABS 31010DO002\_20193 Australian Demographic Statistics Mar 2019, Table 8 ERP by age and sex at 30 June 2018.

While the rate of females accessing subsidised testosterone remains small, it has increased each year since 2015 (Figure 7). The increase coincides with the restriction change on 1 October 2015, which removed the population criterion “patient must be male.” Use was most common in females 15-19 years (Figure 8). Females accounted for more first initiations of testosterone in 2018 than males in the 15-19, 20-24 and 25-29 year age groups.



**Figure 9: Prescribers of testosterone to initiating patients 2015-2018**

Source: DHS supplied prescriptions database, accessed November 2019

Figure 9 shows the contribution of different prescriber types to patients' first prescriptions for subsidised testosterone. The most substantial change in the composition of prescribers initiating testosterone was the reduction in the proportion of GPs between 2015 and 2016. The proportion of initial prescribers accounted for by specialists in paediatric medicine has increased slightly.

## Discussion

Use of testosterone has remained steady since the April 2015 restriction change. The restriction changes that have occurred since then have not affected the overall trend in testosterone use.

While the rate of females accessing subsidised testosterone remains small, it has increased each year since 2015. The increase coincided with the restriction change on 1 October 2015, which removed the population criterion "patient must be male." Use was most common in females 15-19 years. Females accounted for more first initiations of testosterone in 2018 than males in the 15-19, 20-24 and 25-29 year age groups.

The most substantial change in the composition of prescribers initiating testosterone was the reduction in the proportion of GPs between 2015 and 2016. This was likely due to the changes to the testosterone restrictions for androgen deficiency. The proportion of initial prescribers accounted for by specialists in paediatric medicine has increased slightly. The changes to the restrictions on 1 June 2017 to add specialist general paediatricians may have contributed to this. However, the reduction in use of subsidised testosterone in older men also means that children now represent a higher proportion of patients than they did prior to the changes to the androgen deficiency restriction in 2015.

## DUSC Consideration

Use of testosterone has remained steady since the April 2015 restriction change. The restriction changes that have occurred since then have not affected the overall trend in testosterone use.

After the restriction change in 2015, the number of prevalent patients treated under the non-established androgen deficiency code decreased, while there was an increase in patients supplied testosterone under the established androgen deficiency code. This increase was not as substantial as the decrease in people supplied under the non-androgen deficiency code. However, the increase in patients supplied under the established androgen deficiency code cannot be accounted for by new patients. DUSC noted this pattern of use implies prevalent patients qualified for subsidised testosterone under the non-established androgen deficiency restriction, but then switched to established androgen deficiency codes after the restriction change. DUSC considered it possible that these people legitimately fulfilled the requirements of the established androgen deficiency restriction; although some use outside the restriction could possibly be implied.

While the rate of females accessing subsidised testosterone remains small, it has increased each year since 2015. The increase coincided with the restriction change on 1 October 2015, which removed the population criterion “patient must be male.” Use was most common in females 15-19 years. Females accounted for more initiations of testosterone in 2018 than males in the 15-19, 20-24 and 25-29 year age groups.

The most substantial change in the composition of prescribers initiating testosterone was the reduction in the proportion of GPs between 2015 and 2016. This was likely due to the changes to the testosterone restrictions for androgen deficiency. The proportion of initial prescribers accounted for by specialists in paediatric medicine has increased slightly. The changes to the restrictions on 1 June 2017 to add specialist general paediatricians may have contributed to this. However, the reduction in use of subsidised testosterone in older men also means that children now represent a higher proportion of patients than they did prior to the changes to the androgen deficiency restriction in 2015. DUSC noted that the contribution of sexual health medicine prescribers in prescribing testosterone to new patients increased each year of the study period (2015-2018). This trend seemed to coincide with the opening up of the restriction to remove “male” from the population criteria.

One sponsor response indicated that the changes to the restriction for androgen deficiency in 2015 were too narrow and do not address the needs of older men. DUSC recalled that the goal of the androgen deficiency restriction changes in 2015 was to limit access where there wasn't evidence. DUSC decided the results of the analysis did not warrant further consultation with clinical or consumer groups at this stage. Any suggested amendments to the restrictions would require an application to the PBAC with appropriate evidence.

One sponsor considered the restriction being Authority Required and requiring access to a specialist contributed to low uptake of their product. DUSC considered patient preference is a factor in uptake of the different testosterone products. DUSC noted that not all forms of testosterone have low uptake and therefore this is not an access issue.

## **DUSC Actions**

DUSC requested that the report be provided to the PBAC for consideration.

## **Context for Analysis**

The DUSC is a Sub Committee of the Pharmaceutical Benefits Advisory Committee (PBAC). The DUSC assesses estimates on projected usage and financial cost of medicines.

The DUSC also analyses data on actual use of medicines, including the utilisation of PBS listed medicines, and provides advice to the PBAC on these matters. This may include outlining how the current utilisation of PBS medicines compares with the use as recommended by the PBAC.

The DUSC operates in accordance with the quality use of medicines objective of the National Medicines Policy and considers that the DUSC utilisation analyses will assist consumers and health professionals to better understand the costs, benefits and risks of medicines.

The utilisation analysis report was provided to the pharmaceutical sponsors of each drug and comments on the report were provided to DUSC prior to its consideration of the analysis.

## **Sponsors' Comments**

Bayer Australia Ltd: The sponsor has no comment.

Besins Healthcare Australia Pty Ltd: The sponsor has no comment.

Ferring Pharmaceuticals Pty Limited: The sponsor has no comment.

Lawley Pharmaceuticals Pty Ltd: The sponsor has no comment.

Merck Sharp & Dohme Pty Ltd: The sponsor has no comment.

Teva Pharma Australia Pty Limited: The sponsor has no comment.

## **Disclaimer**

The information provided in this report does not constitute medical advice and is not intended to take the place of professional medical advice or care. It is not intended to define what constitutes reasonable, appropriate or best care for any individual for any given health issue. The information should not be used as a substitute for the judgement and skill of a medical practitioner.

The Department of Health (DoH) has made all reasonable efforts to ensure that information provided in this report is accurate. The information provided in this report was up-to-date when it was considered by the Drug Utilisation Sub-committee of the Pharmaceutical Benefits Advisory Committee. The context for that information may have changed since publication.

To the extent provided by law, DoH makes no warranties or representations as to accuracy or completeness of information contained in this report.

To the fullest extent permitted by law, neither the DoH nor any DoH employee is liable for any liability, loss, claim, damage, expense, injury or personal injury (including death), whether direct or indirect (including consequential loss and loss of profits) and however incurred (including in tort), caused or contributed to by any person's use or misuse of the information available from this report or contained on any third party website referred to in this report.

## Appendices

### Appendix A:

**Table A.1: Restriction codes since 1 October 2015**

Restriction code	Indication	Restriction	Summary of change	Date onto PBS	Date off PBS
5449	Micropenis	Population criteria: * Patient must be under 18 years of age. Treatment criteria: * Must be treated by a specialist paediatric endocrinologist, specialist urologist, specialist endocrinologist or a registered member of the Australasian Chapter of Sexual Health Medicine; or in consultation with one of these specialists; or have an appointment to be assessed by one of these specialists. The name of the specialist must be included in the authority application.	Removed population criterion "patient must be male"	1 October 2015	31 July 2016
5460	Pubertal induction				
5471	Constitutional delay of growth or puberty				
5511	Androgen deficiency	Clinical criteria: * Patient must have an established pituitary or testicular disorder. Treatment criteria: * Must be treated by a specialist paediatric endocrinologist, specialist urologist, specialist endocrinologist or a registered member of the Australasian Chapter of Sexual Health Medicine; or in consultation with one of these specialists; or have an appointment to be assessed by one of these specialists. The name of the specialist must be included in the authority application.			
5474		Clinical criteria: * Patient must not have an established pituitary or testicular disorder, AND * The condition must not be due to age, obesity, cardiovascular diseases, infertility or drugs. Population criteria: * Patient must be aged 40 years or older.			

Restriction code	Indication	Restriction	Summary of change	Date onto PBS	Date off PBS
		<p>Treatment criteria:  * Must be treated by a specialist urologist, specialist endocrinologist or a registered member of the Australasian Chapter of Sexual Health Medicine; or in consultation with one of these specialists; or have an appointment to be assessed by one of these specialists.</p> <p>Androgen deficiency is defined as:</p> <ul style="list-style-type: none"> <li>(iii) testosterone level of less than 6 nmol per litre; OR</li> <li>(iv) testosterone level between 6 and 15 nmol per litre with high luteinising hormone (LH) (greater than 1.5 times the upper limit of the eugonadal reference range for young men, or greater than 14 IU per litre, whichever is higher).</li> </ul> <p>Androgen deficiency must be confirmed by at least two morning blood samples taken on different mornings. The dates and levels of the qualifying testosterone and LH measurements must be, or must have been provided in the authority application when treatment with this drug is or was initiated. The name of the specialist must be included in the authority application.</p>			
6322	Micropenis	<p>Population criteria: * Patient must be under 18 years of age.</p> <p>Treatment criteria: * Must be treated by a specialist paediatric</p>	<p>"registered member" of the Australasian Chapter of Sexual Health Medicine changed to "Fellow"</p>	<p>1 August 2016</p>	<p>31 May 2017</p>
6312	Pubertal induction	<p>endocrinologist, specialist urologist, specialist endocrinologist or a Fellow of the Australasian Chapter of Sexual Health Medicine; or in</p>			
6316	Constitutional delay of growth or puberty	<p>consultation with one of these specialists; or have an appointment to be assessed by one of these specialists. The name of the specialist must be included in the authority application.</p>			

Restriction code	Indication	Restriction	Summary of change	Date onto PBS	Date off PBS
6304	Androgen deficiency	Clinical criteria: * Patient must have an established pituitary or testicular disorder. Treatment criteria: * Must be treated by a specialist paediatric endocrinologist, specialist urologist, specialist endocrinologist or a Fellow of the Australasian Chapter of Sexual Health Medicine; or in consultation with one of these specialists; or have an appointment to be assessed by one of these specialists. The name of the specialist must be included in the authority application.			
6324		<p>Clinical criteria:</p> <ul style="list-style-type: none"> <li>* Patient must not have an established pituitary or testicular disorder, AND</li> <li>* The condition must not be due to age, obesity, cardiovascular diseases, infertility or drugs.</li> </ul> <p>Population criteria:</p> <ul style="list-style-type: none"> <li>* Patient must be aged 40 years or older.</li> </ul> <p>Treatment criteria:</p> <ul style="list-style-type: none"> <li>* Must be treated by a specialist urologist, specialist endocrinologist or a Fellow of the Australasian Chapter of Sexual Health Medicine; or in consultation with one of these specialists; or have an appointment to be assessed by one of these specialists.</li> </ul> <p>Androgen deficiency is defined as:</p> <ul style="list-style-type: none"> <li>(i) testosterone level of less than 6 nmol per litre; OR</li> <li>(ii) testosterone level between 6 and 15 nmol per litre with high luteinising hormone (LH) (greater than 1.5 times the upper limit of the eugonadal reference range for young men, or greater than 14 IU per litre, whichever is higher).</li> </ul> <p>Androgen deficiency must be confirmed by at least two morning blood samples taken on different mornings. The dates and levels of the qualifying testosterone and LH measurements must be, or must have been provided in the authority application when treatment with this</p>			N/A

Restriction code	Indication	Restriction	Summary of change	Date onto PBS	Date off PBS
		drug is or was initiated. The name of the specialist must be included in the authority application.			
6933	Micropenis	Population criteria: * Patient must be under 18 years of age. Treatment criteria: * Must be treated by a specialist general	Added "specialist general paediatrician"	1 June 2017	N/A
6919	Pubertal induction	paediatrician, specialist paediatric endocrinologist, specialist urologist, specialist endocrinologist or a Fellow of the Australasian Chapter of Sexual Health Medicine; or in consultation with one of these			
6934	Constitutional delay of growth or puberty	specialists; or have an appointment to be assessed by one of these specialists. The name of the specialist must be included in the authority application.			
6910	Androgen deficiency	Clinical criteria: * Patient must have an established pituitary or testicular disorder. Treatment criteria: * Must be treated by a specialist general paediatrician, specialist paediatric endocrinologist, specialist urologist, specialist endocrinologist or a Fellow of the Australasian Chapter of Sexual Health Medicine; or in consultation with one of these specialists; or have an appointment to be assessed by one of these specialists. The name of the specialist must be included in the authority application.			

## Appendix B:

**Table B.1: Dose and administration information for PBS-listed testosterone (at December 2019)**

Brand name and sponsor	Product	Dose and frequency of administration
Reandron® Bayer Australia Ltd	Testosterone undecanoate intramuscular injection	1 g every 10 to 14 weeks IM where testosterone deficiency has been confirmed by clinical features and biochemical tests.
Andriol Testocaps® Merck Sharp & Dohme Pty Ltd	Testosterone undecanoate oral capsules	The initial dose is usually 120-160 mg/day for 2-3 weeks. Subsequent dosage (40-120 mg/day) should be based on the clinical effect obtained in the first weeks of therapy. Must be taken orally with the morning and evening meal. If an uneven number of capsules are to be taken, the greater dose should be taken in the morning.
Testogel® Besins Healthcare Australia Pty Ltd	Testosterone topical gel in sachets	5 g of gel (i.e. 50 mg of testosterone which equates to four pump actuations, two 25 mg sachets or one 50 mg sachet) applied once daily at about the same time, preferably in the morning. The daily dose should be adjusted by the doctor depending on the clinical or laboratory response in individual patients, not exceeding 10 g of gel per day. The adjustment of dosage should be achieved by 2.5 g of gel steps.
Testogel® Besins Healthcare Australia Pty Ltd	Testosterone topical gel in pump pack	Each pump actuation delivers 12.5 mg of testosterone in 1.25 g of gel and to obtain the equivalent of 50 mg of testosterone, 4 pump actuations are needed. Dose titration as above.
Androforte® Lawley Pharmaceuticals Pty Ltd	Testosterone cream	The recommended dose is 2 mL of cream (i.e. 100 mg of testosterone) applied once daily at about the same time, preferably in the morning. The daily dose should be adjusted by the doctor depending on the clinical or laboratory response in individual patients, not exceeding 4 mL of cream per day. The adjustment of dosage should be achieved by 1 mL of cream steps.
Androderm® Teva Pharma Australia Pty Limited	Testosterone transdermal patch	5 mg/day transdermal patch applied nightly (approximately 10.00pm) and worn for 24 hours, providing approximately 5 mg testosterone per day. The dose can be adjusted up to 7.5 mg/day (i.e., one 5 mg/day and one 2.5 mg/day patches or three 2.5 mg/day patches) nightly or down to 2.5 mg/day (i.e., one 2.5 mg/day patch) nightly depending on the serum testosterone measured in the morning after the application.

Brand name and sponsor	Product	Dose and frequency of administration
		<p>Measurement of serum testosterone should be repeated taking care to ensure proper patch adhesion and correct time of application before the dose is adjusted.</p> <p>Treatment in non-virilised patients may be initiated with one Androderm® 2.5 mg/day patch applied nightly. The dose should be adjusted as appropriate.</p> <p>Three patches per day may be required for men with a higher body weight (&gt;130 kg). The duration of treatment and frequency of testosterone measurements is determined by the physician.</p>
<p>Testavan® Ferring Pharmaceuticals Pty Limited</p>	<p>Testosterone gel in a metered-dose dispenser with a cap applicator</p>	<p>In adult men, the recommended starting dose is 23 mg testosterone (one pump actuation) applied once daily, preferably in the morning.</p> <p>To ensure proper dosing, serum testosterone levels should be periodically measured and dose titrated to maintain serum testosterone levels.</p> <p>Dose titration should be based on both serum testosterone levels and the existence of clinical signs and symptoms related to testosterone deficiency.</p> <p>The maximum recommended dose is 69 mg testosterone per day, which is equivalent to 3 pump actuations of TESTAVAN.</p>