

# Attention Deficit Hyperactivity Disorder: Utilisation Analysis

## Drug utilisation sub-committee (DUSC)

*May 2018*

### **Abstract**

#### ***Purpose***

To review the utilisation of Pharmaceutical Benefits Scheme and Repatriation Pharmaceutical Benefits Scheme (R/PBS) listed medicines used in the management of attention deficit hyperactivity disorder (ADHD). This includes a predicted versus actual analysis of lisdexamfetamine in the first 24 months of R/PBS listing. Lisdexamfetamine was first R/PBS-listed for this indication on 1 September 2015.

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

- Dexamfetamine - 1 December 1973
- Methylphenidate immediate release (IR) - 1 August 2005
- Methylphenidate modified release (MR) (Concerta<sup>®</sup>) - 1 April 2007
- Methylphenidate modified release (MR) (Ritalin LA<sup>®</sup>) - 1 April 2008
- Atomoxetine - 1 July 2007 requiring authority approval. On 1 August 2014, the restriction was simplified and changed to streamlined authority
- Lisdexamfetamine - 1 September 2015

Subsidy of lisdexamfetamine, atomoxetine and the two modified-release forms of methylphenidate (Ritalin LA<sup>®</sup> and Concerta<sup>®</sup>) is limited to patients diagnosed between the ages of 6 and 18 years of age inclusive. In addition, for modified-release methylphenidate, patients need to have demonstrated a response to immediate-release methylphenidate with no emergence of adverse events. Lisdexamfetamine and Concerta<sup>®</sup> are for patients requiring coverage over 12 hours. Ritalin LA<sup>®</sup> is for patients requiring coverage over 8 hours.

Atomoxetine is subsidised for patients unable to take dexamfetamine, lisdexamfetamine or methylphenidate due to specific circumstances set out in the PBS restriction. Patients need to have been diagnosed by a paediatrician or psychiatrist according to the DSM-5 criteria.

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

The analysis used data from the Department of Human Services (DHS) supplied prescriptions database.

## **Key Findings**

Over the five year period 2013-2017:

- The number of patients treated with R/PBS medicines for ADHD has risen at a yearly average growth rate of 9.9%.
- The number of prescriptions also increased at similar growth rates.
- The most commonly used medicine in terms of prevalent patients is the modified-release formulation of methylphenidate.
- More males than females were treated, although the ratio is decreasing over time.
- Children aged 6-12 years old account for over 40% of R/PBS ADHD medicines supplied.

A snapshot of medicine use in 2017 shows that:

- The majority of prescriptions were written by paediatricians or psychiatrists. Most Australian states and territories restrict the prescribing of methylphenidate, lisdexamfetamine and dexamfetamine for the treatment of ADHD to specialists.
- Rates of prescribing vary across states and territories. The rates of treatment in school-aged children were highest in the ACT, NSW and Queensland. Rates of treatment in adults were highest in Western Australia.

Lisdexamfetamine:

- The increase in growth of overall ADHD medicines supplied may be attributed to the listing of lisdexamfetamine in September 2015 and a lack of offset from substitution of other ADHD medicines.
- 17,366 and 26,858 R/PBS patients were treated with lisdexamfetamine in the first two years of listing respectively. This was approximately [REDACTED] fold higher than predicted.
- The total number of lisdexamfetamine prescriptions supplied in Year 1 (83,246) was similar to predicted. However, prescriptions in Year 2 (2,435,807) were [REDACTED] more than expected.
- A closer look at the distribution of the number of prescriptions per patient in the 12 months after initiation found that 15% of patients had one supply, while 30% of patients had two to five prescriptions supplied in that period. The reasons for lower than expected prescriptions per patient are not known, but may be due to the submission not accounting for a half cycle correction, adverse effects discontinuation, drug holidays and combination use with other ADHD medicines.
- The expected cost offset from substitution of other ADHD medicines to lisdexamfetamine has not been realised.

## Purpose of analysis

To review the utilisation of PBS-listed medicines used in the management of attention deficit hyperactivity disorder (ADHD). This includes a predicted versus actual analysis of lisdexamfetamine in the first 24 months of PBS listing (September 2015).

The ADHD medicines considered in this analysis are:

- dexamfetamine
- methylphenidate (immediate release (IR) and modified release (MR) forms)
- atomoxetine
- lisdexamfetamine

## Background

### Clinical situation

ADHD is characterised by a persistent pattern of inattentiveness, hyperactivity and/or impulsiveness that is associated with learning, behavioural and emotional impairment.

In 2013-2014, the prevalence of ADHD in Australian children and adolescents aged 4-17 was estimated to be 7.4%.<sup>1</sup> The prevalence of ADHD is higher in males than females at 10.4% compared to 4.3% of females having ADHD.<sup>1</sup> Many children with ADHD continue to have symptoms as adults.<sup>2</sup>

Comorbid psychiatric conditions are also common in patients with ADHD including anxiety disorders and mood disorders.<sup>2</sup>

The most current ADHD guidelines by the NHMRC<sup>2</sup> in 2012 and Therapeutic Guidelines<sup>3</sup> in 2013 recommend an individualised multimodal management plan for the management of ADHD. Behavioural and educational interventions may be used as non-pharmacological management of ADHD symptoms, either alone or in combination with medicines. In young children, it is recommended to start on non-pharmacological interventions. This report focuses on pharmacological management.

In Australia, psychostimulants are considered the first-line pharmacological treatment for ADHD.<sup>2,3,4</sup> The Therapeutic Guidelines recommend that, with rare exceptions, methylphenidate and dexamfetamine should not be used in children aged younger than 4 years.<sup>3</sup> Atomoxetine should be considered for children, adolescents and adults with

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<sup>1</sup> Lawrence D, Johnson S, Hafekost J, Boterhoven De Haan K, Sawyer M, Ainsley J, Zubrick SR 2015. The Mental Health of Children and Adolescents. Report on the second Australian Child and Adolescent Survey of Mental Health and Wellbeing. Canberra: Department of Health

<sup>2</sup> National Health and Medical Research Council (2012), Clinical Practice Points on the diagnosis, assessment and management of Attention Deficit Hyperactivity Disorder in children and adolescents. Canberra.

<sup>3</sup> Attention deficit hyperactivity disorder: pharmacological treatment [revised July 2013]. In eTG complete [Internet]. Melbourne: Therapeutic Guidelines Limited; 2018 Feb. Accessed 2018 Feb 9 <<http://online.tg.org.au/complete/desktop/index.htm>>.

<sup>4</sup> Tonge, B. (2013). 'Principles for managing attention deficit hyperactivity disorder'. Australian Prescriber, 36:162-5.

severe ADHD who are contraindicated to, do not respond to, or are intolerant of, stimulants.<sup>3,4</sup>

Since 2012, there has been the addition of two new medicines for the management of ADHD that is not reflected in available guidelines. Lisdexamfetamine was registered in July 2013 as a long-acting psychostimulant for the pharmacological management of ADHD. Lisdexamfetamine should not be used in children younger than 6 years as there is a lack of studies in this age group.<sup>5</sup>

In August 2017, guanfacine was registered for the management of ADHD in children 6-17 years old, as monotherapy where psychostimulants or atomoxetine are not suitable, not tolerated or have been shown to be ineffective; or as adjunctive therapy to psychostimulants (where there has been a sub-optimal response to psychostimulants).<sup>6</sup>

Methylphenidate, lisdexamfetamine and dexamfetamine are Schedule 8 controlled drugs where additional prescribing restrictions apply in all states and territories (refer to [Appendix A](#)).

There is some evidence of benefit for the use of clonidine in children over 5 years old.<sup>3,4</sup> There is limited evidence for the use of other pharmacological treatments including modafinil, bupropion and tricyclic antidepressants.<sup>3,7</sup>

This utilisation analysis does not consider use of bupropion, modafinil, tricyclic antidepressants or clonidine as these medicines are not TGA-indicated and are not PBS-subsidised for the treatment of ADHD. Furthermore, this utilisation analysis does not report the use of guanfacine, as the positive recommendation for PBS listing had not been implemented at the time the report was prepared<sup>8</sup> and a minor submission to extend the approved listing is subject for consideration at the July 2018 PBAC meeting.<sup>9</sup>

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<sup>5</sup> Shire Australia Pty Ltd (2018), Product Information: Vyvanse® (Lisdexamfetamine dimesilate). Approved 22 July 2013. Most recent amendment 24 January 2018. Accessed on: 9 February 2018, at:

<https://www.ebs.tga.gov.au/ebs/picmi/picmirepository.nsf/pdf?OpenAgent&id=CP-2013-PI-02051-1>

<sup>6</sup> Shire Australia Pty Ltd (2017), Product Information: Intuniv (Guanfacine hydrochloride). Approved 22 August 2017. Most recent amendment 22 August 2017. Accessed on: 9 February 2018, at:

<https://www.ebs.tga.gov.au/ebs/picmi/picmirepository.nsf/pdf?OpenAgent&id=CP-2017-PI-02254-1&d=2018022716114622483>

<sup>7</sup> Royal Australasian College of Physicians (2009), Draft Australian Guidelines on Attention Deficit Hyperactivity Disorder.

<sup>8</sup> Department of Health (2017), July 2017 PBAC Outcomes- Positive Recommendations. Accessed on: 9 February 2018, at:

<http://www.pbs.gov.au/industry/listing/elements/pbac-meetings/pbac-outcomes/2017-07/positive-recommendations-2017-07.pdf>

<sup>9</sup> Department of Health (2018), PBAC Meeting Agenda. Accessed on: 27 April 2018, at:

<http://www.pbs.gov.au/info/industry/listing/elements/pbac-meetings/agenda>

## Pharmacology

The exact mechanism of action of ADHD medications is not fully established but is thought to be due to modification of dopaminergic and noradrenergic activity in the brain. Dexamfetamine, lisdexamfetamine and methylphenidate hydrochloride are central nervous system stimulants.<sup>5,10,11</sup> Lisdexamfetamine is a prodrug of dexamfetamine and is broken down into active dexamfetamine after ingestion.<sup>5</sup> Atomoxetine is a selective noradrenaline reuptake inhibitor.<sup>12</sup> Guanfacine is a selective  $\alpha_{2A}$ -adrenergic receptor agonist.<sup>6</sup>

## Therapeutic Goods Administration (TGA) approved indications and PBS restrictions

Table 1 shows the TGA indications and PBS restricted uses of medicines used to manage ADHD.

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<sup>10</sup> Aspen Pharma Pty Ltd (2018), Product Information: Aspen Dexamfetamine Tablets. Approved 14 October 1991. Most recent amendment 13 October 2017. Accessed on: 9 February 2018, at:

<https://www.ebs.tga.gov.au/ebs/picmi/picmirepository.nsf/pdf?OpenAgent&id=CP-2017-PI-01667-1>

<sup>11</sup> NOVARTIS Pharmaceuticals Australia Pty Limited (2017), Product Information: RITALIN® 10/RITALIN® LA (methylphenidate). Approved 02 August 1991. Most recent amendment 4 October 2017. Accessed on: 9 February 2018, at:

[www.ebs.tga.gov.au/ebs/picmi/picmirepository.nsf/pdf?OpenAgent&id=CP-2010-PI-03175-3](https://www.ebs.tga.gov.au/ebs/picmi/picmirepository.nsf/pdf?OpenAgent&id=CP-2010-PI-03175-3)

<sup>12</sup> Eli Lilly Australia Pty Limited (2018), Product Information: STRATERA® (atomoxetine hydrochloride). Approved 27 January 2004. Most recent amendment 04 April 2016. Accessed on: 9 February 2018, at:

<https://www.ebs.tga.gov.au/ebs/picmi/picmirepository.nsf/pdf?OpenAgent&id=CP-2010-PI-04269-3>

**Table 1: TGA indications and PBS restricted uses for ADHD medicines**

Drug	TGA indications	PBS restricted uses
Dexamfetamine	<ul style="list-style-type: none"> <li>• Hyperkinetic behaviour disorders in children</li> <li>• Narcolepsy</li> </ul>	<ul style="list-style-type: none"> <li>• ADHD</li> <li>• Narcolepsy</li> </ul>
Methylphenidate IR	<ul style="list-style-type: none"> <li>• ADHD</li> <li>• Narcolepsy</li> </ul>	<ul style="list-style-type: none"> <li>• ADHD</li> </ul>
Methylphenidate MR	<ul style="list-style-type: none"> <li>• ADHD</li> </ul>	<ul style="list-style-type: none"> <li>• ADHD in a patient diagnosed between ages 6 to 18, who require continuous coverage and has demonstrated a response to IR methylphenidate.</li> </ul>
Atomoxetine	<ul style="list-style-type: none"> <li>• ADHD as defined by the DSM-IV criteria for people aged ≥6 years.</li> </ul>	<ul style="list-style-type: none"> <li>• ADHD as defined by the DSM-V criteria, diagnosed by a paediatrician or psychiatrist, in patients diagnosed between ages 6 to 18, who are contraindicated to or intolerant of stimulant treatment.</li> </ul>
Lisdexamfetamine	<ul style="list-style-type: none"> <li>• ADHD treatment commenced by specialist</li> <li>• Moderate to severe Binge Eating Disorder in adults when non-pharmacological treatment is unsuccessful or unavailable. Must be commenced and managed by specialist.</li> </ul>	<ul style="list-style-type: none"> <li>• ADHD in a patient diagnosed between ages 6 to 18, who require continuous coverage over 12 hours.</li> </ul>
Guanfacine	<ul style="list-style-type: none"> <li>• ADHD in children and adolescents aged 6-17 years old, as monotherapy (when stimulants or atomoxetine are not suitable, not tolerated or have been shown to be ineffective) or as adjunctive therapy to psychostimulants.</li> </ul>	<ul style="list-style-type: none"> <li>*Not listed on the PBS at the time of report but was recommended by the PBAC for listing at its July 2017 meeting.</li> <li>*Minor submission to extend the PBS approved listing to be considered on the July 2018 PBAC Meeting</li> </ul>

Sources: Therapeutic Goods Administration (2018), [Australian Register of Therapeutic Goods](#). Accessed: February 2018. Department of Health (2018), [Schedule of Pharmaceutical Benefits](#). Effective 1 February 2018. Accessed February 2018.

### **Black box warnings**

Dexamfetamine, lisdexamfetamine and methylphenidate have black box warnings concerning drug dependence. They should be used cautiously in people with a history of drug or alcohol dependence. Chronic abuse may lead to tolerance, psychological dependence and abnormal behaviour.<sup>5,10,11</sup> Supervision is required during withdrawal from abusive use since severe depression may occur. Withdrawal following chronic therapeutic use may unmask symptoms of the underlying disorder that may require follow-up.

Atomoxetine has a black box warning to monitor patients for suicidal thoughts and behaviours. Short-term placebo-controlled studies showed a positive signal for suicidal thoughts and behaviours in children aged 12 years and under.<sup>12</sup>

## **Safety alerts**

The TGA issued a safety alert for atomoxetine in November 2011 advising that the medication can cause clinically significant increases in heart rate and blood pressure in some patients and that its use is contraindicated in patients with symptomatic cardiovascular diseases, moderate to severe hypertension, or severe cardiovascular disorders, whose condition would be expected to deteriorate if they experienced increases in blood pressure or in heart rate.<sup>12</sup>

The TGA issued another safety alert for atomoxetine in October 2013 advising the risk of suicidal ideation and behaviour in children and adolescents.<sup>13</sup> The advice reinforced that while the risks of suicidal ideation and behaviour are well known, it is important that health professionals adequately inform parents and caregivers of the risks of suicidal ideation and behaviour in children and adolescents taking atomoxetine.

In October 2014, the TGA issued a safety alert advising health professionals that in very rare cases, treatment with methylphenidate may potentially lead to prolonged and sometimes painful erections.<sup>14</sup>

## **Dosage and administration**

Treatment is usually commenced on dexamfetamine, lisdexamfetamine or the immediate release (IR) formulation of methylphenidate. Doses are started low and then up-titrated weekly to optimal doses.<sup>3</sup>

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<sup>13</sup> Therapeutic Goods Administration (2013), Atomoxetine and suicidality in children and adolescents. Accessed on: 09 February 2018, at: <https://www.tga.gov.au/publication-issue/medicines-safety-update-volume-4-number-5-october-2013#atomoxetine>

<sup>14</sup> Therapeutic Goods Administration (2014), Methylphenidate and priapism. Accessed on: 09 February 2018, at: <https://www.tga.gov.au/publication-issue/medicines-safety-update-volume-5-number-5-october-2014-0#methylphenidate>

**Table 2: Dosage and administration of ADHD Medications**

Brand name and sponsor	Product	Dose and frequency of administration
Aspen Dexamfetamine Aspen Pharma Pty Ltd	Dexamfetamine sulfate 5mg tablets	2.5mg daily in divided doses, with 2.5mg weekly increments until optimal response. Maximum of 40mg daily in two divided doses.
Ritalin Novartis Pharmaceuticals Australia Pty Ltd	Methylphenidate hydrochloride 10mg tablets	5mg, once or twice daily with gradual increments of 5-10mg weekly (children and adolescents). Total daily dose to be administered in divided doses.  Maximum of 60mg daily in children and adolescents.
Ritalin LA Novartis Pharmaceuticals Australia Pty Ltd	Methylphenidate hydrochloride 10mg, 20mg, 30mg, 40mg tablets	Dose taken once daily and should equal to the total daily dose of IR formulation OR 20mg once daily with gradual increments until response.  Maximum of 60mg daily in children and adolescents, and 80mg in adults.
Concerta Janssen-Cilag Pty Ltd	Methylphenidate hydrochloride 18mg, 27mg, 36mg, 48mg tablets	Dose should approximately equal to total daily dose of IR formulation OR 18mg once daily with gradual increments of 9mg (children and adolescents) or increments of 18mg (adults) until optimal response.  Maximum of 54mg daily in children and adolescents, and 72mg in adults.
Vyvanse Shire Australia Pty Ltd	Lisdexamfetamine dimesilate 30mg, 50mg, 70mg capsules	30mg once daily, with 20mg weekly increments until optimal response.  Maximum of 70mg daily.
Strattera Eli Lilly Australia Pty Ltd	Atomoxetine 10mg, 18mg, 25mg, 40mg, 60mg, 80mg capsules	Initial: 0.5mg/kg/day or 40mg/day (whichever is less)  Maximum: 1.4mg/kg/day or 100mg/day (whichever is less)

Source: Product information for dexamfetamine<sup>10</sup>, methylphenidate<sup>11</sup>, lisdexamfetamine<sup>5</sup> and atomoxetine<sup>12</sup>

Patients taking methylphenidate IR may switch to long-acting methylphenidate once responsive and dose stabilised. Alternative treatments should be considered if the maximum stimulant dose has been reached and significant improvement in symptoms has not occurred after a month or unacceptable side effects have developed.<sup>4</sup>

There are no established guidelines for the length of time a child should be maintained on stimulants.

Full details on dosing and titration schedules can be found in the Product Information. The current Product Information (PI) and Consumer Medicine Information (CMI) are available from [the TGA \(Product Information\)](#) and [the TGA \(Consumer Medicines Information\)](#).



## **PBS listing details (as at February 2018)**

The PBS listing of medicines for the management of ADHD is listed in Appendix B.

### ***Restriction***

#### **Dexamfetamine**

##### **Authority required**

Attention deficit hyperactivity disorder

Treatment must be in accordance with the law of the relevant State or Territory

**Note:** Care must be taken to comply with the provisions of State/Territory law when prescribing this drug

**Note:** 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.

#### **Methylphenidate IR**

##### **Authority required**

Attention deficit hyperactivity disorder. Treatment must be in accordance with the law of the relevant State or Territory

**Note:** Care must be taken to comply with the provisions of State/Territory law when prescribing methylphenidate hydrochloride.

**Note:** 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.

#### **Methylphenidate MR (Ritalin LA®)**

##### **Authority Required**

Attention deficit hyperactivity disorder

##### **Population criteria:**

- Patient must be or have been diagnosed between the ages of 6 and 18 years inclusive.

##### **Clinical criteria:**

- Patient must have demonstrated a response to immediate-release methylphenidate hydrochloride with no emergence of serious adverse events,

##### **AND**

- Patient must require continuous coverage over 8 hours.

**Note:** Care must be taken to comply with the provisions of State/Territory law when prescribing methylphenidate hydrochloride.

**Note:** 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.

## **Methylphenidate MR (Concerta®)**

### **Authority Required**

Attention deficit hyperactivity disorder

### **Population criteria:**

- Patient must be or have been diagnosed between the ages of 6 and 18 years inclusive.

### **Clinical criteria:**

- Patient must have demonstrated a response to immediate-release methylphenidate hydrochloride with no emergence of serious adverse events,

### **AND**

- Patient must require continuous coverage over 12 hours.

**Note:** Care must be taken to comply with the provisions of State/Territory law when prescribing methylphenidate hydrochloride.

**Note:** 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.

## **Atomoxetine**

### **Authority required (STREAMLINED)**

**6279**

Attention deficit hyperactivity disorder

Treatment Phase: Initial treatment

### **Clinical criteria:**

- The condition must be or have been diagnosed by a paediatrician or psychiatrist according to the DSM-5 criteria, AND
- Patient must have a contraindication to dexamphetamine, methylphenidate or lisdexamfetamine as specified in TGA-approved product information; OR
- Patient must have a comorbid mood disorder that has developed or worsened as a result of dexamphetamine, methylphenidate or lisdexamfetamine treatment and is of a severity necessitating treatment withdrawal; OR
- Patient must be at an unacceptable medical risk of a severity necessitating permanent stimulant treatment withdrawal if given a stimulant treatment with another agent; OR
- Patient must have experienced adverse reactions of a severity necessitating permanent treatment withdrawal following treatment with dexamphetamine, methylphenidate and lisdexamfetamine (not simultaneously).

**Population criteria:**

- Patient must be or have been diagnosed between the ages of 6 and 18 years inclusive.

**Authority required (STREAMLINED)**

**4578**

Attention deficit hyperactivity disorder

Treatment Phase: Continuing treatment

**Clinical criteria:**

- Patient must have previously been issued with an authority prescription for this drug.

**Note:** No increase in the maximum quantity or number of units may be authorised.

**Note:** No increase in the maximum number of repeats may be authorised.

**Lisdexamfetamine**

**Authority Required**

Attention deficit hyperactivity disorder

**Clinical criteria:**

- Patient must require continuous coverage over 12 hours

**Population criteria:**

- Patient must be or have been diagnosed between the ages of 6 and 18 years inclusive.

**Note:** Care must be taken to comply with the provisions of State/Territory law when prescribing methylphenidate hydrochloride.

**Note:** No increase in the maximum quantity or number of units may be authorised.

**Note:** No increase in the maximum number of repeats may be authorised.

**Note:** Special Pricing Arrangements apply

**Note:** 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.

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

***Date of listing on PBS***

The dates of listing and changes to listing for these medicines are available in [Appendix C](#).

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

## ***Relevant aspects of consideration by the Pharmaceutical Benefits Advisory Committee (PBAC)***

The PBAC recommendations for all ADHD medicines listed prior to 2014 are provided in Appendix D. Most medicines have been recommended on a cost-minimisation basis to existing therapies.

### **Lisdexamfetamine (Vyvanse®)**

In July 2013, the PBAC rejected the submission for the listing of lisdexamfetamine on the basis of insufficient clinical evidence to support claims of superiority in comparative effectiveness, non-inferiority in comparative safety and unacceptable cost-effectiveness compared with long-acting methylphenidate. The PBAC considered that some use of lisdexamfetamine would replace dexamfetamine but the majority of use would replace the long acting methylphenidate formulations, as represented by methylphenidate OROS (MPH-OROS). Therefore, dexamfetamine was also considered a suitable comparator for patients in the first-line or initiating treatment setting and methylphenidate OROS was a suitable comparator in the second-line or treatment experienced patients who require longer duration therapy.<sup>15</sup>

In July 2014, the PBAC considered the resubmission and recommended the listing of lisdexamfetamine (Vyvanse®) 30mg, 50mg, 70mg on a cost-minimisation basis compared with long-acting methylphenidate. The PBAC considered that the evidence in the submission demonstrated non-inferiority to long-acting methylphenidate in terms of effectiveness, and inferiority to long-acting methylphenidate in terms of safety. The PBAC noted that weight loss was the most worrying adverse effect.<sup>16</sup>

The resubmission's nominated comparators for lisdexamfetamine are MPH-OROS for first line use and placebo for patients who have not demonstrated an adequate response to MPH-OROS but need longer acting treatment. The ESC did not consider placebo an appropriate comparator on the basis that it would be highly unlikely for clinicians to leave patients completely untreated in the event that they do not respond to MPH-OROS. The ESC considered the appropriate comparators for lisdexamfetamine to be dexamfetamine (where MPH-OROS could be used as the price reference to account for increased compliance and extended duration of effect compared with dexamfetamine) and MPH-OROS.<sup>16</sup>

The resubmission presented a cost-minimisation analysis versus MPH-OROS in children aged 6 to 12, cost-utility analysis versus MPH-OROS in adolescents aged 13-17 and cost-utility analysis versus 'no pharmacological treatment' or 'placebo' as proxy for standard of care in patients who have failed MPH-OROS. The ESC noted that disutilities associated with

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<sup>15</sup> Department of health (2014), PBAC Meeting Public Summary Documents: Lisdexamfetamine dimesilate, capsules 30mg, 50mg and 70mg, Vyvanse®, July 2013. Accessed on: 12 February 2018, at: <http://www.pbs.gov.au/info/industry/listing/elements/pbac-meetings/psd/2013-07/lisdexamfetamine>

<sup>16</sup> Department of Health (2014), PBAC Meeting Public Summary Documents: Lisdexamfetamine dimesilate, capsules, 30mg, 50mg and 70mg, Vyvanse®, July 2014. Accessed on: 12 February 2018, at: <http://www.pbs.gov.au/industry/listing/elements/pbac-meetings/psd/2014-07/lisdexamfetamine-psd-07-2014.pdf>

weight loss over time had not been adequately accounted for, and that this was a concerning limitation in the model. The ESC stated that the only appropriate economic evaluation is a cost-minimisation analysis of lisdexamfetamine versus MPH-OROS.<sup>16</sup>

The PBAC recommended the proposed listing of LDX as an authority required benefit in patients diagnosed between the ages of 6 and 18 years (inclusive). For the restriction, PBAC considered that there should be no requirement for patients to demonstrate response to dexamfetamine, as use of dexamfetamine does not give guidance of dose or tolerability of lisdexamfetamine. The PBAC recommended that lisdexamfetamine should not be treated as interchangeable with any other drugs.<sup>16</sup>

Copies of the PBAC Meeting Outcomes and Public Summary Documents are available on the [PBAC Meetings](#) website.

### Previous reviews by DUSC

DUSC reviewed this therapeutic area in October 2010, as part of the 24 month Predicted versus Actual (PvA) review of atomoxetine. DUSC noted that there was lower than expected utilisation of atomoxetine, which may have been influenced by the listing of Concerta® three months before the listing of atomoxetine and possible over-estimation of the number of patients with the required contraindications to stimulants to meet the restriction.<sup>17</sup>

DUSC reviewed ADHD medicines in June 2012, with further analyses requested by DUSC considered in October 2012.<sup>18</sup> When considering all people treated with ADHD medicines, highest use was in children aged 10 years. DUSC noted that there was steady growth in the utilisation of ADHD medicines between January 2005 and October 2011. PBS benefits paid for ADHD medicines in November 2010–October 2011 totalled around \$24.6 million, up 4.2% from the previous year. The highest cost medicine to the PBS was Concerta® at \$11.2 million, followed by atomoxetine at \$6.2 million, despite its low utilisation.<sup>18</sup>

The DUSC reviewed ADHD medicines again in June 2015.<sup>19</sup> Key findings were:

- The analyses suggested steady growth in the utilisation of ADHD medicines between 2010 and 2014.
- Over 875,000 prescriptions were dispensed at a cost to the PBS of approximately \$30 million in 2014.
- The most commonly used medicine was methylphenidate. The majority of prescriptions supplied for methylphenidate were as the modified release forms.
- The majority of prescriptions were written by a specialist, usually a paediatrician or psychiatrist. Most Australian states and territories restrict the prescribing of

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<sup>17</sup> Drug Utilisation Sub-Committee. DUSC Predicted versus Actual analysis of atomoxetine. Canberra: Australian Department of Health: 2010. Unpublished.

<sup>18</sup> Drug Utilisation Sub-Committee. DUSC Reviews of ADHD Drugs June and October 2012. Canberra: Australian Department of Health: 2010. Unpublished.

<sup>19</sup> Drug Utilisation Sub-Committee. ADHD Utilisation Analysis October 2015. Canberra: Australian Department of Health. Accessed on 12 February 2018, at: <http://www.pbs.gov.au/pbs/industry/listing/participants/public-release-docs/2015-06/attention-deficit-hyperactivity-disorder-2015-06-prd>

methylphenidate and dexamfetamine for the treatment of ADHD to specialist medical prescribers.

- Rates of prescribing varied across states and territories. The rates of treatment in school-aged children were highest in the ACT, NSW and Queensland. Rates of treatment in adults were highest in Western Australia.

## Methods

PBS and RPBS prescription data for PBS-listed ADHD medicines were extracted from the Department of Human Services (DHS) prescription database for the period April 2012 to December 2017 inclusive, based on the date that the prescription was supplied. Data for this period includes all R/PBS supplies regardless of whether a subsidy was paid; i.e. both over co-payment and under co-payment. As dexamfetamine is PBS-listed for both ADHD and narcolepsy, the prescription data for dexamfetamine was merged with the authority approvals database and limited by the ADHD authority restriction number to obtain only the supplies related to ADHD.

The R/PBS prescription data were used to determine the number of prescriptions supplied, R/PBS expenditure, age, sex, state/territory of residence and prescriber type. These prescription data were also used to count the number of patients, both incident (new to pharmacological treatment) and prevalent (number treated) in each time period. The number of prevalent patients was determined by counting the number of people supplied at least one PBS prescription using person-specific numbers (non-identifying) in the data for the specified time periods. Patient initiation date was defined as the date of supply of the first PBS or RPBS prescription of the ADHD medicine (since April 2012).

An analysis of scripts per patient in the 12 months after initiation of PBS lisdexamfetamine was also performed. This analysis was limited to patients that initiated from September 2015 to the end of August 2016, as this cohort of patients had at least 12 months of follow-up data after initiation.

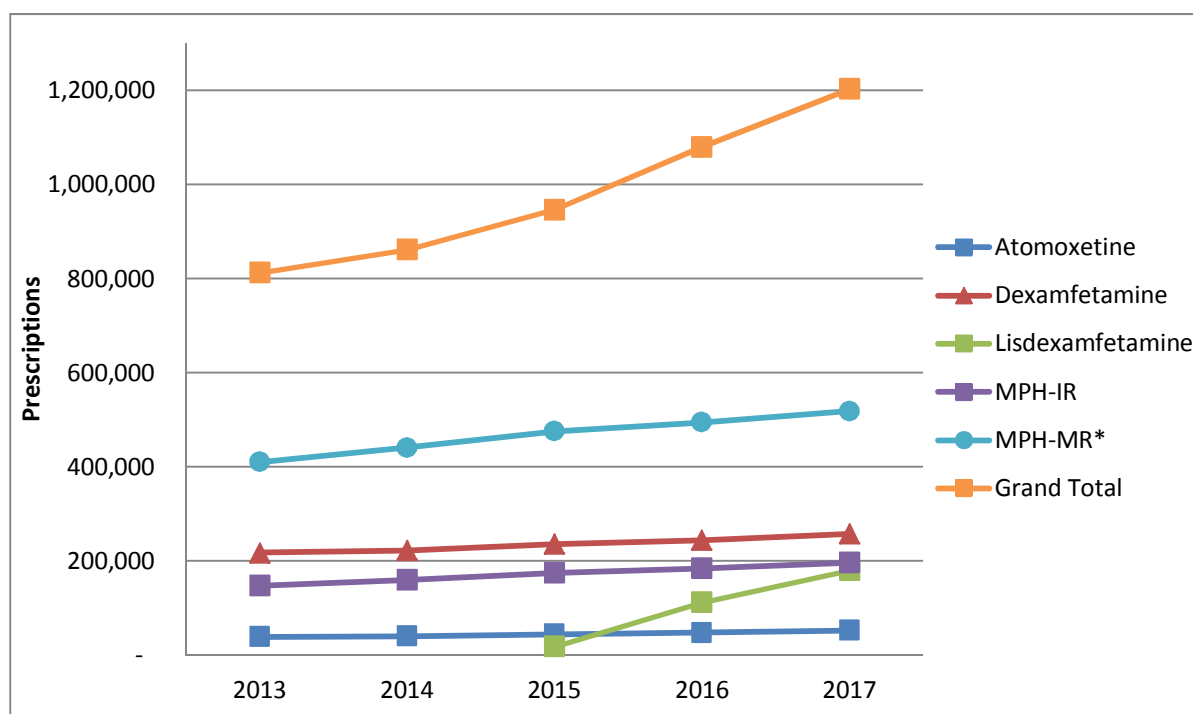
As this analysis uses date of supply prescription data, there may be small differences compared with publicly available Department of Human Services (DHS) Medicare date of processing data. The publicly available DHS Medicare data only includes subsidised R/PBS prescriptions with prescriptions under the patient co-payment not included.

## Results

### Analysis of drug utilisation

#### Overall utilisation

The number of R/PBS prescriptions for ADHD medications supplied per calendar year since 2013 is shown in Figure 1.



**Figure 1: Number of PBS/RPBS ADHD prescriptions supplied per year**

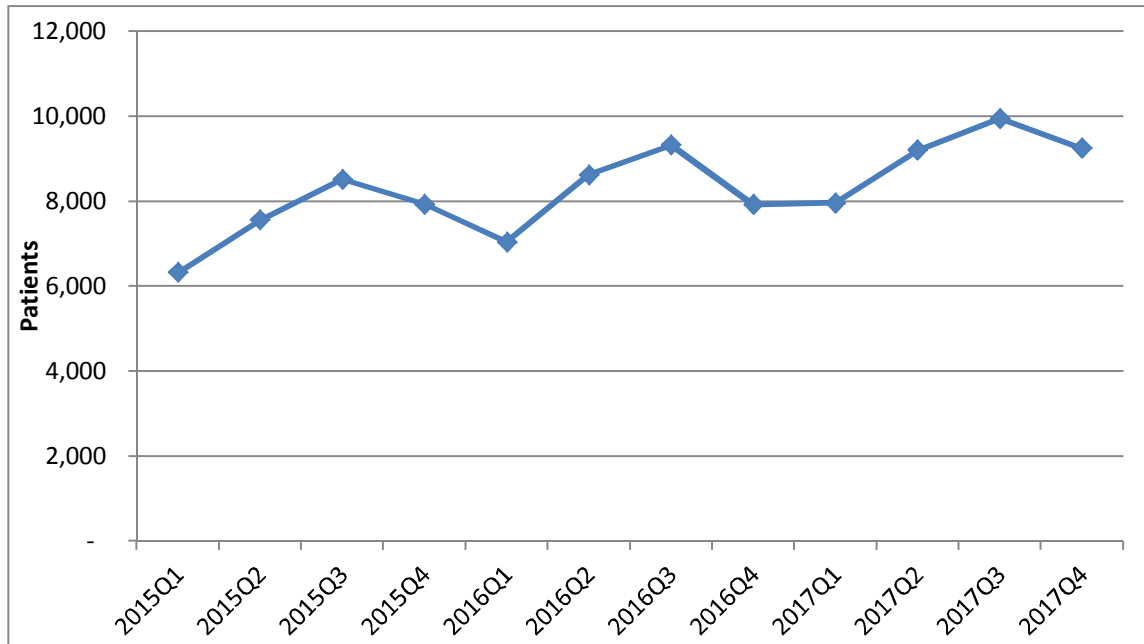
Source: DHS prescriptions database, extracted February 2018

\*MPH-MR consists of both Concerta® and Ritalin LA®

Figure 1 shows an overall increase in the rate of growth in PBS ADHD prescriptions supplied during 2013 to 2017. The average annual growth rate during this period was 10.3%.

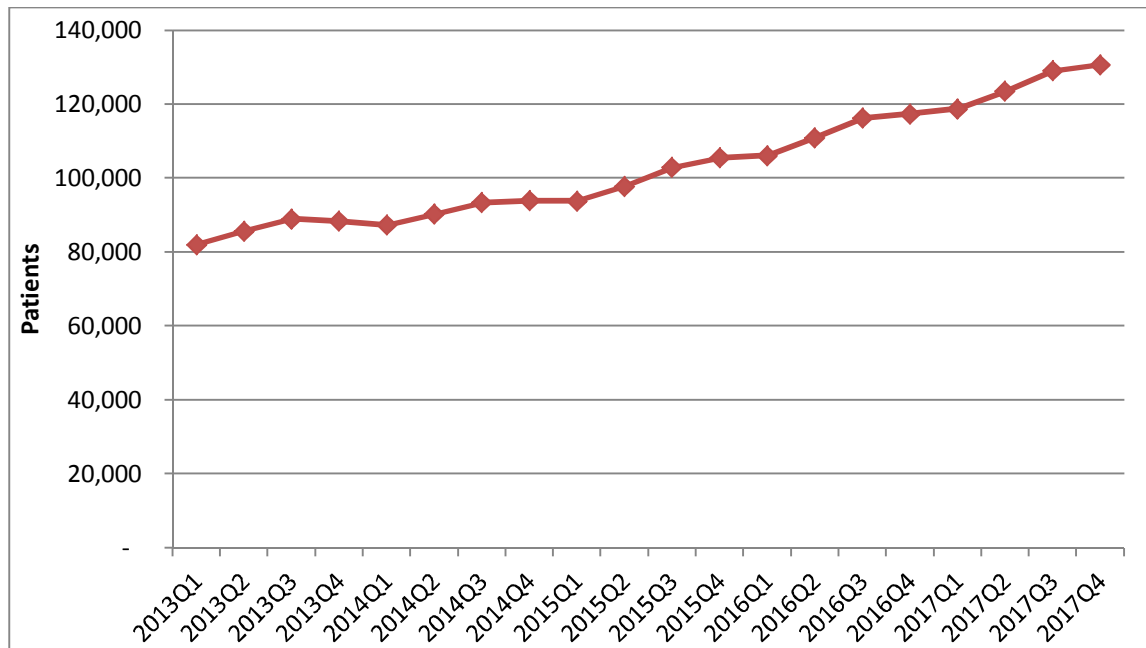
**Patients initiating and prevalent to ADHD therapy**

The total number of new patients starting ADHD medicines (initiating) and the number of patients treated with PBS-listed ADHD medicines each quarter (prevalent) are shown in Figure 2 and 3 respectively.



**Figure 2: Number of patients initiating ADHD therapy per quarter**

Source: DHS prescriptions database, extracted February 2018



**Figure 3: Total number of patients on ADHD therapy per quarter**

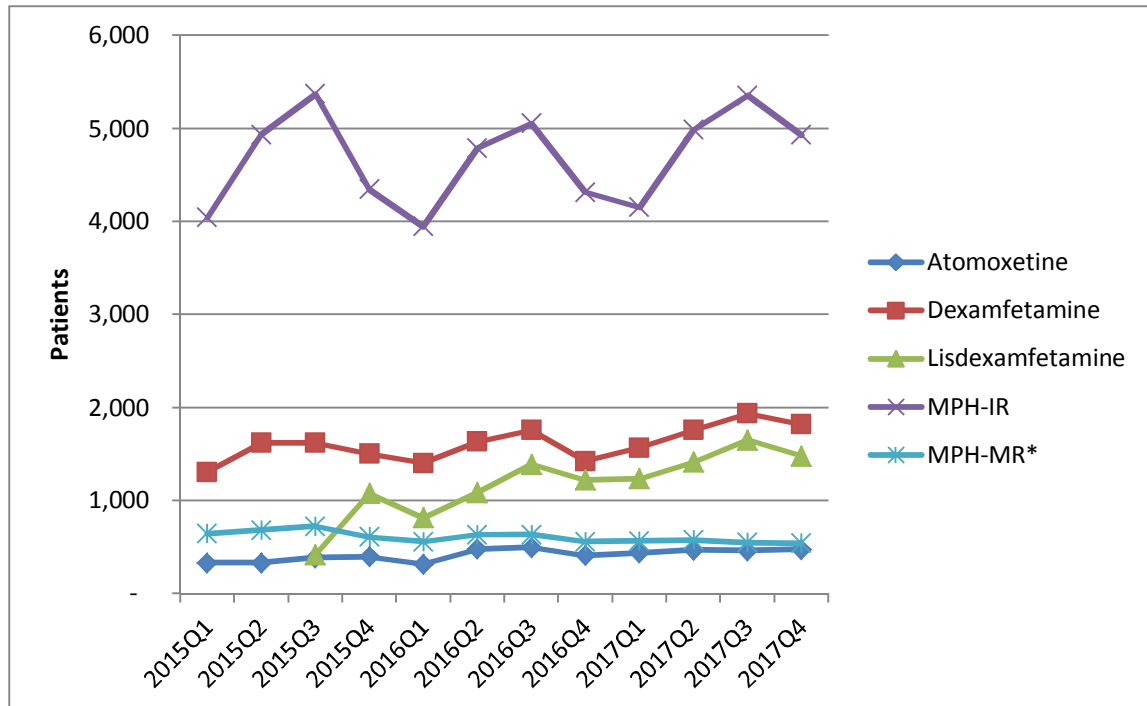
Source: DHS prescriptions database, extracted February 2018



The number of new patients (Figure 2) tends to increase during the year reaching a peak in the third quarter.

The total number of patients on ADHD medicines has increased over time (Figure 3). The average annual growth rate from 2013 to 2017 was 9.9%. Similarly, the number of initiating patients had an average annual growth rate of 9.5% over 2015 to 2017 (Figure 2).

Figure 4 shows the volume of new patients per quarter by their first ever PBS-subsidised ADHD medicine supplied in 2015 to 2017.



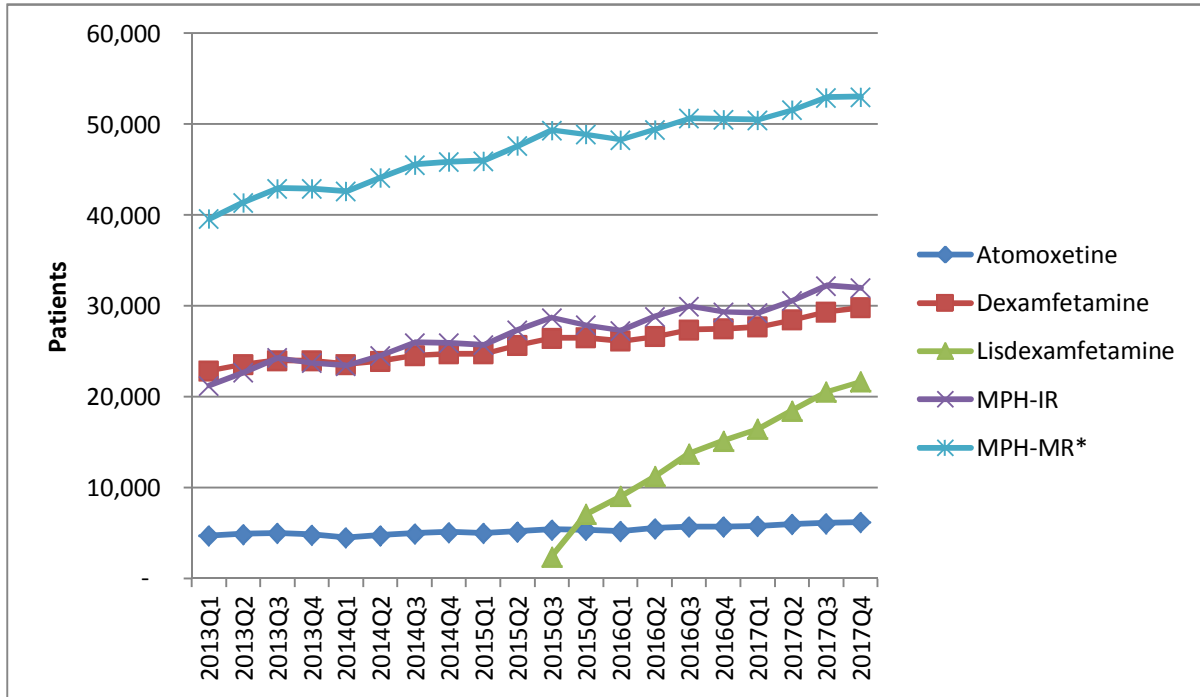
**Figure 4: Number of new patients treated per quarter by initiating ADHD medicine (first ever prescription for ADHD)**

Source: DHS prescriptions database, extracted February 2018

\*MPH-MR Consists of both Concerta® and Ritalin LA®

The majority of new patients (Figure 4) commence PBS ADHD therapy with short-acting medicines; that is, short-acting methylphenidate or dexamfetamine. There has been considerable uptake in lisdexamfetamine as the first ADHD medicine supplied since its PBS listing in 2015, accounting for approximately 15% of the first ADHD medicine supplied to new patients initiating ADHD therapy in 2016 and in 2017.

Figure 5 depicts the volume of all patients per quarter of each ADHD medicine supplied in 2013 to 2017. In Figure 5, patients may be double counted if they are supplied more than one ADHD medicine in the same quarter.



**Figure 5: Total number of patients treated with each ADHD medicines per quarter**

Source: DHS prescriptions database, extracted February 2018

\*MPH-MR Consists of both Concerta® and Ritalin LA®

When considering the total volume of patients treated across all years (Figure 5), long-acting methylphenidate was the most commonly used ADHD medicine. Atomoxetine is used in a small proportion of patients. The use remains stable in light of the change from authority required to streamlined authority listing from August 2014.

***Number of patients by age and gender***

The number of patients treated with PBS-listed medicines for ADHD is shown in Tables 4 and 5. The data is presented as the number of new patients starting PBS-subsidised treatment for ADHD for the first time (Table 4) from 2015 to 2017 and total patients treated (Table 5) from 2013 to 2017, by age group and gender.

**Table 4. Number of new patients treated with PBS-listed ADHD medicines by age group and gender per calendar year**

	2015	2016	2017
<6 years male	1,646	1,796	1,990
<6 years female	450	471	499
6-12 years male	11,719	12,607	13,617
6-12 years female	3,389	3,753	4,310
13-17 years male	2,485	2,510	2,809
13-17 years female	1,224	1,296	1,482
18+ years male	5,736	6,370	6,859
18+ years female	3,680	4,106	4,787
Unknown	7	<=5	<=5
<b>Total New patients</b>	<b>30,336</b>	<b>32,914</b>	<b>36,357</b>
<b>% growth from previous year</b>		8.5%	10.5%

Source: DHS prescriptions database, extracted February 2018. Unknown denotes age and sex not available in the data. Patient counts may be slightly perturbed to protect confidentiality.

**Table 5. Total number of patients treated with PBS-listed ADHD medicines by age group and gender per calendar year**

	2013	2014	2015	2016	2017
<6 years male	2,226	2,277	2,334	2,518	2,807
<6 years female	521	516	619	653	676
6-12 years male	38,216	40,870	45,506	50,726	55,880
6-12 years female	9,716	10,471	11,672	13,312	15,195
13-17 years male	19,310	19,793	21,129	22,729	24,916
13-17 years female	5,397	5,742	6,314	6,996	7,871
18+ years male	23,500	25,088	27,898	31,508	35,022
18+ years female	13,634	14,727	16,632	18,834	21,583
Unknown	77	73	79	16	33
<b>Total New patients</b>	<b>112,597</b>	<b>119,557</b>	<b>132,183</b>	<b>147,292</b>	<b>163,983</b>
<b>% growth from previous year</b>		6.2%	10.6%	11.4%	11.3%

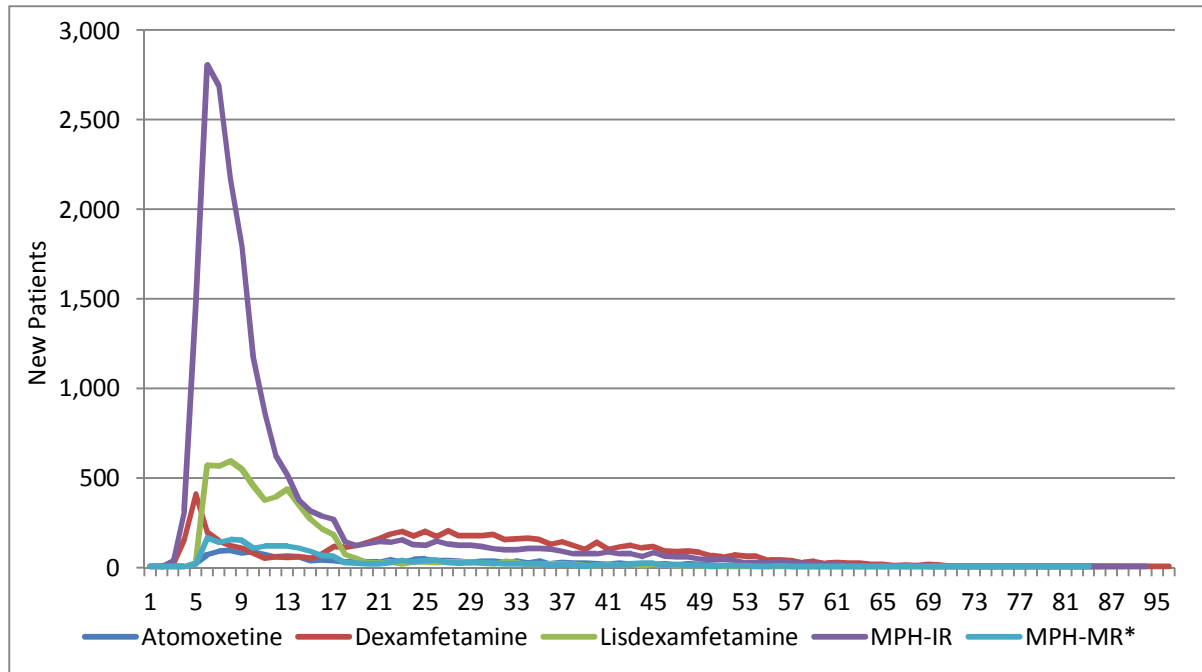
Source: DHS prescriptions database, extracted February 2018. Unknown denotes age and sex not available in the data.

Children aged 6-12 years constituted 40% of all patients treated with ADHD medicines from 2013 to 2017. In addition, over the same period, approximately two thirds of patients supplied PBS ADHD medicines were less than 18 years of age.

The average annual growth rate between 2013 and 2017 differed slightly in males and females; with females at a higher rate of 11.6% and males at 9.3%. The ratio of males to females receiving an ADHD medicine gradually decreased from 2.8 in 2013 to 2.6 in 2017.

Figure 6 depicts the age distribution of patients new to PBS-subsidised ADHD therapy in 2017 by the first ever ADHD medicine they were supplied. Figure 7 shows the age distribution for all patients supplied an ADHD medicine in 2017 by medicine. In Figure 7,

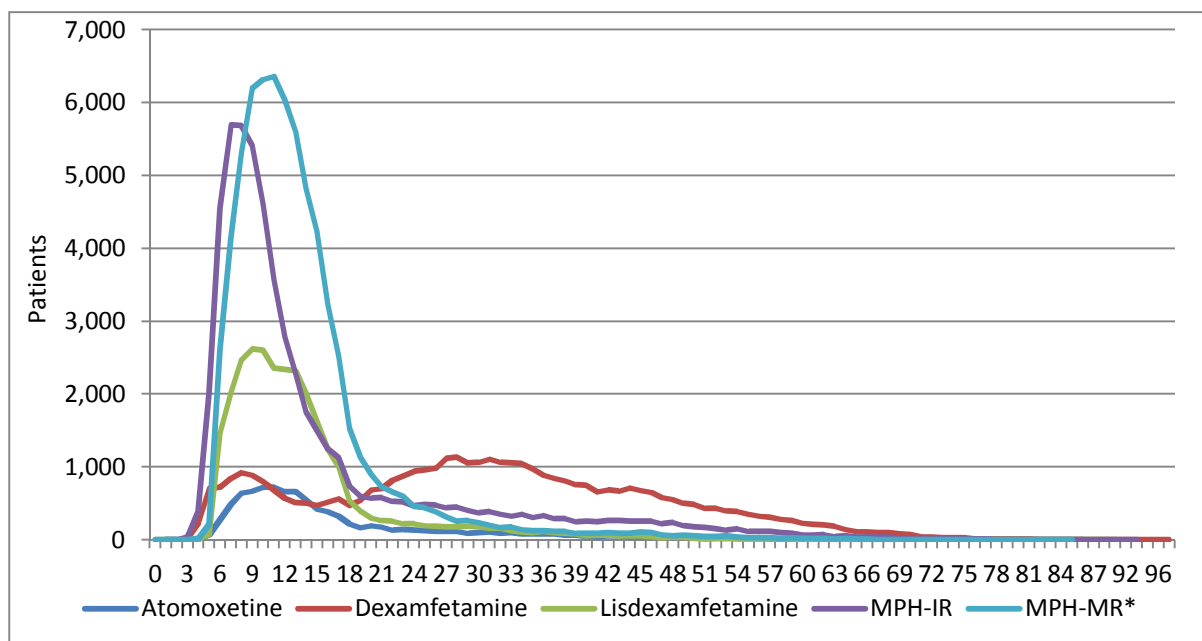
patients may be double counted if they are supplied more than one ADHD medicine in the same year.



**Figure 6: Age distribution of patients new to ADHD therapy by first ever ADHD medicine supplied, 2017**

Source: DHS prescriptions database, extracted February 2018. Note: where the patient count is between 1 and 5 (inclusive), the data point has been set to 5 to protect confidentiality.

\*MPH-MR Consists of both Concerta® and Ritalin LA®



**Figure 7: Age distribution of prevalent patients by ADHD medicine, 2017**

Source: DHS prescriptions database, extracted February 2018. Note: where the patient count is between 1 and 5 (inclusive), the data point has been set to 5 to protect confidentiality.

\*MPH-MR Consists of both Concerta® and Ritalin LA®

In children and adolescents, the most common initiating medicine for ADHD is short-acting methylphenidate followed by lisdexamfetamine (Figure 6). While short-acting methylphenidate is the most used initiating medicine in school-aged children, long-acting methylphenidate formulations are also largely used in this age group (Figure 7). This indicates that children either switch therapy from short-acting to long-acting formulations or that long-acting formulations are added to short-acting therapy.

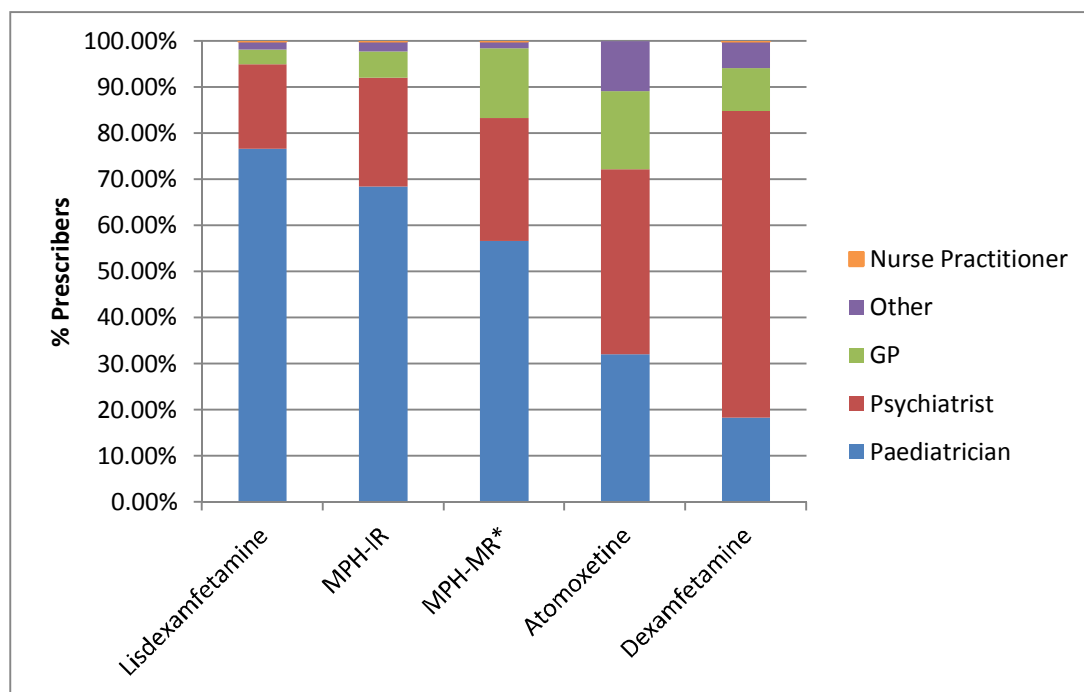
In adults commencing PBS-subsidised therapy for the first time, dexamfetamine is the most common medicine, followed by short-acting methylphenidate (Figure 6). Dexamfetamine is most commonly used in all adults receiving ADHD therapy over the age of 21 (Figure 7).

**Prescribers**

Each State and Territory law stipulates the conditions under which medical practitioners are able to prescribe ADHD medicines. This is summarised in Appendix A.

The PBS restriction for atomoxetine requires that the diagnosis is made by a paediatrician or psychiatrist according to the DSM-5 criteria. Nurse practitioners can prescribe continuing therapy for all ADHD medicines except atomoxetine providing they also comply with State/Territory law.

Figure 8 shows the type of prescribers for each first PBS ADHD medicine supplied to all new patients in 2017.



**Figure 8: Initial prescriptions<sup>a</sup> in 2017 by ADHD medicine and prescriber type**

Source: DHS prescriptions database, extracted February 2018

\*MPH-MR Consists of both Concerta® and Ritalin LA®

<sup>a</sup> initial prescription = first prescription for patients who received their first PBS ADHD medicine in 2017

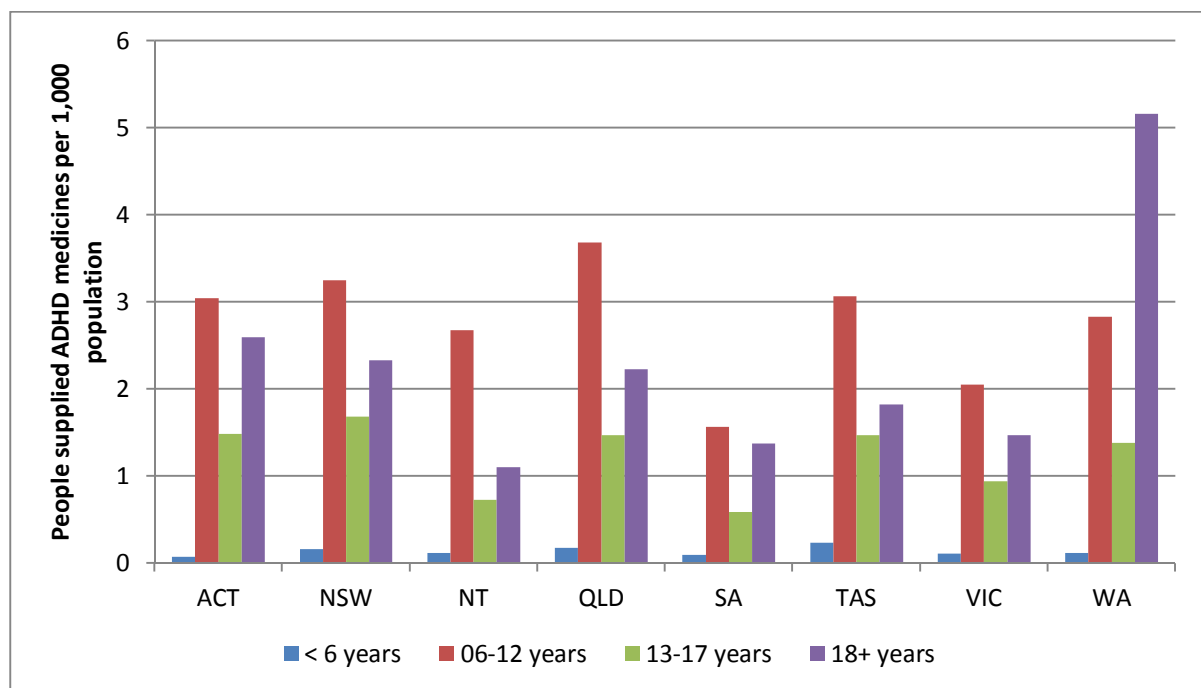
The initial prescriber for commencing an ADHD medicine is influenced by state and territory regulations. The initial prescriber type for initiating ADHD medicines is also influenced by the age of the patient.

For first prescriptions of lisdexamfetamine and methylphenidate, a large proportion of initial prescribers were paediatricians. As the age distribution of lisdexamfetamine and methylphenidate use were more common in adults under 18 years (Figure 7), paediatricians are more likely to be involved in the management of ADHD.

First prescriptions of dexamfetamine were more commonly prescribed by psychiatrists. As the age distribution of dexamfetamine use were more common in adults over 18 years (Figure 7), psychiatrists are more likely to be involved in the management of ADHD.

### Utilisation by State/Territory

Figure 9 shows the number of people supplied ADHD medicines per 1,000 population in 2017, broken down by age and patient state/territory, and adjusted to account for the size and age distribution in each state/territory for 2017.



**Figure 9: Number of people supplied an ADHD medicine per 1000 population in 2017 by patient state/territory and age group**

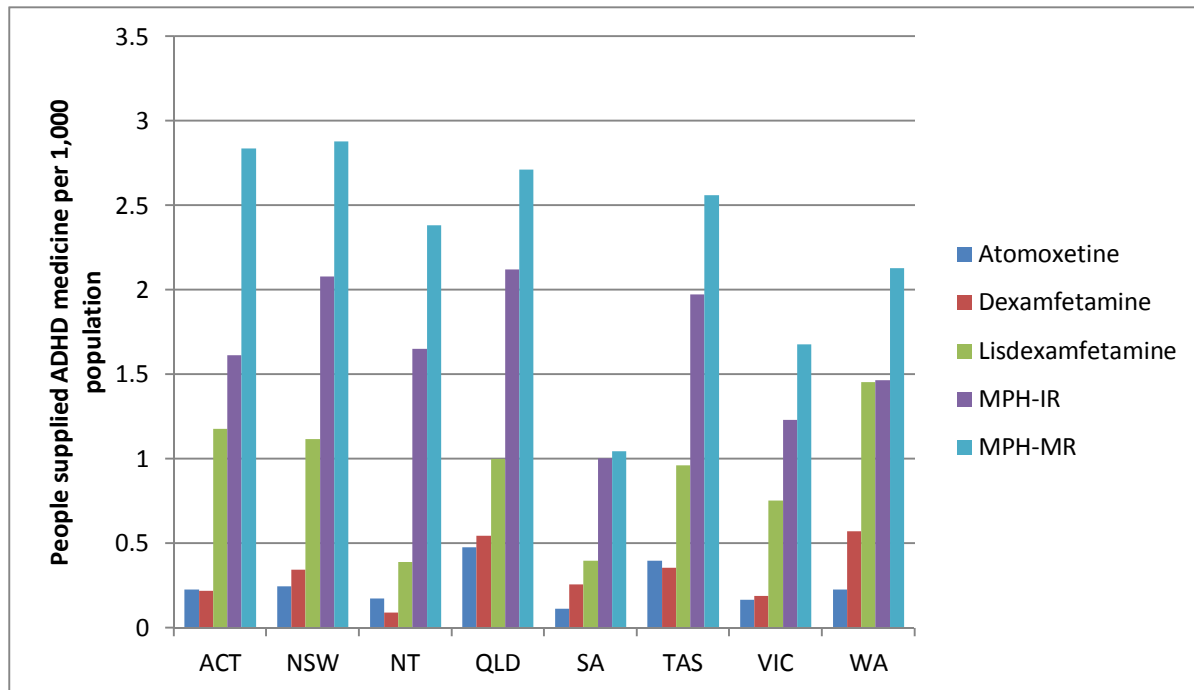
Source: DHS prescriptions database, extracted February 2018

For children under 6 years, the rate of ADHD medicine supply was low, ranging from 0.07/1000 population in the ACT to 0.23/1000 population in Tasmania.

The rate of ADHD medicine supply in the 6-12 year age group was highest in QLD. The rate of ADHD medicine supply in adolescents was highest in NSW, followed by the ACT. For

adults, the rate of supply of ADHD medicine was much higher in WA than all other states and territories, consistent with the findings in previous DUSC reports.

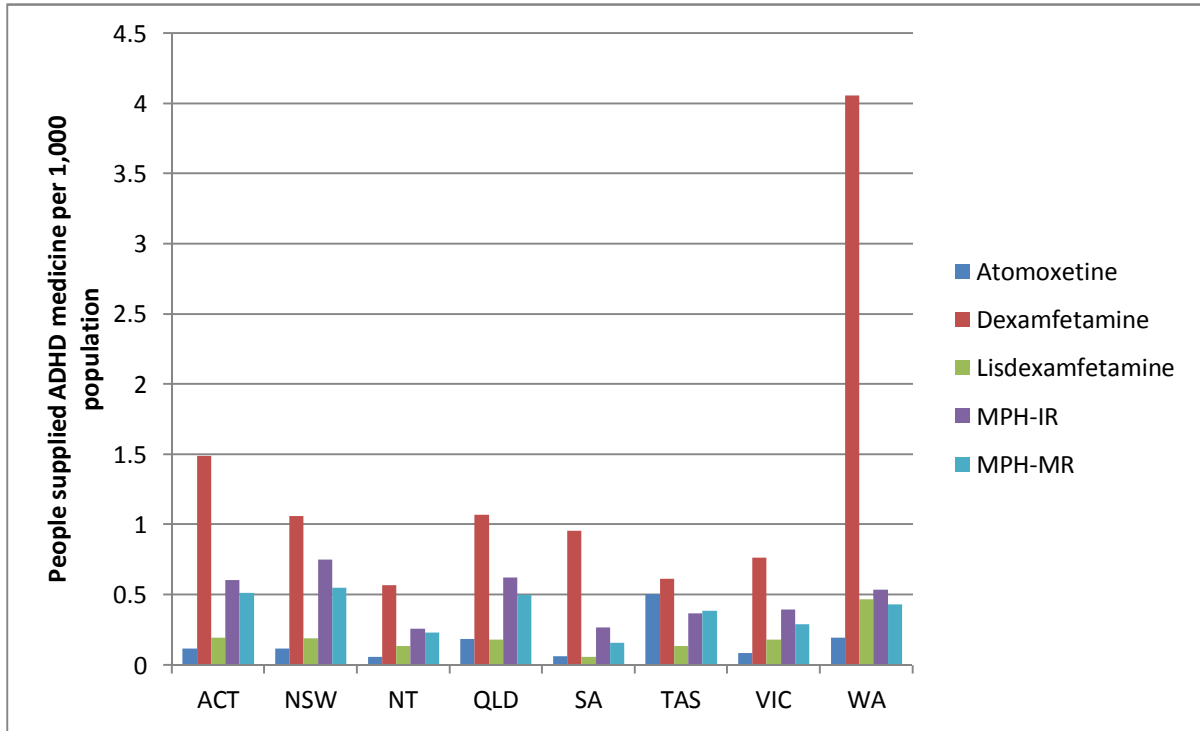
Figures 10 and 11 depict the number of people supplied ADHD medicines per 1,000 population in 2017 for patients under the age of 18 and those over 18, respectively. The figures are presented by medicine and patient state/territory, and are adjusted to account for the population size and age distribution in each state/territory in 2017.



**Figure 10: Number of people aged  $\leq 17$  years supplied an ADHD medicine per 1,000 population in 2017 by patient state/territory and medicine (age adjusted<sup>b</sup>)**

Source: DHS prescriptions database, extracted February 2018

<sup>b</sup> based on 2017 ABS estimated residential population data



**Figure 11: Number of people aged  $\geq 18$  years supplied an ADHD medicine per 1,000 population in 2017 by patient state/territory and medicine (age adjusted<sup>b</sup>)**

Source: DHS prescriptions database, extracted February 2018

<sup>b</sup> based on 2017 ABS estimated residential population data

The pattern of ADHD medicines use varied across the states and territories. In age groups (under 18s and those 18 and older), the rate of patients supplied lisdexamfetamine and dexamfetamine is higher in Western Australia compared to other states and territories.

Conversely, South Australia had the lowest rate of supply in patients aged less than 18 years for most ADHD medicines (atomoxetine, lisdexamfetamine, short-acting methylphenidate and long-acting methylphenidate).



## Approach taken to estimate utilisation

\*\*\*Commercial-in-confidence\*\*\*

[REDACTED]

[REDACTED]

[REDACTED]

[REDACTED]



## Analysis of actual versus predicted utilisation

Table 7 presents the predicted versus actual utilisation of lisdexamfetamine. The results presented are based on date of supply. As a result, there may be small differences between publicly available DHS Medicare dates of processing data.

**Table 7. Lisdexamfetamine: actual versus predicted utilisation**

		Year 1	Year 2
<b>Patients</b>	Predicted	████	████
	Actual	17,366	26,858
	% Difference	████	████
<b>Prescriptions</b>	Predicted	████	████
	Actual	83,246	158,405
	% Difference	██	██
<b>Prescriptions per patient (Average)</b>	Predicted	████	████
	Actual	4.79	5.90
	% Difference	████	████
<b>Published Expenditure*</b>	Predicted	████████	████████
	Actual	\$8,073,510	\$15,361,999
	% Difference	████	████

Source: Lisdexamfetamine Final Estimates (predicted), DHS prescriptions database (actual), extracted February 2018.

Predicted values are in packs and actuals are in prescriptions; these units are equivalent in this instance

\*Expenditure does not include special pricing arrangement.

In the first year of listing, the total number of patients that received a prescription for lisdexamfetamine was much higher (████ fold) than the number predicted. However, the total number of packs supplied and expenditure to the R/PBS was slightly less than the numbers predicted.

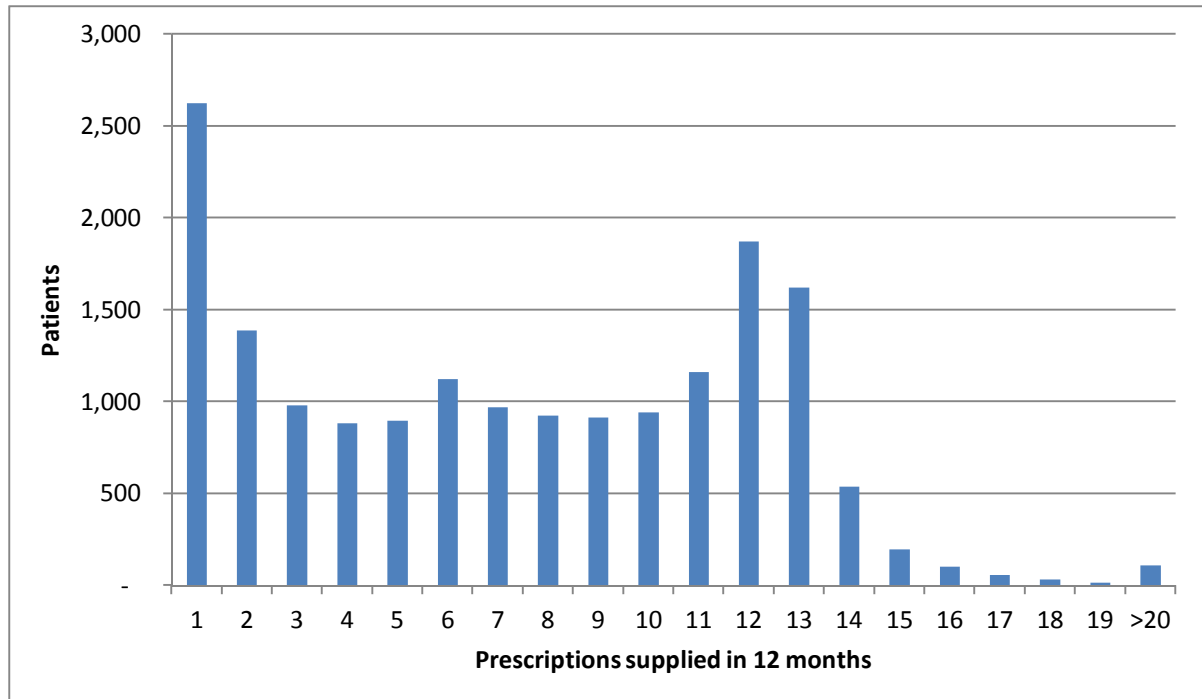
In the second year of listing, the total number of patients was also substantially higher at █████ fold above the expected number. This translated to only a slightly higher than expected volume of packs supplied and expenditure.

### **Prescriptions per patient**

The difference between the predicted and actual patients and prescription volume (Table 7) arises from patients receiving fewer prescriptions per year than predicted. The agreed estimate assumed that each patient would receive █████ prescriptions per year. This did not account for patients that commence or cease treatment part way through the first listing year.

The number of prescriptions per patient in the 12 months after initiation was calculated (Figure 12) for lisdexamfetamine patients that initiated from September 2015 to the end of

August 2016 (n=17,366); to allow for 12 months of follow-up for each patient. Prescriptions supplied include all strengths of lisdexamfetamine.



**Figure 12: Distribution of the number of lisdexamfetamine prescriptions per patient in 12 months post-initiation**

Source: DHS prescriptions database, extracted February 2018

Out of the 17,366 patients starting on lisdexamfetamine, 15% received no further prescriptions in the 12 month period (Figure 12). A further 30% of patients had between two and six scripts dispensed in the 12 month period. On average, patients received seven prescriptions per year in the first year of therapy; much lower than predicted in the submission. *This might be due to discontinuation of lisdexamfetamine. In the SPD489-326 open-label study involving children and adolescents aged 6-17 years, 40% of patients discontinued from the trial.<sup>20</sup> 15.9% of enrolled patients were found to have discontinued due to adverse events and 7.6% due to a lack of efficacy.<sup>20</sup> Most adverse events were found to occur within the first four weeks of treatment initiation.<sup>21</sup>*

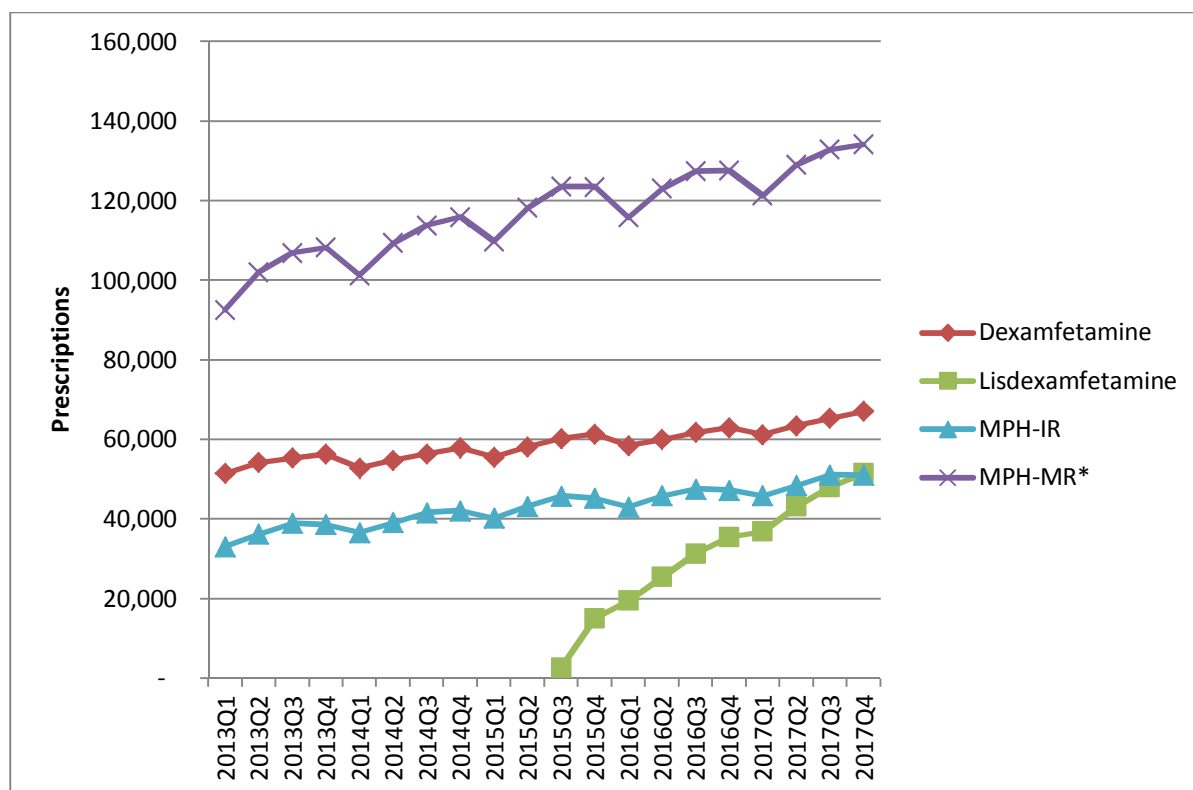
<sup>20</sup> Coghill D, Banachewski T, Lecendreyx M, Johnson M, Zuddas A, Squires L, et al. Maintenance of efficacy of lisdexamfetamine dimesilate in children and adolescents with attention-deficit/hyperactivity disorder: randomized-withdrawal study design. *Journal of The American Academy of Child and Adolescent Psychiatry* [serial on the Internet]. (2014, June), [cited April 23, 2018]; 53(6):647-657.e1. Available from: MEDLINE with Full text

<sup>21</sup> Coghill DR, Caballero B, Sorooshian S, Civil R. A Systematic Review of the Safety of Lisdexamfetamine Dimesylate. *CNS Drugs*. (2014, May). [cited April 23, 2018]; 2014;28(6):497-511. Available from: MEDLINE with Full text

### Changes in the use of other medicines for ADHD

Figure 13 depicts another version of Figure 1, representing the total prescriptions supplied for several key ADHD medicines (methylphenidate IR, methylphenidate MR, dexamfetamine and lisdexamfetamine) for Q1 2013 to Q4 2017.

This data is provided to investigate if the listing of lisdexamfetamine has affected the prescription volumes for these agents. The submission estimated the proportion of switching to lisdexamfetamine and the associated offset in cost.



**Figure 13: PBS/RPBS ADHD prescriptions supplied per quarter**

Source: DHS prescriptions database, extracted February 2018

\*MPH-MR Consists of both Concerta® and Ritalin LA®

The rate of growth in prescriptions supplied for methylphenidate IR, methylphenidate MR and dexamfetamine were largely unchanged by the listing of lisdexamfetamine. The submission predicted a reduction of [REDACTED] prescriptions of long-acting methylphenidate in the first year of listing of lisdexamfetamine due to substitution. This decline was not observed in Figure 13.

The listing of lisdexamfetamine has resulted in growth of the overall PBS ADHD medicine market. Lisdexamfetamine had been expected to mostly substitute for long-acting formulations of methylphenidate. Further analysis may be warranted to investigate the medicines used before, with and after lisdexamfetamine to better understand the way it is being used in practice.

## Discussion

Overall, the utilisation of ADHD medicines listed on the R/PBS increased between 2013 and 2017. This trend is consistent for prescriptions and patient data over this period.

The pattern of use in relation to age and gender has not changed over time. Children aged 6-12 constitute 40% of patients treated with ADHD medicines. The ratio of males to females is decreasing over time, potentially due to increased rates of diagnosis in females.

The graphs representing the pattern of use across states and territories were age adjusted for the 2017 population and are not directly comparable to the previous DUSC review in 2015.<sup>19</sup> However, the trend across the states and territories were similar and have not considerably changed over time. The greater rate of ADHD medicines supplied to adults in WA compared with other states was consistent in 2014 and in 2017. A slightly higher rate of dexamfetamine supply was also observed in WA for children and adolescents under 18 years.

The sponsor of lisdexamfetamine anticipated substitution of other ADHD treatments and considered that the listing of lisdexamfetamine would not cause growth in the market. However, there was higher growth observed in prescriptions supplied, patients and expenditure from 2016; the listing of lisdexamfetamine increased the rate of growth beyond the previous trend. A breakdown of total prescriptions by medicine did not show substitution of lisdexamfetamine for other ADHD treatments. Therefore, the drug cost offsets estimated in the submission have not been realised.

In the first two years of lisdexamfetamine listing, the total number of patients was much higher than the number projected. While the number of patients supplied lisdexamfetamine was higher than predicted, these patients received fewer prescriptions per year than anticipated. This translated to a total volume of prescriptions that was similar to the expected value in the first year and slightly higher in the second year.

The observed prescriptions supplied per patient are less than predicted due to differences between the assumptions in the sponsor's submission and use of lisdexamfetamine in practice. Possible explanations for this include that the submission did not account for:

- A "half-cycle correction" that allows for some patients commencing treatment part way through the year
- Cessation of use due to adverse effects, as lisdexamfetamine is more likely to cause weight loss than long-acting methylphenidate<sup>16</sup>
- Drug holidays (periods of intended cessation) that are commonly taken in children with ADHD<sup>22</sup>
- Combination use with other ADHD medicines to optimally manage the condition

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<sup>22</sup> Ibrahim K, Donyai P. Drug Holidays From ADHD Medication: International Experience Over the Past Four Decades. *Journal of Attention Disorders* [serial on the internet]. (2015, July), [cited March 1, 2018]; 19(7):551-568. Available from: MEDLINE with Full text.

## DUSC consideration

DUSC noted that clinical practice guidelines for the management of ADHD have not been updated with the addition of new medicines to the market (i.e. lisdexamfetamine and guanfacine). Patients requiring ADHD treatment are usually commenced on a low dose of dexamfetamine, lisdexamfetamine or the short-acting formulation of methylphenidate and up-titrated to optimal doses. Once dose stabilised, patients may switch from short-acting to long-acting methylphenidate. While a co-administration analysis was not performed in this review, DUSC noted that there is a degree of co-prescribing of short and long-acting formulations in clinical practice. The dosing of ADHD therapy is complex and dependant on multiple external factors (e.g. timing required for symptomatic control during school hours). DUSC considered that input from clinicians and consumers would help understand the patterns of use for future reviews of ADHD medicines.

The utilisation of ADHD medicines increased between 2013 and 2017 in terms of both prescriptions and patients. DUSC expressed concern that the average rate of growth during this period was high. DUSC considered that the growth in the market could be due to improved diagnosis and recognition, but may also be due to overdiagnosis and overtreatment of ADHD. Additionally, DUSC discussed potential off-label use (e.g. fatigue and depression) or diversion and abuse as factors that may contribute to the growth in the market. DUSC also noted that the listing of lisdexamfetamine contributed to the market growth.

Although more males than females were treated, DUSC commented on the higher rate of growth in females, as evidenced by the almost doubling of the number of females treated between 2013 and 2017 (Table 5 of the report).

With respect to utilisation by age, the number of adult patients over the age of 18 initiating ADHD treatment and the total number of adult patients steadily increased over time. Short-acting methylphenidate and dexamfetamine restrictions do not require that patients must be diagnosed in their paediatric years and only require that the treatment must be in accordance with the law of the relevant State or Territory. This may explain why adults are more likely to receive dexamfetamine and short-acting methylphenidate (Figure 6 of the report).

The majority of ADHD prescriptions were written by paediatricians or psychiatrists. Most Australian states and territories restrict the prescribing of stimulants for the treatment of ADHD to specialists. DUSC considered that specialists may have preferences over the prescribing of specific formulations of ADHD medicines; psychiatrist's preference for dexamfetamine compared to paediatrician's preference for methylphenidate.

DUSC noted that rates of prescribing varied across states and territories, and that the trend has not changed over time.

The predicted versus actual analysis of lisdexamfetamine showed that the number of patients who received lisdexamfetamine was higher than predicted for the first two years, while prescriptions were slightly lower in the first year and only slightly higher in the second year. DUSC noted that while more patients were supplied lisdexamfetamine than

predicted, these patients received fewer prescriptions per year than anticipated. DUSC further noted that the addition of lisdexamfetamine caused an increase in growth of the overall market.

## **DUSC actions**

- DUSC requested that the report be provided to the PBAC

## **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**

No comments were received from sponsors (Aspen Pharma Pty Ltd; Novartis Pharmaceuticals Australia Pty Limited; Janssen-Cilag Pty Ltd; Eli Lilly Australia Pty Ltd; Arrow Pharma Pty Ltd; Apotex Pty Ltd; Amneal Pharmaceuticals Pty Ltd; Sandoz Pty Ltd; Shire Australia Pty Ltd).



## **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: Summary of state and territory regulations for the prescribing of psychostimulants**

Dexamfetamine, lisdexamfetamine and methylphenidate are Schedule 8 medicines under the Standard for the Uniform Scheduling of Medicines and Poisons (SUSMP). Schedule 8 medicines have a high potential for abuse and dependence. The prescribing and supply of Schedule 8 medications are tightly regulated, and regulations vary between each state and territory. A summary of these regulations is presented below in Table A.

Most Australian states and territories restrict the prescribing of psychostimulants for the treatment of ADHD to specialist medical practitioners, including psychiatrists, neurologists and paediatricians. These specialist prescribers are generally required to obtain prior authorisation from the relevant state or territory regulatory body for each patient. Prescribing of psychostimulants to patients under the age of 2 years is generally prohibited, and there are additional regulatory requirements to prescribe psychostimulants to patients aged between 2 to 3 years old.

There are some variations and exceptions to the regulatory requirements between states and territories. For example, some jurisdictions:

- Allow GPs to continue prescribing psychostimulants where treatment was initiated by an appropriate specialist and there is periodic review by a specialist.
- Allow authorised specialists to prescribe psychostimulants without making an application for each patient, but they may be required to provide notifications of treatment and monthly data on prescribing.
- Limit the number of patients a practitioner may treat with psychostimulants, without an additional authorisation.
- Allow treatment on a short term basis without an authority

**Table A. Summary of state and territory regulations for prescribing stimulant medications**

State	Summary of Regulations
ACT <sup>23,24</sup>	<p>A prescriber must have either an approval from the Chief Health Officer (CHO) for each patient, or a standing approval to prescribe a controlled medicine such as methylphenidate.</p> <p><u>CHO Approval:</u> With regard to ADHD medicines, a prescriber must obtain a CHO approval when they intend to prescribe a controlled medicine for &gt;2 months to a patient, or where the patient has been prescribed a controlled medicine in the last 2 months. Prescriptions must be annotated with the details of the CHO approval number. Another doctor at the same clinic may prescribe under the relevant CHO approval for a patient.</p> <p>Certain criteria must be met for a CHO approval to be issued for the prescription of amphetamines for the treatment of ADHD:</p> <ul style="list-style-type: none"> <li>• Patients under 4 years: Initial applications must be submitted by a paediatrician, appropriate psychiatrist or neurologist, and supported by a second clinician from these specialities. Applications for initial treatment will be referred to the Medicines Advisory Committee for determination. Continuing applications should be submitted by the initiating specialist.</li> <li>• Patients aged 4–19 years: Initial applications must be submitted by a paediatrician, appropriate psychiatrist or neurologist. Continuing applications may be submitted by a GP if the treatment has been reviewed by an appropriate specialist within 2 years.</li> <li>• Patients over 19 years: Initial applications must be submitted by a neurologist or psychiatrist. Continuing applications may be submitted by a GP if the treatment has been reviewed by an appropriate specialist within 3 years, and there is no increase in dosage.</li> </ul> <p><u>Standing Approval:</u> A standing approval means that a prescriber is automatically authorised to prescribe a controlled substance and applies where the patient is an in-patient at a hospital or hospice, or a CHO approval is not required (see requirements above). The Standing approval process allows timely initiation of treatment and dose titration prior to seeking CHO approval for a patient. Except for in-patients, prescriptions must be annotated, e.g. with the words ‘Standing short term approval’.</p> <p>Legislation: <i>Medicines, Poisons and Therapeutic Goods Act 2008</i> and the Medicines, Poisons and Therapeutic Goods Regulation 2008.</p>

<sup>23</sup> ACT Health (2018), Guidelines for Prescribers Prescribing Controlled Medicines. Accessed on: 27 February 2018, at: <http://www.health.act.gov.au/health-services/population-health/health-protection-service/pharmaceutical-services/controlled-medicines>

<sup>24</sup> ACT Health (2018), Criteria for the issue of approvals to prescribe amphetamines for Attention Deficit Hyperactivity Disorder (ADHD). Accessed on: 27 February 2018, at: <http://www.health.act.gov.au/health-services/population-health/health-protection-service/pharmaceutical-services/controlled-medicines>

State	Summary of Regulations
NSW <sup>25, 26,27,28</sup>	<p>Dexamfetamine, methylphenidate and lisdexamfetamine may be prescribed only with the prior written authority of the NSW Ministry of Health.</p> <p><u>Authorities for individual patients:</u> Authorities for individual patients are only issued to relevant specialists, usually paediatricians, psychiatrists and neurologists for the treatment of ADHD, but some GPs may also apply. Authorities to prescribe psychostimulants for the treatment of ADHD are only issued in accordance with the TG 181 'Criteria for the Diagnosis and Management of Attention Deficit Hyperactivity Disorder in Children and Adolescents and TG 190 'Criteria for the Diagnosis and Management of Attention Deficit Hyperactivity Disorder in Adults'.</p> <p><u>General authorities for specialists:</u> Psychiatrists, neurologists and paediatricians may apply for a general authority number (S28c number) to prescribe psychostimulant medication for the treatment of ADHD. These prescribers must notify the Ministry of their psychostimulant prescribing on a monthly basis. Individual patient applications must still be made for patients who do not meet the routine prescribing criteria (e.g. higher dosage than the specified range, history of substance abuse, or significant co-morbidities or side-effects).</p> <p>Legislation: <i>Poisons and Therapeutic Goods Act 1966</i> and the Poisons and Therapeutic Goods Regulation 2008.</p>
NT <sup>29,30</sup>	<p>Authorisation from the CHO is required for each patient before dexamfetamine, lisdexamfetamine or methylphenidate is prescribed. Treatment must be initiated by a paediatrician, psychiatrist, physician, neurologist, or registrar in training in one of these disciplines. Other medical practitioners and nurse practitioners (NP) may continue the supply of these medicines, but the patient must see an appropriate specialist or registrar every 2 years. If the specialist is based interstate or overseas, a medical practitioner or NP may continue to supply the relevant medicine for up to 6 months, before review by an appropriate NT based specialist or registrar. Paediatricians may initiate supply without an authorisation if the supply is for less than 30 days. If the patient is under 4 years old, it is recommended that a second specialist opinion is obtained.</p> <p>The authority to supply for a specific patient must be renewed every 2 years where the patient is being managed by a neurologist, psychiatrist, physician or a registrar in these disciplines, or being co-managed by a medical practitioner or NP. Where the patient is being managed by a paediatrician or their registrar, the authority is valid until the patient turns 18 years old. Generally, no more than one months' supply is to be dispensed at any one time.</p> <p>Changes between medications and cessation of treatment must be notified to the CHO.</p>

<sup>25</sup> NSW Ministry for Health (2016), Requirements for an Authority to Prescribe Drugs of Addiction under Section 28 of the Poisons and Therapeutic Goods Act 1966. Accessed on: 27 February 2018, at: <http://www.health.nsw.gov.au/pharmaceutical/Documents/section28-requirements.pdf>

<sup>26</sup> NSW Ministry for Health (2016), Prescribe a psychostimulant medication. Accessed on: 27 February 2018, at: <http://www.health.nsw.gov.au/pharmaceutical/doctors/Pages/prescribe-psychostimulant.aspx>

<sup>27</sup> NSW Ministry for Health (2016), Criteria for the Diagnosis and Management of Attention Deficit Hyperactivity Disorder in Children and Adolescents (TG181/9). Accessed on: 27 February 2018, at: <http://www.health.nsw.gov.au/pharmaceutical/Documents/adhd-criteria-child.pdf>

<sup>28</sup> Health, N.M.f. (2015), Criteria for the Diagnosis and Management of Attention Deficit Hyperactivity Disorder in Adults. Accessed on: 27 February 2018, at: <http://www.health.nsw.gov.au/pharmaceutical/Documents/adhd-criteria-adult.pdf>

<sup>29</sup> Northern Territory Government Department of Health (2014), Code of Practice. Schedule 8 Substances. Volume 1 - Issuing prescriptions supplying Schedule 8 substances. Accessed on: 27 February 2018, at: <http://hdl.handle.net/10137/897>

<sup>30</sup> Northern Territory Government Department of Health (2014), Medicines and Poisons Control Information Sheet No. 320.1. Summary of requirements for medical practitioners. Accessed on: 27 February 2018, at: <http://hdl.handle.net/10137/891>

State	Summary of Regulations
	Legislation: <i>Medicines, Poisons and Therapeutic Goods Act 2012</i> and Medicines, Poisons and Therapeutic Goods Regulations.
QLD <sup>31</sup>	<p>Doctors may only prescribe methylphenidate, dexamfetamine and lisdexamfetamine for the treatment of narcolepsy, brain damage in a child at least 4 years old, or with attention deficit disorder. Paediatricians and psychiatrists may only prescribe these drugs for the treatment of brain damage or attention deficit disorder in a child.</p> <p>Doctors must seek approval from the Chief Executive to prescribe psychostimulants to patients aged 18 years and over.</p> <p>Legislation: <i>Health (Drugs and Poisons) Regulation 1996</i></p>
SA <sup>32</sup>	<p>An authority from the Minister for Health is required to prescribe psychostimulants to a patient for a period exceeding 2 months, which includes periods of treatment provided by other prescribers. The authority will stipulate the conditions under which the drug may be supplied, including dosage and quantity. Treatment should generally be initiated by a relevant specialist, such as a neurologist, paediatrician or psychiatrist for a child, or a psychiatrist for an adult. Authorities may be granted to GPs to continue prescribing stimulants to a patient with ADHD, conditional on support and annual review by a relevant specialist. Prescriptions should be limited to no more than three months' supply.</p> <p>Legislation: <i>Controlled Substances Act 1984</i> and Controlled Substances (Poisons) Regulations 2011.</p>
TAS <sup>33,34</sup>	<p>Before issuing a prescription for a psychostimulant for ADHD, authority must be obtained from the Secretary of the Department of Health and Human Services. For children and adolescent patients, authorities are only issued to child psychiatrists, paediatricians, and specialist physicians. The specialist may request that the authority list a GP as a co-prescriber under their direction. Applications for patients outside the routine authorisation criteria (e.g. higher than recommended dosage, and patients with significant side-effects or severe psychiatric co-morbidity) are referred to the Psychostimulant Advisory Panel, which may request additional reports or opinions.</p> <p>Prescribing these medicines for children under 2 years of age is not permitted. For children aged 2 years, a second specialist opinion is required and the maximum authority length is 3 months. Both the prescriber and second specialist must provide reports indicating that the treatment is appropriate on all authority applications until the child reaches age 3. An authority for a child aged 3 years also requires a second specialist opinion. For children aged over 3 years, authorisations remain in effect until the patient reaches 18 years of age or has completed secondary school.</p>

<sup>31</sup> Queensland Government, Health (Drugs and Poisons) Regulation 1996

<sup>32</sup> SA Health (2017), Authorities for prescribing drugs of dependence Accessed on: 27 February 2018, at:

<http://www.sahealth.sa.gov.au/wps/wcm/connect/public+content/sa+health+internet/clinical+resources/clinical+topics/medicines+and+drugs/prescribing+medicines+regulations+and+requirements/prescribing+drugs+of+dependence/authorities+for+prescribing+drugs+of+dependence>

<sup>33</sup> Tasmanian Department of Health and Human Services (2005), Prescribing of psychostimulants (dexamphetamine and methylphenidate) in adults. Accessed on: 27 February 2018, at:

[http://www.dhhs.tas.gov.au/\\_data/assets/pdf\\_file/0007/46519/Adult\\_Psychostimulant\\_guidelines2005\\_updated\\_2009\\_.pdf](http://www.dhhs.tas.gov.au/_data/assets/pdf_file/0007/46519/Adult_Psychostimulant_guidelines2005_updated_2009_.pdf)

<sup>34</sup> Tasmanian Department of Health and Human Services (2005), Stimulant Prescribing Children and Adolescents. Accessed on: 27 February 2018, at:

[http://www.dhhs.tas.gov.au/\\_data/assets/pdf\\_file/0005/46517/ADHD\\_Criteria\\_for\\_Children\\_and\\_Adolescents.pdf](http://www.dhhs.tas.gov.au/_data/assets/pdf_file/0005/46517/ADHD_Criteria_for_Children_and_Adolescents.pdf)

State	Summary of Regulations
	<p>For adults, initial authorisations are for 3 months, to facilitate appropriate reassessment, and continuing authorisations are for 12–24 months. In general, only psychiatrists may initiate psychostimulant treatment of adults with ADHD. However, the psychiatrist may request that a patient’s GP take over prescribing following the initial application.</p> <p>Legislation: <i>Poisons Act 1971</i> and <i>Poisons Regulations 2008</i>.</p>
VIC <sup>35</sup>	<p>A medical practitioner must hold a permit for each patient from the Drugs and Poisons Regulation Group, Victorian Department of Health, before prescribing psychostimulants. However, there is an exemption from this requirement for paediatricians and psychiatrists where:</p> <ul style="list-style-type: none"> <li>• The patient is being treated for ADHD and the treatment is not expected to be for greater than 8 weeks (including a preceding period of treatment) – no permit or notification is required.</li> <li>• The patient is under the age of 18 years and being treated for ADHD for a period greater than 8 weeks – the specialist must provide notification of the treatment (section 34D notification).</li> </ul> <p>Adult patients being treated for ADHD for greater than 8 weeks require a permit. GPs may be issued with a permit to prescribe psychostimulants for a patient where the application indicates that diagnosis was undertaken by a specialist and there are at least yearly reviews by a specialist. Other clinicians at the same clinic may prescribe under the same permit. Permits are not required for patients in prison or a residential aged care service, or hospital in-patients.</p> <p>Legislation: <i>Drugs, Poisons and Controlled Substances Act 1981</i> and <i>Drugs, Poisons and Controlled Substances regulations 2017</i>.</p>
WA <sup>36</sup>	<p>Authorised specialists may prescribe psychostimulants to patients who meet the clinical criteria in the Stimulant Prescribing Code (the Code). These specialists are issued a Stimulant Prescriber Number by the Department of Health. Treatment of ADHD with stimulants may only be initiated by a neurologist, paediatric neurologist, paediatrician, psychiatrist, a child and adolescent psychiatrist or a medical practitioner approved by the Department of Health. Psychostimulants may not be prescribed for patients with a history of psychosis or drug abuse, or a diagnosis of bi-polar disorder, or have a record of drug dependence or oversupply. Annual drug screening of patients aged over 13 years is required.</p> <p>To prescribe outside the clinical criteria in the Code, special authorisation must be obtained by an authorised specialist from the Department of Health. Psychostimulants must not be prescribed to patients under two years of age, and prescribing for patients aged 2-3 years requires a special authorisation. Patients under 6 years must not be treated with lisdexamfetamine.</p> <p>Legislation: <i>Poisons Act 1964</i> and <i>Poisons Regulations 1965</i>.</p>

**Abbreviations:** ADHD = Attention Deficit Hyperactivity Disorder; CHO = Chief Health Officer

<sup>35</sup> Victorian Government Department of Health (2017), Prescribing psychostimulants to treat ADHD and narcolepsy. Permit and notification requirements. Accessed on: 27 February 2018, at: [https://www2.health.vic.gov.au/getfile/?sc\\_itemid=%7ba7b6d794-fe16-4d50-a83a-e7922f374d71%7d&title=Prescribing%20psychostimulants%20to%20treat%20ADHD%20or%20narcolepsy%20-%20permit%20and%20notification%20requirements](https://www2.health.vic.gov.au/getfile/?sc_itemid=%7ba7b6d794-fe16-4d50-a83a-e7922f374d71%7d&title=Prescribing%20psychostimulants%20to%20treat%20ADHD%20or%20narcolepsy%20-%20permit%20and%20notification%20requirements)

<sup>36</sup> Government of Western Australia Department of Health (2017), Schedule 8 medicines prescribing code. Accessed on: 27 February 2018, at: [http://www2.health.wa.gov.au/~media/Files/Corporate/general%20documents/medicines%20and%20poisons/PDF/MP00001.1\\_Schedule-8-Medicines-Prescribing-Code.pdf](http://www2.health.wa.gov.au/~media/Files/Corporate/general%20documents/medicines%20and%20poisons/PDF/MP00001.1_Schedule-8-Medicines-Prescribing-Code.pdf)

## Appendix B: PBS listing details (as at February 2018)

**Table B: PBS listings of medicines used in the treatment of ADHD**

Item	Name, form & strength, pack size	Max. quant.	Rpts	DPMQ	Brand name and manufacturer
1165H	DEXAMFETAMINE SULFATE Tablet 5 mg, 100	1	5	\$21.58	Aspen Pharma Pty Ltd
8839F	METHYLPHENIDATE HYDROCHLORIDE Tablet 10 mg, 100	1	5	\$23.24	Ritalin 10 Novartis Artige Novartis
2387P	METHYLPHENIDATE HYDROCHLORIDE Tablet 18 mg (modified release) , 30	1	5	\$51.79	Concerta Janssen-Cilag Pty Ltd
2172H	METHYLPHENIDATE HYDROCHLORIDE Tablet 27 mg (modified release), 30	1	5	\$55.93	Concerta Janssen-Cilag Pty Ltd
2388Q	METHYLPHENIDATE HYDROCHLORIDE Tablet 36 mg (modified release) , 30	1	5	\$60.06	Concerta Janssen-Cilag Pty Ltd
2432B	METHYLPHENIDATE HYDROCHLORIDE Tablet 54 mg (modified release) , 30	1	5	\$69.21	Concerta Janssen-Cilag Pty Ltd
3440C	METHYLPHENIDATE HYDROCHLORIDE Capsule 10 mg (modified release), 30	1	5	\$35.77	Ritalin LA Novartis
2276T	METHYLPHENIDATE HYDROCHLORIDE Capsule 20 mg (modified release), 30	1	5	\$45.04	Ritalin LA Novartis
2280B	METHYLPHENIDATE HYDROCHLORIDE Capsule 30 mg (modified release), 30	1	5	\$52.50	Ritalin LA Novartis
2283E	METHYLPHENIDATE HYDROCHLORIDE Capsule 40 mg (modified release), 30	1	5	\$55.03	Ritalin LA Novartis
9092M	ATOMOXETINE Capsule 10 mg, 28	2	5	\$168.11	Strattera Eli Lilly Australia Pty Ltd  Atomerra Arrow Pharma Pty Ltd  Apo-Atomoxetine Apotex Pty Ltd  Atomoxetine Amneal

Item	Name, form & strength, pack size	Max. quant.	Rpts	DPMQ	Brand name and manufacturer
					Amneal Pharmaceuticals Pty Ltd  Atomoxetine Sandoz Sandoz Pty Ltd
9093N	ATOMOXETINE Capsule 18 mg, 28	2	5	\$168.11	Strattera Eli Lilly Australia Pty Ltd  Atomerra Arrow Pharma Pty Ltd  Apo-Atomoxetine Apotex Pty Ltd  Atomoxetine Amneal Amneal Pharmaceuticals Pty Ltd  Atomoxetine Sandoz Sandoz Pty Ltd
9094P	ATOMOXETINE Capsule 25 mg, 28	2	5	\$168.11	Strattera Eli Lilly Australia Pty Ltd  Atomerra Arrow Pharma Pty Ltd  Apo-Atomoxetine Apotex Pty Ltd  Atomoxetine Amneal Amneal Pharmaceuticals Pty Ltd  Atomoxetine Sandoz Sandoz Pty Ltd
9095Q	ATOMOXETINE Capsule 40 mg, 28	2	5	\$168.11	Strattera Eli Lilly Australia Pty Ltd  Atomerra Arrow Pharma Pty Ltd  Apo-Atomoxetine Apotex Pty Ltd  Atomoxetine Amneal Amneal Pharmaceuticals Pty Ltd  Atomoxetine Sandoz Sandoz Pty Ltd
9096R	ATOMOXETINE Capsule 60 mg, 28	2	5	\$168.11	Strattera Eli Lilly Australia Pty Ltd  Atomerra Arrow Pharma Pty Ltd



Item	Name, form & strength, pack size	Max. quant.	Rpts	DPMQ	Brand name and manufacturer
					Apo-Atomoxetine Apotex Pty Ltd  Atomoxetine Amneal Amneal Pharmaceuticals Pty Ltd  Atomoxetine Sandoz Sandoz Pty Ltd
9289X	ATOMOXETINE Capsule 80 mg, 28	1	5	\$113.15	Strattera Eli Lilly Australia Pty Ltd  Atomerra Arrow Pharma Pty Ltd  Apo-Atomoxetine Apotex Pty Ltd  Atomoxetine Amneal Amneal Pharmaceuticals Pty Ltd  Atomoxetine Sandoz Sandoz Pty Ltd
9290Y	ATOMOXETINE Capsule 100 mg, 28	1	5	\$113.15	Strattera Eli Lilly Australia Pty Ltd  Atomerra Arrow Pharma Pty Ltd  Apo-Atomoxetine Apotex Pty Ltd  Atomoxetine Amneal Amneal Pharmaceuticals Pty Ltd  Atomoxetine Sandoz Sandoz Pty Ltd
10486X	LISDEXAMFETAMINE DIMENSILATE Capsule 30mg, 30	1	5	\$117.10	Vyvanse Shire Australia Pty Ltd
10474G	LISDEXAMFETAMINE DIMENSILATE Capsule 50mg, 30	1	5	\$117.10	Vyvanse Shire Australia Pty Ltd
10492F	LISDEXAMFETAMINE DIMENSILATE Capsule 70mg, 30	1	5	\$117.10	Vyvanse Shire Australia Pty Ltd

Source: Department of Health (2018), Schedule of Pharmaceutical Benefits Effective 1 February 2018, Canberra.

Notes: Novartis = Novartis Pharmaceuticals Australia Pty Limited.

## Appendix C: Key PBS listing dates for ADHD medicines and changes to listing dates

**Table C.1. Date of listing of PBS medicines used in the treatment of ADHD**

Date	Drug name	Brand name	Strength	Item
Dec 1973	Dexamfetamine	-	5 mg	1165H
Aug 2005	Methylphenidate IR	Ritalin 10	10 mg	8839F
Dec 2005	Methylphenidate IR	Attenta*	10 mg	8829F
April 2007	Methylphenidate MR	Concerta	18 mg	2387P
			36 mg	2388Q
			54 mg	2432B
July 2007	Atomoxetine	Strattera	10 mg	9092M
			18 mg	9093N
			25 mg	9094P
			40 mg	9095Q
			60 mg	9096R
Aug 2007	Methylphenidate MR	Concerta	27 mg	2172H
April 2008	Methylphenidate MR	Ritalin LA	20 mg	2276T
			30 mg	2280B
			40 mg	2283E
Dec 2008	Atomoxetine	Strattera	80mg	9289X
			100 mg	9290Y
Aug 2010	Methylphenidate MR	Ritalin LA	10mg	3440C
Sep 2015	Lisdexamfetamine	Vyvanse	30mg	10486X
			50mg	10474G
			70mg	10492F

Notes: \* The Attenta® brand of methylphenidate IR was delisted in March 2009.

**Table C.2. Changes to PBS restrictions of ADHD medicines**

Date	Drug name	Change to the restriction/s
Aug 2007	Methylphenidate MR (Concerta®)	Replacement of "...child or adolescent aged 6 to 18 years inclusive" with "...patient aged 6 to 18 years inclusive".
Nov 2008	Atomoxetine (all items)	<p>The restrictions were changed to remind prescribers that atomoxetine is not PBS subsidised for use with other ADHD medicines. "Initial treatment..." was replaced by "Initial sole PBS-subsidised treatment...", and "Continuing treatment..." was replaced by "Continuing sole PBS-subsidised treatment...".</p> <p>A note was also added, "No applications for increased maximum quantities and/or repeats will be authorised", as the listing of the 80 mg and 100 mg doses was considered to negate the need for increased maximum quantities.</p>
Oct 2009	Methylphenidate (modified release) (all items)	<p>The restrictions were modified to extend the listing to the treatment of patients aged over 18 years who were diagnosed between ages 6–18. "Treatment of attention deficit hyperactivity disorder (ADHD) in a patient between the ages of 6 and 18 years inclusive" was changed to "Treatment of attention deficit hyperactivity disorder (ADHD) in a patient <i>diagnosed</i> between the ages of 6 and 18 years inclusive".</p>
Aug 2014	Atomoxetine (all items)	<p>The restriction was simplified and changed from Authority Required to Authority Required (STREAMLINED). The requirement for diagnosis using the DSM-IV criteria was updated to the DSM-V. The emphasis on "sole PBS-subsidised treatment" use was removed. References in the previous restriction to specific contraindications and adverse events were generally removed.</p>
July 2016	Methylphenidate (modified release) (all items)	<p>The restriction criteria remains the same but was contents were restructured to separately define population criteria and clinical criteria.</p>
July 2016	Dexamfetamine 5mg, tablets	<p>The restriction criteria remains the same but was contents were restructured to separately define the two criteria for prescribing.</p>
July 2016	Atomoxetine (all items)	<p>The restriction was modified to account for the new listing of lisdexamfetamine. The criteria were further limited by adding the requirement for contraindication to lisdexamfetamine before prescribing. "Patient must have a contraindication to dexamphetamine, methylphenidate or <i>lisdexamfetamine</i> as specified in TGA-approved product information;"</p>

## **Appendix D: PBAC recommendations for listing of ADHD medicines (Prior to 2014)**

Copies of the PBAC Meeting Outcomes and Public Summary Documents are available on the [PBAC Meetings](#) website.

### ***Methylphenidate IR***

At the March 2005 meeting, the PBAC recommended listing on a cost-minimisation basis compared to dexamfetamine sulfate, with the equi-effective doses being methylphenidate hydrochloride 10 mg and dexamfetamine sulfate 5 mg.<sup>37</sup> The PBAC was concerned over the possible extent of use of the product and requested that the DUSC monitor this.

### ***Methylphenidate MR (Concerta®)***

At the November 2006 meeting the PBAC recommended listing of methylphenidate MR (Concerta®) as an authority required benefit on a cost effectiveness basis over methylphenidate IR. Although the extent of any clinical benefit over methylphenidate IR remained uncertain, the Committee agreed that the likely improvements in compliance and in ease of administration, particularly in relation to the removal of the need for a dose of medication at school, were sufficient to justify listing.<sup>38</sup>

In July 2012 the PBAC rejected a submission to extend the listing to include patients diagnosed with ADHD after the age of 18 years, on the basis of uncertain efficacy and safety in the proposed population, and high and highly uncertain cost to the PBS.<sup>39</sup>

### ***Methylphenidate MR (Ritalin LA®)***

In November 2007, the PBAC recommended listing of methylphenidate hydrochloride modified release (Ritalin LA®) capsules on the PBS on a cost-minimisation basis compared with methylphenidate hydrochloride modified release tablets (Concerta®) at the same price per day, as reflected by the equi-effective doses.<sup>40</sup>

### ***Atomoxetine (Strattera®)***

The PBAC recommended the listing of atomoxetine (Strattera®) 10 mg, 18mg, 25 mg, 40 mg and 60 mg in November 2006, on a cost-effectiveness basis over placebo. The PBAC

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<sup>37</sup> Department of Health (2005), March 2005 PBAC Outcomes - Positive Recommendations. Accessed on: 27 February 2018, at: <http://www.pbs.gov.au/info/industry/listing/elements/pbac-meetings/pbac-outcomes/2005-03/positive-recommendations>

<sup>38</sup> Department of Health (2007), PBAC Meetings Public Summary Documents: Methylphenidate Hydrochloride, extended release tablets, 18 mg, 36 mg and 54 mg, Concerta® November 2006. Accessed on: 27 February 2018, at: <http://www.pbs.gov.au/info/industry/listing/elements/pbac-meetings/psd/2006-11/pbac-psd-methylphenidate-nov06>

<sup>39</sup> Department of Health (2012), PBAC Meetings Public Summary Documents: Methylphenidate hydrochloride, Tablets, 18 mg, 27 mg, 36 mg, and 54 mg,(extended release) Concerta® - July 2012 Accessed on: 27 February 2018, at: <http://www.pbs.gov.au/info/industry/listing/elements/pbac-meetings/psd/2012-07/methylphenidate-hydrochloride>

<sup>40</sup> Department of Health (2007), November 2007 PBAC Outcomes - Positive Recommendations. Accessed on: 27 February 2018, at: <http://www.pbs.gov.au/info/industry/listing/elements/pbac-meetings/pbac-outcomes/2007-11/positive-recommendations>

considered that there was a clinical need for the product and that the proposed restriction targeted the appropriate population.<sup>41</sup>

In July 2008, the PBAC recommended the listing of two additional strengths of atomoxetine (Strattera®), 80 mg and 100 mg, but rejected a submission to extend the use of atomoxetine to patients diagnosed with ADHD as adults due to insufficient evidence of clinical and cost-effectiveness. The submission claimed that the new strengths were unlikely to increase atomoxetine use or cost to the PBS.<sup>42</sup>

In March 2014, the PBAC recommended that the current Authority required restriction for atomoxetine be changed to Authority Required (STREAMLINED).<sup>43</sup>

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<sup>41</sup> Department of Health (2007), PBAC Meetings Public Summary Documents: Atomoxetine Hydrochloride, capsules, 10 mg, 18 mg, 25 mg, 40 mg and 60 mg, Strattera® November 2006. Accessed on: 27 February 2018, at:

<http://www.pbs.gov.au/info/industry/listing/elements/pbac-meetings/psd/2006-11/pbac-psd-atomoxetine-nov06>

<sup>42</sup> Department of Health (2008), PBAC Meeting Public Summary Documents: Atomoxetine hydrochloride, capsules, 80 mg and 100 mg, Strattera®, July 2008 Accessed on: 27 February 2018, at: <http://www.pbs.gov.au/info/industry/listing/elements/pbac-meetings/psd/2008-07/pbac-psd-atomoxetine-hydrochloride-july08>

<sup>43</sup> Department of Health (2014), March 2014 PBAC Outcomes - Positive Recommendations. Accessed on: 27 February 2018, at: <http://www.pbs.gov.au/info/industry/listing/elements/pbac-meetings/pbac-outcomes/pbac-recommendations-march-2014>