Lisdexamfetamine for attention deficit hyperactivity disorder (ADHD)

nps.org.au/radar/articles/lisdexamfetamine-adult-diagnosis-of-adhd

Key points

- **From 1 February 2021, adults retrospectively diagnosed with ADHD after the age of 18 years can be prescribed lisdexamfetamine on the PBS**
  Previously, adults were only eligible if their diagnosis of ADHD had been made between the ages of 6 and 18 years.
- **Before this change, adults diagnosed with ADHD after 18 years were only eligible to receive short-acting ADHD medicines on the PBS**
  Access to lisdexamfetamine, a long-acting, once-daily ADHD medicine, may improve adherence and sustained response.
- **Diagnosis of ADHD after the age of 18 years requires a retrospective confirmation of childhood symptoms**
  This involves documentation of an in-depth clinical interview and/or obtaining supporting evidence that supports the presence of childhood symptoms.
- **The changes to the PBS listings now align with ADHD guidelines**
  These changes will help adults with ADHD access effective treatment options and achieve control of symptoms.

What's changed?

On 1 February 2021, changes were made to the listings of lisdexamfetamine (Vyvanse) on the PBS General Schedule (Section 85) for attention deficit hyperactivity disorder (ADHD).[1]

Adults who have been retrospectively diagnosed with ADHD after the age of 18 years are now included in the population criteria of the listings. Previously, adults were only included if they had been diagnosed when they were aged between 6 and 18 years inclusive and were continuing treatment after the age of 18. Instructions for making a retrospective diagnosis of ADHD in adults were also added to the listings.[1,2] These changes are summarised in Table 1.

Table 1: Changes to the population criteria in the PBS listings of lisdexamfetamine[1,2]

Before 1 February 2021	After 1 February 2021

Age of diagnosis	Age of diagnosis	Retrospective diagnosis instructions
Patient must be or have been diagnosed between the ages of 6 and 18 years inclusive.	Patient must be aged between the ages of 6 and 18 years inclusive, or Patient must have had a diagnosis of ADHD prior to turning 18 years of age if PBS-subsidised treatment is continuing beyond 18 years of age, or Patient must have a retrospective diagnosis of ADHD if PBS-subsidised treatment is commencing after turning 18 years of age; or Patient must have had a retrospective diagnosis of ADHD if PBS-subsidised treatment is continuing in a patient who commenced PBS-subsidised treatment after turning 18 years of age.	(i) the presence of pre-existing childhood symptoms of ADHD (onset during the developmental period, typically early to mid-childhood); and (ii) documentation in the patient's medical records that an in-depth clinical interview with, or obtainment of evidence from, either a: (a) parent, (b) teacher, (c) sibling, (d) third party, has occurred and which supports point (i) above.

Other changes have also been made to the listings. These are:[1]

- Intention for once-daily dosing only, stating that divided dosing is not intended (eg, 20 mg in the mornings, 30 mg in the evenings) and where applications (either on the same day or on separate days) for multiple strengths are sought, repeats should only be sought for the listed target strength.
- No increase in the maximum quantity or number of units may be authorised.
- No increase in the maximum number of repeats may be authorised.

See the PBS website for complete details for each item.

Why were the changes made?

PBS-listed ADHD medicines

Various ADHD medicines are listed on the PBS. These include:[3]

- short-acting ADHD stimulant medicines, such as immediate-release (IR) dexamfetamine and IR methylphenidate. These are rapidly absorbed and act within 30 minutes, with the peak within 1–3 hours. The effect is mostly gone after 4–6 hours. These medicines may be taken once or twice daily initially.[4]
- long-acting ADHD stimulant medicines such as lisdexamfetamine and modified-release (MR) methylphenidate. MR methylphenidate and lisdexamfetamine are taken once daily and effects last 8–12 hours.[4,5]

The PBS listings for all ADHD medicines, including lisdexamfetamine, formerly stated that patients must be or have been diagnosed between the ages of 6 and 18 years (except for guanfacine which is between 6 and 17 years).[3]

In September 2019, the PBAC asked the Royal Australian and New Zealand College of Psychiatrists (RANZCP) whether the age of diagnosis for PBS-listed ADHD medicines was problematic for prescribers or patients. It also asked whether the restrictions were inconsistent with the current evidence-based standards of care for people with ADHD. The PBAC requested this advice after concerns were raised about the age of diagnosis by individuals, clinicians and organisations.[2]

The RANZCP advised that:[2]

- access to PBS-listed ADHD medicines is limited by the age of diagnosis criteria
- short-acting ADHD medicines may be more susceptible to abuse by people with substance use disorder
- short-acting ADHD medicines require multiple daily doses which may lead to poor adherence and clinical outcomes
- poorly managed ADHD can lead to a greater risk of failure at school, work and in relationships, as well as significantly increase rates of suicide, serious accidents, substance abuse and imprisonment, and
- improved access to treatment would significantly reduce the societal costs of ADHD in Australia.

Lisdexamfetamine

At the March 2020 PBAC meeting, the PBAC considered a submission from the sponsor of lisdexamfetamine, along with comments from individuals, health professionals and organisations, evidence from eight randomised placebo-controlled trials and recent systematic literature reviews, and safety information in the TGA-approved Product Information (PI).[2]

As people diagnosed with ADHD after 18 years of age were, at that time, only eligible to receive short-acting ADHD medicines on the PBS, the submission nominated IR dexamfetamine as the main comparator and IR methylphenidate as a secondary comparator. The PBAC agreed that these were the appropriate comparators.[2] The submission included evidence on lisdexamfetamine versus placebo, which was presented to show the efficacy of lisdexamfetamine in adults, as well as an estimation of the relative treatment effect sizes of lisdexamfetamine and short-acting medicines versus placebo.

These comparisons were informative and the PBAC noted that lisdexamfetamine is likely to be equally effective in improving ADHD core symptoms in adults, compared to the short-acting stimulant medicines. In terms of safety, PBAC considered that lisdexamfetamine may have a lower potential for abuse or dependence compared to short-acting stimulants and was likely to be similar with regard to other potential harms.[2]

The PBAC noted and welcomed health professional input describing the benefits of improved adherence because of once-daily dosing, and sustained response to the medicine. Individuals discussed their experiences of improvements in quality of life with lisdexamfetamine, but also of the financial hardship caused by having to access this medicine via a private prescription because their diagnoses of ADHD were made in adulthood. ADHD Australia also supported the requested change to the listing and emphasised that not all people with ADHD have the benefit of a diagnosis in their early life.[2] The PBAC acknowledged that there is now a greater acceptance in the medical community of the diagnosis of ADHD in adulthood and considered that there is a moderate unmet clinical need for effective treatments for these patients.[2]

The PBAC considered it appropriate that the restriction should be amended to require retrospective confirmation of childhood symptoms. The change is in alignment with international classification systems; the International Statistical Classification of Diseases and Related Health Problems 11th Revision (ICD-11)[6] and Diagnostic and Statistical Manual of Mental Disorders 5th edition (DSM-5).[2]

The listing change for the intention of once-daily dosing is in alignment with the PI. The changes stipulating no increase in the maximum quantity or number of units and no increase in the maximum number of repeats that may be authorised are designed to prevent prescribers from requesting increased quantities for the purpose of split dosing.[7]

The PBAC also recommended at its March 2020 meeting that the adult ADHD listing changes for lisdexamfetamine should flow on to all other long-acting ADHD medicines on the PBS, including methylphenidate (Concerta and Ritalin LA) and atomoxetine (Strattera).[2]

As of 1 February 2021, no decision has been made about the flow on of changes relating to adult or retrospective diagnosis to other medicines.[1]

However, the PBAC has made changes stipulating once-daily dosing and no increase in the maximum quantity and number of repeats to the listing for long-acting methylphenidate.[1]

Read more about 1 February 2021 listing changes to methylphenidate.

Will the changes affect current prescribing?

The Therapeutic Guidelines do not offer specific guidance on management of ADHD in adults. The RANZCP recommends the Canadian ADHD Practice Guidelines and the UK National Institute for Health Care and Excellence (NICE) Guidelines.[2]

The changes to the PBS listings bring them in line with these guidelines. Both the Canadian ADHD Practice Guidelines and UK NICE Guidelines state that long-acting stimulants, such as lisdexamfetamine and methylphenidate, are first-line treatment options for adults with ADHD.[8,9]

With greater acceptance of the diagnosis of ADHD in adulthood and the recommendation in guidelines that long-acting ADHD medicines are first-line for adults with ADHD, the changes to the listings will enable and reinforce increased prescribing of lisdexamfetamine for these patients.

What else should health professionals know?

A diagnosis of ADHD is made on reported symptoms and impairment, rather than just on direct observation by a health professional. Symptoms of ADHD may not be observed during an appointment.[8]

Obtaining a developmental history in adults may be difficult. A parent or close relative who is familiar with the person's early life may be helpful in obtaining a complete childhood development history.[8]

Stimulants produce small increases in systemic adrenergic activity that may lead to small increases in blood pressure and heart rate. These should be measured initially before starting an ADHD medicine and during follow-up.

In 2006, the US Food and Drug Administration and Health Canada raised concerns about ADHD medicines after reports of sudden death in children.[8] Sudden death related to cardiac causes, stroke and myocardial infarction occurring in adults taking usual ADHD doses is discussed in the PI for lisdexamfetamine.[7] Cardiac problems may alone increase the risk of sudden death, and adults may have a greater likelihood of cardiac problems than children. Adults with pre-existing structural cardiac abnormalities or other serious cardiac problems should not be treated with stimulant medicines.[7]

Long-acting ADHD medicines may help maintain privacy for individuals and families at school, work and social situations,[8] by removing the need for additional doses to be taken during the day.[2]

Long and short-acting ADHD medicines have varying benefits. For example, while psychostimulant medicines can be diverted or misused, long-acting ADHD medicines have less abuse potential than IR preparations.[8] The NICE guidelines state that IR preparations may be suitable if more flexible dosing regimens are required, or during the initial dose titration to determine correct dosing levels.[9]

All states and territories within Australia have their own laws on prescribing of psychostimulant medicines.[10] See the Australian ADHD Professionals Association (AADPA) website for more information.

What else should patients know?

Common side effects of psychostimulants include nausea, diarrhoea, dry mouth, loss of appetite, weight loss, anxiety, irritability, insomnia, headache, dizziness, aggression, tachycardia, palpitations and blood pressure changes (usually increases).[5]

As lisdexamfetamine is taken once daily, patients should avoid taking doses after the early afternoon to minimise sleep disturbances.[5]

During the dose titration period when an ADHD medicine is first prescribed, it is important to regularly review the dose and monitor physical health, side effects and social and personal well-being, until the ADHD is stabilised.[8]

Patients who are moving between states or territories, may run into problems with the different laws on prescriptions for stimulant medicines, as some states/territories will not accept prescriptions from other areas.[10] Patients should ask their doctors or pharmacists for more information about this.

Changes to prescribing information and processes

Active ingredient prescribing

On 31 October 2019, active ingredient prescribing regulations were introduced by the PBS under the National Health Act 1953. Active ingredient prescribing is part of a wider government strategy to ensure consistent and standardised medicines information.[11]

Active ingredient prescribing aims to:[11]

- ensure the identification of active ingredient names on all PBS prescriptions
- increase patient understanding of the medicines they are taking
- promote the uptake of generic and biosimilar medicines.

Under the regulations, prescribers:[11]

- are required to include the active ingredient on all PBS prescriptions (excluding handwritten prescriptions, paper-based medication charts in residential aged care settings, and medicines with four or more active ingredients).
- can include a brand after the active ingredient on a prescription, if the medicine prescribed is likely to pose a patient safety risk if the brand is not specified or to ensure medicine continuance where a patient is familiar with a particular brand of their regular medicine.

A transition period has been arranged to ensure prescribers have sufficient time to update prescribing software to versions which meet the new active ingredient prescribing requirements.

Community level electronic prescriptions

On 31 October 2019, Commonwealth legislation changed to recognise electronic prescriptions as a legal prescription for the purpose of PBS-listed medicine supply. Electronic prescribing is part of a wider government strategy to support safer medicine management and improve the efficiency of the PBS. It will not be mandatory but provides prescribers and their patients with a safe and secure alternative choice to paper prescriptions.

Electronic prescribing aims to:

- improve efficiency in prescribing and dispensing medications
- remove the need for handling and storing a physical paper prescription
- support digital health services such as telehealth services to ensure continuity of patient care

To support the legislative changes, technical upgrades are currently underway to ensure safe, secure and seamless transmission of information of electronic prescriptions between prescribing and dispensing clinical software and to PBS payment systems.

Once in place, two models will be available to support electronic prescription; Token and Active Script List.

More information about electronic prescriptions is available:

- NPS MedicineWise
- Department of Health
- Australian Digital Health Agency FAQs for prescribers and for pharmacists.