

**6.02 MODAFINIL,
Tablet, 100 mg,
ARMODAFINIL
Tablet 50 mg, 150 mg and 250 mg,
Various Sponsors**

1 Purpose of Item

- 1.1 To request General Schedule Authority Required listings of modafinil and armodafinil for the first-line treatment of patients with narcolepsy.

2 Background

Previous PBAC consideration

- 2.1 The Australasian Sleep Association (ASA) made a minor submission to the July 2020 PBAC meeting requesting the removal of the following clinical criteria from the restrictions of armodafinil and modafinil:
- The treatment must be for use when therapy with dexamfetamine poses an unacceptable medical risk; OR
 - The treatment must be for use when intolerance to dexamfetamine is of a severity to necessitate treatment withdrawal.
- 2.2 At the July 2020 meeting, the PBAC deferred making a recommendation to change the PBS listing of armodafinil and modafinil to allow use as a first-line therapy for the treatment of narcolepsy and requested the Department undertake further analysis of available data to assess the comparative cost-effectiveness and determine the financial implications of the requested change.
- 2.3 The PBAC noted that, under section 101(3B) of the Act, a significant improvement in efficacy or reduction of toxicity over the alternative therapy or therapies is required to list armodafinil and modafinil at a higher price than dexamfetamine for the same place in therapy. The PBAC noted that no clinical evidence directly comparing armodafinil and modafinil to dexamfetamine was provided to support the clinical claim of superior comparative effectiveness and safety and therefore concluded that there was insufficient evidence to support a higher price.
- 2.4 Further information is available in the July 2020 PBAC Public Summary Document of armodafinil and modafinil.

Registration status

- 2.5 Armodafinil and modafinil are registered by the Therapeutic Goods Administration (TGA) for the following indications:
- To improve wakefulness in patients with excessive daytime sleepiness associated with narcolepsy
 - To treat excessive sleepiness associated with moderate to severe chronic shift work disorder where non-pharmacological interventions are unsuccessful or inappropriate
 - As an adjunct to continuous positive airways pressure (CPAP) in obstructive sleep apnoea/hypopnoea syndrome in order to improve wakefulness.
- 2.6 Armodafinil is PBS listed in the following strengths: 50 mg, 150 mg, and 250 mg tablets. Armodafinil 50 mg tablets have a maximum PBS quantity of 60 tablets, while the 150 mg and 250 mg tablets have a maximum quantity of 30 tablets. Nuvigil® is the only brand of armodafinil registered by the TGA and its patent is due to expire on 18 December 2028.
- 2.7 Modafinil 100 mg tablets is PBS listed at a maximum quantity of 120 tablets. There are currently six listed brands of modafinil on the PBS (APO-Modafinil®, Modafin®, Modafinil GH®, Modafinil Mylan®, Modafinil Sandoz®, Modavigil®).

For more detail on PBAC's view, see section 4 PBAC outcome.

3 Current situation

- 3.1 The dispensed prices per maximum quantity (DPMQ) for dexamfetamine, modafinil and armodafinil as at 1 May 2022 are:
- Dexamfetamine 5 mg, 100 tablets: \$23.30
 - Modafinil 100 mg, 120 tablets: \$206.88
 - Armodafinil 50 mg, 60 tablets: \$102.18
 - Armodafinil 150 mg, 30 tablets: \$148.98
 - Armodafinil 250 mg 30 tablets: \$243.57

Methodology

- 3.2 PBS utilisation data for dexamfetamine, armodafinil and modafinil for the treatment of narcolepsy was extracted from 1 January 2012 to 31 December 2021 based on the date of supply and was used to estimate the financial implications of listing armodafinil and modafinil as equal first line treatments with dexamfetamine for narcolepsy.

- 3.3 Dexamfetamine is PBS listed for the first-line therapy of both narcolepsy and attention deficit hyperactivity disorder (ADHD). To identify supplies for the narcolepsy indication only, patient identifiers were obtained from the Authorities data for the Authority codes of narcolepsy only ('6227', '1236'). The PINs for these Authority codes were then matched to the PBS claims data for dexamfetamine. The supplies of dexamfetamine that were not matched to a PIN for the Authorities data were assumed to be for ADHD and removed from the analysis.
- 3.4 Incident patients (i.e. new patients with a first ever supply of a PBS listing) were identified from the first ever supply from 1 January 2016. A look back period to 1 January 2012 was used to identify new patients.
- 3.5 The sequence of supply was based on first ever initiators from 1 January 2016 with a follow up to 31 December 2021.
- 3.6 The following assumptions were used to estimate the population for the existing listings into the forward estimates:
- The narcolepsy market growth will remain stable, consistent with what was observed in 2020 and 2021 (with no impact of global shortages or other circumstances that would significantly shift the market growth).
 - If the clinical criteria for modafinil and armodafinil are updated to allow for the first line treatment of narcolepsy, 40% of the forecasted dexamfetamine using population will switch to modafinil therapy and 40% to armodafinil therapy.
- 3.7 As the PBAC has advised that there was insufficient evidence to support a higher price for armodafinil and modafinil over dexamfetamine in the first line setting, the DPMQ per patient per annum of armodafinil and modafinil was matched to that of dexamfetamine at the maximum doses for the treatment of narcolepsy (250 mg, 400 mg, and 60 mg respectively).
- 3.8 As armodafinil was supplied through three different listings, the proportions of patients dispensed each listed item was based on the proportions in 2021.

Equi-effective doses

- 3.9 The respective product information of dexamfetamine, modafinil and armodafinil shows that the maximum dose for the treatment of narcolepsy is 60 mg, 400 mg, and 250 mg respectively. Therefore, the equi-effective doses are dexamfetamine 60 mg \equiv modafinil 400 mg \equiv armodafinil 250 mg.

Drug cost/patient/year

- 3.10 Assuming that a patient takes the maximum dose for the treatment of narcolepsy, the current drug costs/patient/year using the DPMQ as at May 2022 for dexamfetamine, modafinil and armodafinil are:

Public Summary Document – May 2022 PBAC Meeting

- Dexamfetamine 5 mg at a dose of 12 tablets per day: \$1,020.54
- Modafinil 100 mg at a dose of 4 tablets per day: \$2,517.04
- Armodafinil 50 mg at a dose of 5 tablets per day¹: \$3,107.98
- Armodafinil 150 mg at a dose of 1 tablet per day: \$1,812.59
- Armodafinil 250 mg at a dose of 1 tablet per day¹: \$2,963.44

Financial implications

3.11 Assuming a consistent market growth and no changes to the current PBS restrictions and DPMQ, the estimated costs of armodafinil, dexamfetamine, and modafinil over the forward estimates (2022-2027) would be:

- Armodafinil: \$30 million to < \$40 million
- Dexamfetamine: \$0 to < \$10 million
- Modafinil: \$20 million to < \$30 million
- Total cost: \$60 million to < \$70 million

3.12 If the PBS listings of armodafinil and modafinil were changed to allow the equal first line treatment of narcolepsy, assuming a market share split as outlined in paragraph 3.6, and at a similar annual cost to dexamfetamine, the estimated cost over the forward estimates would be:

- Armodafinil: \$10 million to < \$20 million
- Dexamfetamine: \$0 to < \$10 million
- Modafinil: \$10 million to < \$20 million
- Total cost: \$20 million to < \$30 million

¹ PI recommended dose is 150-250 mg/day. Maximum dose used for a conservative estimate.

Public Summary Document – May 2022 PBAC Meeting

Table 1: Estimated usage and financial expenditure of armodafinil, modafinil, and dexamfetamine

| | 2022 | 2023 | 2024 | 2025 | 2026 | 2027 |
|--|---------------|---------------|---------------|---------------|---------------|---------------|
| Patients | ¹ | ¹ | ¹ | ¹ | ¹ | ¹ |
| Dexamfetamine scripts | ² | ² | ² | ² | ² | ² |
| Modafinil scripts | ³ | ³ | ³ | ³ | ³ | ³ |
| Armodafinil scripts | ⁴ | ⁴ | ⁴ | ⁵ | ⁵ | ⁵ |
| Dexamfetamine cost with proposed DPMQ | | | | | | |
| Cost | ⁶ | ⁶ | ⁶ | ⁶ | ⁶ | ⁶ |
| Co-payments | ⁶ | ⁶ | ⁶ | ⁶ | ⁶ | ⁶ |
| Cost less co-payments | ⁶ | ⁶ | ⁶ | ⁶ | ⁶ | ⁶ |
| Modafinil cost with proposed DPMQ | | | | | | |
| Cost | ⁶ | ⁶ | ⁶ | ⁶ | ⁶ | ⁶ |
| Co-payments | ⁶ | ⁶ | ⁶ | ⁶ | ⁶ | ⁶ |
| Cost less co-payments | ⁶ | ⁶ | ⁶ | ⁶ | ⁶ | ⁶ |
| Armodafinil cost with proposed DPMQ | | | | | | |
| Cost | ⁶ | ⁶ | ⁶ | ⁶ | ⁶ | ⁶ |
| Co-payments | ⁶ | ⁶ | ⁶ | ⁶ | ⁶ | ⁶ |
| Cost less co-payments | ⁶ | ⁶ | ⁶ | ⁶ | ⁶ | ⁶ |
| Net cost to PBS | ⁶ | ⁶ | ⁶ | ⁶ | ⁶ | ⁶ |
| Cost to PBS at current DPMQ | ⁶ | ⁶ | ⁶ | ⁷ | ⁷ | ⁷ |
| Financial impact to Government | ⁻⁶ | ⁻⁶ | ⁻⁶ | ⁻⁶ | ⁻⁶ | ⁻⁶ |

DPMQ = dispensed price per maximum quantity, PBS = Pharmaceutical Benefits Scheme

The redacted values correspond to the following ranges:

¹10,000 to < 20,000

²25,000 to < 10,000

³30,000 to < 40,000

⁴40,000 to < 50,000

⁵50,000 to < 60,000

⁶\$0 to < \$10 million

⁷\$10 million to < \$20 million

3.13 It was estimated that if the clinical criteria of armodafinil and modafinil were revised to allow equal first-line use for the treatment of narcolepsy, using a similar annual cost to dexamfetamine and the assumptions outlined in paragraph 3.6, there would be a net saving to government of \$30 million to < \$40 million over the forward estimates.

For more detail on PBAC's view, see section 4 PBAC outcome.

4 PBAC Outcome

4.1 The PBAC recommended the listing of modafinil and armodafinil as first-line treatment for patients with narcolepsy on a cost-minimisation basis to dexamfetamine.

Public Summary Document – May 2022 PBAC Meeting

- 4.2 The PBAC noted that, under section 101(3B) of the Act, a significant improvement in efficacy or reduction of toxicity over the alternative therapy or therapies is required to recommend armodafinil or modafinil at a higher price than dexamfetamine. The PBAC considered that there was no clinical evidence to suggest that modafinil or armodafinil have superior comparative effectiveness or safety compared to dexamfetamine. The PBAC therefore considered that both armodafinil and modafinil should not be more costly than dexamfetamine if listed for the first-line treatment of narcolepsy.
- 4.3 The PBAC considered that the equi-effective doses are dexamfetamine 60 mg ≡ modafinil 400 mg ≡ armodafinil 250 mg.
- 4.4 The PBAC noted that there are currently no head-to-head comparison data for dexamfetamine versus modafinil or armodafinil.
- 4.5 The PBAC considered that an extension to listing for armodafinil and/or modafinil should not result in additional net cost to Government.

Outcome:

Recommended

5 Recommended listing

5.1 Amend existing listing as follows:

| Name, Restriction, Manner of administration and form | PBS item code | Max. qty packs | Max. qty units | №.of Rpts | Proprietary Name and Manufacturer |
|--|---------------|----------------|----------------|-----------|-----------------------------------|
| MODAFINIL modafinil 100 mg tablet, 60 | 8816B | 2 | 120 | 5 | Various brands and sponsors |

| Name, Restriction, Manner of administration and form | PBS item code | Max. qty packs | Max. qty units | №.of Rpts | Proprietary Name and Manufacturer |
|--|---------------|----------------|----------------|-----------|--|
| ARMODAFINIL armodafinil 50 mg tablet, 30 | 10922W | 2 | 60 | 5 | Nuvigil Teva Pharma Australia Pty Ltd |
| armodafinil 150 mg tablet, 30 | 10912H | 1 | 30 | 5 | |
| armodafinil 250 mg tablet, 30 | 10919Q | 1 | 30 | 5 | |

Restriction Summary / Treatment of Concept:

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|--|
| Category / Program: GENERAL – General Schedule (Code GE) |
| Prescriber type: <input checked="" type="checkbox"/> Medical Practitioners |
| Restriction type / Method: <input checked="" type="checkbox"/> Authority Required – (in writing only via post/HPOS upload) |
| Note: This drug is not PBS-subsidised when used in combination with PBS-subsidised dexamfetamine sulfate or modafinil/armodafinil |
| Indication: Narcolepsy |
| Treatment Phase: Treatment phase: Initial 1 - treatment of narcolepsy without cataplexy |
| Treatment criteria: |
| Must be treated by a qualified sleep medicine practitioner or neurologist |

Public Summary Document – May 2022 PBAC Meeting

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|--|---|
| | Clinical criteria: |
| | The treatment must be for use when therapy with dexamfetamine sulfate poses an unacceptable medical risk; or |
| | The treatment must be for use when intolerance to dexamfetamine sulfate is of a severity to necessitate treatment withdrawal |
| | AND |
| | Patient must have experienced excessive daytime sleepiness, recurrent naps or lapses into sleep occurring almost daily for at least 3 months |
| | AND |
| | Patient must have a mean sleep latency less than or equal to 10 minutes on a Multiple Sleep Latency Test (MSLT); or |
| | Patient must have an electroencephalographic (EEG) recording showing the pathologically rapid development of REM sleep |
| | AND |
| | Patient must not have any medical or psychiatric disorder that could otherwise account for the hypersomnia |
| | The presence of any one of the following indicates treatment with dexamfetamine sulfate poses an unacceptable medical risk: (a) a psychiatric disorder; (b) a cardiovascular disorder; (c) a history of substance abuse; (d) glaucoma; (e) any other absolute contraindication to dexamfetamine sulfate as specified in the TGA approved Product Information. |
| | The MSLT must be preceded by nocturnal polysomnography. Sleep prior to the MSLT must be at least 6 hours in duration. |
| | The authority application must be made in writing and must include the following: (a) a completed authority prescription form; and (b) a completed Narcolepsy Initial PBS authority application and Supporting information form; and (c) details of the contraindication or intolerance to dexamfetamine sulfate; and (c) either: (i) the result and date of the polysomnography test and Multiple Sleep Latency Test (MSLT) conducted by, or under the supervision of, a qualified sleep medicine practitioner; or (ii) the result and date of the electroencephalograph (EEG), conducted by, or under the supervision of, a neurologist. The polysomnography, MSLT or EEG test reports must be provided with the authority application. |
| | Administrative Advice: Any queries concerning the arrangements to prescribe may be directed to Services Australia on 1800 700 270 (hours of operation 8 a.m. to 5 p.m. EST Monday to Friday). Prescribing information (including Authority Application forms and other relevant documentation as applicable) is available on the Services Australia website at www.servicesaustralia.gov.au Applications for authority to prescribe should be submitted online using the form upload facility in Health Professional Online Services (HPOS) at www.servicesaustralia.gov.au/hpos Or mailed to: Services Australia Complex Drugs Reply Paid 9826 HOBART TAS 7001 |
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Public Summary Document – May 2022 PBAC Meeting

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|--|--|
| | <input checked="" type="checkbox"/> Authority Required – (telephone/online PBS Authorities system) - |
| | Note: This drug is not PBS-subsidised when used in combination with PBS-subsidised dexamfetamine sulfate or modafinil/armodafinil |
| | Treatment Phase: Treatment phase: Initial 2 - treatment of narcolepsy with cataplexy |
| | Treatment criteria: |
| | Must be treated by a qualified sleep medicine practitioner or neurologist |
| | Clinical criteria: |
| | The treatment must be for use when therapy with dexamfetamine sulfate poses an unacceptable medical risk; or |
| | The treatment must be for use when intolerance to dexamfetamine sulfate is of a severity to necessitate treatment withdrawal |
| | AND |
| | Patient must have experienced excessive daytime sleepiness, recurrent naps or lapses into sleep occurring almost daily for at least 3 months |
| | AND |
| | Patient must have a definite history of cataplexy documented in their medical records for auditing purposes, |
| | AND |
| | Patient must not have any medical or psychiatric disorder that could otherwise account for the hypersomnia |
| | The presence of any one of the following indicates treatment with dexamfetamine sulfate poses an unacceptable medical risk: (a) a psychiatric disorder; (b) a cardiovascular disorder; (c) a history of substance abuse; (d) glaucoma; (e) any other absolute contraindication to dexamfetamine sulfate as specified in the TGA approved Product Information. |
| | Administrative Advice: Applications for authorisation under this restriction may be made in real time using the Online PBS Authorities system (see www.servicesaustralia.gov.au/HPOS) or by telephone by contacting Services Australia on 1800 700 270 (hours of operation 8 a.m. to 5 p.m. EST Monday to Friday). |

This restriction may be subject to further review. Should there be any changes made to the restriction the sponsor(s) will be informed.

6 Context for Decision

The PBAC helps decide whether and, if so, how medicines should be subsidised through the Pharmaceutical Benefits Scheme (PBS) in Australia. It considers applications regarding the listing of medicines on the PBS and provides advice about other matters relating to the operation of the PBS in this context. A PBAC decision in relation to PBS listings does not necessarily represent a final PBAC view about the merits of the medicine or the circumstances in which it should be made available through the PBS. The PBAC welcomes applications containing new information at any time.

7 Sponsor's Comment

The sponsor had no comment.