

11.02 MIDAZOLAM,

Oromucosal solution in pre-filled syringe 2.5 mg in 0.25 mL,

Oromucosal solution in pre-filled syringe 5 mg in 0.5 mL,

Oromucosal solution in pre-filled syringe 7.5 mg in 0.75 mL,

Oromucosal solution in pre-filled syringe 10 mg in 1 mL,

Zyamis[®],

Clinect Pty Ltd

1 Purpose

- 1.1 The Category 3 submission requested a Section 85, Authority Required (telephone/online) listing of midazolam oromucosal solution in pre-filled syringes (2.5 mg, 5 mg, 7.5 mg and 10 mg), for the treatment of generalised convulsive status epilepticus (GCSE) in patients aged over 6 months. The purpose of the submission was to provide revised financial estimates and a revised risk sharing arrangement (RSA) for PBAC consideration.
- 1.2 In November 2022, the PBAC recommended midazolam for this indication. The PBAC advised that the cost-effectiveness of midazolam would be acceptable at the price proposed in the early re-entry resubmission (AEMP \$| per syringe) with an RSA and 100% rebate above caps to address concerns about financial uncertainty. The recommended caps were based on the estimates proposed by the sponsor in November 2022 (net cost to PBS/RPBS of \$20 million to < \$30 million over 6 years).
- 1.3 The submission stated that it was presented “to formalise negotiations between the Sponsor and the Department following the positive PBAC recommendation at its November 2022 meeting”. The submission noted sponsor concerns including financial risks associated with uncertain utilisation, high import costs, short shelf life and write off risks (especially in relation to multiple presentations being proposed for listing).

2 Background

Registration status

- 2.1 Midazolam oromucosal solution was listed on the Australian Register of Therapeutic Goods (ARTG) on 22 April 2022. The TGA-approved indication for midazolam

oromucosal solution is for the treatment of generalised convulsive status epilepticus (GCSE), in those over 6 months old.

- 2.2 The pre-PBAC response noted that as part of the TGA registration, the sponsor was required to implement a local Risk Management Plan. It was stated that key aspects of this plan include TGA approved education and training materials for families, carers, clinicians, and pharmacists.

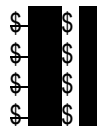
Previous PBAC consideration

- 2.3 This is the third PBAC consideration of midazolam oromucosal solution for the treatment of GCSE. It was previously considered in July 2022 (Category 2 submission) and November 2022 (early re-entry resubmission).
- 2.4 In November 2022, the PBAC recommended the listing of midazolam oromucosal solution in pre-filled syringes (2.5 mg, 5 mg, 7.5 mg and 10 mg), for the treatment of generalised convulsive status epilepticus (GCSE) in patients aged over 6 months. When recommending midazolam for PBS listing in November 2022, the PBAC considered that the cost-effectiveness of midazolam oromucosal solution would be acceptable at the price proposed in the resubmission (AEMP of \$| per syringe) with an appropriate risk sharing arrangement based on the estimates presented by the sponsor in November 2022 (Midazolam Public Summary Document (PSD), November 2022, paragraphs 5.5 – 5.6).




3 Requested listing

- 3.1 The requested listing and suggested wording for the restriction as proposed by the Secretariat is presented below (additions are in italics, deletions in strikethrough).

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MEDICINAL PRODUCT Medicinal Product Pack	Maximum Quantity Packs	Maximum Quantity Units	No. of repeats	Dispensed Price Maximum Quantity	Proprietary Name and Manufacturer
MIDAZOLAM MALEATE Pre-filled oral syringe 2.5 mg in 0.25 mL solution 5 mg in 0.5 mL solution 7.5 mg in 0.75 mL solution 10 mg in 1.0 mL solution	2 2 2 2	2 2 2 2	1 1 1 1		Zyamis® Clinect Pty Ltd
Category / Program: GENERAL – General Schedule (Code GE)					
Restriction type: <input checked="" type="checkbox"/> Authority Required (telephone/online PBS Authorities system)					
Indication: Generalised Convulsive Status Epilepticus					
Treatment Phase: Initial treatment					
Prescriber type: <input checked="" type="checkbox"/> Medical Practitioners					
Clinical criteria:					
Patient must have been assessed to be at significant risk of status epilepticus					
AND					
Clinical criteria:					
Patient must have experienced at least one prolonged seizure (>five minutes duration) requiring emergency medical attention within the previous 5 years					
Population criteria:					
Patient must be at least six months of age					
AND					
Treatment criteria:					
Treatment must be initiated by a specialist physician experienced in the treatment of epilepsy.					
Prescribing Instructions:					
<i>At the time of the authority application, medical practitioners should request the appropriate quantity to cater for the patient's circumstances. Up to a maximum of 10 syringes can be authorised.</i>					
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 888 333.*					
Treatment Phase: Continuing treatment					
Prescriber type: <input checked="" type="checkbox"/> Medical Practitioners <input checked="" type="checkbox"/> Nurse Practitioners					
Clinical criteria:					
Patient must have previously received PBS-subsidised treatment with this drug for this condition					
Prescribing Instructions:					
<i>At the time of the authority application, medical practitioners should request the appropriate quantity to cater for the patient's circumstances. Up to a maximum of 10 syringes can be authorised.</i>					
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 888 333.*					

*PBS approvals system should be programmed to allow higher quantities on request if justified for individual patients requiring more frequent doses, but not more than 10 syringes could be authorised per prescription.

3.2 The submission requested an ex-manufacturer price of \$  per syringe. The corresponding DPMQ for a maximum quantity of 2 syringes is \$  based on current fees, this has been amended in the requested listing above (the submission had calculated \$  based on outdated fees).

- 3.3 The proposed price for 2 syringes remains considerably higher than the price of 10 midazolam hydrochloride ampoules which are currently used off label for this indication (DPMQ = \$40.76 for midazolam 5 mg/mL injection, 10 x 1 mL ampoules, refers to DPMQ for the Prescriber Bag Schedule for PBS Item 10178Q).
- 3.4 The requested restriction was consistent with the PBAC's November 2022 recommendation, other than the requested number of repeats. The submission requested a maximum quantity of 2 syringes with 1 repeat, whereas the PBAC had recommended a maximum quantity of 2 syringes with 2 repeats (Section 6 of the November 2022 PBAC PSD). Based on the submission's estimates, many patients would require fewer than 4 syringes per 12-month period (an average of 3.8 syringes was estimated for patients experiencing 3 PACS per year; Table 1). The pre-PBAC response stated that a maximum quantity of 2 syringes with 1 repeat would meet the requirements for a large proportion of patients, and for patients with higher than the average number of seizures, 2 repeats would be appropriate.
- 3.5 The submission stated that the PBS approvals system should be programmed to allow higher quantities on request if justified for individual patients requiring more frequent doses, but not more than 10 syringes could be authorised per script. This is consistent with the PBAC's November 2022 advice (paragraph 5.3). The Secretariat proposed to include this information in a Prescribing Instruction.
- 3.6 The submission requested an Authority Required listing (telephone/online PBS Authorities system). This is consistent with the PBAC's November 2022 recommendation.
- 3.7 The Secretariat notes that two sets of item codes will be required, one for initial treatment and one for continuing. This is to enable the addition of Nurse Practitioner prescribing for continuing treatment.
- 3.8 *For more detail on PBAC's view, see section 5 PBAC outcome.*

4 Consideration of the evidence

Sponsor hearing

- 4.1 There was no hearing for this item.

Consumer comments

- 4.2 The PBAC noted and welcomed the input from individuals (18), health care professionals (9) and organisations (7) via the Consumer Comments facility on the PBS website. The comments were generally consistent with those considered previously by the PBAC in November 2022 (1) and July 2022 (6), describing the benefits of timely and accurate treatment. Midazolam was described as an essential emergency medication. It was noted that midazolam in pre-filled syringes would improve access to effective medication particularly for those living far from hospital settings, and support parents/carers experiencing difficulties using the ampoules. Concerns were

raised about affordability if the drug is not PBS listed. The input discussed the serious risks associated with prolonged seizures, including Sudden Unexpected Death in Epilepsy (SUDEP). The input stated that rapid management of seizures of more than 5 minutes duration was a critical action to reduce morbidity and potential mortality from severe epilepsy. The input described the need for adequate training regarding midazolam administration, and the need to update epilepsy management plans. The input noted training would be a critical safety factor for patients in a wide variety of settings in addition to the home, such as school, day care and sporting situations, with different people supervising care.

- 4.3 The PBAC noted the advice received from Epilepsy ACT, The Epilepsy Centre (SA & NT), Epilepsy Australia, SCN2A Australia, Epilepsy Action Australia, Epilepsy Society of Australia and the National Paediatric Medicines Forum, supporting the proposed PBS listing. Three of the organisations had also provided comment in July 2022 (Epilepsy Action Australia, Epilepsy Australia, and National Paediatric Medicines Forum). Main themes described in the comments included ease of administration during a stressful medical situation and reducing the risk of overdosing or underdosing. The comments indicated that compared with the off-label use of ampoules, pre-filled syringes would lead to more effective use of the drug as correct dosages would be given, there was less risk of harm from incorrect dosing, and there was reduced risk of midazolam loss/abuse.

Estimated PBS usage and financial implications

- 4.4 The submission stated that changes were made to improve the accuracy of the utilisation estimates. The main change was to explicitly estimate the number of syringes needed for treatment of patients with high frequency seizures as shown in Table 1.
- 4.5 The submission estimates were derived from a Delphi survey conducted in the UK which explored the frequency distribution of prolonged seizures in the general epileptic population per 6-month period, and common patterns of prescribing (Ludwig and Fisher 2020¹). This study was described in the July 2022 PSD (paragraph 3.3) and November 2022 PSD (paragraph 3.6).
- 4.6 The submission estimated between 0 to 31.6 scripts per patient per year, and a weighted average of 2.15 compared with 1.00 scripts per year estimated in November 2022 (Table 1). The submission did not consider replacement of syringes due to expiry. According to the ARTG public summary, 2.5 mg, 5 mg and 7.5 mg strengths have a lifetime of 14 months and the 10 mg strength has a lifetime of 18 months.

¹ Ludwig C, and Fisher L. 2020. "Buccal Midazolam Solution for the Management of Prolonged Acute Convulsive Seizures: A Cost Analysis." *Pharmacoeconomics* 4:171-9.

4.7 The pre-PBAC response stated that the model provided a weighted average calculation across the expanded patient cohort allowing for prevalent patients to replace their medication annually, if expired, or more frequently when utilised.

Table 1: Annual prescriptions estimated by the submission based on PACS frequency

PACS per 12 months	Proportion of population	Syringes used per year	Scripts per year (assumes 2 syringes per script)
0	30.5%	0.0	0.0
1	13.5%	1.3	0.0
2	10.9%	2.5	1.3
3	8.7%	3.8	1.9
4	7.0%	5.0	2.5
5	5.7%	6.3	3.2
6	4.6%	7.6	3.8
7	3.7%	8.8	4.4
8	2.9%	10.1	5.0
9	2.4%	11.4	5.7
10	1.9%	12.6	6.3
11	1.5%	13.9	6.9
12	1.2%	15.1	7.6
13	1.0%	16.4	8.2
14	0.8%	17.7	8.8
15	0.6%	18.9	9.5
16	0.5%	20.2	10.1
17	0.4%	21.5	10.7
18	0.3%	22.7	11.4
19	0.3%	24.0	12.0
20	0.2%	25.2	12.6
21	0.2%	26.5	13.3
22	0.1%	27.8	13.9
23	0.1%	29.0	14.5
24 – 50 (calculated individually) ^a	0.5%	30.3 to 63.1	15.1 to 31.6
Weighted average in November 2023 submission		4.4774178	2.1535571
Weighted average in November 2022 resubmission		2.00346	1.00173

a. The proportions for patients experiencing 24 to 50 PACS per year were estimated using an exponential trendline of the reported data.

Source: 3a. Scripts – proposed sheet.

PACS= Prolonged acute convulsive seizures

4.8 A summary of changes to the financial estimates is shown in Table 2.

Table 2: Summary of changes to financial estimates

Assumption	Initial submission July 2022	Early re-entry resubmission November 2022	Category 3 submission November 2023
Max qty per script	1	2	2
AEMP	\$ [REDACTED]	\$ [REDACTED] per syringe (\$ [REDACTED] for 2)	\$ [REDACTED] per syringe (\$ [REDACTED] for 2)
DPMQ	\$ [REDACTED]	\$ [REDACTED] (for 2)	\$ [REDACTED] (for 2) (\$ [REDACTED] with current fees)
Fees and mark ups	Fees applying January 2022	Fees applying August 2022	Fees applying June 2023
Patient co-pays	\$41.30 for general benefit patients and \$6.60 for concessional patients	\$42.50 for general benefit patients and \$6.80 for concessional patients	\$30.00 for general benefit patients and \$7.30 for concessional patients
Average scripts per month	0.0834775 doses per month; (=1.00173/12, see below)	0.0834775 doses per month; no change.	0.1794630 doses per month Two changes were noted: 1. Distribution of scripts was estimated based on UK Delphi survey (Ludwig and Fisher 2020). 2. Weighted average treatment failure rate estimated from two clinical trials (Baysun 2005 ² and McIntyre 2005 ³) and assumed to represent the proportion of patients requiring two syringes per episode (26% need two syringes, 74% one syringe).
Average scripts per year	1.00173 The submission assumed one script for all patients in their first year of treatment, and estimated utilisation for used and expired stock based on the proportion of patients experiencing a GCSE event per year and requiring replacement scripts (based on Sillanpaa 2002); and the assumption that patients without an event will require 1 script per year due to expiry (14 month shelf-life with an effective dispensed expiry of 12 months).	1.00173 No change	2.15356 The submission did not consider replacement of syringes due to expiry.
First year of PBS listing	2022	2022	2024 (results in higher patient estimates based on ABS data)

Source: Submission Table 5, page 7.

² Baysun, Ş, Ö F. Aydin, E. Atmaca, and Y. K. Yavuz Güler. 2005. "A comparison of buccal midazolam and rectal diazepam for the acute treatment of seizures." *Clinical Pediatrics* 44 (9):771-776.

³ McIntyre, J., S. Robertson, et al. 2005. "Safety and efficacy of buccal midazolam versus rectal diazepam for emergency treatment of seizures in children: a randomised controlled trial." *Lancet* 366 (9481):205-210.

- 4.9 The estimated financial implications are presented in Table 3. The submission stated that the estimates in the November 2022 resubmission did not account for patients with high frequency seizures, and presented revised estimates which increased the net cost to PBS/RPBS to \$50 million to < \$60 million over 6 years (base case).
- 4.10 The PBAC noted the submission's rationale for increasing the estimated utilisation from an average of 1 script per year to 2.15 scripts per patient per year (Table 1) by incorporating estimates for patients with high frequency seizures based on the UK Delphi survey (Ludwig and Fisher 2020). In addition, the PBAC noted that the study by Ludwig and Fisher reported that most patients (55%) in the general epilepsy population would experience low frequency seizures (zero to one prolonged seizure per 6-month period) and 34% of the population would experience zero prolonged seizures per 6-month period. Based on these estimates it was likely that in many cases, the medicine would need replacement due to product expiry rather than use.
- 4.11 The PBAC considered that a modest increase in the previously recommended utilisation estimates was justified to account for the utilisation of high-frequency patients. The PBAC recommended a 10% increase to the November 2022 estimates, noting that the vast majority of patients would experience less than one prolonged seizure per month based on the estimates in Table 1 (89.9% of patients). The PBAC advised it would be appropriate to revise the estimates such that Year 1 was assumed to be 2024, rather than 2022 as had been assumed in the previous set of estimates that were considered in November 2022. The revised estimates incorporating the PBAC's advice are shown in Table 3, ranging from \$0 to < \$10 million in Year 1 to \$0 to < \$10 million in Year 6.

Table 3: Estimated use and financial implications

	Year 1	Year 2	Year 3	Year 4	Year 5	Year 6
Total Australian population	1	1	1	1	1	1
Children aged 0-17 years diagnosed in Years 1-6						
Incident epilepsy patients	2	2	2	2	2	2
Experiencing GCSE	2	2	2	2	2	2
Treatment uptake	60.00%	80.00%	90.00%	90.00%	90.00%	90.00%
Incident patients	2	2	2	2	2	2
Total incident/persistent treated	2	2	2	2	2	2
Children aged 0-17 years with historical diagnosis up to 6 years prior to Year 1						
Children treated	2	2	2	2	2	2
Total children treated	2	2	2	3	3	3
Adults aged 18-100 years diagnosed in Years 1-6						
Incident epilepsy patients	4	4	4	4	4	4
Experiencing GCSE	2	2	2	2	2	2
Treatment uptake	30.00%	40.00%	50.00%	55.00%	55.00%	55.00%
Incident patients	2	2	2	2	2	2
Total incident/persistent treated	2	2	2	2	3	3
Adults aged 18-100 years with historic diagnosis up to 6 years prior to Year 1						
Adults treated	3	3	3	3	3	3
Total adults treated	3	3	4	4	4	4
Total treated population						
Total patients treated	3	4	4	4	4	4
Estimated cost of midazolam oromucosal solution to the PBS/RPBS						
Number of scripts	5	5	6	6	6	7
Net cost to the PBS	6	8	8	8	8	9
Net cost to the RPBS	6	8	8	8	8	8
Net cost to the PBS/RPBS	6	8	8	9	9	9
Revised PBAC estimates - November 2023, assumes two syringes per script						
Patient years of treatment	4	4	4	4	5	5
Number of scripts	4	4	4	5	5	5
Net cost PBS / RPBS	8	8	8	8	8	8
November 2022 early re-entry resubmission, assumes two syringes per script						
Total patients treated	3	4	4	4	4	4
Number of scripts	3	4	4	4	4	4
Net cost to the PBS/RPBS	8	8	8	8	8	8
July 2022 estimated utilisation and cost (after correction by Evaluator), assumes one syringe per script						
Total patients treated	3	4	4	4	4	4
Number of scripts	3	4	4	4	4	4
Net cost to the PBS/RPBS	8	8	8	8	8	8

Source: Submission Table 8 and Table 9, Table 9 in November 2022 PBAC PSD, and Table 8 in July 2022 PBAC PSD.

Numbers above match the Section 4 UCM workbook of the submission, however the data have not been independently evaluated.

The redacted values correspond to the following ranges:

¹ > 10,000,000

² 500 to < 5,000

³ 5,000 to < 10,000

⁴ 10,000 to < 20,000

⁵ 20,000 to < 30,000

⁶ 30,000 to < 40,000

⁷ 40,000 to < 50,000































⁸ \$0 to < \$10 million

⁹ \$10 million to < \$20 million

Financial Management – Risk Sharing Arrangements

- 4.12 In November 2022 (paragraph 5.5), the PBAC considered that the cost-effectiveness of midazolam oromucosal solution would be acceptable at the price proposed in the resubmission with an appropriate Risk Sharing Arrangement. At that time, the PBAC also advised that a Risk Sharing Arrangement with 100% rebate above annual cap thresholds should be implemented in order to address its concerns about financial uncertainty and that the financial caps should be based on the estimates proposed in the resubmission (net cost to PBS/RPBS ranged from \$0 to < \$10 million in Year 1 to \$0 to < \$10 million in Year 6).
- 4.13 The submission stated that an RSA requiring 100% rebate above the threshold was not viable for the sponsor. The submission stated that the cost of goods for this product is more complex than the cost of the drug alone. It was stated that the costliest components are the custom packaging and device (including tamper proof container), and the high manual component of the production. It was stated that increases in the volume of production do not translate directly to lower costs due to fixed batch sizes, increased risk of batch rejections and device batch failures. The submission also stated there was uncertainty regarding time to reach ‘steady utilisation’ which was estimated to be evident by Year 3.
- 4.14 The pre-PBAC response stated that the sponsor questioned the need for an RSA when the eligibility for the product will be defined by PBS restrictions and managed as authority prescriptions. The pre-PBAC response stated there was no genuine risk of an expanded patient population or use beyond the criteria defined by the restriction.
- 4.15 The details of the RSA proposed by the submission, and the details corresponding to PBAC advice are shown in Table 4 (see paragraph 5.4).

Table 4: Estimated net cost to PBS/RPBS for midazolam and proposed RSA

	Year 1	Year 2	Year 3	Year 4	Year 5	Year 6
Submission						
Estimated net cost to PBS/RPBS (\$)	 ¹	 ¹	 ¹	 ²	 ²	 ²
Proposed RSA threshold (\$)	 ¹	 ¹	 ¹	 ²	 ²	 ²
Proposed rebate above cap (%)	 ¹	 ¹	 ¹	 ¹	 ¹	 ¹
November 2023 PBAC advice						
Estimated net cost to PBS/RPBS (from Table 3) (\$)	 ¹	 ¹	 ¹	 ¹	 ¹	 ¹
RSA threshold (\$)	 ¹	 ¹	 ¹	 ¹	 ¹	 ¹
Rebate above cap (%)	80%	80%	80%	80%	80%	80%

The redacted values correspond to the following ranges:

¹ \$0 to < \$10 million

² \$10 million to < \$20 million

For more detail on PBAC’s view, see section 5 PBAC outcome.

5 PBAC Outcome

- 5.1 The PBAC recommended the listing of midazolam oromucosal solution in pre-filled syringes (2.5 mg, 5 mg, 7.5 mg and 10 mg), for the treatment of generalised convulsive status epilepticus (GCSE) in patients aged over 6 months. The PBAC noted that GCSE presents stressful situations for parents and carers, and considered that the proposed listing, offered clinically meaningful benefits by improved quality use of medicines with easier and more accurate administration. Consistent with its November 2022 advice, the PBAC's recommendation for listing was based on, among other matters, its assessment that the cost-effectiveness of midazolam oromucosal solution in pre-filled syringes would be acceptable if it were cost-minimised against off label use of midazolam ampoules. However, the PBAC recognised there were additional health outcome benefits to this formulation associated with the accurate and timely administration of midazolam during an acute health emergency that justified a significant price premium under the specific circumstances of the restriction. The PBAC noted that the submission had presented revised financial estimates and a revised risk sharing arrangement for PBAC consideration. The PBAC considered that a modest increase in the utilisation estimates was justified to account for the utilisation of patients experiencing high-frequency seizures.
- 5.2 The PBAC reaffirmed that the proposed PBS listing of midazolam oromucosal solution provided in pre-filled syringes, that would be prescribed according to patient body weight, would provide clinically meaningful benefits over the currently used ampoules.
- 5.3 The PBAC noted that the resubmission estimated a net cost to PBS/RPBS that was substantially higher than was presented by the sponsor in the early re-entry resubmission in November 2022, totalling \$50 million to < \$60 million over 6 years compared with \$20 million to < \$30 million in November 2022 (Table 3). The PBAC considered that an increase of this magnitude was not justified by the evidence presented (paragraphs 4.10 to 4.11). The PBAC considered that a modest increase in the previously recommended utilisation estimates was justified to account for the utilisation of high-frequency patients, and that Year 1 should reflect 2024 estimates as presented in Table 3.
- 5.4 The PBAC advised that midazolam could be considered cost-effective at the price proposed in the submission (AEMP of \$ | per syringe) with an appropriate risk sharing arrangement. The PBAC advised that the thresholds for the RSA should be set at the estimated net cost to PBS/RPBS based on PBAC advice (ranging from \$0 to < \$10 million in Year 1 to \$0 to < \$10 million in Year 6), and that 80% rebate above the expenditure threshold should be applied as presented in Table 4.
- 5.5 The PBAC recalled that it had previously sought advice from paediatric neurologists in relation to the proposed restriction (Midazolam PSD November 2022 meeting, paragraph 5.3). The advice noted considerable variability in the frequency and duration of seizures across the population. In acknowledgement of this variability the

PBAC maintained that a risk sharing arrangement was necessary for midazolam, to address concerns about financial uncertainty. The PBAC noted that limited data were available to inform the financial estimates and therefore considered that a utilisation review would be valuable to characterise utilisation patterns in the PBS population. The PBAC requested that the Drug Utilisation Sub Committee (DUSC) undertake an analysis after 3 years of listing, to review the actual utilisation of midazolam in comparison with predicted utilisation.

- 5.6 The PBAC accepted the sponsor’s proposal of a maximum quantity of 2 pre-filled syringes and 1 repeat, whilst retaining the prescribing instruction that up to a maximum of 10 syringes can be authorised for patients with high frequency seizures. The PBAC advised that no increase in the number of repeats should be permitted.
- 5.7 The PBAC advised that midazolam is suitable for prescribing by nurse practitioners for continuing therapy in collaborative practice.
- 5.8 The PBAC recommended that the Early Supply Rule should not apply.
- 5.9 The PBAC found that the criteria prescribed by the *National Health (Pharmaceuticals and Vaccines – Cost Recovery) Regulations 2022* for Pricing Pathway A were not met. Specifically, the PBAC found that in the circumstances of its recommendation for midazolam:
 - a) The treatment is not expected to provide a substantial and clinically relevant improvement in efficacy, or reduction of toxicity, over alternative therapies;
 - b) The treatment is not expected to address a high and urgent unmet clinical need because midazolam ampoules are currently used (off label) for this indication;
 - c) It was not necessary to make a finding in relation to whether it would be in the public interest for the subsequent pricing application to be progressed under Pricing Pathway A because one or more of the preceding tests had failed.
- 5.10 The PBAC noted that this submission is not eligible for an Independent Review as it received a positive recommendation.

Outcome:

Recommended

6 Recommended listing

- 6.1 Add new medicinal item follows:

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MEDICINAL PRODUCT Medicinal Product Pack	Maximum Quantity Packs	Maximum Quantity Units	No. of repeats	Proprietary Name and Manufacturer
MIDAZOLAM				
midazolam maleate 2.5 mg in 0.25 mL solution, pre-filled oral syringe	2	2	1	Zyamis® Clinect Pty Ltd
midazolam maleate 5 mg in 0.5 mL solution, pre-filled oral syringe	2	2	1	
midazolam maleate 7.5 mg in 0.75 mL solution, pre-filled oral syringe	2	2	1	
midazolam maleate 10 mg in 1.0 mL solution, pre-filled oral syringe	2	2	1	

Restriction Summary [new] / Treatment of Concept: [new]	
	Category / Program: GENERAL – General Schedule (Code GE)
	Restriction type: <input checked="" type="checkbox"/> Authority Required (telephone/online PBS Authorities system)
	Indication: Generalised Convulsive Status Epilepticus
	Treatment Phase: Initial treatment
	Prescriber type: <input checked="" type="checkbox"/> Medical Practitioners
	Clinical criteria:
	Patient must have been assessed to be at significant risk of status epilepticus
	AND
	Clinical criteria:
	Patient must have experienced at least one prolonged seizure (>five minutes duration) requiring emergency medical attention within the previous 5 years
	Population criteria:
	Patient must be at least six months of age
	AND
	Treatment criteria:
	Treatment must be initiated by a specialist physician experienced in the treatment of epilepsy.
	Prescribing Instructions: <i>At the time of the authority application, medical practitioners should request the appropriate quantity to cater for the patient's circumstances. Up to a maximum of 10 syringes for each repeat prescription can be authorised.</i>
	Administrative Advice: <i>No increase in the maximum number of repeats may be authorised.</i>
	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 888 333.
	Treatment Phase: Continuing treatment
	Prescriber type: <input checked="" type="checkbox"/> Medical Practitioners <input checked="" type="checkbox"/> Nurse Practitioners
	Clinical criteria:
	Patient must have previously received PBS-subsidised treatment with this drug for this condition
	Prescribing Instructions: <i>At the time of the authority application, medical practitioners should request the appropriate quantity to cater for the patient's circumstances. Up to a maximum of 10 syringes for each repeat prescription can be authorised.</i>
	Administrative Advice: <i>No increase in the maximum number of repeats may be authorised.</i>

	<p>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 888 333.</p>
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This restriction may be subject to further review. Should there be any changes made to the restriction the Sponsor will be informed.

7 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.

8 Sponsor's Comment

The sponsor had no comment.