

11.02 RISPERIDONE

500 microgram and 1 mg tablet

1mg/mL oral liquid,

Various Sponsors.

1 Purpose of Application

- 1.1 To seek PBAC's advice on proposed changes to the PBS-listing of risperidone for use in the context of behavioural and psychological symptoms of dementia (BPSD).

2 Requested listing

- 2.1 The proposal requests the following changes to the existing restriction. Suggestions and additions to the requested listing are added in italics and suggested deletions are crossed out with strikethrough.

Name, Restriction, Manner of administration and form	Max. Qty	No. of Rpts	Proprietary Name and Manufacturer
RISPERIDONE			Various
500 microgram tablet, 20	3	2	
500 microgram tablet, 60	1	2	
1 mg tablet, 60	1	2	
1mg/mL oral liquid, 100 mL	1	2	

Category / Program:	GENERAL – General Schedule (Code GE)
Prescriber type:	<input type="checkbox"/> Dental <input checked="" type="checkbox"/> Medical Practitioners <input checked="" type="checkbox"/> Nurse practitioners <input type="checkbox"/> Optometrists <input type="checkbox"/> Midwives
Episodicity:	-
Severity:	-
Condition:	Behavioural disturbances
PBS Indication:	Behavioural disturbances
Treatment phase:	<i>Commencement of a course of treatment (12 weeks)</i>
Restriction Level / Method:	<input checked="" type="checkbox"/> Streamlined
Clinical criteria:	The condition must be characterised by psychotic symptoms and aggression AND Patient must have dementia of the Alzheimer type AND Patient must have failed to respond to non-pharmacological methods of treatment AND The treatment must be limited to a maximum duration of 12 weeks
Prescriber Instructions:	<i>A patient may only qualify for PBS-subsidised treatment under this restriction once in a 12 month period.</i>

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2.2 In addition to changing the existing restriction for risperidone, the proposal requested adding an additional streamlined authority code for use beyond the first 12 weeks of treatment, as outlined below.

Name, Restriction, Manner of administration and form	Max. Qty	No. of Rpts	Proprietary Name and Manufacturer
RISPERIDONE			Various
500 microgram tablet, 20	3	2	
500 microgram tablet, 60	1	2	
1 mg tablet, 60	1	2	
1mg/mL oral liquid, 100 mL	1	2	

Category / Program:	GENERAL – General Schedule (Code GE)
Prescriber type:	<input type="checkbox"/> Dental <input checked="" type="checkbox"/> Medical Practitioners <input checked="" type="checkbox"/> Nurse practitioners <input type="checkbox"/> Optometrists <input type="checkbox"/> Midwives
Episodicity:	-
Severity:	-
Condition:	<i>Behavioural disturbances</i>
PBS Indication:	<i>Behavioural disturbances</i>
Treatment phase:	<i>Trial of reduction or cessation of treatment; or Recommencement or continuation of treatment</i>
Restriction Level / Method:	<input checked="" type="checkbox"/> Streamlined
Clinical criteria:	<i>The condition must be characterised by psychotic symptoms and aggression AND Patient must have dementia of the Alzheimer type AND Patient must have responded to an initial course of treatment with this drug for this condition AND The treatment must be for dose tapering purposes as part of a trial of treatment reduction or cessation OR Patient must have trialed a period of treatment reduction or cessation with this drug for this condition and experienced worsening or re-emergence of symptoms during this trial AND Patient must be optimised on non-pharmacological methods of treatment.</i>

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<p>Prescriber Instructions:</p>	<p><i>The patient's response to treatment and trial of treatment reduction or cessation must be discussed formally with a psychiatrist or geriatrician or in a documented clinical governance review process involving a least one other medical practitioner; or the patient has been reviewed by a psychiatrist or geriatrician.</i></p> <p><i>Response to treatment is defined as a significant reduction in symptoms of psychosis or aggression.</i></p> <p><i>Patients must cease treatment if there is no improvement in symptoms of psychosis and aggression, or worsening of symptoms with therapy.</i></p> <p><i>Patients must be monitored for adverse effects such as falls, drowsiness leading to reduced self care, incontinence, reduced nutrition, reduced ability to communicate needs/wishes and take part in activities and therapy ceased if harms of therapy outweigh benefits.</i></p> <p><i>Trials of reduction or cessation of therapy should be considered periodically with the intention of maintaining symptom control through non-pharmacological measures wherever possible and/or lowest effective dose therapy.</i></p> <p><i>Evidence of patient benefit from therapy, failure of non-pharmacological approaches to manage symptoms in the absence of therapy, and recurrence of symptoms following reduction or cessation of therapy, trialled on at least 1 occasion, must be documented in the patient's medical records.</i></p>
<p>Administrative Advice:</p>	<p><i>No increase in the maximum quantity or number of units may be authorised</i></p> <p><i>No increase in the maximum number of repeats may be authorised.</i></p>

3 Background

3.1 Risperidone is currently listed on the PBS for the treatment of the following indications:

- schizophrenia and related psychoses;
- acute mania associated with bipolar I disorder;
- behavioural disturbances in dementia;
- conduct and other disruptive disorders in children (over 5 years), adolescents and adults with sub average intellectual functioning or mental retardation in whom destructive behaviours (e.g. aggression, impulsivity and self-injurious behaviours) are prominent; and
- behavioural disorders associated with autism in children and adolescents.

3.2 At the November 2015 PBAC meeting, the PBAC recommended an amendment be made to the risperidone restriction for the treatment of dementia to align with the revised TGA indication, restricting use to moderate to severe dementia of the Alzheimer's type and limiting duration of treatment to 12 weeks.

3.3 The natural history of behavioural disturbance in dementia is a waxing and waning of severity in response to precipitants (clinical and environmental factors) and disease

progression. Whilst improvement in some behaviours may occur in the initial phase of treatment with antipsychotics including risperidone, there is minimal evidence of efficacy beyond 3 months since trials beyond 12 weeks have not been done.

- 3.4 A Cochrane review that investigated withdrawal vs continuation of chronic antipsychotics for behavioural symptoms of dementia found that, in general, antipsychotic discontinuation appeared to make minimal to no difference in overall symptoms as measured by the Neuropsychiatric Inventory.ⁱ Conversely, Patel et al reported that people with severe hallucinations at baseline were significantly more likely to relapse with the cessation of risperidone, compared with those with mild or no hallucinations.ⁱⁱ Devenand et al found that patients with psychosis or agitation–aggression who had a sustained response to antipsychotic treatment for 4 to 8 months had a significantly increased risk of relapse for at least 4 months after discontinuation of risperidone.ⁱⁱⁱ
- 3.5 Deprescribing guidelines that address antipsychotic use for behavioural disturbances of dementia provide regimens to taper and stop antipsychotics in collaboration with the patient and caregiver for persons who have been treated for 3 months or more and whose symptoms are controlled or have had no response to therapy.^{iv v}
- 3.6 The former Minister for Senior Australians and Aged Care, the Hon Ken Wyatt AM MP, requested the Australian Government Chief Medical Officer, Professor Brendan Murphy, to establish and chair a Clinical Advisory Committee to consider options to reduce the inappropriate use of chemical restraint in residential aged care. The Committee consisted of a range of clinicians with expertise in their fields and aged care, including GPs, psychiatrist, nurse practitioners, pharmacist, as well as a representative from the Australian Commission on Safety and Quality in Healthcare, and the Aged Care Quality and Safety Commission’s interim Chief Clinical Advisor. The Committee explored a range of measures across the themes of education, workforce, best practice prescribing behaviours, alternative approaches (e.g. diversional therapies) and clinical governance.
- 3.7 The Committee provided an options paper to Minister Wyatt that included a number of recommendations to be further scoped for implementation. One of these recommendations was *‘Exploring the potential for stronger prescribing restrictions on antipsychotic drugs beyond the initial 12-week trial with an additional streamlined authority code being required for prescriptions for risperidone after the initial 12 weeks. This would also include detailed guidance material for the prescriber’*.
- 3.8 As part of the Chief Medical Officer’s witness statement and evidence to the Royal Commission into Aged Care Quality and Safety (the Royal Commission), he discussed this recommendation and that work was underway to firstly ensure the current streamlined authority for risperidone includes a ‘hard stop’ after 12 weeks and also including a new streamlined authority to be used in the instances where risperidone is effective and required in treating a person’s symptoms.

- 3.9 However, there are no mechanisms currently available to implement a ‘hard stop’ when using streamlined authority codes. The proposed restriction changes therefore aim to provide greater clarity to prescribers around appropriate use of risperidone in this population and would enhance the ability for the Department of Health to undertake compliance activities to identify inappropriate prescribing, however the changes would not prohibit inappropriate prescribing.

4 Current situation

- 4.1 There have been media reports and published studies of the overuse of antipsychotic medications in residential aged care. The Royal Commission has also received commentary from a range of audiences on this issue.
- 4.2 The Aged Care Clinical Advisory Committee noted that there was a clear problem with the overuse of antipsychotic medications and benzodiazepines in residential aged care. It suggested that a small proportion (estimated at about 10%) of the current use was justified in the treatment of often pre-existing, mental illness and some rare, acutely psychotic, manifestations of dementia.
- 4.3 Non-pharmacological therapy is equally or more effective than antipsychotics in most people with behavioural disturbance of dementia and must be first line therapy. Antipsychotics are effective in approximately one in five people with dementia for short-term management of significant agitation, aggression and psychosis.^{vi}

5 PBAC Outcome

- 5.1 The PBAC recommended the proposed changes to the PBS listing for initiation of risperidone for BPSD and the proposed listing for continuation of risperidone for BPSD (as outlined in section 6).
- 5.2 The PBAC noted that the intent of the proposed restriction changes for risperidone is to reduce inappropriate prescribing in patients beyond 12 weeks. The PBAC noted there is minimal evidence of efficacy beyond 3 months since trials beyond 12 weeks have not been conducted (see paragraphs 3.3-3.4) and was concerned with the over-use of chemical restraints in patients with lesser severity of BPSD and as a substitute for first line non-pharmacological treatments. It acknowledged that there is a place in therapy for using risperidone to control moderate to severe BPSD beyond 12 weeks, but that this is likely to be a very small patient group.
- 5.3 The PBAC noted that the proposed restriction changes would allow the Department to undertake retrospective utilisation analyses of patients continuing on risperidone beyond 12 weeks and may assist in identifying inappropriate prescribing. The PBAC further noted that these analyses may be used to inform compliance activities.
- 5.4 The PBAC recommended the level of authority for risperidone for BPSD for initial listing be Authority Required (STREAMLINED), and for the new continuing listing for

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BPSD be Authority Required (Telephone) to further support the intent of the changes in reducing inappropriate prescribing of risperidone in BPSD beyond 12 weeks. The PBAC noted there may be practical considerations relating to increasing the level of authority and requested that the Department investigate whether this change could be feasibly implemented.

- 5.5 The PBAC expressed concern about the availability of specialists (psychiatrists and geriatricians) to advise whether continuation is appropriate, however it noted that the restriction also included a review process with another medical practitioner as an option and the PBAC was satisfied that this would overcome any equity issues that may occur in accessing specialists.
- 5.6 The PBAC considered that the wording ‘documented clinical governance review process’ may cause confusion. The PBAC recommended the wording change to ‘documented clinical review process’ and noted that prescribers should be familiar with the *Guiding principles for medication management in residential aged care facilities 2012*.^{vii}
- 5.7 The PBAC considered that prescribers would mostly have an intermittent view of patients as opposed to the long-term and intimate view of caregivers and family members of patients in relation to assessing their symptoms and response to treatments.
- 5.8 The PBAC noted that risperidone is the most prescribed antipsychotic on the PBS, followed by olanzapine and quetiapine. Risperidone has the most evidence for use in controlling moderate to severe BPSD and is the only drug listed on the PBS for behavioural disturbances.
- 5.9 The PBAC was concerned that this restriction change may result in an increase in off-label prescribing of other more sedating or harmful agents such as: other antipsychotics (e.g. olanzapine and quetiapine), benzodiazepines (e.g. diazepam), and older antipsychotics (e.g. haloperidol). The PBAC also noted that low strength quetiapine is known to be used off-label and prescribed privately as a sedative in dementia. In this regard, the PBAC noted a review into the effects of restriction changes where a significant increase in the discontinuation of 25mg quetiapine after initiation was recorded when the repeat was removed from the listing in January 2014 (Brett et al, 2017)^{viii}.
- 5.10 The PBAC noted that risperidone and the medicines referred to in the above paragraph are relatively inexpensive, and the changes will not prevent prescribers writing these medicines on a private prescription. It considered that the inappropriate prescribing of chemical restraints is a broader problem not exclusive to risperidone, even though these other medicines may not be listed or registered for use in controlling BPSD. The PBAC considered this change should form part of a broader suite of measures to improve the quality use of medicines in people with dementia in residential aged care.

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- 5.11 The PBAC recommended that a review of the utilisation of risperidone and as well as other antipsychotics and benzodiazepines (see paragraph 5.9) be conducted at no later than 2 years following the restriction changes.
- 5.12 The PBAC noted the recommendation from the Clinical Advisory Committee (see paragraph 3.7) included “detailed guidance material for the prescriber” and referred this back to the Department to facilitate.
- 5.13 The PBAC advised that the new listing for risperidone in the continuation phase is suitable for prescribing by nurse practitioners.
- 5.14 The PBAC recommended that the Early Supply Rule should not apply to the new listing for risperidone in the continuation phase.

6 Recommended listing

6.1 Amend existing listing as follows:

Name, Restriction, Manner of administration and form	Max. Qty	No. of Rpts	Proprietary Name and Manufacturer
RISPERIDONE			Various
500 microgram tablet, 20	3	2	
500 microgram tablet, 60	1	2	
1 mg tablet, 60	1	2	
1mg/mL oral liquid, 100 mL	1	2	

Category / Program:	GENERAL – General Schedule (Code GE)
Prescriber type:	<input type="checkbox"/> Dental <input checked="" type="checkbox"/> Medical Practitioners <input checked="" type="checkbox"/> Nurse practitioners <input type="checkbox"/> Optometrists <input type="checkbox"/> Midwives
Episodicity:	-
Severity:	-
Condition:	Behavioural disturbances
PBS Indication:	Behavioural disturbances
Treatment phase:	<i>Commencement of a course of treatment (12 weeks) Initial treatment</i>
Restriction Level / Method:	<input checked="" type="checkbox"/> Streamlined
Clinical criteria:	The condition must be characterised by psychotic symptoms and aggression AND Patient must have dementia of the Alzheimer type AND Patient must have failed to respond to non-pharmacological methods of treatment AND The treatment must be limited to a maximum duration of 12 weeks <i>Patient must not receive more than 12 weeks of treatment under this restriction.</i>
Prescriber Instructions:	<i>A patient may only qualify for PBS-subsidised treatment under this restriction once in a 12 month period.</i>

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6.2 Add new item:

Name, Restriction, Manner of administration and form	Max. Qty	No. of Rpts	Proprietary Name and Manufacturer
RISPERIDONE			Various
500mcg tablet, 20	3	2	
500 mcg tablet, 60	1	2	
1 mg tablet, 60	1	2	
1mg/mL oral liquid, 100 mL	1	2	

Category / Program:	GENERAL – General Schedule (Code GE)
Prescriber type:	<input type="checkbox"/> Dental <input checked="" type="checkbox"/> Medical Practitioners <input checked="" type="checkbox"/> Nurse practitioners <input type="checkbox"/> Optometrists <input type="checkbox"/> Midwives
Episodicity:	-
Severity:	-
Condition:	Behavioural disturbances
PBS Indication:	Behavioural disturbances
Treatment phase:	<i>Trial of reduction or cessation of treatment; or Recommencement or continuation of treatment Continuing treatment</i>
Restriction Level / Method:	<input checked="" type="checkbox"/> Streamlined <input checked="" type="checkbox"/> Authority Required – Telephone, Electronic
Clinical criteria:	The condition must be characterised by psychotic symptoms and aggression AND Patient must have dementia of the Alzheimer type AND Patient must have responded to an initial course of treatment with this drug for this condition AND The treatment must be for dose tapering purposes as part of a trial of treatment reduction or cessation OR Patient must have trialed a period of treatment reduction or cessation with this drug for this condition and experienced worsening or re-emergence of symptoms during this trial AND Patient must be optimised on non-pharmacological methods of treatment.

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<p>Prescriber Instructions:</p>	<p>The patient’s response to treatment and trial of treatment reduction or cessation must be discussed formally with a psychiatrist or geriatrician or in a documented clinical governance review process involving a least one other medical practitioner; or the patient has been reviewed by a psychiatrist or geriatrician.</p> <p>Response to treatment is defined as a significant reduction in symptoms of psychosis or aggression.</p> <p>Patients must cease treatment if there is no improvement in symptoms of psychosis and aggression, or worsening of symptoms with therapy.</p> <p>Patients must be monitored for adverse effects such as falls, drowsiness leading to reduced self care, incontinence, reduced nutrition, reduced ability to communicate needs/wishes and take part in activities and therapy ceased if harms of therapy outweigh benefits.</p> <p>Trials of reduction or cessation of therapy should be considered periodically with the intention of maintaining symptom control through non-pharmacological measures wherever possible and/or lowest effective dose therapy.</p> <p>Evidence of patient benefit from therapy, failure of non-pharmacological approaches to manage symptoms in the absence of therapy, and recurrence of symptoms following reduction or cessation of therapy, trialled on at least 1 occasion, must be documented in the patient’s medical records.</p>
<p>Administrative Advice:</p>	<p>No increase in the maximum quantity or number of units may be authorised</p> <p>No increase in the maximum number of repeats may be authorised.</p>

7 Context for Decision

7.1 The PBAC helps decide whether and, if so, how medicines should be subsidised in Australia. It considers submissions in this context. A PBAC decision not to recommend listing, or not to recommend changing a listing does not represent a final PBAC view about the merits of the medicine.

ⁱ Van Leeuwen E, Petrovic M, van Driel ML, De Sutter AI, Vandeer Stickele R, Declercq T et al. Withdrawal versus continuation of long-term antipsychotic drug use for behavioural and psychological symptoms in older people with dementia. The Cochrane database of systematic reviews. 2018; 3: Cd007726.

ⁱⁱ Patel AN, Lee S, Andrews HF, Pelton GH, Schultz SK, Sultzer DL et al. Prediction of relapse after discontinuation of antipsychotic treatment in Alzheimer’s Disease: the role of hallucinations. The American Journal of Psychiatry 2017; 174(4): 362-9.

ⁱⁱⁱ Devenand DP, Mintzer J, Schultz SK, Andrews HF, Sultzer DL, de la Pena D et al. Relapse risk after discontinuation of risperidone in Alzheimer’s Disease. N Engl J Med 2012; 367: 1497-507.

^{iv} Primary Health Tasmania. A guide to deprescribing antipsychotics. 2019.

^v Bjerre LM, Farrell B, Hogel M, Graham L, Lemay G, McCarthy L et al. Deprescribing antipsychotics for behavioural and psychological symptoms of dementia and insomnia. Evidence-based clinical practice guideline. 2018; 64(1): 17-27.

^{vi} A Guide to Deprescribing Antipsychotics, <https://www.primaryhealthtas.com.au/wp-content/uploads/2018/09/A-Guide-to-Deprescribing-Antipsychotics-2019.pdf>

^{vii} <https://www1.health.gov.au/internet/main/publishing.nsf/Content/guide-med-mgmt-aged-care>

^{viii} Jonathan Brett, Andrea Schaffer, Timothy Dobbins, Nicholas A. Buckley, Sallie-Anne Pearson. The impact of permissive and restrictive pharmaceutical policies on quetiapine dispensing: Evaluating a policy pendulum using interrupted time series analysis. Pharmacoepidemiol Drug Saf. 2018;1–8.