



Therapeutic brief

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www.dva.gov.au/health/veteransmates

Antipsychotics in dementia

Behavioural and psychological symptoms of dementia (BPSD) are common.^{1,2} These are distressing for patients and carers, and are often a trigger for moving to residential care.^{1,2,3,4,5,6} Symptoms include agitation, aggression, psychosis, wandering, depression, calling out and intrusiveness. These can be difficult to manage.^{1,2,3,4,7,8,9,10}

Antipsychotic agents are frequently used for the management of BPSD (also called neuropsychiatric symptoms of dementia).^{2,11,12,13} Approximately 80% of all prescriptions for antipsychotics in Australia are written by GPs.¹⁴ Almost 6000 veterans living in the community were dispensed an antipsychotic over a 12 month period (December 2004 to December 2005). In the aged-care setting, more than 30% of veterans with high care needs and 20% with low care needs were dispensed an antipsychotic agent.¹⁵

Antipsychotics have limited efficacy for BPSD, and they can cause serious adverse effects in the elderly.³ In many cases non-drug approaches can be used to address mild to moderate behavioural changes in dementia. However, pharmacotherapy may be required when behaviour is excessively disruptive, unsafe, or interferes with the delivery of care.

This therapeutic brief discusses appropriate management strategies for BPSD.

Key points

- Behavioural and environmental interventions should be utilised for the management of BPSD.
- The onset, progress, resolution and relapses of BPSD are unpredictable, as is response to pharmacotherapy.
- Antipsychotics have limited efficacy in BPSD and adverse effects such as accelerated cognitive decline can be counter-productive.
- If an antipsychotic is used, then:
 - Start with a low dose and titrate upwards very slowly according to clinical response; and
 - Review regularly for efficacy and adverse effects, and continue for no longer than 3 months before a dose reduction/trial cessation.

Non-pharmacological management of BPSD

Addressing behavioural and environmental changes may be more clinically useful than pharmacological intervention. Utilise non-pharmacological interventions with pharmacotherapy.^{16,17}

Consider the 'ABC' for the assessment of BPSD:

- **Antecedents** (what causes the behaviour, what leads up to it?)
- **Behaviour** (what is the nature of the behaviour?)
- **Consequences** (what are the consequences of the behaviour for self and others?)

This assessment may be done by family, carers and/or aged-care staff before seeking medical intervention. An understanding of these factors may reveal simple and effective behavioural and environmental interventions.



② Non-pharmacological management of BPSD (cont)

Behavioural problems may result from a mismatch between a patient's care needs and their environment/ care-giver. A change may be as simple as changing times of bathing or placing familiar objects in a patient's room.¹ Recent evidence provides some support for the efficacy of activity programs, familiar music, light therapy, behaviour therapy and changes to physical environment.^{1,2,18}

Environmental factors can cause disorientation, loneliness, boredom, worry, discomfort or humiliation, leading to BPSD. These may include sitting all day in an

uncomfortable position; hunger or thirst; poor lighting; improper heating; excessive noise; being surrounded by unfamiliar people; disruption to normal routines; lack of opportunity to participate in meaningful and useful activities; needing assistance with private tasks such as bathing or toileting and feeling pressured to do tasks that are difficult for the person.

The National Dementia Behaviour Advisory Service (1800 699 799) provides information about managing behavioural problems.

Pharmacological management of BPSD

Behavioural problems in dementia may be due to underlying and remediable conditions such as pain, depression, anxiety or delirium.¹ Common causes of delirium in the elderly are respiratory and urinary tract infections, anticholinergic drug load and benzodiazepines.¹ Nevertheless, severe behavioural disturbances may need intervention (possibly pharmacological) until the underlying cause is resolved.

Antipsychotic medications provide limited improvements for a minority of patients with BPSD.^{3,19} There are, however, few (if any) effective alternative medications.

Pharmacotherapy with antipsychotic agents is often used as the first line treatment for these disorders, despite evidence of only limited efficacy.³ Factors related to the caregiver and the caring situation may significantly influence the decision to use antipsychotics.¹⁰ These include patient distress, caregiver despair, a lack of formal training and resources for non-pharmacological approaches such as behavioural interventions or environmental changes and few alternative pharmacological approaches.⁶

Table 1. Clinical practice points for pharmacotherapy in BPSD

1. Before starting an antipsychotic

- Explore environmental changes and behaviour modification for patients with BPSD.^{2,20}
- Assess and treat any underlying conditions such as pain, delirium or urinary tract infection, which may cause behavioural problems.
- Consider pharmacotherapy as the initial management strategy for patients with BPSD when severe symptoms cannot be easily contained and when the patient or others are at risk of harm.⁶
- Inform the patient and their family of risks and benefits of proposed pharmacotherapy.²
- Do not use conventional (typical) antipsychotics where dementia with Lewy bodies is suspected, or when the patient has Parkinson's disease, because of an increased risk of adverse effects.²¹ Cardinal features of dementia with Lewy bodies are delirium, visual hallucinations, parkinsonism and extreme sensitivity to antipsychotic agents.

2. Initiating an antipsychotic

- Initiate with a low dose (usually below therapeutic doses used for schizophrenia) and titrate upwards very slowly according to clinical response. The Australian Medicines Handbook recommended dosing for risperidone in BPSD is 0.25 mg orally twice daily, increasing by 0.25 mg orally every 2 or more days with a maximum dose of 2mg (including prn medication) per 24 hours.²²
- Consider a prn regimen when clinical circumstances are episodic or rapidly changing. Specifically define the parameters to govern the prn administration of antipsychotic drugs, including the symptoms to trigger administration, doses, frequency, duration and maximum

daily dose. Carefully defined prn regimens and drug free days can help minimise overall psychotropic burden. Consider a short-term order as an alternative to prn regimen.

- Use a time-limited regimen of antipsychotic drug therapy for BPSD. Use for no longer than 3 months before tapering the dose (see below) and undertaking a trial cessation.^{1,2,6} Monitor for recurrence of symptoms and adjust regimen accordingly.
- **Do not use more than one antipsychotic at any one time.**²³

3. Reviewing antipsychotic use

- Regularly review any underlying medical condition and the use of antipsychotics in people with dementia for clinical efficacy, adverse effects and harm/benefit ratio.¹ Clinical improvement (if it occurs) should be seen within several weeks.²⁴ An HMR or RMMR can provide an opportunity to check duration of treatment, dosing and adverse effects (e.g. over-sedation, cognitive decline).
- Cease the medication if no convincing improvement is seen with an antipsychotic. Revisit non-pharmacological approaches (behavioural and environmental changes) and/or trial another antipsychotic or other psychotropic agent.
- **Do not stop antipsychotics abruptly;** they should be gradually withdrawn to avoid withdrawal symptoms (e.g. dizziness, nausea, vomiting, headache, tremors, insomnia and anxiety). Dose should be tapered by 50% every 2 weeks and stopped after 2 weeks on the minimum dose.
- SSRIs can potentiate the effects of antipsychotics and increase the risk of extra-pyramidal adverse effects.

Table 1. Clinical practice points for pharmacotherapy in BPSD (cont)

4. Other medications

- Consider a short-acting benzodiazepine prn rather than an antipsychotic for acute anxiety or agitation. Most guidelines suggest that benzodiazepines should not be used continuously for longer than 2 weeks. They may exacerbate cognitive impairment in dementia and may increase the risk of falls and associated injuries in older people.²¹
- The potential benefit of anticholinesterases [donepezil (Aricept); galantamine (Reminyl); rivastigmine (Exelon)] and memantine (Ebixa), for BPSD has not been proven. These drugs do not cause cognitive decline, can improve quality of life and have a good safety profile. For less severe behavioural problems when there are other indications, one of these drugs may be preferable to an antipsychotic, but they do not work quickly.
- Antidepressants may be appropriate for depressive symptoms in dementia, but are not recommended for BPSD. Assessment of depression may be difficult in this patient group and specialist assistance may be needed.
- There is insufficient evidence to support the use of valproate, carbamazepine, lithium or gabapentin for BPSD.²

Benefits and risks of antipsychotics in BPSD

Although several clinical trials provide some support for using atypical antipsychotics to treat BPSD, there is no clear evidence of the clinical value of these agents.^{7,19}

Psychotic features, agitation and aggression in people with dementia is difficult to manage and antipsychotics may be modestly effective when used judiciously.^{2,24}

The elderly are particularly susceptible to serious adverse effects from these agents and they should be used with great caution.²⁰ As many as 23% of all adverse drug events in nursing homes are associated with antipsychotic use.²

Table 2. Benefits and risks of antipsychotic therapy for BPSD

Symptoms of BPSD where there is some evidence supporting the use of antipsychotics ³	psychotic features, aggression, agitation
Symptoms of BPSD where there is little or no evidence for efficacy of antipsychotics	depression, apathy, calling out, wandering, sexual disinhibition
Atypical antipsychotics with most evidence of efficacy ³	risperidone (most evidence), olanzapine There is insufficient evidence to systematically evaluate the efficacy of any of the other atypical antipsychotics for BPSD. ³
Conventional vs. atypical antipsychotics	There are insufficient data to make definitive conclusions regarding the relative efficacies of conventional and atypical antipsychotics for BPSD. ²⁵
Response to therapy	Cannot be predicted in individual patients. ²⁴
Mortality risk ¹²	The US Food and Drug Administration (FDA) has determined that the treatment of behavioural disorders or psychosis in elderly patients with dementia with atypical (and possibly conventional) antipsychotics is associated with increased mortality. ^{7,26} This increased risk of death with antipsychotics in the elderly is not supported by all studies. ²⁷
Adverse effects	An increased risk of falls and drowsiness are common to most classes of psychotropic drugs. Additional problems such as cognitive decline, confusion, parkinsonism, akathisia, tardive dyskinesia, social withdrawal, QT prolongation, diabetes, postural hypotension and stroke may occur with antipsychotics. ^{3,28}

PBS subsidy and dosing of antipsychotics in BPSD

Not all atypical antipsychotics are approved for the treatment of behavioural and psychological disturbances in dementia. In Australia, risperidone is the only atypical agent that is both TGA approved and PBS subsidised for this indication.^{1,29} Use of olanzapine for BPSD is therefore off-label. The conventional antipsychotic haloperidol is PBS subsidised without restriction.

Table 3. Oral antipsychotics for BPSD^{1,21,22}

Atypical antipsychotics		
Risperidone (Risperdal)	A total daily dose of 0.5 to 2 mg, administered in 1 or 2 divided doses.	Maximum total dose (including prn medication) not to exceed 2 mg in 24 hours.
Olanzapine (Zyprexa)	A total daily dose of 2.5 to 10 mg, administered in 1 or 2 divided doses.	Maximum total dose (including prn medication) not to exceed 10 mg in 24 hours.
Conventional antipsychotics		
Haloperidol (Serenace)	0.5 mg at night, increase up to 1 mg twice daily as necessary.	Normal final dose is 1-2 mg daily.

What to tell your veteran patient/family/carer

Antipsychotic medicines might help with some behavioural disturbances in dementia, but not all people benefit.

Older people are more vulnerable to serious adverse effects from these medicines and there may be an increased risk of stroke and death, but if severe BPSD are left unmanaged, this in itself may increase the risk of death or serious injury.

Some adverse effects such as sedation, dizziness, confusion, falls and accelerated cognitive decline may appear soon after starting the medicine. Other adverse effects such as Parkinsonism, diabetes and heart problems are more likely after long-term use.

For drug information, including precautions, adverse effects, interactions and contraindications, refer to the AMH Drug Choice Companion: Aged Care²³ and approved product information.

Useful websites and contact numbers

National Dementia Helpline 1800 100 500

National Dementia Behaviour Advisory Service 1800 699 799

Alzheimer's Australia website <https://fightdementia.org.au/>

References

- Byrne GJ. *Pharmacological treatment of behavioural problems in dementia*. Australian Prescriber 2005;28(3):67-69
- Woodward M. *Pharmacological Treatment of Challenging Neuropsychiatric Symptoms of Dementia*. Journal of Pharmacy Practice and Research 2005;35(3):228-234
- Ballard C, Waite J, Birks J. *Atypical antipsychotics for aggression and psychosis in Alzheimer's disease*. Cochrane Database of Systematic Reviews 2006, Issue 1. Art. No.: CD003476. DOI: 10.1002/14651858.CD003476.pub2
- Lawlor BA. *Behavioral and Psychological Symptoms in Dementia: The Role of Atypical Antipsychotics*. Journal of Clinical Psychiatry 2004;65(Supplement 11):5-10.
- Tariot PN. *Clinical Effectiveness of Atypical Antipsychotics in Dementia*. Journal of Clinical Psychiatry 2004;65(Supplement 11):3-4
- Ballard C, Howard R. *Neuroleptic drugs in dementia: benefits and harms*. Nature Reviews Neuroscience 2006;7:492-500.
- Karlavish J. *Alzheimer's Disease – Clinical Trials and the Logic of Clinical Purpose*. New England Journal of Medicine 2006;355(15):1604-1606.
- Pitkala KH, Laurila JV, Strandberg TE, Tilvis RS. *Behavioral symptoms and the administration of psychotropic drugs to aged patients with dementia in nursing homes and in acute geriatric wards*. International Psychogeriatrics 2004;169(1):61-74.
- Bonner C. *Reducing stress-related behaviours in people with dementia: care-based therapy*. June 2005. Jessica Kingsley Publishers London.
- Lövheim H, Sandman P-O, Kallin K. *Relationship between antipsychotic drug use and behavioral and psychological symptoms of dementia in old people with cognitive impairment living in geriatric care*. International Psychogeriatrics, Vol 18(4), Dec 2006. pp. 713-726.
- Rapopart M, Mamdani M, Shulman KI, Hermann N, Rochon PA. *Antipsychotic use in the elderly: shifting trends and increasing costs*. International Journal of Geriatric Psychiatry 2005;20:749-753.
- Hollis J, Touyz S, Grayson D, Forrester L. *Antipsychotic medication dispensing and associated odds ratios of death in elderly veterans and war widows, 2001*. Australian and New Zealand Journal of Psychiatry 2006;40:981-986.
- Ruths S, Straand J, Nygaard HA. *Psychotropic drug use in nursing homes – diagnostic indications and variations between institutions*. European Journal of Clinical Pharmacology 2001;57:523-528.
- Mond J, Morice R, Owen C, Korten A. *Use of antipsychotic medications in Australia between July 1995 and December 2001*. Australian and New Zealand Journal of Psychiatry 2003;37:55-61.
- Veterans' Datamart, University of South Australia, QUMPRC, Accessed 2006
- Bird M, Llewellyn-Jones R, Smithers H, Korten A. *Psychosocial approaches to challenging behaviour in dementia: A controlled trial*. Commonwealth Department of Health and Ageing 2002
- Fossey J, Ballard C, Juszcak E, James I, Alder N, Jacoby R, Howard R. *Effect of enhanced psychosocial care on antipsychotic use in nursing home residents with severe dementia: cluster randomised trial*. BMJ 2006;332:756-761
- Ayalon L, Gum AM, Feliciano L, Areal PA. *Effectiveness of non-pharmacological interventions for the management of neuropsychiatric symptoms in patients with dementia: a systematic review*. Archives of Internal Medicine 2006;166:2182-2188
- Schneider LS, Tariot PN, Dagerman KS, Davis SM, Hsiao JK, Ismail S, Lebowitz BD, Lyketsos CG, Ryan JM, Stroup TS, Sultzer DL, Weintraub D, Lieberman JA, for the CATIE-AD Study Group. *Effectiveness of Atypical Antipsychotic Drugs in Patients with Alzheimer's Disease*. New England Journal of Medicine 2006; 355(15):1525-1538
- Osborne CA, Hooper R, Li KC, Swift CG, Jackson SHD. *For the management of behavioural and psychological symptoms of dementia*. Age and Ageing 2002;31:435-439.
- Therapeutic Guidelines: Psychotropic*. 5th edition 2003. Therapeutic Guidelines Ltd.
- Rossi S, et al, editors. *Australian Medicines Handbook*. January 2007 online edition. Adelaide: Australian Medicines Handbook Pty Ltd, 2007
- Australian Medicines Handbook Drug Choice Companion: Aged Care 2006*. Australian Medicines Handbook Pty Ltd.
- Schneider LS, Dagerman K, Insel PS. *Efficacy and Adverse Effects of Atypical Antipsychotics for Dementia: Meta-analysis of Randomized, Placebo-Controlled Trials*. American Journal of Geriatric Psychiatry 2006;14(3):191-210
- Carson S, McDonagh MS, Peterson K. *A Systematic Review of the Efficacy and Safety of Atypical Antipsychotics in Patients with Psychological and Behavioral Symptoms of Dementia*. Journal of the American Geriatrics Society 2006;54:354-361.
- US Food and drug Administration. *FDA Public Health Advisory: Deaths with antipsychotics in elderly patients with behavioural disturbances*. Available at: <http://www.fda.gov/cder/drug/advisory/antipsychotics.htm>
Also, *FDA Alert (4/11/2005): Increased Mortality in Patients with Dementia-Related Psychosis*. Available at: <http://www.fda.gov/cder/drug/InfoSheets/HCP/ziprasidoneHCP.htm>
- Barak Y, Baruch Y, Mazeh D, Paleacu D, Aizenberg D. *Cardiac and Cerebrovascular Morbidity and Mortality Associated With Antipsychotic Medications in Elderly Psychiatric Inpatients*. American Journal of Geriatrics 2007;15(4):354-356.
- Mamdani M, Rapoport M, Shulman KI, Hermann N, Rochon PA. *Mental Health-Related Drug Utilization Among Older Adults: Prevalence, Trends, and Costs*. American Journal of Geriatric Psychiatry 2005;13(10):892-900
- Snowdon J, Day S, Baker W. *Why and how antipsychotic drugs are used in 40 Sydney nursing homes*. International Journal of Geriatric Psychiatry 2005;20:1146-1152.