Recent changes to the Pharmaceutical Benefits Scheme (PBS) highlight the risks and benefits of the use of antipsychotics in the management of behavioural and psychological symptoms of dementia (BPSD). Risperidone is the only atypical antipsychotic approved in Australia and listed on the PBS for use in behavioural disturbances in dementia.

Risperidone has the strongest evidence for treating psychosis associated with dementia. Risperidone and olanzapine (Zyprexa) have the strongest evidence for treating agitation/aggression, with weaker evidence for aripiprazole (Abilify).

The efficacy of risperidone in the treatment of behavioural disturbances, such as aggressiveness (verbal outburst, physical violence), activity disturbances (agitation, wandering) and psychotic symptoms (paranoid and delusional ideation, hallucinations) in patients with dementia has been demonstrated in numerous trials. Risperidone, at a daily dose above 0.75 mg, effectively reduces the severity and frequency of aggressiveness symptoms in this population.

Antipsychotics are less effective for some types of behavioural problems, for example, wandering, calling out, and hypersexuality. Non-pharmacological therapy is equally or more effective than antipsychotics in many residents with BPSD.

In Lewy body dementia, even low dose antipsychotics can cause deterioration in cognitive and motor function, and may cause paradoxical increase in agitation and worsen behaviour. Although off-label, low-dose quetiapine is sometimes prescribed due to lower potential for extrapyramidal side effects (EPSE).

PBS criteria
For risperidone to be prescribed on the PBS, the resident must have dementia of the Alzheimer type and must be characterised by psychotic symptoms and aggression. The resident must have failed to respond to non-pharmacological methods of treatment, and treatment must be limited to a maximum duration of 12 weeks. Approval now limited to treatment (up to 12 weeks) of moderate to severe dementia only of the Alzheimer type.

Initiation of treatment
According to the Clinical Practice Guidelines and Principles of Care for People with Dementia the following conditions should be met:

- Full discussion with the person with dementia and their carers and family about the possible benefits and risks of treatment
- Target symptoms should be identified, quantified and documented
- Effect of comorbid conditions, such as depression, should be considered
- Choice of antipsychotic should be made after an individual risk–benefit analysis
- Dose should be initially low and titrated upwards if necessary
- Monitoring for adverse effects including the metabolic syndrome should occur
- If there is no efficacy observed within a relatively short timeframe (usually one to two weeks), treatment should be discontinued

Treatment should be reviewed every four to 12 weeks, considering the need for antipsychotics and possible cessation of medication. Review should include regular assessment and recording of changes in cognition and target symptoms. If behavioural symptoms are controlled by risperidone use, no worsening is commonly seen when the antipsychotics are stopped.

Adverse effects
Common adverse effects associated with antipsychotics include:

- Sedation, anxiety, agitation
- Extrapyramidal side effects
- Orthostatic hypotension
- Tachycardia
- Weight gain
- Sexual adverse effects
- Hyperprolactinaemia
- Anticholinergic effects e.g. blurred vision, dizziness, constipation, dry mouth, urinary retention

Less common adverse effects are tardive dyskinesia,
dystonias, akathisia, neuroleptic malignant syndrome, ECG changes, arrhythmias, anaemia, hepatic fibrosis, and seizures.

Trial data show an excess of approximately 1 death for each 100 people with dementia treated with risperidone, olanzapine, quetiapine or aripiprazole for 10–12 weeks. Deaths appeared to be cardiovascular or infectious (e.g. pneumonia) in nature.

If 1000 people were treated with an antipsychotic for 12 weeks:
- Only 91-200 people show clinically significant improvements
- 10 additional deaths
- 18 additional cerebrovascular events
- 58-94 people with disturbed gait

Monitoring for adverse effects including metabolic effects should occur regularly. Metabolic adverse effects include weight gain, diabetes and the development of metabolic syndrome. NPS MedicineWise recommends routine monitoring for residents prescribed antipsychotics:
- Weight and waist circumference
- Blood pressure
- Fasting serum lipids
- Fasting blood glucose
- Electrocardiogram

The use of antipsychotics in older people is associated with an increased risk of stroke and death. Cerebrovascular risk factors should be assessed and the possible increased risk of stroke/transient ischaemic attack and possible adverse effects on cognition discussed. The Australian Medicines Handbook (AMH) suggests the risk is greatest early in treatment and with higher doses.

Akathisia or a feeling of restlessness, usually occurs 2 to 3 days after starting treatment, but may present up to several weeks after initiation. It may subside spontaneously, but usually improves on dosage reduction.

Risperidone and other antipsychotics may prolong the QT interval and can exacerbate or precipitate arrhythmias and syncope.

Antipsychotics are also associated with an increased risk of falls.

Deprescribing
Antipsychotics should be withdrawn or “deprescribed” gradually. The dose can be tapered by 50% every 2 weeks and continue for 2 weeks on the minimum dose before stopping.

Depression
Comorbid conditions, such as depression, should be considered when assessing residents with dementia and BPSD. Depression is common in patients with dementia. As many as 40% of patients with dementia have significant depressive symptoms at some stage. Reducing symptoms such as irritability may aid in the treatment of BPSD.

Selective serotonin reuptake inhibitors (SSRIs) may play an important role in the psychotic symptoms of dementia. The class of antidepressants may have “neuroleptic” effects by reducing dopaminergic outflow. Serotonergic deficits in AD contribute to aggressive verbal and physical outbursts, sleep disturbance, depression and psychosis. However, only citalopram has demonstrated efficacy. Citalopram is the most selective SSRI, with moderate potency and high bioavailability.

Citalopram has shown to significantly reduce agitation, hostility and suspicion in people with BPSD. Psychotic and nonpsychotic behavioural disturbances may improve acutely with citalopram.

Summary
Whilst antipsychotics are frequently used in the management of BPSD, their effectiveness is limited in most people. All antipsychotics are associated with a risk of serious adverse effects when used for BPSD. Use of risperidone for the treatment of behavioural and psychological symptoms of dementia of Alzheimer’s type should be at the lowest possible dose for the shortest time. Risperidone’s approved indication for use has been limited to people with Alzheimer’s dementia, for no more than 12 weeks.

References
NPS News 74, Aug 2011.