

Quarterly Medication Review Deprescribing Focus

LONG TERM CARE

Antipsychotic Use in BPSD

July to September 2022



Background

- 22% (range 19.3—37.1%) of residents in Canadian LTC facilities take an antipsychotic without a diagnosis of psychosis¹
- In Canada, 62% of residents in LTC have been diagnosed with dementia¹ and antipsychotics are often used in the elderly to control behavioural and psychological symptoms of dementia (BPSD) including delusions, hallucinations, aggression, and agitation¹
 - ◇ Antipsychotics have been found to be minimally effective in managing responsive behaviours and the clinical value may be limited due to serious adverse events including stroke and death
 - ◇ Antipsychotic medications have the potential for considerable harm, and the risk of harm is higher with prolonged use and in the elderly.² Stopping or tapering antipsychotics may decrease all cause mortality^{3,4}
- It is prudent to regularly assess antipsychotic usage to ensure that therapy continues to be safe, effective, and warranted. If use is deemed necessary, using antipsychotics for the shortest duration possible is advised



For the quarterly medication reviews from July to September 2022, reassess all residents currently receiving an antipsychotic (oral formulations and/or long acting injectables) to determine whether or not they are a candidate for deprescribing.

- Determine when and why the antipsychotic was started. Document this information on the QMR form adjacent to the antipsychotic medication the resident is using
- Refer to Table 4 “**Indication Based Criteria for Deprescribing Antipsychotics**” (on page 5) to assess for deprescribing
- For situations where deprescribing can be considered, refer to the [deprescribing.org](https://www.deprescribing.org) resources for guidance on deprescribing antipsychotic medications:
 - ⇒ [Antipsychotic deprescribing algorithm](#)⁵
 - ⇒ [Antipsychotic deprescribing guideline information pamphlet](#)
 - ⇒ [Antipsychotic deprescribing infographic](#)
 - ⇒ [Whiteboard video on using the Antipsychotic Deprescribing Algorithm](#) (10 mins)
- If the antipsychotic was prescribed for BPSD and has been used for less than 3 months:
 - * Determine if there has been objective improvement in the targeted behaviour(s) using behaviour mapping or DOS
 - * Review for any changes in functioning (e.g. increased fall rate, somnolence, increased cognitive decline)
 - * Assess for the emergence of any adverse effects (refer to the *Antipsychotic Side Effects infographic*)
 - * Deprescribe if there is no improvement in behaviour and/or the risks outweigh the benefits
- For indications where the antipsychotic medication is warranted and should not be deprescribed:
 - * Assess for treatment effect and/or the emergence of adverse effects (refer to the *Antipsychotic Side Effects infographic*)
 - * Assess if consulting a specialist (e.g., RACE Psychiatry) is required in order to optimize the treatment and if deprescribing or switching to an alternate medication is warranted (e.g., if adverse effects are occurring or treatment is not effective)

QMR Contents:

- Management of BPSD and the Appropriate Use of Antipsychotics → page 2
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Attachments included with QMR:

- Antipsychotic deprescribing algorithm
- Regional antipsychotic use data report
- Antipsychotic infographics:
 - ◇ Will an antipsychotic help?
 - ◇ Side effects: Antipsychotic Medication
- First 3 Steps to Management of Behavioural Symptoms of Dementia infographic

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Management of BPSD and the Appropriate Use of Antipsychotics

- Evaluate the resident’s symptoms and assess if there are any potential underlying causes for BPSD (e.g., constipation, infection, pain, hearing/vision problems, insomnia)
- Identify if the BPSD could be being caused by reversible factors such as recent environmental changes, changes to routine, sleep pattern or social situations, physical health, medication changes, or possible contributing adverse effects^{5,6,9}
- Refer to the Centre for Effective Practice [Use of Antipsychotics in Behavioural and Psychological Symptoms of Dementia \(BPSD\) Discussion Guide](#) for more on clinical evaluation of BPSD in LTC
- In most cases, the recommended first line treatment for BPSD is to create a safe and supportive environment for the resident and utilize resident centred **non-pharmacological approaches**
 - ◊ Antipsychotics have a modest role in the management of aggression, agitation and psychosis in patients with dementia. Compared to placebo, antipsychotic treatment results in benefit for 1 in 5 people treated for 12 weeks⁹
 - ◊ In BPSD trials, antipsychotics were only 18% more effective than placebo, reflecting the high rates of spontaneous resolution of BPSD and the value of psychosocial approaches in trials^{8,16}
 - ◊ For non-pharmacological recommendations, see the *First 3 Steps to Management of Behavioural Symptoms of Dementia* infographic and the Centre for Effective Practice [Use of Antipsychotics in Behavioural and Psychological Symptoms of Dementia \(BPSD\) Discussion Guide](#)
- Treatment with an antipsychotic may be required before trialing non-pharmacological approaches if there is an **imminent safety risk to the resident and/or others,⁷ or symptoms are disturbing, distressing or dangerous⁹**
- If potential underlying causes for BPSD have been treated and non-pharmacological approaches are unsuccessful or alone are not sufficient to manage BPSD⁹, a trial of antipsychotic treatment may be considered^{2,9}
- When the use of an antipsychotic for behavioral disturbances is being considered:
 - ◊ Determine whether the undesirable behavior will be responsive to an antipsychotic (see Table 1 below and the *Will an antipsychotic help?* infographic)
 - ◊ Review the evidence for the risks and benefits of using an antipsychotic in dementia (see section on page 3). Discuss the risks and benefits with the resident or family/caregiver prior to starting treatment (see resources on page 6).
- When prescribing an antipsychotic, resident-specific factors including medical conditions (e.g., stroke, TIA, diabetes, Parkinson’s, other comorbidities), allergies/intolerances, and concomitant medications must be considered when assessing risks versus benefits of using an antipsychotic medication for the resident.
- When starting an antipsychotic for BPSD, initiate it at the lowest possible dose⁹ and trial one antipsychotic at a time¹². Continue non-pharmacological therapies throughout antipsychotic treatment⁹ as this may help prevent the use of higher doses of an antipsychotic.
- Knowledge of relative adverse effects of common antipsychotic drugs may help guide most appropriate therapy selection (see Table 2 & 3 on page 4 and *Side Effects: Antipsychotic Medication* infographic).

Table 1: Antipsychotic Response for BPSD Management^{7, 9, 10}

| Behaviors/symptoms <u>likely to respond to antipsychotics</u> | Behaviors/symptoms <u>unlikely to respond to antipsychotics</u> | |
|---|--|--|
| - Delusions - Hallucinations - Misidentification - Suspiciousness - Defensive or physically reactive behaviours - Agitation - Restlessness - Anxiousness | - Verbally reactive behaviours - Resistance to care - Dressing/undressing - Pacing, wandering without reactive behaviour - Exit seeking - Repetitive actions or verbalizations - Mania (euphoria, irritability, pressured speech) - Apathy (amotivation, lack of interest, withdrawn) | - Hiding or hoarding - Social or sexual disinhibition - Calling out - Inappropriate voiding - Sleep disturbances |

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Evidence of Antipsychotics Efficacy and Risks

- Risperidone is the only antipsychotic with an official Health Canada indication for management of responsive behaviors in dementia;⁹ however it should still be restricted to short-term use for aggression or psychotic symptoms in patients with severe Alzheimer's dementia when non-pharmacological approaches have not worked.
 - ◇ Risperidone is not indicated for vascular or mixed dementia due to the higher risk of cerebrovascular adverse effects¹⁷
 - ◇ Risperidone has the most evidence for efficacy for aggression at dosages of 1 mg/day or less and for psychosis at dosages of 2 mg/day or less¹³
- A 2011 systematic review and meta-analysis assessed efficacy of atypical antipsychotics for off-label indications including use in elderly patients with dementia for symptoms of psychosis, aggression, and mood changes, as well as generalized anxiety disorder. Significant improvement in global behavioural symptom scores for aripiprazole, olanzapine and risperidone was reported. Quetiapine did not demonstrate statistically significant results for behavioural symptoms; however, it showed benefit in generalized anxiety disorder.¹⁸
- The CATIE-AD trial compared olanzapine, quetiapine, and risperidone to placebo and showed limited benefit for long-term atypical antipsychotic use for BPSD. Results showed 80% of participants stopped therapy by 39 weeks due to adverse effects, intolerance or death¹⁹
- Paliperidone oral tablets are not covered by Manitoba Pharmacare based on the recommendations from CADTH
- Severe adverse effects of antipsychotics include a 1.6 fold increase in the risk for death⁹ and greater than 2-fold increase in the risk for cerebrovascular accident^{27,28}
 - ◇ For every 100 people treated, only 20 are likely to benefit from the antipsychotic, 79 are likely to have no benefit, and 1 person is likely to have a stroke or die⁹
 - ◇ Factors associated with higher risk of death from antipsychotics are older age, male gender, functional impairment, severe dementia and possibly medication dose, with increased risk persisting up to 2 years after beginning treatment
 - ◇ Specific antipsychotics are not considered safer than others for risk of stroke or death, however there is some evidence that risperidone may carry a greater stroke risk¹³



- : Likely to be helped by antipsychotics
- : Likely to have **no benefit** from using antipsychotics
- : Likely to have a stroke or die*

*There is research to show that for every 100 people with dementia who take antipsychotics one person is likely to have a stroke or die (mostly related to heart failure, sudden death, pneumonia). However, it is hard to tell if the antipsychotic medicine was the cause, because those with dementia are often at high risk even when not taking an antipsychotic.

Long-Acting Injectable Antipsychotics and Dementia

- The American Psychiatric Association recommends against the use of long-acting injectable antipsychotics for BPSD unless a patient also has a chronic psychiatric disorder (e.g., schizophrenia)²¹.
- Long-acting antipsychotics may pose increased risk to older adults due to their longer duration of action and pharmacokinetic changes associated with age (e.g. body composition changes, renal and/or hepatic impairment)²¹.
- These changes can result in increased drug exposure and greater risk of adverse effects because stopping the medication will not immediately stop the medication effect.²¹
- There have been few studies assessing use of long-acting injectable antipsychotics in the elderly and no trials to assess the use in patients with dementia.²²
- Long-acting antipsychotic injections such as risperidone (Rispedal Consta), aripiprazole (Abilify Maintena), and paliperidone (Invega Sustenna and Invega Trinza) are not covered for BPSD and expensive for residents to pay for

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Lewy body dementia commonly presents with symptoms of visual hallucinations and delusions, fluctuations in level of consciousness, and parkinsonian movements due to dysfunction in dopamine.^{14,15}

- Cholinesterase inhibitors are likely the most effective treatment for Lewy body dementia as they may help to improve cognition, performance of activities of daily living, and manage behavioural symptoms¹⁴
- AVOID first generation antipsychotics because their side effect may worsen the symptoms of Lewy body dementia
- Cautious use of second generation antipsychotics may be considered if required, however there is little evidence for efficacy
- Higher potency second generation antipsychotics (e.g. risperidone, olanzapine) may pose greater risk to parkinsonian symptoms compared to low-potency (e.g. quetiapine)¹⁵

Monitoring Antipsychotic Medications

- After starting or increasing the dose of an antipsychotic, reassess in 3-7 days to review for response to treatment, tolerability and adverse effects (see Tables 2 and 3 and *Side Effects: Antipsychotic Medication* infographic)¹³
- Continue to monitor for improvement in targeted behaviour weekly and for emergence of adverse effects over 1-3 weeks⁹
- The goal is improvement in target symptoms⁹; however, individuals may respond differently, ranging from no response, to partial or full response, therefore ongoing reassessment is essential
- Monitor for the specific behaviour and document using integrated progress notes, behaviour mapping, or the dementia observation system (DOS) for objective monitoring of effectiveness
- Consider if dividing or timing doses according to the behaviour would be of benefit (e.g., for agitation exhibited near the end of the day, a lunchtime dose may be appropriate¹¹)
- Based on response, the dose may be gradually increased every 1-2 weeks. Response often demonstrated within 2 weeks¹³
- Antipsychotic treatment should be reviewed every 3 months to determine if residents are receiving ongoing benefit and assess if the medication is still needed.¹³ Continue to monitor for any other health conditions that could be worsened by the use of antipsychotics

Table 2: Comparison of Antipsychotics and their Effects

| Drug | Anticholinergic | Sedation | Orthostatic Hypotension | EPS | TD | Weight Gain | Diabetes |
|--------------|-----------------|----------|-------------------------|-----|-----|-------------|----------|
| Aripiprazole | + | ++ | + | + | + | + | - |
| Olanzapine | +++ | +++ | + | ++ | + | +++ | +++ |
| Quetiapine | +++ | +++ | ++ | + | + | ++ | +++ |
| Risperidone | ++ | ++ | ++ | ++ | + | +++ | ++ |
| Haloperidol | + | + | + | +++ | +++ | ++ | ++ |
| Loxapine | ++ | +++ | ++ | +++ | +++ | - | + |

EPS = extrapyramidal symptoms; TD = tardive dyskinesia. Table was adapted from the Centre for Effective Practice and is intended as a general guide for comparison only. There is variability in relative adverse effects reported in other resources.

Table 3: Risks and Safety Concerns of Antipsychotic Use in BPSD^{2, 5, 12, 13}

Some of the most common adverse effects associated with antipsychotic use include:

| | |
|---|---|
| <ul style="list-style-type: none"> - Dizziness - Sedation - Postural hypotension - Falls, fractures - Abnormal gait - Extrapyramidal symptoms (akinesia, rigidity, stiffness) - Tardive dyskinesia - Constipation | <ul style="list-style-type: none"> - Dry mouth - QT prolongation* - Metabolic disturbances (hyperglycemia, hyperlipidemia, weight gain) - Infection (pneumonia, urinary tract infections)^{24,25} - Per Health Canada (2016) there are cases of sleep apnea linked to atypical antipsychotics.²⁶ <p>*QT prolongation can contribute to arrhythmias and sudden cardiac death</p> |
|---|---|

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Deprescribing Antipsychotics

- Antipsychotic treatment initiated for BPSD is often continued chronically despite lacking ongoing indications for use
- Individuals with dementia may present with varying degrees of progression and severity of cognitive, behavioural and psychological symptoms, which may improve and resolve over time;¹³ therefore, routine long-term use of antipsychotics for BPSD may not be required and is not recommended.
- The DART-AD trial compared patients continuing their antipsychotic after 3 months of use versus switching to placebo. Results showed that stopping long-term antipsychotics reduced mortality by ~25% at 2 years. There was no significant difference between treatment or placebo groups in BPSD outcomes, except in verbal fluency which favoured placebo^{13, 20}
- For BPSD, reducing or stopping antipsychotics has been shown to be safe²⁷, and can often be completed without residents' symptoms returning or experiencing withdrawal.
- Consider deprescribing antipsychotics if BPSD symptoms are controlled or the resident is not benefiting from the medication



Recommendation: At the QMR, follow the [Antipsychotic \(AP\) Deprescribing Algorithm](#) for steps to safely deprescribe antipsychotic medications where appropriate.

Table 4: Indication Based Criteria for Deprescribing Antipsychotics^{5,6}

| Indications where deprescribing the antipsychotic should be considered | Indications where continued antipsychotic use is warranted and should not be deprescribed |
|--|--|
| <ul style="list-style-type: none"> - BPSD treated for 3 or more months and targeted symptoms are under control - BPSD treated for 3 or more months* with NO improvements - For symptoms of BPSD not likely to respond to antipsychotics (see Table 1) - Insomnia (any duration) <p><i>*Assess new treatment(s) over 1-3 weeks, documenting any benefits. If symptoms persist or worsen, adjust therapy (e.g. change to alternate medication) or consider a referral to a specialist. If after 3 months there is no response despite treatment, consider deprescribing the antipsychotic(s) and other medications being used for BPSD⁹</i></p> | <ul style="list-style-type: none"> - Schizophrenia or schizoaffective disorder - Bipolar disorder - Developmental disorders with chronic aggression and psychosis - Obsessive-compulsive disorder - Huntington's chorea - Tourette's syndrome - Tic disorders - Autism - Parkinson's disease psychosis - Adjuvant treatment for major depressive disorder - Less than 3 months of treatment for BPSD if improving and manageable side effects - 3 or more attempts have been made to deprescribe for BPSD without success (e.g. targeted symptoms return when deprescribing) |

Recommendations for Deprescribing Antipsychotics^{5,6}:

- Taper slowly, reducing the dose of the antipsychotic by 25-50% every 1-2 weeks until discontinued⁵. Slower tapering may be required depending on the individual's response.
- If dose reductions result in withdrawal symptoms or recurrence of severe behaviours posing risk to self/others, resume the previous dose when behaviours were under control or when the resident was not experiencing withdrawal symptoms. Deprescribing may require a slower approach or may need to be continued at a later time⁶
- If tapering or discontinuation is unsuccessful (e.g. antipsychotic indicated symptoms recur), use non-pharmacological approaches and consider restarting the antipsychotic at the lowest effective dose or trial another medication. Reassess again in 3 months and consider deprescribing at a slower pace if symptoms are stable. At least 2 additional deprescribing attempts should be made⁵
- Document each deprescribing attempt including the resident's response and outcome of intervention.¹²
- Continuing with non-pharmacological approaches after deprescribing antipsychotics may minimize resident stressors and help improve the success of deprescribing (see the *First 3 Steps to Management of Behavioural Symptoms of Dementia* infographic)
- If the antipsychotic was prescribed at a low dose for insomnia, tapering is not necessary.⁵ For more information, refer to the *QMR Deprescribing Focus: Sedatives for Insomnia* from October-December 2019
- If the antipsychotic was prescribed for acute delirium, antipsychotics can be stopped once the underlying cause of delirium has resolved (e.g. delirium caused by an infection or a medication)⁷, and can usually be stopped 7 to 10 days after symptom

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Monitoring Suggestions for Tapering and Discontinuing Antipsychotic Therapy^{6,13}

- Monitor for the following every 1-2 weeks (or more closely if the initial baseline symptoms were severe):
 - ◇ **Benefits:** improved alertness, gait, less or no extrapyramidal symptoms and fewer falls
 - ◇ **Withdrawal symptoms:** e.g. nausea and vomiting, abdominal pain, diarrhea, headache, tachycardia, vertigo, increased perspiration, dry mucous membranes, myalgia, restlessness, anxiety, tension, insomnia, and hyperkinesia
 - ◇ **Return of targeted behaviours**

 In Manitoba LTC facilities, medication reviews must be conducted every 3 months, providing opportunity for antipsychotic reassessment on a quarterly basis at a minimum. More frequent reassessment (1-2 weeks) should be considered when antipsychotics are started, stopped or dose changes occur.²³

Resident/Family Discussions

- It is important to involve family members and caregivers so they are well informed and a part of the decision making when initiating or deprescribing antipsychotics.
- Discussing the risks compared to benefits of antipsychotics and allowing them to ask questions provides an opportunity for clear communication and developing understanding of prescribing and deprescribing intentions.
- By involving caregivers, the healthcare team can also gain insight into triggers for worsening BPSD, and can provide ideas for effective non-pharmacological management strategies.²⁹

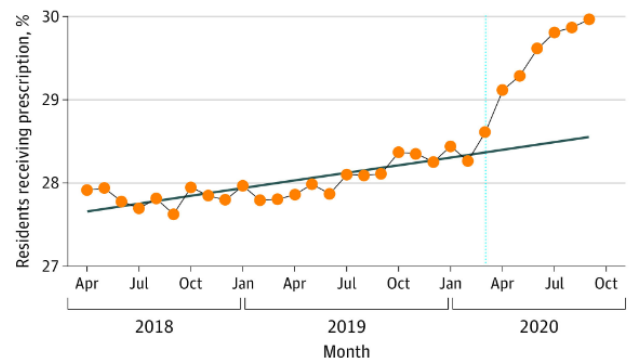


Resources:

[How Antipsychotic Medications are Used to Help People with Dementia: A Guide for Residents, Families, and Caregivers](#)
[Deprescribing: Reducing Medications Safely to Meet Life's Changes Focus on Antipsychotics](#)
[Treating Disruptive Behaviour in People with Dementia: Antipsychotic drugs are usually not the best choice](#)

Antipsychotics Use and the COVID-19 Pandemic³³

- An Ontario study showed that since the COVID-19 pandemic in Canada, antipsychotic prescribing for nursing home residents increased from March to September 2020.
- The absolute increase in proportion of residents receiving antipsychotic prescriptions was 1.7%.
- Some challenges identified as contributing to this increase in use include social isolation from COVID-19 infection prevention/control procedures, staff shortages, and possible minimized focus on non-pharmacological management of BPSD.³³
- This pattern of increased use is also reflected in the CIHI data for the Winnipeg region, where rates of potentially inappropriate antipsychotic use was 20.1% in 2018-2019, increasing to 21.9% in 2020-2021.¹ Given these trends and our knowledge of the risks of antipsychotic use, ongoing active reassessment of these drugs is necessary.



Changes in Psychotropic Drug Prescribing Among Nursing Home Residents in Ontario, Canada, From April 2018 to September 2020

Antipsychotic Use Data

Attached to the QMR are region-specific antipsychotic reports with data up to the end of quarter 4 (Jan-Mar 2022). This data includes all antipsychotic medications dispensed for residents, regardless of indication, at LTC facilities serviced by MediSystem Pharmacy. While some of these antipsychotic medications may be appropriate, it provides a regional and provincial comparison to facilitate discussion on target usage and deprescribing strategies.

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Additional Resources for Healthcare Providers:

Deprescribing.org: [Deprescribing antipsychotics for behavioural and psychological symptoms of dementia and insomnia](#)

Centre for Effective Practice: [Use of Antipsychotics in Behavioural and Psychological Symptoms of Dementia \(BPSD\) Discussion Guide](#)

Canadian Foundation for Healthcare Improvement: [Appropriate Use of Antipsychotics Resources](#)

INESSS: [Deprescribing antipsychotics in residents of residential and long-term care centres](#)

Alberta Health Services: [Appropriate Use of Antipsychotics \(AUA\) Toolkit](#)

Choosing Wisely Canada: [Toolkit for Reducing Inappropriate Use of Antipsychotics in Long Term Care](#)

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