Promoting the Appropriate Use of Antipsychotics

A Toolkit for North Simcoe Muskoka Long-Term Care Home Prescribers

May 30, 2017

Developed by the North Simcoe Muskoka Specialized Geriatric Services Program in partnership with the County of Simcoe and the Royal Victoria Regional Health Centre
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“The aging population is not a tsunami . . . it’s an iceberg. The only way you get hit by an iceberg is if you don’t get out of the way in time”.

Michael Rachlis
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GLOSSARY OF TERMS

ABC Antecedent, Behaviour, Consequence Documentation Framework
ALC Alternate Level of Care
BPSD Behavioural and psychological symptoms of dementia
CMAI Cohen Mansfield Agitation Inventory
DOS Dementia Observation Scale
CV Cardiovascular
EPS Extrapyramidal side effects
FDA Food & Drug Act, Canada
FGA First Generation Antipsychotic
Harm Physical injury or mental damage
LHIN Local Health Integration Network
LTC Long Term Care
LTCH Long Term Care Home
NSM North Simcoe Muskoka
ODT Orally disintegrating tablet
Severe Distress Causing discomfort by extreme character or conditions
Serious Harm Mental Health Act, R.S.O. 1990, c. M.7 s. 15(1); 2000, c.9, s. 3(1).
This is the indication for a psychiatric assessment (equivalent to the Future Test in Form 1).
SDM Substitute Decision Maker
SGA Second Generation Antipsychotic
SGS Specialized Geriatric Services
SS Statistically significant
TD Tardive Dyskinesia
TGA Third Generation Antipsychotic
INTRODUCTION

In November 2015, a Behaviour Concurrent Review was completed as part of the NSM LHIN ALC Review project. In this review, an Expert Panel was convened by the Behaviour Task Force to review all ALC patients in all NSM hospital sites with responsive behaviours delaying their discharge. A key finding was the variation in practice across the NSM. The review highlighted opportunities related to standardization, resource awareness and medication management. Based on the recommendations from the Expert Panel, the Behaviour Task Force developed a work plan, which included exploring LTCH sector interest in developing and implementing a program related to the review of psychotropic medications.

In June 2016, the NSM SGS Program met with NSM LTCH administrators at the LHIN LTCH Sector Summit. The SGS Program presented the findings from the Behaviour Concurrent Review, provided physician-led education related to the appropriate use of antipsychotics and presented findings from a review of all NSM LTCH Quality Improvement Plans related to the appropriate use of antipsychotics. Given the overlap in priorities between the Behaviour Task Force and LTCHs related to antipsychotic use, the SGS Program opened discussion with attendees regarding collaborative project opportunities. Regional LTCHs identified the greatest need to be education of prescribers on the appropriate use of antipsychotics.

In the fall of 2016, a survey was sent to NSM LTCH prescribers (Medical Directors and NPs) to support project planning. The purpose of the survey was to gain an understanding of the interest among prescribers for this education and the best way to deliver the information. The survey generated 26 responses and confirmed interest in this education. Prescribers who responded identified that case-based education and quick reference tools would be most beneficial for their practice.

These results reflect the broader need for tools to fill the gap between existing evidence and clinical relevant and evidence-based strategies to appropriate antipsychotic prescribing. Scientific guidelines focus heavily on the important need to weigh efficacy and risks of psychotropic drugs in clinical trials and meta-analysis, but lack specifics of prescribing, monitoring and maintaining or tapering these medications\(^1\).

This toolkit has been developed as a resource for interested NSM LTCH prescribers. It is intended to address the gap between scientific guidelines and everyday practice thereby promoting a more standardized approach to care while improving resident and system outcomes. The aim is not to replace scientific guidelines, but rather to provide additional support to clinical practitioners for their decision making process when assessing antipsychotics in the geriatric population.

OVERVIEW

Antipsychotic use in the geriatric population is a complex and often controversial subject. For Ontario’s seniors, antipsychotics play an important role in managing mental illness, particularly those with illnesses with psychoses and sometimes the behavioural issues found in dementia\(^2\). The use of these medications can be controversial because their use is associated with sedation, higher risk of falls and a low but significant risk of death\(^3\).

Antipsychotics have a broad range of prescribed indications and are a mainstay of treatment for schizophrenia and other mental illnesses. In 2013, 18.3% of residents aged 65+ in Ontario LTC had a diagnosis of psychosis. 69.6% were diagnosed with dementia and 12.1% were not diagnosed with psychosis or dementia\(^2\). At that time almost 50% of those with psychosis were prescribed antipsychotics, but 26.9% of residents with dementia and 12.0% of patients without a diagnosis of psychosis or dementia were prescribed antipsychotic treatment\(^2\) (see Figure 1). Between 2012 and 2020 there is a projected increase in the number of cases of dementia in NSM from 7,570 to 10,340 (37%), the fourth highest percent increase in the province\(^4\).

Figure 1 – Health Quality Ontario. Looking for Balance\(^2\)

**Percentage of long-term care home residents 65 years or older who were using antipsychotic medication with a diagnosis of a specific medical condition on March 31, 2013, in Ontario**

<table>
<thead>
<tr>
<th>Condition</th>
<th>Use of Antipsychotic Medication</th>
</tr>
</thead>
<tbody>
<tr>
<td>Residents with psychosis</td>
<td>47.2%</td>
</tr>
<tr>
<td>Residents with dementia</td>
<td>26.9%</td>
</tr>
<tr>
<td>Residents without psychosis or dementia</td>
<td>12.0%</td>
</tr>
</tbody>
</table>

Data sources: CCRS, DAD, ODB claims database, OHIP claims database, OMMIIS and RPDB, provided by ICES. Notes: Antipsychotic use values were adjusted for sex, age group and comorbidity. Residents were identified as having a documented diagnosis of psychosis or dementia based on physician, drug and hospital claims data (DAD, ODB claims database, OHIP claims database and OMMIIS). Residents with neither psychosis nor dementia according to the administrative sources listed above may have a diagnosis of psychosis or dementia noted in other data sources, such as the PMS-MDS data in the CCPS. See the online technical appendix for more information.


Care Connections – Partnering for Healthy Communities
Between April 2008 and March 2013, the Ontario Drug Policy Research Network identified that, 34,195 of community and 24,804 LTC seniors with dementia were newly initiated on antipsychotics\(^5\). 80% of these were started on second-generation antipsychotics and of these users half (50-60\%) were on this therapy for at least one year\(^4\). It is generally accepted that 20-30\% of LTC residents are appropriately prescribed long-term antipsychotic therapy; however, a target of 15-30\% reduction in antipsychotic use in LTC homes has been recommended to address inappropriate antipsychotic use in this population\(^4\).

**TOOLKIT SCOPE**

It is important to note the following at this time:

- This toolkit addresses general use of antipsychotics in seniors and, while we discuss use in dementia, we focus primarily on Alzheimer’s dementia. Recommendations of which antipsychotics to use do not extend to Parkinson’s dementia, Lewy Body dementia, or less common subclasses of dementia. However, in assessing antipsychotic therapy and whether or not discontinuation is appropriate, the suggestions recommended herein are relevant.

- The authors recognize that antipsychotic prescribing may not always be a linear process. This toolkit was developed to help give guidance in the assessment and reassessment of antipsychotic medications in this vulnerable population.

- The knowledge, skill and judgement of individual clinicians remain the foundation of antipsychotic prescribing, titration and deprescribing. This toolkit is not intended to usurp the practice of clinicians. Instead, it is meant as a resource for interested NSM LTCH prescribers.

- It is important to emphasize the treatment of the condition when prescribing any medication. While this toolkit focuses on antipsychotic medications, other classes of psychotropic medications (specifically benzodiazepines and other hypnotics) are at times prescribed to older adults with dementia. The intent of this toolkit is not to support the prescription of alternative psychotropic medications in place of antipsychotics. The goal is always to ensure the individual receives the right care to meet their needs.

- Although the focus of this toolkit is on antipsychotic use, clinicians are always encouraged to explore non-pharmacological approaches to care as a first line of support and management of responsive behaviours when clinically appropriate.

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ANTIPSYCHOTICS

Figure 2 - Early Antipsychotic Advertising

The first antipsychotic commercially available hit the market in 1950: chlorpromazine hydrochloride. Prior to the publication of clinical research into its use, it was marketed for “prompt control of senile agitation, control of nausea and vomiting in children, arthritis, alcoholism” and the list went on. While scientific research has narrowed the indications for use of antipsychotics today, they are frequently used to treat mental health concerns for which evidence is sparse, or even contradicting.

Antipsychotics generally work by altering control and release of dopamine and serotonin in various parts of the brain. Antipsychotics have been found effective in the management of positive symptoms of psychosis (hallucination, delusions, hostility and aggression) but lack data to support their use in cognitive and negative symptoms of psychosis (flat affect, alogia, amotivation). They do not cause physical or psychic dependence but generally require slow tapers on discontinuation to prevent rebound symptoms and side effects.

Since the discovery of chlorpromazine, newer antipsychotics have been developed. A classification system of first, second and third generation antipsychotics is used to distinguish them (primarily based on the risks of use). In Canada, there are eight second generation antipsychotics available: asenapine, clozapine, lurasidone, olanzapine, paliperidone, quetiapine, risperidone and ziprasidone. Aripiprazole, and newly approved brexpiprazole, are the only third-generation antipsychotics available in Canada.

In 2005, Health Canada issued a black box warning for a small but significant increase in overall mortality in elderly patients with dementia receiving treatment with SGAs and aripiprazole. Thirteen placebo-control trials were assessed and from these a pooled “3965 patients, showed a mean 1.6 fold-increase in death rate in the drug-treated patients”, most

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of which were due to cardiovascular causes (e.g., heart failure, sudden death) or infection (pneumonia)\textsuperscript{10}. Subsequent studies have suggested that there is a similar risk with FGAs and in 2008 similar warnings were made for use of FGAs by the FDA.

The studies cited were relatively short term and so the absolute risks beyond 10-12 weeks of therapy are still unknown, as are benefits when antipsychotics are used to treat aggression and psychosis that are not associated with mental illness\textsuperscript{11}.

### Antipsychotics in Mental Illness

It is beyond the scope of this resource to review treatment algorithms for mental illnesses. However, it is important to note that there are valid indications for long-term antipsychotic use. Specific criteria that justify long-term use of antipsychotics are reviewed in the Antipsychotic Deprescribing Algorithm on page 22. Careful history taking and assessment must be made in order to select the patient population that would benefit from antipsychotic deprescribing. 20-30\% of current antipsychotic use in Ontario LTCHs may be considered appropriate\textsuperscript{4}. While this tool strongly promotes always using the lowest effective dose for disease management, it would be potentially harmful to recommend a blanket-approach to antipsychotic dose adjustment and medication discontinuation.

### Antipsychotics in Dementia

Management of the condition of dementia is not reviewed in this resource. Antipsychotic therapy is not indicated in dementia or the management of behavioural and psychological symptoms of dementia (BPSD) UNLESS there is severe distress, risk of harm and/or psychosis.

BPSD are the “non-cognitive symptoms of disturbed perception, thought content, mood or behaviour” that can develop among patients with dementia\textsuperscript{12}. These generally include delusions, hallucinations, agitation/aggression, depression, anxiety, euphoria, apathy, irritability, motor behaviour (purposeful wandering, shadowing, etc.), sleep disturbances, changes in eating behaviour\textsuperscript{13}.

These symptoms have been documented as “problematic, disturbing, difficult, inappropriate and challenging", which records the negative experience of someone other than the patient, rather than focusing on the person-centered experience\textsuperscript{9}. Terminology now focuses

on ‘responsive behaviours’ as our understanding is now that these behaviours are a form of communication about an unmet need of the person with dementia, rather than random or without cause.¹¹

Not all responsive behaviours respond to psychotropic medications, including antipsychotics. Behaviours exhibited by a person with dementia NOT (usually) responsive to medication include¹⁴:
1. Aimless wandering
2. Inappropriate urination/defecation
3. Inappropriate dressing/undressing
4. Annoying perseverative activities
5. Vocally repetitious behaviour
6. Hiding/hoarding
7. Pushing wheelchair bound co-patient
8. Eating inedibles
9. Tugging at/removal of restraint

It is estimated that up to 20% of LTCH dementia patients can have agitation and aggression⁸, however given the side effect profile of antipsychotics, their use for responsive behaviour must be limited to cases of severe distress and/or risk of harm.

As demonstrated in figures 3 and 4, haloperidol has been proven superior to placebo in the treatment of BPSD (SS), but it is significantly worse than the second or third generation antipsychotics for safety outcomes (mortality, falls, EPS and weight changes)⁴. In assessing comparisons of efficacy, only olanzapine has been proven to manage behavioural and psychological symptoms of dementia better than haloperidol and the other second and third generation antipsychotics (SS).⁴

Figure 3: Safety of atypical antipsychotics for the management of behavioural and psychological symptoms of dementia⁴

Risperidone is the only antipsychotic approved by Health Canada for short term treatment of severe dementia and inappropriate behaviour due to aggression and/or psychosis\textsuperscript{4, 15}, however risperidone, olanzapine, quetiapine and aripiprazole are all used to treat BPSD with severe distress and/or risk of harm\textsuperscript{4, 7}.

If using an antipsychotic for BPSD with severe distress and/or risk of harm, consent to treat with antipsychotics must be obtained from the patient (or, if incapable, the SDM). Behaviour tracking should be done regularly for each specific behaviour. Side effect monitoring must be assessed as clinically indicated, at a minimum at week 1, week 2 and monthly while on antipsychotic therapy (see Monitoring Plan pg. 20-21). If antipsychotics are only being used for BPSD, reassessment for tapering and deprescribing should be conducted no later than after 3 months of antipsychotic therapy (additional details presented in “Antipsychotic Deprescribing Notes” pg. 23).

**Considerations for Use in Seniors**

Aging is associated with many pharmacokinetic and pharmacodynamic changes (decreased cardiac output, renal and hepatic blood flow, changes in hepatic metabolism and CYP enzyme processing, as well as total body weight and lean body mass)\textsuperscript{6}.

Medications and lab monitoring for medication should be reviewed in partnership with a pharmacist at least every 3 months or as clinically indicated.

With respect to antipsychotic use in the geriatric population, olanzapine, quetiapine, risperidone and aripiprazole are all primarily metabolized hepatically, although olanzapine, quetiapine and risperidone are also significantly eliminated renally\textsuperscript{7}.

Seniors are more sensitive to psychotropic medications and drug-drug or drug-disease interactions. Strategies to optimize therapy may include:

- Consult a pharmacist prior to starting an antipsychotic for a medication review and drug interaction analysis
- Start low and go slow, using the lowest effective dose
- Avoid medications with anticholinergic properties
- In BPSD, avoid antipsychotic therapy solely for insomnia, depression, nonspecific agitation and anxiety.
TOOLKIT FOR APPROPRIATE ANTIPSYCHOTIC USE IN SENIORS

The following steps are from an algorithm developed by Dr. Geoff Daniel. This algorithm was developed to assist the prescriber when considering psychotropic medication, including antipsychotics in the support and management of responsive behaviours. See Figure 5, page 18.

Assess R.I.S.K.S.

To understand the behaviour and/or psychological symptom in dementia, one must assess the risk to the person and others. Evaluating R.I.S.K.S. \(^{16}\) will help you to determine the urgency of the situation and the next step in your assessment and treatment plan.

R Roaming – wandering (purposeful or aimless)
I Imminent physical risk of harm (to self or others) – frailty (e.g. delirium, physical illness), falls, fire, firearms
S Suicide Ideation
K Kinship Relationships (risk of harm to others OR to the person by others due to the behaviour, including avoidance of the person)
S Self-neglect, safe driving and substance abuse

Things to Consider when Assessing Risk

- How imminent is the risk? Is the risk increasing?
- Consider the ability of the individual to use supports to reduce risk / or the inability to use supports which may increase risk.
- Consider the social and physical environments in terms of increasing or reducing risk.
- Always consider risks in the context of the person's values, wishes, beliefs and life experience.
- Be aware of one's own values and beliefs and how they affect interpretation and decision-making

For the purposes of the Toolkit, the definition of “harm” includes a wider scope than “serious harm” as defined by the Mental Health Care Act.

*It is highly recommended that delusions of persecution/paranoia or of jealousy be assessed as a risk of harm and psychotropic medications be started immediately.*

For patients with an identified risk of harm to self or others OR if the patient is in severe distress, it is recommended that a psychotropic medication be initiated.

In order to determine which medication to prescribe, a diagnosis needs to be established.

Even if the level of harm OR distress does not indicate the prescription of a psychotropic medication at this point in time, the first step is to establish an accurate diagnosis.

Once risks have been assessed, it is prudent to establish the diagnosis. This allows one to quickly treat what is treatable, including delirium, and to have a guide if and when psychotropic medication is warranted.

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### Establish accurate **DIAGNOSIS**

The 3Ds is a familiar way to remember the two most common treatable conditions that can be mislabeled as dementia.

#### *Diagnosis*

Think 3 Ds - Dementia, Delirium, Depression

#### *What drives Irritability/Agitation/Aggression* CHECKLIST

- Depression – irritability
- Delirium (CAM - Confusion Assessment Method)
- Psychosis – especially delusions of paranoia/jealousy
- Frontal Lobe Symptoms – disinhibition
- Personality – premorbid
- Other – Longstanding Psychiatric Diagnosis: Bipolar 2, Impulse Dyscontrol, ADHD, +/- Anxiety Disorders
  - Medication Side Effect – Akathisia
  - Medical conditions including Pain, etc

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**Practice hint:**

Depression – often has symptoms of irritability in seniors.

Delirium – the Confusion Assessment Method (CAM) is a reliable and valid screening tool.

Pain – often may be a causative factor. Recommend comprehensive assessment and treatment of all pain or discomfort.
The CHECKLIST digs deeper into symptoms and/or diagnosis that may “drive” the behaviour witnessed. By accurately identifying the core issue, one can choose medication that has a greater chance of being effective. This principle can be applied even when quickly moving to psychotropic medication when risk is high.

**TARGET & DOCUMENT Specific Behaviours**

Prior to developing a treatment plan, the specific behaviour needs to be described and documented. Vague descriptions of behaviours lead to interventions that are not individualized to the person. Describing the person as aggressive is not as beneficial as describing a person who pushes away, slaps and scratches the hands of the care provider when personal hygiene is attempted.

There are many methods to track and document behaviours including:

(i) Cohen Mansfield Agitation Inventory (CMAI),
(ii) Dementia Observation Scale (DOS) and
(iii) Documenting the Antecedent, Behaviour and Consequence (ABC).

The benefit of these tools is that they provide a clear description of the behaviour, identify trends during the day/evening/night and establish frequency and severity of behaviours.

**Assess CAUSATIVE / CONTRIBUTING Factors**

Establishing the specific behaviour and documenting trends, frequency and/or severity assists in the assessment of causative / contributing factors. Many tools, algorithms and frameworks are available to support identifying these factors. The P.I.E.C.E.S.™ framework is a comprehensive, interdisciplinary approach that identifies medical, psychological and social factors that may lead to responsive behaviours.

The following chart identifies the area for consideration under each letter in the word P.I.E.C.E.S. and provides a checklist for clinicians to use when assessing the causative factor under each area.

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17 Available at: [https://www.google.ca/search?q=pieces+responsive+behaviour+chart&source=lnms&tbm=isch&sa=X&ved=0ahUKEwj8yP2Khc_TAhWCxYMKHdmcDNoQ_AUJBiq8&biw=1920&bih=911#imgrc=WcYQj3SKA9XaM](https://www.google.ca/search?q=pieces+responsive+behaviour+chart&source=lnms&tbm=isch&sa=X&ved=0ahUKEwj8yP2Khc_TAhWCxYMKHdmcDNoQ_AUJBiq8&biw=1920&bih=911#imgrc=WcYQj3SKA9XaM) Accessed on May 1, 2017

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*Care Connections – Partnering for Healthy Communities*
Determine whether intervention is NECESSARY

Often, medication is not necessary to support individuals with responsive behaviours. Within the comprehensive assessment undertaken in the steps above, think about the behaviour in terms of overall context and what is reasonable. Think about the behaviour within that person’s norms as well as impact on quality of life if any or certain interventions are done or not done. Ask “whose problem is it”? Psychotropic medications, especially antipsychotics, should not be prescribed to make things easier for the caregiver unless risk has been identified.

Attempt INDIVIDUALIZED NON-PHARMACOLOGICAL APPROACH

If risk of harm to self/others OR severe distress of the patient has not been identified, best practice indicates that non-pharmacological interventions should be exhausted prior to initiating medication management.

Due to the complexity of responsive behaviours, an individualized approach allows for flexibility and creativity in the development of interventions. Interventions should target the specific behaviour and be customized to fit the psychological and social factors of
the person with dementia. Ensure that care plans and interventions are documented and easily accessible to all direct care providers. Continue to use tools such as the DOS, CMAI and ABC charting to evaluate the effectiveness of the care plan. A referral to NSM Behavioural Support System (BSS) services may be beneficial to assist direct care providers in creating and implementing an individualized care plan.

Psychotropic MEDICATION
If needed.

When R.I.S.K.S. is high or the non-pharmacological approach is not sufficient to support the behaviour, the next step is consideration of medication. Remember, the individualized non-pharmacological approach should be continued in conjunction with medication management. The “What drives Irritability / Agitation / Aggression Checklist” remains valid at this step to help determine the most appropriate psychotropic medication to prescribe.
**Diagnosis**
Think 3 Ds - Dementia, Delirium, Depression

*What drives Irritability/Agitation/Aggression CHECKLIST*
- Depression – irritability
- Delirium (CAM - Confusion Assessment Method)
- Psychosis – especially delusions of paranoia/jealousy
- Frontal Lobe Symptoms – disinhibition
- Personality – premorbid
- Other – Longstanding Psychiatric Diagnosis: Bipolar 2, Impulse Dyscontrol, ADHD, +/- Anxiety Disorders
  - Medication Side Effect – Akathisia
  - Medical conditions including Pain, etc

*Assessing Risk*
**R.I.S.K.S. acronym**
- R roaming
- I mminent Physical Danger (FIRE, FALLS, FRAILTY)
- S uicidal
- K inship relationships – risk of harm by older person or to the older person due to the behaviours; includes avoidance of the person
- S elf Neglect
- S ubstance Abuse
- S afe Driving

**GENERAL PRINCIPLES FOR PRESCRIBING PSYCHOTOPICS IN BPSD**

Dr. Geoff Daniel, MD, FRCP, March 2017©
**Recommended Dosing and Risk Factors to Consider Prior to Prescribing**\
This Toolkit provides dosing and risk factor information on aripiprazole, olanzapine, quetiapine and risperidone given the evidence for efficacy and safety of antipsychotics in seniors for BPSD (Antipsychotics in Dementia, page 9). These medications are listed in alphabetical order.

<table>
<thead>
<tr>
<th>Drug</th>
<th>Usual starting and maximum dose when used for short term therapy of BPSD</th>
<th>Available Dosage Forms</th>
<th>Additional Considerations:</th>
</tr>
</thead>
<tbody>
<tr>
<td>Aripiprazole</td>
<td>• 2-5 mg PO daily, increase at intervals of 1 week&lt;br&gt;• No evidence to support doses greater than 10 mg/day for BPSD&lt;br&gt;• Adult maximum 30 mg/day&lt;br&gt;• Geriatric maximum 15 mg/day</td>
<td>Tablets: 2mg, 5 mg, 10 mg, 15 mg, 20 mg, 30 mg&lt;br&gt;ODT: 10 mg, 15 mg&lt;br&gt;Tablets and ODT have equivalent bioavailability.</td>
<td>• Low incidence of CV side effects (~2% reported orthostatic hypotension, tachycardia, ECG abnormalities/QT prolongation).&lt;br&gt;• Least impact on endocrine (sexual dysfunction, galactorrhea, weight gain (some reports of weight loss), hyperglycemia, hyperlipidemia)&lt;br&gt;* Please note: newer to market and so less data altogether.&lt;br&gt;• Morning administration can minimize activation effects.</td>
</tr>
<tr>
<td>Olanzapine</td>
<td>• 1.25 mg PO daily, may increase to 5 mg PO daily at intervals of 1 week&lt;br&gt;• Psychosis may require up to 15mg/day&lt;br&gt;• Adult maximum 20 mg/day&lt;br&gt;• Geriatric maximum 10 mg/day</td>
<td>Tablets: 2.5 mg, 5 mg, 7.5 mg, 10 mg, 15 mg, 20 mg&lt;br&gt;ODT: 5 mg, 10 mg, 15 mg, 20 mg&lt;br&gt;Short acting injectable: 10 mg/vial *Not covered by ODP&lt;br&gt;Tablets and ODT have equivalent bioavailability.</td>
<td>• Low incidence of CV side effects (10% tachycardia at higher dose but ~2% reported orthostatic hypotension, ECG abnormalities / QT prolongation).&lt;br&gt;• The half life of olanzapine is up to 1.5x longer in patients over 65.&lt;br&gt;• Injectable administration peaks in 15-45 minutes and Cmax is 4-5 times higher than the same dose administered orally.</td>
</tr>
</tbody>
</table>

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18 See Citation list for Recommended Dosing, Risk Factors and Monitoring of Antipsychotics page ---
<table>
<thead>
<tr>
<th>Drug</th>
<th>Usual starting and maximum dose when used for short term therapy of BPSD</th>
<th>Available Dosage Forms</th>
<th>Additional Considerations:</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td></td>
<td>IR tab: 25 mg, 100 mg, 150 mg, 200 mg, 300 mg, 400 mg&lt;br&gt;XR tab: 50 mg, 150 mg, 200 mg, 300 mg, 400 mg&lt;br&gt;Conversion from IR to XR can be done directly using the same total daily dose</td>
<td>Lowest incidence of EPS but most anticholinergic side effects.</td>
</tr>
<tr>
<td>Quetiapine</td>
<td>• Immediate release tab: 6.25 - 25 mg PO, may increase by 12.5-25 mg PO BID per day as tolerated&lt;br&gt;• Extended release tab: 50-150 mg PO HS, may increase by up to 150 mg/day as tolerated – see below&lt;br&gt;• Adult maximum 800 mg/day&lt;br&gt;• Geriatric maximum 800 mg/day</td>
<td>Tabs: 0.25 mg, 0.5 mg, 1 mg, 2 mg, 3 mg, 4 mg&lt;br&gt;Oral solution: 1mg/mL&lt;br&gt;Cannot be administered with beverages containing tannin or pectinate (cola or tea).&lt;br&gt;Compatible with water, coffee, orange juice or low fat milk&lt;br&gt;ODT: 0.5 mg, 1 mg, 2 mg, 3 mg, 4 mg</td>
<td>Highest risk EPS, least sedation reported.</td>
</tr>
<tr>
<td>Risperidone</td>
<td>• 0.25 mg PO daily, increase by 0.25 mg no sooner than Q7d to optimal dose of 0.5 mg PO BID or (high dose) 1 mg BID&lt;br&gt;• No evidence to support doses above 10 mg/day in adult population&lt;br&gt;• Adult maximum 16 mg/day and 8mg/dose&lt;br&gt;• Geriatric maximum 2 mg per day for BPSD</td>
<td></td>
<td>Low incidence of CV side effects (10% experience orthostatic hypotension at higher dose but ~2% reported tachycardia, ECG abnormalities/QT prolongation). Only antipsychotic indicated for short term treatment of severe dementia / inappropriate behaviour due to aggression and/or psychosis in Canada.</td>
</tr>
</tbody>
</table>
Monitoring Antipsychotic Use

When a patient presents with antipsychotic medications, assess if the indication was originally for short term use (e.g. acute psychosis, BPSD, etc.) or if the patient has an underlying condition that requires long term antipsychotic therapy.

Antipsychotic Monitoring Plan

Listed below are considerations for prescribing clinicians to support the monitoring of seniors on antipsychotic medications.

- Obtain a thorough history, including all baseline labs, if available.

- **Electrolytes, CBC*, serum creatinine, liver function tests (AST, ALT, etc.), thyroid function**
  - at baseline and Q3months OR as clinically indicated**

- *Agranulocytosis/leukopenia/neutropenia may not be time dependent. If neutrophil count is low, monitor closely for fever and signs/symptoms of infection. Discontinue and reassess antipsychotic if Absolute Neutrophil Count less than 1.5x10^9.

- **Q3month review should include a pharmacist

METABOLIC DISORDER

Typically comes on late in the course of therapy but some factors (particularly weight gain) can appear earlier in treatment. Prevention is easier to manage than treatment, making early monitoring important.

- **Weight** at initiation/dose change, then monthly x3 months, then Q3months while stable

- **HbA1C** at baseline, then 3 months after initiation/dose change, then annually*
  - *May increase to Q3-6months in patients with obesity, family history of DM, weight gain greater than 5% body weight

- **+/− Fasting/random blood glucose** at baseline, then 3 months after initiation/dose change, then annually OR as clinically indicated

EXTRAPYRAMIDAL SYMPTOMS & TARDIVE DYSKINESIA

EPS typically have early onset (within the first few days), but akathisia and pseudoparkinsonism can occur within the first 6 weeks (more common with first generation antipsychotics vs. second and third generation antipsychotics, but can occur in SGA/TGAs, particularly risperidone and aripiprazole). TD is thought to be related to the duration of treatment and total dose. Prophylaxis not usually indicated in this population.

- Evaluate **motor signs/symptoms** (motor restlessness, rigidity, shuffling gait, cog wheeling, tremor, difficulty swallowing, etc.) at baseline AND Q3months AND as clinically indicated
CARDIOVASCULAR RISK

- Orthostatic vitals* at initiation and with dose titrations AND Q3months in patients with CV risk factors**, particularly when using asenapine, clozapine, risperidone, quetiapine, chlorpromazine and ziprasidone

- ECG to assess QT interval at baseline in patients with CV risk factors* AND as part of differential diagnosis in the setting of dizziness, fainting spells, palpitations, nausea/vomiting
  From most to least QT prolonging: ziprasidone > quetiapine = risperidone = olanzapine = haloperidol > clozapine (ref: 2009 schizophrenia PORT treatment recommendation)

- Serum potassium and magnesium at baseline and as clinically indicated in patients with CV risk factors

- Lipids 3months after initiation/dose change and annually thereafter

*To accurately assess for orthostatic change, take vitals at least 1-minute post position change.
** Heart failure, recent myocardial infarction, preexisting conduction abnormalities, syncope, family history of sudden cardiac death (before age 40), long QT syndrome

ANICHOLINERGIC EFFECTS

Typically early onset

- Monitor patient for dry mouth, dry eyes, blurry vision (usually transient and only near vision affected), constipation, urinary retention, confusion and delirium

NEUROLEPTIC MALIGNANT SYNDROME (NMS)

- In the setting of fever, rigidity, diaphoresis/autonomic instability, test CBC for WBC and CPK level.
  If suspicion of NMS, immediately discontinue the antipsychotic(s), ensure patient avoids dehydration and initiate management of NMS

PROLACTIN LEVELS

- In the setting of decreased libido, erectile or ejaculatory dysfunction, menstrual changes, galactorrhea, monitor prolactin Q1month x 3 months, then annually

* While these symptoms may be part of natural aging, antipsychotics may be used for the management of BPSD and other conditions in a younger population
Stopping Antipsychotics

To support deprescribing, clinicians are encouraged to consider the Antipsychotic Deprescribing Algorithm and Notes developed through deprescribing.org\(^{19}\). Available at: [http://www.open-pharmacy-research.ca/evidence-based-deprescribing-algorithm-for-antipsychotics/\(^{20}\)]


NOTE: The recommendation in the above algorithm is for all antipsychotic medication prescribed for BPSD be reviewed at least every 3 months for trial of tapering and/or deprescribing. As dementia and other neurological conditions with related responsive behaviours are progressive in nature, over time changes in the responsive behaviours will occur with minimal or no responsive behaviours in the later stages of the disease.

NOTE: “Tapering doses”
In cases where the initial R.I.S.K.S. was due to:
(i) delusions of persecution/paranoia or of jealousy,
(ii) psychosis causing risk to self/others AND/OR
(iii) psychosis causing severe distress.
The following tapering dose schedule and monitoring is highly recommended for clinician consideration:
- Reduce to 25% (or lower) of original dose every 4 weeks or more
- Monitor closely for original signs/symptoms of psychosis.
CONFLICTS OF INTEREST

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SUPPORTING DOCUMENTS

Quick Reference Card A
General Principles for Prescribing Psychotropics for BPSD
Antipsychotic Medication MONITORING PLAN

Quick Reference Card B
Antipsychotic Deprescribing Algorithm
Antipsychotic Deprescribing Notes

CITATIONS FOR RECOMMENDED DOSING, RISK FACTORS & MONITORING OF ANTIPSYCHOTICS


Lexicomp Online. Aripiprazole, Olanzapine, Quetiapine, Risperidone. [On-line]


Schneider LS; Tariot PN; Dagerman KS; Davis SM; Hsiao JK; Ismail MS; Lebowitz BD; Lyketsos CG; Ryan JM; Stroup TS; Sultzer DL; Weintraub D; Lieberman JA; CATIE-AD Study Group. (2006) Effectiveness of atypical antipsychotic drugs in patients with Alzheimer's disease. The New England Journal of Medicine, 355(15), 1525-1538.

Street JS; Clark WS; Kadam DL; Mitjan SJ; Julian BE; Feldman PD; Breier A. (2001). Long-term efficacy of olanzapine in the control of psychotic and behavioural symptoms in nursing home patients with Alzheimer's dementia. International Journal of Geriatric Psychiatry. 16(1), S62-70


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