Dementia Antipsychotic Prescribing Guide

**General Guidelines:**

1. **Rule out reversible causes** prior to using a drug.
2. **Try non-drug management strategies first.**
3. **Clearly document treatment targets** (symptoms) before and after a treatment strategy is tried.
4. **Justify use of an antipsychotic.** The treatment target symptom must present a danger to the person or others according to CMS guidelines for antipsychotic use in nursing homes and must also fail to respond to non-drug interventions. If symptoms are due to schizophrenia or related disorders, severe mood disorders or psychosis then antipsychotic use may be appropriate. In non-nursing home settings where these CMS regulations do not apply, many clinicians would consider antipsychotic use for persistent distressing symptoms related to hallucinations, delusions, or agitation, even if they do not clearly pose a danger to the patient or others. A key determinant is whether the antipsychotic appears to improve the patient’s quality of life.
5. **See Guidance for Special Populations**, if the patient has frontotemporal dementia, Parkinson’s disease, Lewy body dementia, renal impairment, or hepatic impairment.
6. **Consider the impact of side effects on comorbidities** when choosing a drug, and **start with a low dose.**
7. **If the drug doesn’t help, stop it** (use appropriate tapering).

**Appropriate antipsychotic treatment targets:**
- Aggressive behavior (especially physical)
- Hallucinations (if distressing)
- Delusions (note: memory problems are often mistaken for delusions, e.g. thinks people are stealing lost items)
- Possibly other severely distressing agitation (see #4 above)

**Inappropriate antipsychotic treatment targets:**
- Wandering
- Insomnia
- Poor self-care
- Restlessness
- Uncooperativeness without aggressive behavior
- Inattention or indifference to surroundings
- Sadness or crying alone that is not related to depression or another psychiatric disorder

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**Antipsychotic Efficacy**

Evidence supports modest symptom improvements with **aripiprazole**, **haloperidol**, **olanzapine**, **quetiapine**, and **risperidone**, but not with use of other antipsychotics in dementia. All antipsychotics appear to increase risk of death. The table below summarizes the strength of evidence supporting the efficacy of each **atypical antipsychotic** for different symptom domains.

<table>
<thead>
<tr>
<th></th>
<th>Aripiprazole</th>
<th>Olanzapine</th>
<th>Quetiapine</th>
<th>Risperidone</th>
</tr>
</thead>
<tbody>
<tr>
<td>Dementia overall</td>
<td>++</td>
<td>+</td>
<td>+</td>
<td>++</td>
</tr>
<tr>
<td>Dementia psychosis</td>
<td>+</td>
<td>+/-</td>
<td>+/-</td>
<td>++</td>
</tr>
<tr>
<td>Dementia agitation</td>
<td>+</td>
<td>++</td>
<td>+/-</td>
<td>++</td>
</tr>
</tbody>
</table>

++ = moderate or high evidence of efficacy
+ = low or very low evidence of efficacy
*/- = mixed results in randomized trials

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**Adverse Effects Comparison Table**

<table>
<thead>
<tr>
<th>Drug</th>
<th>Urinary incontinence</th>
<th>Urine glucose↑</th>
<th>Weight gain↑</th>
<th>Edema</th>
<th>Orthostatic hypotension</th>
<th>Confusion, delirium</th>
<th>Cognitive worsening</th>
<th>Weight gain/glucose↑</th>
<th>Triglyceride↑</th>
<th>Weight gain/glucose↑</th>
<th>Edema</th>
<th>Orthostatic hypotension</th>
<th>Confusion, delirium</th>
<th>Cognitive worsening</th>
<th>Weight gain/glucose↑</th>
<th>Triglyceride↑</th>
</tr>
</thead>
<tbody>
<tr>
<td>Aripiprazole (2-10mg)</td>
<td>0</td>
<td>0</td>
<td>0</td>
<td>0</td>
<td>0</td>
<td>0</td>
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<tr>
<td>Haloperidol (0.25-2mg)</td>
<td>0</td>
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<td>0</td>
<td>0</td>
<td>0.25</td>
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</tr>
<tr>
<td>Olanzapine (2.5-7.5mg)</td>
<td>0</td>
<td>0</td>
<td>0</td>
<td>0</td>
<td>0.5</td>
<td>0</td>
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<td>0</td>
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</tr>
<tr>
<td>Quetiapine (12.5-150mg)</td>
<td>0</td>
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<td>0</td>
<td>0.25</td>
<td>0</td>
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<td>0</td>
</tr>
<tr>
<td>Risperidone (0.25-2mg)</td>
<td>0</td>
<td>0</td>
<td>0</td>
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<td>0</td>
</tr>
</tbody>
</table>

0 = no clear evidence that the drug causes this side effect in a clinically important way, or very rarely
1 = more based on clinical judgment
2 = weak evidence based on less data
3 = moderate evidence
4 = strong evidence

*Haloperidol has shown efficacy for aggression in randomized trials

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**Movement side effects** (e.g. parkinsonism, akathisia, dystonia, tardive dyskinesia):
- Parkinsonism
- Akathisia (restlessness)
- Dystonia
- Tardive dyskinesia

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**Dementia overall:**
- ++ = moderate or high evidence of efficacy
- + = low or very low evidence of efficacy
- */- = mixed results in randomized trials

**Dementia psychosis:**
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**Dementia agitation:**
- ++ = moderate or high evidence of efficacy
- + = low or very low evidence of efficacy
- */- = mixed results in randomized trials

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**Guidance for Special Populations:**
- If the patient has frontotemporal dementia, Parkinson’s disease, Lewy body dementia, renal impairment, or hepatic impairment.

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**Consider the impact of side effects on comorbidities** when choosing a drug, and **start with a low dose.**
Dementia Antipsychotic Prescribing Guide
Dosing, Special Populations

Dosing

Timing: Usually once daily at night or prior to sundowning. Beware of sedation-related adverse events if given earlier than bedtime.

Dosage forms:
- Regular tablets can be crushed and mixed with food if needed.
- IM antipsychotics used only in emergencies when oral is refused.
- Topical forms, e.g. compounded creams, not recommended. No evidence to guide proper dosing. Absorption is unknown and unpredictable.

<table>
<thead>
<tr>
<th>Medicine</th>
<th>Starting Dose (mg/day)</th>
<th>Max Dose for Maintenance* (mg/day)</th>
<th>Special Dosage Forms**</th>
</tr>
</thead>
<tbody>
<tr>
<td>Aripiprazole</td>
<td>2-5</td>
<td>10</td>
<td>ODT, L, IM</td>
</tr>
<tr>
<td>Haloperidol</td>
<td>0.25</td>
<td>2</td>
<td>L, IM</td>
</tr>
<tr>
<td>Olanzapine</td>
<td>2.5-5</td>
<td>7.5</td>
<td>ODT, L, IM</td>
</tr>
<tr>
<td>Quetiapine</td>
<td>12.5-25</td>
<td>150</td>
<td>XR</td>
</tr>
<tr>
<td>Risperidone</td>
<td>0.25-0.5</td>
<td>2</td>
<td>ODT, L</td>
</tr>
</tbody>
</table>

*per CMS regulations for long-term care facilities. Doses for acute treatment sometimes exceed maintenance doses.

**ODT = orally dissolving tablet, L = liquid, IM = short-acting intramuscular, XR = extended release.

Dosage forms:
- Regular tablets can be crushed and mixed with food if needed.
- IM antipsychotics used only in emergencies when oral is refused.
- Topical forms, e.g. compounded creams, not recommended. No evidence to guide proper dosing. Absorption is unknown and unpredictable.

Guidance for Special Populations

Frontotemporal dementia: Some evidence for trazodone. Mixed for SSRIs. See Iowa Geriatric Education Center website for details.

Parkinson’s disease (PD) and Lewy body dementia (LBD):
- Movement disorder treatments (dopamine agonists, carbidopa-levodopa, anticholinergics) can cause psychosis or delirium. Prior to antipsychotic use, consider reducing the dose of these drugs to see if the psychosis or behaviors resolve or become manageable.
- People with PD and LBD are very sensitive to adverse effects, particularly movement side effects and neuroleptic malignant syndrome. If antipsychotics are used, expert guidelines recommend quetiapine or clozapine due to lower movement side effect risk.

Renal Impairment: Reduce risperidone dose. Titrate slowly.

Hepatic Impairment: Possibly reduce dose of olanzapine.

Dementia Antipsychotic Prescribing Guide
Monitoring for Response and Adverse Effects

Monitoring for Response
- Clearly document treatment target symptoms. If the drug does not help, discontinue the drug. These symptoms may also change over time, with or without drug treatment.
- Do not expect an immediate response. Sedation may explain much of any immediate effect that is seen. Response may take 2-4 weeks.
- Do not increase doses too quickly if the patient doesn’t respond right away. At a stable dose, drug blood levels may rise for several days to a week or more before reaching a steady state level.

Monitoring for Adverse Effects
Other possible adverse effects include: falls, constipation, urinary tract infection, urinary incontinence or retention, stroke, arrhythmias, and neuroleptic malignant syndrome.

<table>
<thead>
<tr>
<th>Side Effect</th>
<th>Monitoring</th>
</tr>
</thead>
<tbody>
<tr>
<td>Movement Side Effects</td>
<td>Observation for tremor, gait changes, difficulty swallowing, signs of parkinsonism, restlessness (akathisia), unusual movements (tardive dyskinesia). Abnormal Involuntary Movement Scale (AIMS) at baseline, every 6 months, or if movement side effects are suspected.</td>
</tr>
<tr>
<td>Central Nervous System</td>
<td>Sedation Observation, sedation scale if needed. Confusion, delirium, or other cognitive worsening Observation for mental status or behavior changes. Delirium screening tool, e.g. CAM (Confusion Assessment Method) if delirium is suspected. Psychotic symptoms Observation for worsening symptoms. Cardiovascular / Metabolic Orthostatic hypotension Observation for signs of dizziness or falls. Orthostatic blood pressure (if feasible). Monthly, or if signs of dizziness occur. More frequent on initiation or after dose increase. Edema Observation for swelling of extremities. Weight gain Monthly weight. Consider weekly for 1 month if overweight. Watch for increased appetite. Hyperglycemia / Diabetes Blood glucose at baseline, 3 &amp; 6 months, then q6 months. Also PRN symptoms or mental status change. Monitor symptoms: increased thirst, urination, hunger, weakness. Triglyceride ↑ Fasting blood lipid panel at baseline, 3 &amp; 6 months, then q6 months. Especially if patient has cardiovascular risk factors: e.g. obesity, diabetes, hyperlipidemia.</td>
</tr>
</tbody>
</table>