

COGNITIVE IMPAIRMENT — PART 2: DIAGNOSIS TO MANAGEMENT Clinical Practice Guideline | February 2017

OBJECTIVE

Alberta primary care physicians and their interdisciplinary teams will be able to assess patients presenting with cognitive concerns and manage the majority of these patients and support their caregivers.

TARGET POPULATION

Older adults, e.g., ≥65 years of age

EXCLUSIONS

Children

Younger adults <65 years of age, i.e., early onset dementia

RECOMMENDATIONS

- Most patients with dementia can be managed within primary care. However, at times
 voluntary agencies, consultants, and both community and facility-based services will be
 required to assist primary care providers.
- The focus of this guideline is on the management of the mild to moderate stages of dementia.

GENERAL MANAGEMENT CHECKLIST

- ✓ Patient-centred and culturally sensitive care should be provided at all times.
- ✓ All patients with dementia and their families who consent should be referred to the local chapter of the Alzheimer Society.
- ✓ Modify management of co-morbidities in the setting of dementia so there is less reliance on patient self-care and a concomitant increase in the role played by both informal and formal caregivers.
- ✓ Determine how medications are being managed. If there is evidence of medication nonadherence, suggest using reminder aids and/or request that a caregiver manage medications.
- ✓ Use with caution medications that may adversely impact cognition (e.g., anticholinergics, benzodiazepines, hypnotics, other psychotropics, opioids).
- ✓ Arrange for regular follow-up visits at four to six month intervals to reassess the patient's general condition, look for adverse effects to medications being used, and monitor the cognitive and non-cognitive symptoms of their dementia.
- ✓ Consider referral to specialty services to address specific concerns that might arise in the care of patients with dementia (see below).



- ✓ Strive to maintain an optimal level of functioning with use of non-pharmacological (e.g., memory aids) and pharmacological interventions. Note that drug treatment alone is of limited value.
- ✓ Actively encourage patients (while they retain capacity) to update their will and complete both a personal directive and an enduring power of attorney. See the Future/Advanced Planning Tools & Tips for Aging Individuals section of the <u>supplemental document</u>.
- ✓ Remain vigilant for and strive to mitigate safety risks particularly in relation to driving, cooking, wandering, financial management and abuse while supporting functional independence wherever possible.
- ✓ Enlist support from family, friends and community resources (e.g., home care, day programs, respite) to maximize functioning and ease caregiver burden See the Professional Services & Resources in Alberta section of the <u>supplemental document</u>.

TREATMENT/MANAGEMENT OF SPECIFIC CONDITIONS

PRACTICE POINT

Many cases of dementia have more than one contributing cause. Management should be based on dealing with the predominant contributing cause(s) of the dementia.

Table 1: Condition and Treatment

Condition	Treatment
Alzheimer Disease (AD)	✓ Consider a trial of any of the three available <u>cholinesterase inhibitors</u> for patients AD or AD with a cerebrovascular component:
	 Know the contraindications and precautions, common adverse effects (and their management), titration regimens and indications for stopping for these agents.
	 Treated patients should be reassessed regularly in order to gauge their response to therapy and/or detect the emergence of adverse effects.
	✓ Consider memantine as an option for patients with moderate to severe AD.
	✓ There is insufficient evidence to recommend for or against combination therapy with a cholinesterase inhibitor and memantine.
Vascular Dementia (VaD)	✓ Identify and mange vascular risk factors (e.g., hypertension, diabetes, smoking, sedentary lifestyle, lipid abnormalities).
	✓ Consider antiplatelet therapies for the prevention of recurrent ischemic events in appropriate patients.
	✓ Consider cholinesterase inhibitors as a treatment option for patients with AD and a cerebrovascular component.
	✓ There is insufficient evidence to recommend for or against the use of cholinesterase inhibitors for VaD.
Dementia with Lewy Bodies (DLB)/ Parkinson	✓ Consider cholinesterase inhibitors for patients with DLB who likely have concurrent AD.

Clinical Practice Guideline Page 2 of 14 Recommendations



Condition	Treatment
Disease Dementia (PDD)	 Consider a trial of levodopa-carbidopa at low dosages for parkinsonism arising in the context of DLB.
	✓ Suggest caregivers modify the sleep environment (e.g., placing mattress on the floor, padding corners of furniture) for patients with sleep-related injuries or REM-sleep behaviour disorder (RBD) emerging in DLB.
	✓ Consider melatonin (few side effects) or a cautious trial of clonazepam for RBD.
	X Avoid use of antipsychotics. If antipsychotics are required, a low dose of an atypical antipsychotic can be attempted but should be managed by a clinician who is experienced, has specialized skills and can provide close follow-up.
Frontotemporal Dementia (FTD)	✓ Emphasize a non-pharmacological approach targeted at controlling symptoms (especially behavioural) and supporting patients and their families.
	✓ Drug options are limited for FTD. Consider:
	✓ Selective serotonin reuptake inhibitors for severity of compulsion, agitation, aggression, impulsivity, and aberrant eating behavior.
	✓ Atypical antipsychotics are reserved for severe agitation and aggression that cannot be managed by other means.
	✓ Refer to a speech and language therapist when language issues are prominent.
	✓ Consider referral to a specialty service because of the unique and challenging nature of this condition.

Note: Alberta Blue Cross requires special authorization for Donepezil, Rivastigmine, Galantamine. See Alberta Health Drug Benefit List and special authorization criteria at: https://idbl.ab.bluecross.ca/idbl/load.do.

PRACTICE POINT

Always use caution when prescribing cholinesterase inhibitors to patients with:

- Previous hypersensitivity or adverse reactions to these drugs
- History of seizures or chronic alcoholism
- Asthma and chronic obstructive airway disease
- History of bradycardia, heart block, and/or syncope
- Gastrointestinal ulcers and those taking non-steroidal anti-inflammatories
- Low body weight or history of weight loss
- Urinary tract obstruction or difficulty with urination

Clinical Practice Guideline Page 3 of 14 Recommendations



BEHAVIOURAL AND PSYCHOLOGICAL SYMPTOMS OF DEMENTIA (BPSD)

- ✓ Use non-pharmacological interventions as "first-line" therapy for BPSD. Refer to "Appropriate Use of Antipsychotics (AUA) Toolkit for Care Teams" for additional details and information regarding assessment and management of responsive behaviours associated with dementia. http://www.albertahealthservices.ca/auatoolkit.asp.
- ✓ Consider the following general approaches for patients with BPSD:
 - Search for and manage the underlying cause of BPSD. Challenging behaviours can arise from delirium or depression.

PRACTICE POINT

Responsive behaviours is a term used to describe how the actions of a person with dementia are a response, often intentional, to something important about their personal, social or physical environment. Management is directed at uncovering what this might be and addressing it. See

http://www.albertahealthservices.ca/assets/about/scn/ahs-scn-srs-responsivebehaviours.pdf.

- Advise caregivers to re-direct and distract the patient, and remove triggers when possible to prevent or ease agitation and aggression.
- Recommend specific training for caregivers so they can provide person-centred care, manage behaviours, and learn communication skills.
- Consider tracking devices, motion detection devices, and home alarms to assist with detecting wandering and locating lost patients.
- Consider music therapy, exercise (for sleep), sensory interventions (e.g., multisensory stimulation, massage and touch therapy) and involvement in activities as possible helpful interventions.
- X There is little to no evidence at this time to support use of any herbal remedies and/or other non-prescriptive agents for the treatment and/or management of BPSD.

GENERAL PHARMACOLOGICAL APPROACHES FOR BPSD

Table 2: Pharmacological Agent and Recommendation

Agent	Recommendation			
Antidepressants	✓ Consider a trial of an antidepressant if the patient had an inadequate response to non-pharmacological interventions or has a major depressive disorder, severe dysthymia, or severe emotional lability.			
	✓ If an antidepressant is used, avoid tricyclics because of their anticholinergic side effects.			
	✓ There is insufficient evidence to recommend for or against the use of selective serotonin reuptake inhibitors or trazodone for managing agitation.			

Clinical Practice Guideline Page 4 of 14 Recommendations



Agent	Recommendation
Atypical Antipsychotics	✓ Potential benefits must be weighed against the significant risks such as cerebrovascular events and mortality.
	✓ Prescribe risperidone, olanzapine and aripiprazole for severe agitation, aggression and psychosis associated with dementia when there is risk of harm to the patient and/or others.
	✓ Start medication at a low dose and then carefully titrate based on response and emerging adverse effects.
	✓ Reassess medications periodically with attempts to taper and discontinue.
	X DO NOT use these medications to manage behavioural concerns e.g., insomnia - especially when safer more effective alternatives are available.
	? There is insufficient evidence to recommend for or against the use of quetiapine.
	Note: risperidone is the only antipsychotic with an indication for short-term use in Canada for the management of the neuropsychiatric symptoms of AD.
Cholinesterase Inhibitors	✓ Cholinesterase inhibitors and/or memantine are generally not recommended for the primary treatment of neuropsychiatric symptoms.
-	opropriate Use of Antipsychotics (AUA) Toolkit for Care Teams" for additional details and regarding assessment and management of responsive behaviours associated with

PRACTICE POINT

Antipsychotics should be avoided in the treatment of patients with Dementia with Lewy bodies. If required to manage troubling behavioural issues that have not responded to other measures, use a low dose of an atypical antipsychotic with extreme caution and careful monitoring for adverse effects.

REFERRAL

- ✓ Consider referral to a specialist/specialty service when:
 - o The patient has early-onset dementia.
 - The patient has rapidly progressive dementia.

dementia: http://www.albertahealthservices.ca/auatoolkit.asp

- The patient has frontotemporal dementia. This is to help confirm the diagnosis and assist in devising, coordinating, and implementing a care plan for patients, caregivers and family.
- There is continuing uncertainty about the patient's diagnosis after initial assessment and follow-up.
- The patient and/or the family request another opinion.
- There is the presence of significant depression, especially if there was an inadequate response to initial treatment.

Clinical Practice Guideline Page 5 of 14 Recommendations



- There is unfamiliarity or problems with specific medications being used to treat Alzheimer disease or another dementia.
- There is need for assistance in patient management (e.g., behavioural problems, functional impairments) or providing caregiver support.
- o Genetic counselling is indicated.
- o The patient and/or family express an interest in research studies.

BACKGROUND

Most patients with dementia can be managed within primary care. However, at times voluntary agencies, consultants, and both community - and facility-based services will be required to assist primary care providers. The focus of this guideline is on the management of the mild to moderate stages of dementia.

TREATMENT/MANAGEMENT OF SPECIFIC CONDITIONS

ALZHEIMER DISEASE (AD)

All patients diagnosed with dementia should be assessed for their suitability for pharmacologic treatment. In AD the cholinergic neuronal pathways that project from the basal forebrain to the cerebral cortex and hippocampus are affected. This has been proposed to account for some of the clinical manifestations of dementia. Please note that many cases of dementia are a result of several contributing conditions. This is typically a combination of AD with other brain pathology. Management of these patients would include addressing the contribution from AD.

VASCULAR DEMENTIA (VAD)

Prevention of the onset and progression of VaD is potentially possible by the management of vascular risk factors. In addition to dealing with smoking, physical inactivity, diet and obesity this could include the use of anti-hypertensives, agents for lipid abnormalities, treatment of diabetes, anticoagulants for certain arrhythmias and other types of heart disease, and platelet inhibitors (e.g., ASA) for secondary prevention in high risk individuals.³ Cholinesterase inhibitors for "pure" VaD (i.e., dementia due to cerebrovascular disease without other pathologies) is not currently an accepted indication for their use.

DEMENTIA WITH LEWY BODIES (DLB)4,5

The core symptoms of DLB were described in the accompanying guideline. Mild hallucinations from this condition may not require pharmacotherapy. When a medication is required, cholinesterase inhibitors typically are tried first (in an effort to protect patients from being exposed to antipsychotics) though evidence on their effectiveness is generally lacking. If ineffective, most experts recommend a cautious trial of atypical neuroleptics such as quetiapine and avoiding standard neuroleptics such as haloperidol because of neuroleptic sensitivity. This should be

preferably overseen by a clinician with specialized skills and/or experience in the treatment of DLB. Cholinesterase inhibitors might help with alertness and the cognitive deficits of this condition. A trial of levodopa-carbidopa at low dosages can be considered for parkinsonism arising in the context of DLB. The motor improvement tends to be less than what is seen with Parkinson disease and its use may worsen the neuropsychiatric symptoms. Modifying the sleep environment is helpful (e.g., placing mattress on the floor, padded corners of furniture) for patients who have had sleep-related injuries for REM-sleep behaviour disorder (RBD) arising in the context of DLB. Other medication options to help manage RBD are melatonin since it has fewer side effects or a cautious trial of clonazepam. As many if not most patients with DLB also have Alzheimer pathology, a trial of a cholinesterase inhibitor can be considered. In Canada rivastigmine has been approved for the treatment of dementia in Parkinson disease.

FRONTOTEMPORAL DEMENTIA (FTD)

There are no disease-modifying therapies available for FTD, and few studies have been done on the treatment options that are available. 9,10,11 Management is directed to controlling symptoms (especially behavioural) and helping patients and their families cope with the impact of the illness. When language issues are prominent, speech and language therapy can assist with communication strategies.

BEHAVIOURAL AND PSYCHOLOGICAL SYMPTOMS OF DEMENTIA (BPSD)

BPSD is also referred to as Responsive Behaviours in Dementia.

Non-pharmacologic interventions for agitation and aggression in dementia include recognition and management of the underlying factors that are contributing to the behaviour (medical, psychiatric, mediations, environmental). For depressive symptoms, a trial of an antidepressant can be considered if the patient has an inadequate response to non-pharmacologic interventions or has a major depressive disorder, severe dysthymia, or severe emotional labiality. 13,14 There is insufficient evidence to recommend for or against the use of selective serotonin reuptake inhibitors or trazodone in the management of agitation. Risperidone, olanzapine, or aripiprazole can be considered for severe agitation, aggression, and psychosis associated with dementia where there is risk of harm to the patient or others. There is insufficient evidence to recommend for or against the use of quetiapine in the management of these behaviours in dementia. 2,8,14 The potential benefit of all antipsychotic medications must be weighed against the substantial risks such as cerebrovascular adverse events and mortality. Valproate should not be used for agitation and aggression in AD.14

PHARMACOTHERAPY - REVIEW OF AVAILABLE AGENTS

CHOLINESTERASE INHIBITORS

Recommendations regarding cholinesterase inhibitors are derived from the Third and Fourth Canadian Consensus Conference on the Diagnosis and Treatment of Dementia.¹⁴ A trial of a cholinesterase inhibitor is recommended for most patients with AD. All three cholinesterase



inhibitors have demonstrated efficacy for mild to severe AD (note: in Canada only donepezil has been approved for the severe stage). Direct comparisons do not suggest significant differences in efficacy between them. Selection of which agent to use will be based on adverse effect profile, ease of use, familiarity, and differences between the agents in their pharmacokinetics and other mechanisms of action. The most common adverse effects are gastrointestinal (e.g., anorexia, nausea, vomiting, diarrhea). Cholinesterase inhibitors might increase the risk of:

- Gastrointestinal bleeding particularly in patients with ulcer disease or those taking nonsteroidal anti-inflammatory (NSAD) drugs including high doses of acetylsalicylic acid (ASA)
- Bradycardia or heart block
- Asthma or obstructive pulmonary disease
- Lower urinary tract symptoms
- Seizures
- Prolonged effects of succinylcholine-type neuromuscular blockers

When a cholinesterase inhibitor is discontinued there may be a decline over the following six weeks in the patient's cognition, function and/or behaviour. If observed, consideration should be given to re-initiating treatment. There is insufficient evidence to advise for or against combining cholinesterase inhibitors and memantine.¹⁵

DONEPEZIL

Donepezil is a reversible inhibitor of acetylcholinesterase (AChE) approved in Canada for the symptomatic treatment of mild, moderate and severe dementia of the Alzheimer's type. It exerts its therapeutic effect through enhancing cholinergic function.* Clinical trials have demonstrated modest benefits with donepezil compared to the placebo arm.* Therapy with donepezil begins with a dose of 5 mg once daily. This is continued for four to six weeks and typically increased to 10 mg if there are no unacceptable adverse effects. Doses over 10 mg are not recommended.* Common side effects include nausea, diarrhea, insomnia, vomiting, muscle cramps, fatigue and anorexia. Side effects are usually mild and temporary. If insomnia or disturbing vivid dreams develop, this may be helped by ensuring the medication is taken in the morning. Caution should be exercised in patients with a history of arrhythmias/conduction abnormalities, gastrointestinal ulcers, urinary retention, seizures, and/or asthma or obstructive pulmonary disease.*

RIVASTIGMINE

Rivastigmine is a reversible inhibitor of both acetylcholinesterase (AChE) and butyrylcholinesterase (BuChE). The activity of BuChE is known to increase with increasing severity of dementia, but the clinical significance of the ability of rivastigmine to inhibit BuChE has not been demonstrated. Clinical trials have shown positive effects on cognition, behaviour and activities of daily living.¹⁶

Rivastigmine in Canada is indicated for the treatment of mild to moderate AD and dementia with Parkinson disease. The dose range is 3.0 mg to 12.0 mg daily with a usual maintenance dose of 6 to 12 mg per day. Titration is done slowly (e.g., at four-week intervals) to reduce the gastrointestinal

See drug monograph info.



side effects.* Rivastigmine is available in a transdermal patch, but this is not covered by the drug benefit plan for seniors through Alberta Blue Cross.

GALANTAMINE

Galantamine is stated to be a modulator of nicotinic receptors as well as cholinesterase inhibitor. The clinical benefits of this dual action remain unproven. Galantamine is available daily at an ER preparation. The starting dose is 8 mg and at four-week intervals can be increased to 16 and 24mg daily.*

Table 3: Comparison of Cholinesterase Inhibitors. Adapted with permission from Compendium of Therapeutic Choices 7th Edition, p65-66.18

Comparison of the Cholinesterase Inhibitors ¹⁸				
Class	Drug	Dose	Adverse Effects	Drug Interactions
Cholinesterase Inhibitors	Donepezil	Initial: 5 mg/day Target: 5-10 mg/day Adjust dose at 4 week intervals	Cholinesterase inhibitors may lower seizure threshold, increase the risk of GI ulceration or bleeding or exacerbate COPD or asthma.	Cholinesterase inhibitors: Concern regarding antagonistic effect when combined with drugs that have anticholinergic effects or if combined with agents that have an additive bradycardic effect (e.g., beta-blockers).
			Donepezil:>10%: headache, nausea, diarrhea.	Donepezil: Toxicity may be increased by inhibitors of CYP2D6 or CYP 3A4 (e.g.,
			<10%: vomiting, anorexia, fatigue, sleep disturbance, syncope, muscle cramps, urinary frequency. Uncommon: bradycardia, heart block.	paroxetine, erythromycin, prednisone, or grapefruit juice. Effectiveness may be reduced by inducers of CYP2D6 or CYP3A4 (e.g., carbamazepine, phenytoin, or rifampin).
	Galantamine	Initial: 8 mg daily. Target: 16-24 mg daily. Adjust dose at 4 week intervals. Take with meals.	See cholinesterase inhibitors above. In addition: Galantamine: >10%: nausea, vomiting, diarrhea. <10%: bradycardia, syncope, dizziness, headache, sleep disturbance, fatigue,	See cholinesterase inhibitors above. In addition, Galantamine: Toxicity may be increased by inhibitors of CYP2D6 or CYP3A4 (e.g., paroxetine, erythromycin, prednisone, or grapefruit juice). Effectiveness may be decreased by inducers of CYP2D5 or CYP3A4 (e.g., carbamazepine, phenytoin, and rifampin).

^{*} See drug monograph info.

Clinical Practice Guideline Page 9 of 14 Background



Comparison of the Cholinesterase Inhibitors ¹⁸				
Class	Drug	Dose	Adverse Effects	Drug Interactions
			abdominal pain, weight loss, UTI, urinary incontinence, rhinitis.	
			Rare: heart block, seizures, delirium.	
	Rivastigmine	Initial: 1.5 mg BID Target: 6-12 mg/day po Adjust dose at 4 week intervals Take with meals	See cholinesterase inhibitors above. In addition, Rivastigmine: >10% headache, dizziness nausea/vomiting, diarrhea, abdominal pain, anorexia (note: topical formulation reported to have lower GI symptoms). <10%: fatigue, insomnia, syncope, dyspepsia, weight loss, UTI, rhinitis. Rare: heart block, delirium, seizures.	See cholinesterase inhibitors above. Rivastigmine: None reported; not metabolized by cytochrome P450 system.
	Rivastignmine - transdermal patch Exelon Patch (not covered by provincial drug benefit plan for seniors).	Initial: Apply 1 Exelon 5 transdermal patch daily; if well tolerated, increase to Exelon 10 patch after at least 4 weeks. If switching from oral rivastigmine, use Exelon 5 for patients taking <3 mg BID and Exelon 10 for patients taking	See rivastigmine oral above.	See rivastigmine oral above.



Comparison of the Cholinesterase Inhibitors ¹⁸				
Class	Drug	Dose	Adverse Effects	Drug Interactions
		3-6 mg BID.		
		Remember to		
		remove patch		
		from previous		
		day before		
		applying new		
		patch.		

Table 4: Other Drugs. Adapted with permission from Compendium of Therapeutic Choices 7th Edition, p65-66.¹⁸

Other Drugs ¹⁸					
Class	Drug	Dose	Adverse Effects	Drug Interactions	
N-methyl-D- aspartate Receptor Antagonists	Memantine	Initial: 5 mg daily; increase by 5 mg daily at weekly intervals, to target dose of 10 mg BID starting at week 4.	Generally well tolerated; most common adverse effects - dizziness (7%), headache (6%), confusion (6%), constipation (5%), nausea/vomiting (3%).	Not affected by cytochrome P450 system. Concurrent use of amantadine, dextromethorphan, and ketamine should be avoided (these compounds act at the same receptor system as memantine and adverse drug reactions may be more frequent or pronounced). Theoretically, urinary alkalizers such as carbonic anhydrase inhibitors may decrease the clearance of memantine.	

Other Agents

There is little to no evidence at this time to support the use of any other pharmaceutical agent or herbal remedy for the treatment and/or management of the cognitive and functional manifestations of dementing illnesses.

ALBERTA BLUE CROSS SPECIAL AUTHORIZATION REQUEST FOR: DONEPEZIL/GALANTAMINE/RIVASTIGMINE

In Alberta coverage for a cholinesterase inhibitor can be requested through Alberta Government sponsored drug programs. A special authorization request form has to be completed (https://www.ab.bluecross.ca/dbl/pdfs/30776.pdf).

Criteria for coverage include a diagnosis of Alzheimer's disease and scoring between 10-26 on a Mini-Mental State Examination OR 1-4 on the interRAI Cognitive Performance Scale (CPS).

CPS is derived from items in the interRAI Resident Assessment Instrument MDS 2.0© (RAI-MDS 2.0©) and Resident Assessment Instrument-Home Care Instrument (RAI-HC©). An algorithm incorporating information on level of consciousness and a person's ability to make daily decisions, be understood, remember and eat is used to assign people into cognitive performance categories.



CPS scores range from 0 (intact) to 6 (very severe impairment). While not an office-based assessment of cognition, if available a current CPS score obtained on a home care client or a supportive living facility resident can be used as an alternative to a MMSE score in an Alberta Blue Cross special authorization request for cholinesterase inhibitor coverage.¹⁷

DISCONTINUATION OF CHOLINESTERASE INHIBITORS

The benefits of discontinuing cholinesterase inhibitors should be considered and balanced against possible worsening of cognition and function after stopping the agent in an individual who has been taking the agent for a prolonged period of time. It is suggested that cholinesterase inhibitors be discontinued when:

- Patient/caregiver/decision-maker decides to stop the agent after being informed of the risks and benefits of continuing and discontinuing the cholinesterase inhibitors.
- Persistent non-adherence with medication to the extent that continued use is futile that is cannot be rectified.
- Rate of cognitive, functional, or behavioural decline is greater on treatment compared to before therapy initiated.
- Intolerable side effects that are definitely or probably related to the cholinesterase inhibitors.
- Comorbidities make continued use of the agent unacceptably risky or futile (e.g., terminal illness).
- The patient's dementia progresses to a stage (e.g., Global Deterioration Scale stage 7) where there would be no meaningful benefit from continued therapy.

It is suggested that the dose be tapered before stopping the agent. If the dose is discontinued because of perceived lack of effectiveness, the patient should be monitored over the next one to three months to observe for evidence of decline with consideration of reinstating therapy if decline occurs.¹⁴

MEMANTINE

Memantine is an N-methyl-D-aspartate (NMDA) receptor antagonist that acts as a partial receptor blocker for the excitatory amino acid glutamate. Compared with placebo, treatment with memantine improved function, cognition, and the global state of patients with advanced dementia in a number of clinical trials.¹⁹ It is approved as monotherapy or adjunctive therapy with cholinesterase inhibitors for the symptomatic treatment of patients with moderate to severe AD (an MMSE score of 14 – 19 to less than 10 respectively).¹⁹ Side effects include headache, nausea, agitation, dizziness, hallucinations, and lowered seizure threshold. Concurrent use of amantadine, dextromethorphan, and ketamine should be avoided. These compounds act at the same receptor system as memantine, and therefore adverse drug reactions (mainly CNS-related) may be more frequent or pronounced. If renal function is low (creatinine clearance 40-60 ml/min/1.73m2) daily dose should be reduced to 10 mg/day (drug monograph info).



Non-Pharmacologic Approaches

Although non-pharmacologic measures are the preferred first line of therapy, there is relatively sparse research evidence supporting the use of these interventions.²⁰ However, experts suggest a variety of options can be tried if patients/caregivers wish to pursue them including re-direction, distraction and removal of trigger when possible to ease agitation and aggression in dementia. Other approaches that can be suggested are music therapy, bright light therapy, exposure to white noise, massage/touch interventions and involvement in recreational activities.^{12,13}

REFERENCES

- 1. Gauthier S, Patterson C, Chertkow H, Gordon M, Herrmann N, Rockwood K, et al. Recommendations of the 4th Canadian Consensus Conference on the Diagnosis and Treatment of Dementia (CCCDTD4). Can Geriatr J. 2012 Dec 4;15(4):120–6.
- 2. Hogan DB, Bailey P, Black S, Carswell A, Chertkow H, Clarke B, et al. Diagnosis and treatment of dementia: 4. Approach to management of mild to moderate dementia. Can Med Assoc J. 2008 Oct 7;179(8):787–93.
- 3. Pase MP, Beiser A, Enserro D, Xanthakis V, Aparicio H, Satizabal CL, et al. Association of ideal cardiovascular health with vascular brain injury and incident dementia. Stroke J Cereb Circ. 2016 May;47(5):1201–6.
- 4. Zupancic M, Mahajan A, Handa K. Dementia with lewy bodies: diagnosis and management for primary care providers. Prim Care Companion. CNS Disord. 2011;13(5).
- 5. Walker Z, Possin KL, Boeve BF, Aarsland D. Lewy body dementias. The Lancet. 2015 Oct;386(10004):1683–97.
- 6. Lucetti C, Logi C, Del Dotto P, Berti C, Ceravolo R, Baldacci F, et al. Levodopa response in dementia with lewy bodies: a 1-year follow-up study. Parkinsonism Relat Disord. 2010 Sep;16(8):522–6.
- 7. Aurora RN, Zak RS, Maganti RK, Auerbach SH, Casey KR, Chowdhuri S, et al. Best practice guide for the treatment of REM sleep behavior disorder (RBD). J Clin Sleep Med JCSM Off Publ Am Acad Sleep Med. 2010 Feb 15;6(1):85–95.
- 8. Herrmann N, Lanctôt KL, Hogan DB. Pharmacological recommendations for the symptomatic treatment of dementia: the Canadian Consensus Conference on the Diagnosis and Treatment of Dementia 2012. Alzheimers Res Ther. 2013 Jul 8;5(Suppl 1):S5.
- 9. Bang J, Spina S, Miller BL. Frontotemporal dementia. The Lancet. 2015 Oct;386(10004):1672–82.
- 10. Barton C, Ketelle R, Merrilees J, Miller B. Non-pharmacological management of behavioral symptoms in frontotemporal and other dementias. Curr Neurol Neurosci Rep. 2016 Feb;16(2):14.
- 11. Warren JD, Rohrer JD, Rossor MN. Frontotemporal dementia. BMJ. 2013 Aug 6;347:f4827.

Clinical Practice Guideline Page 13 of 14 References



- 12. O'Neil ME, Freeman M, Christensen V, Telerant R, Addleman A, Kansagara D. A systematic evidence review of non-pharmacological interventions for behavioral symptoms of dementia [Internet]. Washington (DC): Department of Veterans Affairs; 2011 [cited 2016 Oct 17]. (VA Evidence-based Synthesis Program Reports). Available from: http://www.ncbi.nlm.nih.gov/books/NBK54971/.
- 13. Livingston G, Kelly L, Lewis-Holmes E, Baio G, Morris S, Patel N, et al. Non-pharmacological interventions for agitation in dementia: systematic review of randomised controlled trials. Br J Psychiatry. 2014 Dec 1;205(6):436–42.
- 14. Moore A, Patterson C, Lee L, Vedel I, Bergman H, Canadian Consensus Conference on the Diagnosis and Treatment of Dementia. Fourth Canadian Consensus Conference on the Diagnosis and Treatment of Dementia: recommendations for family physicians. Can Fam Physician Med Fam Can. 2014 May;60(5):433–8.
- 15. Raina P, Santaguida P, Ismaila A, Patterson C, Cowan D, Levine M, et al. Effectiveness of cholinesterase inhibitors and memantine for treating dementia: evidence review for a clinical practice guideline. Ann Intern Med. 2008 Mar 4;148(5):379–97.
- 16. McKeith I, Del Ser T, Spano P, Emre M, Wesnes K, Anand R, et al. Efficacy of rivastigmine in dementia with Lewy bodies: a randomised, double-blind, placebo-controlled international study. Lancet Lond Engl. 2000 Dec 16;356(9247):2031–6.
- 17. Morris JN, Fries BE, Mehr DR, et al: MDS cognitive performance scale. J Gerontol Med Sci. 1994, 49: M174-82.
- 18. Canadian Pharmacists Association. Compendium of therapeutic choices, 7th Edition. 2014. Ottawa, Canada: Canadian Pharmacists Association.
- 19. Reisberg B, Doody R, Stöffler A, Schmitt F, Ferris S, Möbius HJ, et al. Memantine in moderate-to-severe Alzheimer's disease. N Engl J Med. 2003 Apr 3;348(14):1333–41...
- 20. Ngo J, Holroyd-Leduc JM. Systematic review of recent dementia practice guidelines. Age Ageing. 2015 Jan 1;44(1):25–33.

SUGGESTED CITATION

Toward Optimized Practice (TOP) cognitive Impairment CPG Committee 2017 Feb. Cognitive impairment: diagnosis to treatment clinical practice guideline. Edmonton, AB: Toward Optimized Practice. Available from: http://www.topalbertadoctors.org.

This work is licensed under a <u>Creative Commons Attribution-Noncommercial-Share Alike 2.5 Canada</u> <u>License</u> with the exception of external content reproduced with permission for use by TOP.

For more information see www.topalbertadoctors.org

GUIDELINE COMMITTEE

The committee consisted of representatives of family medicine, geriatric medicine and internal medicine.

DATES

February 2017