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Cognitive Impairment: Recognition, Diagnosis and Management in Primary Care

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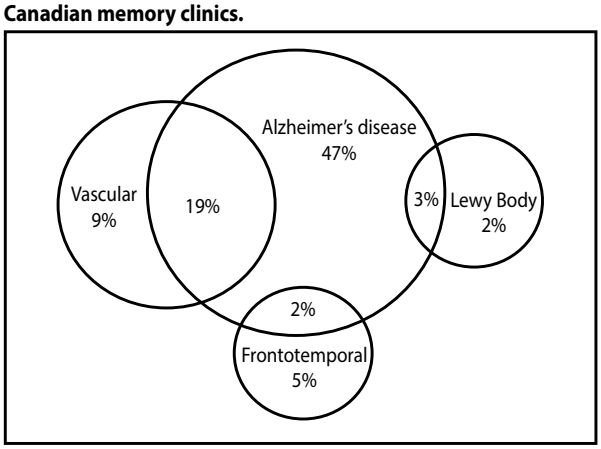
Scope

This guideline provides recommendations for the recognition, diagnosis and management of cognitive impairment in adults ≥ 19 years within the primary care setting. The guideline focuses on Alzheimer's disease, the most common form of dementia seen in primary care. The guideline encourages early recognition and assessment of dementia and supports the development of a care plan that includes the identification of community resources for patients and caregivers.

Key Recommendations

- Do not screen asymptomatic population for cognitive impairment.
- Dementia can be masked in a typically structured office visit; third party observations can be important.
- Imaging is of limited value.
- Always involve the caregiver and plan on several visits to establish and inform patient/caregiver of diagnosis.
- Introduce advance care planning early.
- Polypharmacy and multimorbidity can both be causes and effects of cognitive impairment.
- Drug treatment has limited value; first consider non-pharmacological management of the behavioural and psychological symptoms of dementia.
- Make early and regular use of adjunct services.

Figure 1: Sub-types of dementia commonly seen in Canadian memory clinics.



Definition

Cognitive impairment refers to mild cognitive impairment and dementia. Mild cognitive impairment refers to a cognitive decline that does not significantly impair cognitive function.[1] Dementia refers to Alzheimer's disease and other dementia sub-types, including vascular dementia, mixed forms of dementia and less common forms of dementia such as dementia with Lewy bodies, frontotemporal dementia and Parkinson's disease dementia.

Epidemiology

Alzheimer's disease and other neurodegenerative dementia sub-types are progressive, irreversible brain diseases, which lead to a decline in memory and other cognitive functions sufficient to impact activities of daily living. While Alzheimer's disease is the most common dementia, mixed dementias are becoming increasingly recognized (see Figure 1: Sub-types of dementia commonly seen in Canadian memory clinics).[2]

It is estimated that between 60,000 and 70,000 British Columbians have dementia, 60% of whom are female.[3] Dementia prevalence is positively correlated with age.

Diagnosis

Cognitive Screening

There is no demonstrable benefit to screening asymptomatic patients. Screening is recommended with patients with cerebrovascular disease.

Signs and symptoms

Suspect cognitive impairment when there is a functional decline in work and usual activities. This might be reported by the patient, family, friends, health care workers or other caregivers.* Cognitive impairment symptoms tend to be gradual and insidious. Patients may hide symptoms, making it hard to detect cognitive impairment in visits that are time limited or otherwise structured.

The following are examples of cognitive impairment symptoms that may present during office visits and may require further assessment:

- Missed office appointments;
- Calls office frequently or inappropriately;
- Confused, forgetful or less compliant about medications;
- Defers to family member in answering questions;
- Has suffered a stroke;
- Unexplained falls and fractures;
- Frequent emergency room visits;
- Experiences late life depression, or delirium;
- Patient is unable to recall treatment instructions or recommendations from prior visits; or
- Presents signs of self-neglect (e.g., hygiene, grooming, unexplained weight loss).

Diagnostic Criteria of Dementia, Alzheimer's Disease and Mild Cognitive Impairment

The diagnosis of dementia requires that the patient display the following features: [4]

- Impairment in at least 2 of the following cognitive domains: memory, language, visuospatial, executive function and behavior;
- Impairment causes a significant functional decline in usual activities or work; and
- Impairment not explained by delirium or other major psychiatric disorder.

To diagnose Alzheimer's disease, the patient must display the following features: [4]

- Cognitive changes that are of gradual onset over months to years;
- Two of the following cognitive domains are impaired: memory, language, visuospatial or executive function (memory is the most common);
- Impairment causes a significant functional decline in usual activities or work; and
- Symptoms are not explained by other neurologic disorder (including cerebrovascular disease), psychiatric disorder, systemic disorder or medication.

Although Alzheimer's disease is the most common form of dementia, patients may exhibit symptoms that fit more appropriately into other dementia sub-types (See *Appendix A: Dementia Sub-types*).

A diagnosis of mild cognitive impairment is made when the patient **does not** meet the criteria for dementia either because they lack a second deficit in the cognitive domains or because their deficits are not significantly affecting their usual activities or work.

* *Caregiver refers to the individual(s) primarily responsible for the care of the patient with dementia. The caregiver may be a family member, friend or health care worker.*

Steps to arriving at a diagnosis

1. Conduct a complete medical history including a comprehensive review of medications (including over-the-counter and alternative medications).

2. Encourage patient to allow collateral information be obtained from family and caregivers to assist with diagnosis. Consider administering the Alzheimer's Questionnaire to a family member or other reliable informant (see *Associated Document: The Alzheimer's Questionnaire*).

3. The following tools are recommended to provide objective evidence to support the diagnosis (the patient's cultural and educational background need to be considered when administering and interpreting results of assessment tools):
   - Standardized Mini-Mental State Examination to test cognition (see *Associated Document: Standardized Mini-Mental State Examination*);
   - Clock Drawing Test to test executive functioning (see *Associated Document: Clock Drawing Test*); and
   - Montreal Cognitive Assessment to test for mild cognitive impairment and early dementia (see *Associated Document: Montreal Cognitive Assessment*).[5]

4. Rule out/treat remediable contributory causes of cognitive impairment such as:
   - Delirium and depression (see *Appendix B: Clinical Features of Dementia, Delirium and Depression*);
   - Hyponatremia, thyroid disorders, hypercalcemia, and cobalamin deficiency;
   - Alcohol dependence;
   - Adverse drug effects & polypharmacy; and
   - Co-morbid diseases.[6-8]

5. When contributory causes have been ruled out and/or treated and cognitive impairment persists, suspect mild cognitive impairment or dementia.
   It may take a few visits to complete the diagnostic evaluation.

6. Neuroimaging is not routinely indicated.[6, 9] Magnetic resonance imaging (MRI) of the head is preferable to computerized tomography (CT) if available[10] and should be considered when:
   - The patient is less than 60 years old;
   - The onset has been abrupt or the course of progression rapid;
   - There is a history of significant recent head injury;
   - The presentation is atypical or the diagnosis is uncertain;
   - There is a history of cancer;
   - There are new localizing neurological signs or symptoms;
   - There is a suspicion of cerebrovascular disease;
   - The patient is on anticoagulants or has a bleeding disorder; or
   - The patient has a combination of early cognitive impairment with urinary incontinence and gait disorder (to exclude normal pressure hydrocephalus).

7. Consider using the Global Deterioration Scale to stage dementia (See *Associated Document: Global Deterioration Scale*).

8. When available, consider referral† to secondary services (e.g., specialist, social services, occupational therapist) for the following:
   - Diagnostic uncertainty or atypical features;
   - Rapid decline in cognition;
   - Under 65 years of age;
   - Management issues that are difficult to resolve; or
   - Risk of harm to self or others.

† *Where referral is not possible, a telephone consult may be appropriate. Reimbursement for consultations may be available through the Facility and Community Conferencing Fees billing items; information found through GPSC: www.gpscbc.ca.*

Diagnosis Disclosure

Dementia diagnosis should be disclosed as soon as possible, preferably with a caregiver present. Significant stress can occur to patients and their caregivers. Therefore, the timing and extent of disclosure should be individualized and carried out over several visits. Make an early referral to other support resources (see *Associated Document: Resource Guide for Physicians*). Provide the patient with the *Associated Document: Guide for Patients and Caregivers*.

Exceptions to disclosing dementia diagnosis to the patient include probable catastrophic reaction, severe depression or severe dementia.

Carefully consider mild cognitive impairment diagnosis disclosure to avoid prompting needless anxiety. Reassure the patient and caregiver that it is premature to diagnose Alzheimer's disease or prescribe drugs. Discussing the possibility of progression to dementia may facilitate patient participation in monitoring their cognitive decline. Schedule regular follow-up visits (e.g., every six months) to monitor possible progression of cognitive deficit. Suggest healthy brain activities, such as regular exercise, word games, socialization (see *Resource Guide for Physicians*).

Management

Physicians are encouraged to deliver timely, individualized care to the patient and their caregiver and to support patient independence at a level that is appropriate for their cognitive and physical capabilities. Always start with non-pharmacological interventions.

Specific suggestions include:

- Establish a register of patients with cognitive impairment to aid in scheduling timely patient visits;
- Reassess a patient at planned visits dedicated solely to the care of cognitive impairment (e.g., regular drug reviews, measure cognitive decline and functional changes, reevaluate multimorbidity and polypharmacy[‡] for their effects on cognition);[§]
- Involve the patient and caregiver in setting goals and making decisions. Consider use of clinical action plan (flow sheet). See *Associated Document: Clinical Action Plan (flow sheet)*; and
- Most dementia patients are geriatric patients with other issues. Consider vaccinations, vitamin D supplementation, falls risk assessment and exercise prescriptions. Refer to BCGuidelines.ca for other chronic disease guidelines which may be useful.

General Care and Support for Community Dwelling Patients

Consider the following general care and supplementary supports for patients:[¶]

a. Memory

- Aids like calendars, diaries and telephone reminders;
- Keeping keys, glasses, wallet in same designated place ("landing spot"); and
- Accompaniment to appointments.

b. Behavioural Symptoms

- If patient is considered at risk to others or themselves through reactive, repetitive and wandering behaviours; see the Best Practice Guideline for Accommodating and Managing Behavioural and Psychological Symptoms of Dementia in Residential Care and its related algorithm for guidance on managing these; and
- Carrying identification when out alone; use of an ID bracelet.

c. Nutrition

- Weigh regularly to monitor for weight loss;
- Have the caregiver monitor the refrigerator for food safety; and
- Meal support services (e.g., delivered prepared meals or pre-prepared frozen foods).

d. Shopping

- Use of lists when shopping;
- Shopping assistance from caregiver; and
- Use of shop by phone programs, if available.

‡ *Polypharmacy is a standalone risk for morbidity in all elderly patients; the cognitively impaired are especially at risk.*

§ *Physicians may be eligible for complex care incentives for the management of complex patients; see GPSC for more details: www.gpscbc.ca.*

¶ *All suggested resources are referenced in either the Resource Guide for Physicians and/or the Guide for Patients and Caregivers.*

e. Household Safety

- Monitor kitchen for mishaps (e.g., fires, burned pots); have stove unplugged or automatic stove turn-off device installed;
- Functioning smoke detectors;
- Assess home for other safety hazards (e.g., unsafe smoking, firearms in the home);
- 911 stickers for telephones;
- A personal alarm service in case of patient accident; and
- Referral for home assessment through Home & Community Care.

f. Medication Management

- Use blister packages/dossette trays and suggest caregiver supervision to improve safety and compliance; and
- Medication monitoring through Home & Community Care.

g. Hygiene

- A bathing assistant or bath program through Home & Community Care.

h. Socialization

- Awareness that patients with dementia may become socially withdrawn; and
- Referral to an adult day center through Home & Community Care.

i. Financial & Legal Issues

- Discuss advance care planning as early as possible (e.g., refer to Advance Care Planning Guide for aid in discussing sensitive topics like tube feeding. See also No Cardiopulmonary Resuscitation form); and
- Encourage patient to have an up-to-date will, a power of attorney agreement for financial management, a representation agreement for health management and/or an advance directive.

j. Driving

- Assess patient's competence for driving (see BC Driver Fitness Handbook for Medical Professionals);
- If there are concerns about a patient's functional ability to drive, consider referral to Drivable to have their skills assessed;
- Under Section 230 of the *Motor Vehicle Act*, a physician **must** report to the Office of the Superintendent of Motor Vehicles if:
    - A patient has a medical condition that makes it dangerous to the patient or to the public for the patient to drive a motor vehicle; and
    - A patient continues to drive after being warned of the danger.[1]
- To supplement or replace driving encourage patient to register with HandyDart and TaxiSavers (see *Guide for Patients and Caregivers*).

k. Self-Neglect, Neglect and Abuse

- Be aware of the risks for patient abuse/neglect;
- Help assess patient abuse/neglect using the Re: Act Adult Abuse and Neglect Response Flow Sheet and Assessment Guide;
- Report cases of abuse to designated agencies; and
- In extreme cases of self-neglect use the *Mental Health Act's* Form 4: Medical Certificate (Involuntary Admission).

l. Mental Health and Specialty Services

- Be aware that dementia may co-exist with other complex mental health conditions;
- Involve mental health teams and resources, such as Community Mental Health Services, to help in distinguishing depression from dementia, and assessing and treating significant behavioural problems and managing caregiver stress; and
- Involve allied health professionals (e.g., Home & Community Care case managers, mental health teams, pharmacists, occupational therapists, physiotherapists, dietitians).

m. Caregiver Support

- Discuss needs, coping strategies, support system and stress management with caregiver (respite care through Home & Community Care); and
- Aid in co-ordination, communication and planning during transitions between care environments.

Cognitive Impairment in Culturally and Linguistically Diverse Groups:[11, 12]

The assessment and management of cognitive impairment in diverse individuals can be challenging for several reasons:

- Communication difficulties, cultural factors, low education and literacy impact formal cognitive screening, with poor inter-rater reliability – use interpreter services to assist in more accurate patient screening and assessment;
- Dementia symptoms may be unfamiliar or viewed as part of the aging process, and there may be stigma to mental health issues, resulting in diagnosis delay – provide culturally sensitive patient information on dementia to patients and families;
- Language barriers may result in a lack of awareness of community supports – provide *Guide for Patients and Caregivers;*
- Community supports may not provide culturally appropriate care, resulting in lack of adoption of these services and increase in caregiver stress; and
- Families may share caregiver responsibilities by rotating the residence of the patient amongst family members – this is generally discouraged as it confuses the patient with dementia and complicates the provision of services between the staff of many agencies and the extended family. One familiar, safe and secure environment is encouraged.

Pharmacological Management

The use of acetylcholinesterase inhibitors/memantine is controversial. While data from clinical trials report statistical evidence of benefit, clinical benefits are unclear. It should be noted that drugs may benefit only a small minority of patients, and the evidence for long term use is insufficient. Short term benefits (6-12 months) **may** include cognitive, functional, and global improvement.[13] However, patients and their caregivers should be advised that benefits are limited, and that side effects and drug interactions are common. End points for discontinuation of medication should be discussed.

If considering pharmacological management of Alzheimer's disease, see *Appendix E: Comprehensive Pharmacotherapy Information for Acetylcholinesterase Inhibitors and Memantine.*

Pharmacotherapy of Behavioural and Psychological Symptoms of Dementia (BPSD):

It is preferable to first attempt to treat BPSD using behaviour or environment modification rather than drugs. Identify and correct reversible causes of the behavior first. For detailed guidance on managing BPSD, see Best Practice Guideline for Accommodating and Managing Behavioural and Psychological Symptoms of Dementia in Residential Care and its related algorithm. In very specific situations, antipsychotics have been used to treat symptoms of agitation, aggression, or psychotic manifestations. Typical (first generation) antipsychotics, such as loxapine, and atypical (second generation) antipsychotics, such as olanzapine, quetiapine, and risperidone, may be used.

Resources

References

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Diagnostic Code: 290

Appendices

- Appendix A: Dementia Sub-types
- Appendix B: Clinical Features of Dementia, Delirium and Depression
- Appendix C: Delirium Screening and Assessment Tools – CAM & PRISME
- Appendix D: Depression Screening Tools
- Appendix E: Comprehensive Pharmacotherapy Information for Acetylcholinesterase Inhibitors and Memantine
- Appendix F: Medication Table (for the treatment of cognitive impairment in the elderly)

Associated Documents

The following documents accompany this guideline:

- The Alzheimer's Questionnaire
- Standardized Mini-Mental State Examination
- Clock Drawing Test
- Montreal Cognitive Assessment
- Geriatric Depression Scale (short form)
- Global Deterioration Scale
- Clinical Action Plan (flow sheet)
- Guide for Patients & Caregivers
- Resource Guide for Physicians

This guideline is based on scientific evidence current as of the effective date.

The guideline was developed by the Guidelines and Protocols Advisory Committee, approved by Doctors of BC and adopted by the Medical Services Commission.

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The principles of the Guidelines and Protocols Advisory Committee are to:

- encourage appropriate responses to common medical situations
- recommend actions that are sufficient and efficient, neither excessive nor deficient
- permit exceptions when justified by clinical circumstances

Contact Information:

Guidelines and Protocols Advisory Committee
PO Box 9642 STN PROV GOVT
Victoria, BC V8W 9P1

Email: hlth.guidelines@gov.bc.ca
Website: www.BCGuidelines.ca

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Appendix A: Dementia Sub-types

Alzheimer's disease (AD)	• Cognitive changes that are of gradual onset over months to years. • Two of the following cognitive domains are impaired: memory, language, visuospatial or executive function (memory impairment is the most common presentation). • Impairment causes a significant functional decline in usual activities or work. • Symptoms are not explained by other neurologic disorder (including cerebrovascular disease), psychiatric disorder, systemic disorder or medication.
Vascular dementia (VaD)	• Cerebrovascular disease is a heterogeneous disorder: clinically overt or covert disease, large or small vessel disease, and cortical or subcortical location. • There are differing criteria for the diagnosis of vascular dementia, resulting in varying prevalence rates. • Small vessel disease is common in the elderly (in multiple body systems), and often co-exists with AD. It is not benign and represents an important risk factor for future overt stroke, for gait problems and falls, for urinary incontinence and for cognitive and behavioural decline. • Clinical assessment and neuroimaging evidence support the diagnosis. • Current recommendations suggest screening for vascular cognitive impairment in patients with clinical stroke, covert lacunar or white matter lesions on neuroimaging, and when there is damage to target organs (such as kidney and eyes). • Typically, executive dysfunction and speed of cognitive processing are impacted earlier on in vascular dementia, and memory loss is a later feature. Hence, the MOCA is the preferred cognitive screening tool when VaD is suspected.
Mixed AD/VaD	• The degenerative changes of AD and the vascular changes of VaD commonly co-exist. Most common presentation is AD pattern with significant vascular risk factors +/- small vascular events.
Dementia with Lewy bodies (DLB)	• Core features: o Fluctuating cognition with pronounced variation in attention and alertness (memory decline may not be an early feature) o Recurrent visual hallucinations that are well formed and detailed o Spontaneous motor features of Parkinsonism. • Features supportive of diagnosis: o Repeated falls o Syncope or transient loss of consciousness o Hypersensitivity to antipsychotics (typical and atypical) o Systematized delusions; non-visual hallucinations. • DLB has reduced prevalence of resting tremor and reduced response to L-dopa compared to idiopathic Parkinson's disease dementia. • Presence of REM sleep disorder in the setting of a dementia suggests DLB & related conditions. • Dementia should occur before or concurrently with onset of Parkinsonism for DLB diagnosis.
Parkinson's disease dementia (PDD)	• The cognitive features may appear similar to DLB (deficits in attention and alertness). • For PDD diagnosis, look for motor Parkinsonian symptoms that typically are present many years before the onset of the dementia.
Frontotemporal dementia	• Insidious onset and gradual progression; tends to present in middle-aged patients. • Personality changes present early and include apathy, disinhibition, executive function failure alone or in combination. • Relatively preserved memory, perception, spatial skills and praxis. • Behavioural disorder supportive of diagnosis: decline in hygiene, mental rigidity, distractibility, hyperorality, perseveration. • Prominent language changes frequently occur with reduction in verbal output.

Appendix B: Clinical Features of Dementia, Delirium and Depression

Feature	Dementia	Delirium	Depression
Onset	• Insidious	• Acute	• Gradual; may coincide with life changes
Duration	• Months to years	• Hours to less than one month, seldom longer	• At least two weeks, but can be several months to years
Course	• Stable and progressive; Vascular dementia: usually stepwise	• Fluctuates: worse at night • Lucid periods	• Diurnal: usually worse in mornings, improves as day goes on
Alertness	• Generally normal	• Fluctuates: lethargic or hyper-vigilant	• Normal
Orientation	• May be normal but often impaired for time/later in the disease, place	• Always impaired: time/place/person	• Usually normal
Memory	• Impaired recent and sometimes remote memory	• Global memory failure	• Recent memory may be impaired • Long-term memory intact
Thoughts	• Slowed: reduced interests • Makes poor judgements • Words difficult to find • Perseverates	• Disorganized, distorted, fragmented • Bizarre ideas and topics such as paranoid grandiose	• Usually slowed, preoccupied by sad and hopeless thoughts; somatic preoccupation • Mood congruent delusions
Perception	• Normal • Hallucinations (often visual)	• Distorted: visual and auditory • Hallucinations common	• Intact • Hallucinations absent except in psychotic depression
Emotions	• Shallow, apathetic, labile • Irritable	• Irritable, aggressive, fearful	• Flat, unresponsive or sad and fearful • May be irritable
Sleep	• Often disturbed, nocturnal, wandering common • Nocturnal confusion	• Nocturnal confusion	• Early morning wakening
Other features	• Poor insight into deficits • Careless	• Other physical disease may not be obvious • Inattentive	• Past history of mood disorder • Poor effort on cognitive testing: gives up easily
Standard Tests	• Comprehensive assessment (history, physical, lab, Standardized Mini-Mental State Exam)	• See *Appendix C: Delirium Screening and Assessment Tools - CAM & PRISME*	• See *Appendix D: Depression Screening Tools*

Reference (adapted from): Centre for Health Informatics and Multiprofessional Education, University College London. Dementia tutorial: Diagnosis and management in primary care: A primary care based education/research project. Available from: www.ehr.chime.ucl.ac.uk.

Appendix C: Delirium Screening and Assessment Tools – CAM & PRISME

Predisposing Risk Factors for Delirium:

- Cognitive impairment
- Over 80 years of age
- Chronic illness
- Multiple comorbid conditions
- Sensory deficits
- Alcohol abuse
- Immobility
- Insomnia
- Polypharmacy (5+ medications)

Delirium Screening Tool: Confusion Assessment Method (CAM)

Feature 1: Acute onset and fluctuating course

This feature is usually obtained from a family member or nurse and is shown by positive responses to the following questions:

- Is there evidence of an acute change in mental status from the patient's baseline? Did the (abnormal) behaviour fluctuate during the day, that is, tend to come and go, or increase and decrease in severity?

Feature 2: Inattention

This feature is shown by a positive response to the following question:

- Did the patient have difficulty focusing attention, for example, being easily distracted, or having difficulty keeping track of what was being said?

Feature 3: Disorganized thinking

This feature is shown by a positive response to the following question:

- Was the patient's thinking disorganized or incoherent, such as rambling or irrelevant conversation, unclear or illogical flow of ideas, or unpredictable switching from subject to subject?

Feature 4: Altered level of consciousness

This feature is shown by any answer other than "alert" to the following question:

- Overall, how would you rate this patient's level of consciousness? Alert (normal), vigilant (hyperalert), lethargic (drowsy, easily aroused), stupor (difficult to arouse), or coma (unarousable).

The diagnosis of delirium by CAM requires the presence of features 1 and 2 and either 3 or 4

Reference (adapted from): Inouye, S., van Dyck, C., Alessi, C., et al. Clarifying confusion: The confusion assessment method. Ann Intern Med.1990;113(12);941-948.

PRISME

PRISME is an acronym that can assist in identifying and relieving underlying factors that are modifiable and can contribute to the onset and perpetuation of delirium.

	Assessment	Interventions
P	**Pain** • Regular pain assessment & monitoring • Use consistent pain scale **Poor nutrition** • Dehydration/ malnutrition • ↓ Albumin or protein levels • Swallowing difficulties • Electrolyte/ glucose imbalance • Monitor weight	**Pain** • Regular scheduled analgesia (not prn) • Non-pharmacological support: turning, re-positioning • Document effect of analgesia **Poor nutrition** • Fluid intake at least 1500cc/ 24hrs • Dietary consult • Recent wt loss/ gain (> 10lbs in last year) • Total protein < 64 g/L and Albumin level < 35 g/L • Occupational therapy (OT) consult for swallowing difficulties
R	**Retention** • Determine continence ability; bowel pattern • Assess for urinary retention • Palpate abdomen for distention/ impaction • Evaluate fluid balance/ output **Restraints** • Explore alternatives to restraints whenever possible to maximize functional status and safety	**Retention** • In/ out catheterization if suspect retention • Nurse continence advisor consult if in retention • Regular toileting schedule (minimize use of incontinence pads) • Initiate bowel protocol • Ensure person is well hydrated **Restraints** • Minimize use of restraint: physical/ chemical • Use only if patient is a danger to him/ herself or others • Involve substitute decision maker around informed consent • Engage multi-disciplinary team
I	**Infection/ Illness (new)** • Ongoing monitoring for urinary, chest, wound infection **Immobility** • Determine pre-morbid functional abilities	**Infection/ Illness (new)** • Monitor VS & O2 stats; compare to baseline (note as normal process of aging, temperature may remain normal); ↑↓ BP, postural ↓ BP • Request appropriate diagnostic/ lab tests (e.g. C7S, chest x-ray) **Immobility** • Encourage mobility; implement fall prevention strategies • OT/ Physiotherapy consult
S	**Sleep** • Assess for altered sleep/ wake cycles • Use a sleep pattern record **Skin** • Assess for areas of skin breakdown • Braden Scale **Sensory** • Assess for sensory deficits and aides used	**Sleep** • Document changes in pattern – day/ night reversal • Implement non-pharmacological sleep promotion measures • Intersperse activities during the day with planned rest periods **Skin** • Pressure reducing mattress as indicated; turn q2h • Refer to wound/ continence nurse if wound present **Sensory** • Ensure eyeglasses, hearing aids & dentures are working and used • Use Pocket talker to assist with communication/ assessments

	Assessment	Interventions
M	**Mental Status** • Monitor for sudden changes in ability or cognition • Other causes of behaviour • Grief, loss, emotional trauma **Medications** • Polypharmacy (> 5 meds) • Medication side effects • Withdrawal – alcohol, benzodiazepines, nicotine • Toxicity (digozin, dilantin) **Metabolic** • Monitor for abnormal lab results/ hemodynamic status	**Mental Status** • Maximize non-pharmacological behaviour strategies • Identify self; use a calm/ gentle approach; use cues to orient • Acknowledge and validate fears related to changes in cognition • Use interdisciplinary interventions to support restoration of normal activity (e.g., volunteers/family, mobility, activities, familiar objects and photos, routines, clocks/calendar) **Medications** • Review med profile with pharmacist for recent changes, adverse effects, toxicity, drug interactions • Start Low, Go Slow! • Assess psychotropic med response & report side effects (e.g., ↑ anxiety/ agitation; Parkinson-like symptoms, postural ↓ BP) **Metabolic** • Evaluate lab results and notify physician of abnormalities
E	**Environment** • Self-care activities of daily living's ability • Relocation stress (e.g., unfamiliar surroundings/ routine)	**Environment** • Provide calm & safe environment • Promote normal activities of daily living routines; consistent staff • Encourage family/ support persons to provide support • Provide adequate lighting and exposure to daylight

Reference: Shaw M. PRISME [unpublished work]. Vancouver: Vancouver Coastal Health Authority, 2008.

Appendix D: Depression Screening Tools

Depression Screening Tools	Brief Description or Comments
Screening tools for persons with minor cognitive loss or early stage dementia	
S²IGECAPS	• **S**adness • **S**leep disturbance • Loss of **I**nterest • Inappropriate or excessive feelings of **G**uilt • Decreased **E**nergy and increased fatigue • Diminished ability to think or **C**oncentrate • **A**ppetite change • **P**sychomotor agitation or retardation • **S**uicidal ideation See *BC Guidelines, Major Depressive Disorder in Adults: Diagnosis & Management*.
Geriatric Depression Scale (short form)	• See *Associated Document: Geriatric Depression Scale (short form)*. • **Score Range is 0-15**. A score of > 5 points is suggestive of depression and warrants a follow-up interview. Scores > 10 are almost always depression. • Link to downloads of the Geriatric Depression Scale in English and other languages: www.stanford.edu/~yesavage/GDS.html. • Link to scoring information for the Geriatric Depression Scale: www.stanford.edu/~yesavage/GDS.english.short.score.html.
Patient Health Questionnaire (PHQ)-9	• Link to *BC Guidelines Major Depressive Disorder in Adults: Diagnosis & Management – Associated Document: PHQ-9*: www.bcguidelines.ca/pdf/depression_patient_health_questionnaire.pdf. • **Score Range is 0-27**. A score of > 5 is suggestive of a potential major depressive disorder.
Screening tools for persons with advanced cognitive impairment	
Cornell Assessment Scale for Depression in Dementia	• Link to informant-based tool: img.medscape.com/pi/emed/ckb/psychiatry/285911-1335300-1356106-1392041.pdf. • **Score Range is 0-38**. A score > 10 indicates a potential major depressive episode, while a score >18 is definite for major depressive episode.
RAI-2.0 Depression Rating Scale (Outcome Score)	• This scale can be used as a clinical screen for depression. • **Score Range is 0–14**. A score of three or more may indicate a potential or actual problem with depression.

Note: Choose a depression screening tool based on the remaining cognitive abilities of the person to be screened. Any positive screen should be followed up by a medical assessment and appropriate interventions.

Reference (adapted from): Developed by and shared with permission of the Clinical Review Working Group for the Provincial Best Practice Algorithm for Accommodating and Managing Behavioural and Psychological Symptoms of Dementia www.bcbpsd.ca.

Appendix E: Comprehensive Pharmacotherapy Information for Acetylcholinesterase Inhibitors and Memantine

Acetylcholinesterase Inhibitors (AChEIs)

AChEIs include donepezil (Aricept®), galantamine (Reminyl®) and rivastigmine (Exelon®). AChEIs are approved for the symptomatic treatment of mild to moderate Alzheimer's disease. Donepezil is the only AChEI indicated for severe Alzheimer's disease. Studies report modest improvements or stabilization of dementia symptoms. Benefits were demonstrated in cognitive function, activities of daily living, behavioural and measures of global function but none of these treatment effects are large.[1,2] Currently, there is insufficient evidence for AChEIs in the outcome measures of delayed institutionalisation, mortality, severe disease progression, and reduction of caregiver burden.[3] In studies with global outcomes (subjective assessment by clinician and/or caregiver of change overall), the number needed to treat is 12 (three to six months) for one additional patient to experience stabilization or improvement on global response.[4]

Evidence regarding the long-term use of AChEIs is limited, with the majority of clinical trials being 12 months or less in duration. In one 24 month trial, there were no significant differences between donepezil and placebo on the primary endpoints of institutionalization and progression of disability; however, the results are limited by the trial design, in which patients in the treatment group were subjected to multiple interruptions in treatment.[5]

While some evidence suggests a role for AChEIs in the treatment of symptoms associated with severe Alzheimer's disease and in other types of dementias (vascular dementia and dementia with Lewy bodies),[6, 7] the clinical meaningfulness of randomized controlled trial outcome measures is controversial and donepezil is the only AChEI currently approved by Health Canada for severe Alzheimer's disease. There is no evidence of beneficial effect in progression from mild cognitive impairment to dementia at one, two, and three years of AChEI use in mild cognitive impairment.[8]

Adverse effects

Common adverse events are gastrointestinal effects, particularly nausea, vomiting, diarrhea, and anorexia. Relative to placebo, adverse effects occur in approximately 8% more patients (number needed to harm = 12) on AChEI therapy.[9] Adverse events are the main cause of attrition in the clinical trials, with approximately 29% and 18% of patients treated with AChEIs and placebo, respectively, withdrawing prematurely from the clinical trials.[1]

Summary of the most common adverse events by AChEI type[9, 12]

AChEI	Common adverse effects	NNH
donepezil	Diarrhea	8
	Nausea	20
galantamine	Nausea at 24mg/day	5
rivastigmine (oral)	Nausea	6
	Vomiting	7
rivastigmine (patch)	Administration site skin conditions	8
	Vomiting	33
	Nausea	50

Alzheimer's Drug Therapy Initiative

The Alzheimer's Drug Therapy Initiative (ADTI) was started in British Columbia in 2007 to gather evidence on the efficacy, safety and cost-effectiveness of AChEIs for the treatment of mild to moderate Alzheimer's disease. The ADTI consisted of a meta-analysis and systematic review of AChEIs on patient outcomes in mild to moderate Alzheimer's disease, four research studies completed by the University of Victoria and one research study completed by the University of British Columbia.

The ADTI found that the average change in SMMSE score was +1.6 points (out of 30) in AChEI-naive patients at 6 months; this was consistent with observations in RCTs and was considered to be a small change compared to natural fluctuations between the first and second SMMSE in individual patients. There were no differences in outcomes for the different AChEIs.

The results of the ADTI showed no significant differences in clinical benefit and/or safety between the three AChEIs. The ADTI also reported insufficient evidence of therapeutic benefit of switching to a different AChEI if a patient experiences clinical ineffectiveness on one AChEI. As such, for patients new to AChEIs, prescribers should consider initiating therapy with the least costly AChEI (donepezil). Consider oral rivastigmine or galantamine in patients who are unable to tolerate donepezil.

In patients with mild to moderate Alzheimer's disease, no statistical differences in efficacy between rivastigmine patches and capsules were reported. Relative to rivastigmine capsule, low dose patches were reported to have fewer nausea, vomiting, weight loss, dizziness, decreased appetite, and headache events, but higher rates of diarrhea. High dose patches and capsules demonstrated higher rates of adverse events as compared to low dose patches. The rivastigmine patch is substantially more costly than oral formulations of AChEIs (refer to Appendix F for drug cost and drug coverage information).

For further information on the ADTI research, visit www.gov.bc.ca/pharmacareprescribers.

Initiation of therapy

Decision to initiate AChEI therapy requires an individualized patient assessment, involving the patient and caregivers in the following discussion points:

- Clinician, patient, and caregiver expectations of benefit with AChEI therapy.
- Presence of comorbidities and life expectancy.
- Potential drug interactions with concurrent medications.
- Ability of the patient or caregiver to adhere to pharmacotherapy.
- Potential benefits as compared to potential harms of AChEI therapy.
- Patient and caregiver preferences, including cost of therapy.

If a trial of AChEI therapy is to be initiated, develop and implement a monitoring plan:

- Document baseline symptoms and define goals for therapy.
- Encourage caregivers to maintain a written record of symptoms, adverse drug reactions, sleep disturbances, and personal impressions to support ongoing patient assessment.
- Carefully monitor for adverse effects, particularly during the first three months of therapy. A three month titration period is required to develop tolerance and minimize adverse effects.[1]
- Assess tolerability and adverse effects two weeks after medication initiation and two weeks after each dosage change.[10]
- Until a stable maintenance dose is achieved, schedule regular follow up appointments based on the titration schedule of the medication.
- Once a maintenance dose is reached, monitor for efficacy by assessing changes in cognition, function, behaviour, and global assessment of change every three months. Continue to monitor for adverse effects every three months.[10]

Management strategies for adverse effects of AChEIs [1, 2, 10–19]

- Use a longer titration period. Gastrointestinal adverse effects, such as nausea, vomiting, and diarrhea, are dose related.
- Titration period of up to 12 weeks may be required to develop tolerance and minimize adverse effects.
- Administer oral doses with food.
- A short course of an antiemetic, such as domperidone, may be administered during the titration period. Avoid antiemetics with anticholinergic properties, such as dimenhydrinate, as these agents may worsen cognition or cause delirium.

Rivastigmine transdermal patch [11, 12, 15, 16, 17, 19, 20]

- Rotate application site of rivastigmine patch daily. Do not use the same application site within 14 days.
- Application to upper arm, upper back or chest may reduce the risk of skin irritation relative to application to the abdomen or upper thigh.
- Minimize the use of harsh soaps and do not apply patch immediately after cleansing.
- Trimming hair at application site, as opposed to shaving, may reduce skin irritation.
- Remove patch slowly and delicately.
- Management of dermatitis at the application site by pre-treating the skin site with two puffs of aerolized fluticasone propionate (250µg/puff) prior to patch application has been documented. Following patch removal, the skin site was treated with once daily application of 0.05% betamethasone dipropionate glycol ointment for three days.[20]

See *Appendix F: Medication Table (for the treatment of cognitive impairment in the elderly)*

Relative contraindications

- Patients with serious cardiovascular disease were excluded from clinical trials. Avoid use in patients with cardiac conduction abnormalities (except right bundle branch block), such as sick sinus syndrome, bradycardia, atrioventricular block, or unexplained syncope. Use cautiously in active coronary artery disease and congestive heart failure.
- Increased gastric acid secretion may result from increased cholinergic activity. Use cautiously in patients at risk of ulceration, such as those with peptic ulcer disease or concurrent non-steroidal anti-inflammatory drug use.
- Use cautiously in obstructive urinary disease, as AChEIs may worsen symptoms.
- Use cautiously in patients with history of seizure or seizure disorder, as AChEI may increase seizure risk.
- Increased cholinergic activity due to AChEIs may worsen symptoms in significant bronchospastic disease.
- Dose adjustments or avoidance of use may be necessary in severe renal or hepatic disease (see *Appendix F: Medication Table* for dosing details).

Potential drug interactions

All AChEIs

- Avoid concurrent cholinomimetic agents, such as succinylcholine, neuromuscular blocking agents, or cholinergic agonists, due to synergistic effects (i.e., may potentiate muscle relaxants used during anaesthesia).
- Avoid concurrent use of agents with anticholinergic properties, such as oxybutinin, tricyclic antidepressants, including cyclobenzaprine (Flexeril), paroxetine, or certain nonprescription medications such as dimenhydrinate and diphendyramine, due to antagonistic effects.
- Monitor closely if medications with similar adverse effects as AChEIs are administered concurrently.
- Review product monographs at hc-sc.gc.ca/dhp-mps/prodpharma/databasdon/index-eng.php and regularly review current Health Canada advisories, warnings and recalls at www.hc-sc.gc.ca/ahc-asc/media/advisories-avis/index_e.html.

Donepezil and galantamine

- Substrates of cytochrome P450.
- CYP2D6 and CYP3A4 inhibitors, such as paroxetine, erythromycin, ketoconazole, or quinidine, may increase the risk of toxicity of donepezil and galantamine.
- Cimetidine does not significantly affect metabolism of donepzil, but does increase the bioavailability of galantamine by approximately 16%.[12]
- CYP2D6 and CYP3A4 inducers, such as carbamazepine, phenytoin, phenobarbital, dexamethasone, or rifampin, may decrease the therapeutic effect of donepezil and galantamine.

Rivastigmine

- Primarily metabolized via hydrolysis; therefore, the risk of cytochrome P450 interactions is expected to be minimal.

Switching therapy

There is insufficient evidence demonstrating differences in clinical efficacy between donepezil, galantamine, and rivastigmine.[1, 18, 21] However, tolerability can vary among patients.[10] Considerations in the selection of an alternate AChEI include adverse effect profile, dosing profile, adherence, drug interactions, and comorbidities. When switching to an alternate AChEI, taper the first agent over one to two weeks, while starting the second agent at the lowest possible dose using the same titration schedule as initiation of new therapy.

Discontinuing therapy

In patients with advanced Alzheimer's disease, practitioners and caregivers should routinely re-evaluate the value of continuing therapy. There is insufficient evidence to guide the difficult decision of continuation or discontinuation of AChEI therapy in advanced Alzheimer's disease. Discontinue treatment when the risks of therapy are assessed to outweigh the perceived benefits. Although further research is warranted, discontinuation of donepezil appears to be generally well tolerated.[9, 22] It is important to ensure prompt assessment by a practitioner should symptoms acutely worsen upon discontinuation of an AChEI. To attenuate potential withdrawal symptoms, consider gradual tapering of AChEIs, as opposed to abrupt discontinuation.

N-methyl-D-aspartate Receptor Antagonist - Memantine

Memantine (Ebixa®) is approved by Health Canada as monotherapy or as adjunctive therapy with AChEIs for the symptomatic treatment of patients with moderate to severe Alzheimer's disease. Memantine is not indicated for the treatment of MCI.[12]

Studies suggest that 20 mg per day of memantine offers symptomatic benefit on cognition, behaviour, mood, and functional measures of daily living in moderate to severe Alzheimer's disease at six months.[23] In mild to moderate Alzheimer's disease, studies suggest a marginal benefit in cognitive outcomes and lack of effect on measures of behaviour and activities of daily living.[23] The magnitude of clinical significance and clinically important benefits of memantine remains uncertain.[18] The DOMINO study reported no statistically significant benefits on cognition, function, and behaviour with the addition of memantine to donepezil as compared to donepezil monotherapy in moderate to severe Alzheimer's disease.[24] Memantine may be an option for the symptomatic treatment of moderate to severe Alzheimer's disease in patients with intolerance to or contraindications to AChEI treatment.[18]

Adverse effects

Memantine is generally well tolerated and attrition rates from clinical trials are similar between the treatment and placebo groups.[23] The most common adverse effects of memantine include dizziness, headache, somnolence, constipation, and hypertension.

Relative contraindications

- Renal disease or conditions causing alkalinization of urine, such as renal tubular acidosis, severe urinary tract infection, or drastic dietary changes, may reduce systemic elimination of memantine.
- Use cautiously in patients with history of seizure disorder, as these patients were excluded from clinical trials and memantine may increase seizure risk.
- Use cautiously in patients with cardiovascular conditions, as cardiovascular adverse effects have been observed in clinical trials.
- Hepatic disease (see *Appendix F: Medication Table* for dosing details).
- Ophthalmic disease.

Potential drug interactions

- Not significantly metabolized by cytochrome P450.
- Primarily renally excreted. Elimination of memantine may be reduced with concurrent use of drugs which alkalinize urine, such as sodium bicarbonate or carbonic anhydrase inhibitors.
- Exercise caution with concomitant use of agents which are renally excreted, such as cimetidine, ranitidine, hydrochlorothiazide, triamterene, quinidine, metformin, or nicotine. Plasma levels of both agents may be altered.
- Avoid concurrent use of agents with properties similar to N-methyl-D-aspartate antagonists, such as amantadine, ketamine, or dextromethorphan, due to increased risk of adverse effects (especially central nervous system effects).
- Therapeutic effects of levodopa, dopaminergic agonists, and anticholinergics may be enhanced and may necessitate dosage adjustment of these agents.
- Review product monographs at hc-sc.gc.ca/dhp-mps/prodpharma/databasdon/index-eng.php and regularly review current Health Canada advisories, warnings and recalls at www.hc-sc.gc.ca/ahc-asc/media/advisories-avis/index_e.html.

Other agents

Use of ginkgo biloba, vitamin E, anti-inflammatory drugs (e.g., NSAIDs), estrogen, and statins as pharmacotherapy for dementia is not recommended. There is insufficient evidence of treatment efficacy and/or concerns have been raised regarding the potential risk of negative health impacts.

See *Appendix F: Medication Table*

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Appendix F: Medication Table (for the treatment of cognitive impairment in the elderly)[1-6]

Generic name (trade name) (dosage form, strengths)	Usual effective maximum dose	Annual cost	PharmaCare coverage	Common adverse effects	Therapeutic considerations
Acetylcholinesterase Inhibitors (AChEIs)					
donepezil (Aricept) (tablet: 5 mg, 10 mg) (rapidly disintegrating tablet: 5 mg, 10 mg)	5-10 mg PO once daily in the morning **Dose titration:** initial dose 5 mg once daily for 4-6 weeks; if tolerated, may increase to a maximum of 10 mg once daily. Consider initial dose of 2.5 mg once daily for frail patients or patients whom have experienced adverse effects due to other AChEIs.	$1850	Limited Coverage Rapidly Disintegrating Tablet: No Coverage	**GI**: nausea, vomiting, diarrhea (dose related), anorexia, weight loss, abdominal pain, dyspepsia, constipation **CNS**: dizziness, headache, fatigue, insomnia, somnolence, depression, agitation, confusion, hallucinations, nightmares **CV**: hypertension, bradycardia, syncope **Resp:** rhinitis **MSK**: muscle cramps (donepezil), weakness, tremor, back pain **Urogenital**: urinary incontinence, UTI <u>Rivastigmine patch</u> **Skin**: application site hypersensitivity, urticaria, blister, allergic contact dermatitis	• May be administered without regard to food. • Only AChEI approved for severe dementia of the Alzheimer's type. • Lowest risk of GI adverse effects. • Maximum recommended dose in elderly women of low body weight is 5 mg daily. • Use caution in doses exceeding 5 mg daily in elderly patients with chronic comorbid disease(s).
galantamine (Reminyl ER, G) (ER capsule: 8 mg, 16 mg, 24 mg)	16–24 mg PO once daily in the morning **Dose titration**: initial dose of 8 mg once daily for 4-6 weeks; if tolerated, increase to 16 mg once daily for at least 4 weeks; if tolerated, may further increase to a maximum of 24 mg once daily.	Generic: $1810	Limited Coverage Limited Coverage		• Administer with food. • Some evidence to suggest that 16 mg per day dose appears to be the best tolerated, with similar efficacy to higher doses.[7] If treatment is interrupted for ≥ 3 days, restart treatment as per initial dose titration. • Maximum 16 mg daily in moderate renal (CrCl >10 mL/min) or moderate liver impairment (Child-Pugh 7-9). Not recommended for severe renal (CrCl < 9 mL/min) or severe liver (Child-Pugh 10-15) impairment.
rivastigmine (Exelon, G) (capsule: 1.5 mg, 3 mg, 4.5 mg, 6 mg) (oral solution: 2 mg/mL) (patch: 4.6 mg released per 24 hours [as 9 mg/5cm^2 patch], 9.5 mg released per 24 hours [as 18mg/10cm^2 patch])	3-6 mg PO bid **Dose titration (oral)**: initial dose 1.5 mg bid for 2–4 weeks; if tolerated, may titrate dose by 1.5 mg bid after a minimum of 2 weeks at each dose level to a maximum of 6 mg bid. **Dose titration (transdermal patch)**: initiate 4.6 mg patch once daily for at least 4 weeks; if tolerated, may increase to a maximum dose of one 9.5 mg patch once daily. **Switching from oral to transdermal:** • < 3 mg bid PO: use 4.6 mg patch • 3-6 mg bid PO: use 9.5 mg patch	Generic Capsule: $2050 Transdermal Patch: $1750 Oral Solution: $810 – $3240 (dose dependent)	Capsule: Limited Coverage Oral Solution: Limited Coverage Transdermal Patch: No Coverage		• Administer oral doses with food. • Significantly fewer adverse effects of decreased appetite, nausea, vomiting, dizziness, and asthenia with transdermal patch as compared to oral doses of 6 to 12 mg day.[8] • If treatment is interrupted for > 3 days, restart treatment as per initial dose titration. • For patients > 85 years of age and < 50 kg or patients with renal or mild-moderate hepatic impairment, initiate at 1.5 mg once daily and titrate slowly. Contraindicated in severe hepatic impairment. • The transdermal patch has not been studied in renal or hepatic impairment. Titrate dose cautiously in renal impairment. In mild to moderate hepatic impairment, titrate dose cautiously. In severe hepatic impairment, use in contraindicated.

Generic name (trade name) (dosage form, strengths)	Usual effective maximum dose	Annual cost	PharmaCare coverage	Common adverse effects	Therapeutic considerations
N-methyl-D-aspartate (NMDA) Receptor Antagonist					
memantine (Ebixa, G) (tablet: 10 mg)	10 mg PO bid **Dose titration**: initial dose 5 mg once daily in the morning for at least 1 week. If tolerated, titrate dose to 5 mg bid for at least 1 week, then 10 mg in the morning and 5 mg in the afternoon for at least 1 week, followed by titration to a maximum dose of 10 mg bid.	$920	No coverage	**GI**: diarrhea, constipation, nausea, vomiting **CNS**: dizziness, headache, confusion, somnolence, anxiety, hallucination **CV**: hypertension, angina, bradycardia, cardiac failure **Resp**: cough **MSK**: back pain **Urogenital**: incontinence, UTI **Ocular**: cataract, conjunctivitis	• Use cautious dose titration in moderate renal impairment (CrCl 30-49 mL/min). Maximum 5 mg bid in severe renal impairment (CrCl 15–29 mL/min). • No dosage adjustment in mild-moderate hepatic impairment. Avoid use in severe hepatic impairment.

Abbreviations: **AChEIs**: Acetylcholinesterase Inhibitors; **bid**: twice daily; **cm**: centimeter; **CNS**: central nervous system; **CrCl:** creatinine clearance in millimeters per minute; **CV**: cardiovascular; **ER**: extended release; **G**: generic brands available; **GI**: gastrointestinal; **kg**: kilogram; **mg**: milligrams; **mL**: milliliter; **MSK**: musculoskeletal; **NMDA**: N-methyl-D-aspartate; **PO**: oral; **Resp:** respiratory; **UTI:** urinary tract infection.

Note: Please review product monographs at hc-sc.gc.ca/dhp-mps/prodpharma/databasdon/index-eng.php and regularly review current Health Canada advisories, warnings and recalls at www.hc-sc.gc.ca/ahc-asc/media/advisories-avis/index_e.html.

Pricing is approximate as per PharmaNet 2012/11/14 and does not include dispensing fee or additional markups, updated to PharmaCare coverage made June 2016.

PharmaCare Coverage Definitions
Regular Coverage: also known as regular benefit; does not require Special Authority. Regular benefits may be fully or partially covered.*
Limited Coverage: requires Special Authority for coverage. Limited Coverage benefits approved by Special Authority may be fully or partially covered.*
No coverage: also known as non-benefit; does not fit the above categories.

* Information on which products PharmaCare covers can be obtained using the B.C. PharmaCare Formulary Search (www.health.gov.bc.ca/pharmacare/benefitslookup). In all cases, coverage is subject to drug price limits set by PharmaCare and to the patient's PharmaCare plan rules and deductibles. See: www.health.gov.bc.ca/pharmacare/plans/index.html and www.health.gov.bc.ca/pharmacare/policy.html for further information.

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