Part 2: Pain and Symptom Management
Depression

Effective Date: February 22, 2017

Key Recommendations

- Before diagnosing and treating major depressive disorder, first effectively treat pain and other symptoms, then differentiate the symptoms of depression from normal grieving.
- When prescribing antidepressants for this group of patients, select antidepressants with the least drug interactions.

Assessment

1. Depression occurs in 13–26% of patients with terminal illness,[1, 2] can amplify pain and other symptoms, and is often recognized too late in a patient's life.
2. Patients are at high risk of suicide and have an increased desire for hastened death.[3]
3. A useful depression screening question is, "Have you been depressed most of the time for the past two weeks?"[4]
4. A diagnosis of depression in the terminally ill may be made when at least two weeks of depressed mood is accompanied by symptoms of hopelessness, helplessness, worthlessness, guilt, lack of reactivity, or suicidal ideation.
5. DSM-IV criteria for depression are not very helpful because vegetative symptoms like anorexia, weight loss, fatigue, insomnia, and impaired concentration may accompany end stage progressive illness.
6. Risk factors for depression include:
    - personal or family history of depression;
    - social isolation, concurrent illnesses (e.g., COPD, CHF);
    - alcohol or substance abuse;
    - poorly controlled pain;
    - advanced stage of illness;
    - certain cancers (head and neck, pancreas, primary or metastatic brain cancers);
    - chemotherapy agents (vincristine, vinblastine, asparagines, intrathecal methotrexate, interferon, interleukin);
    - corticosteroids (especially after withdrawal); and
    - abrupt onset of menopause (e.g., withdrawal of hormone replacement therapy, use of tamoxifen).

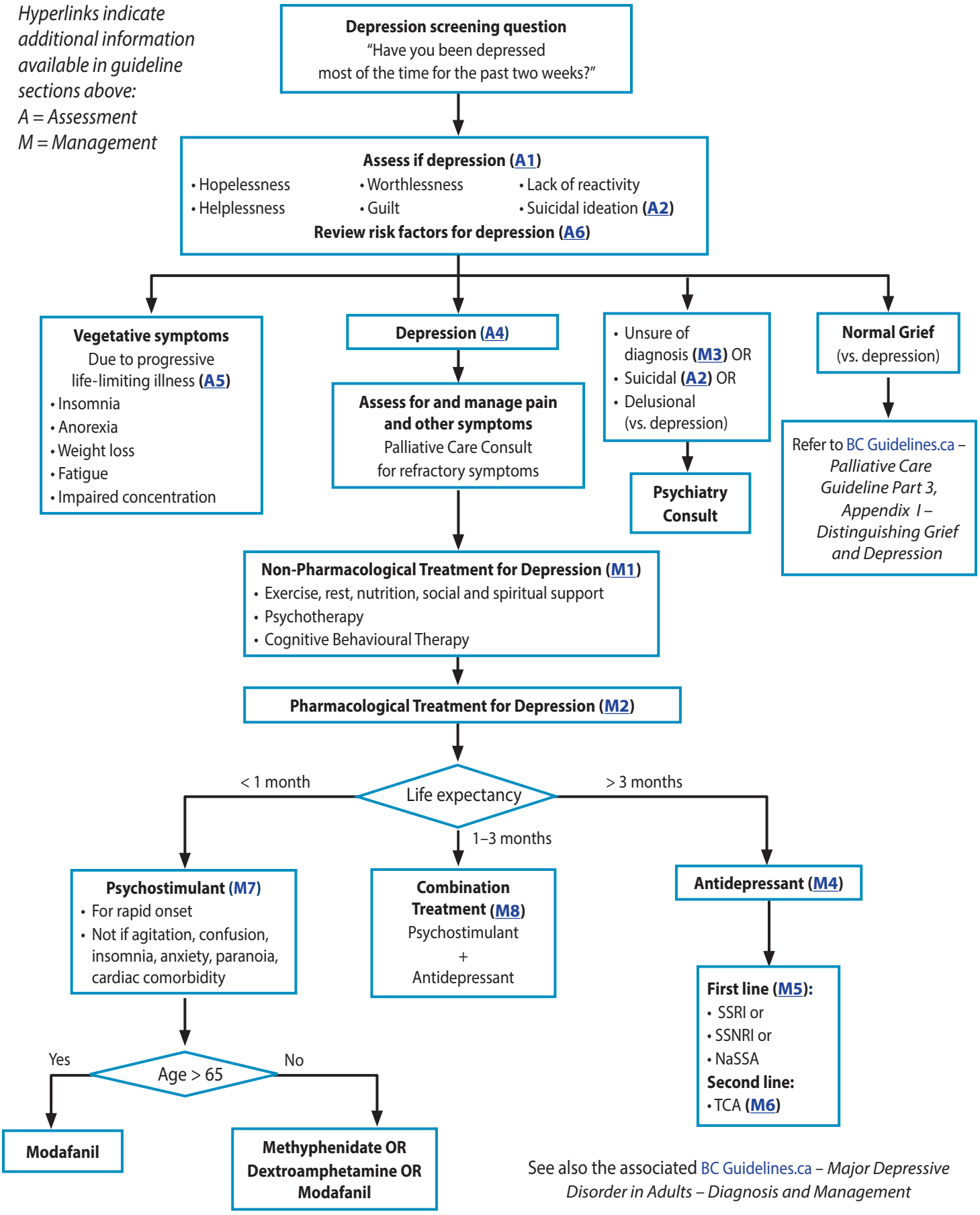
Management

1. Non-pharmacological treatments are the mainstay of treatment for the symptom of depression without a diagnosis of primary affective disorder.
2. Treatment of pain and other reversible physical symptoms should occur before initiating antidepressant medication.
3. If a diagnosis of primary affective disorder is uncertain in a depressed patient, consider psychiatric referral and a trial of antidepressant medication (refer to *Appendix A: Medications Used in Palliative Care for Depression*). Consider drug interactions, adverse side effect profiles, and beneficial side effects when choosing an antidepressant.
4. In the terminally ill, start with half the usual recommended starting dose of antidepressant.[5]
5. First line therapy is with a selective serotonin reuptake inhibitor (SSRI),[2] selective serotonin norepinephrine reuptake inhibitor (SSNRI), or noradrenergic and specific serotonergic antidepressant (NaSSA).

6. Tricyclic antidepressants (especially nortryptiline and desipramine) can be considered due to their co-analgesic benefit for neuropathic pain (refer to *Appendix A – Medications Used in Palliative Care for Depression*). Avoid with constipation, urinary retention, dry mouth, orthostatic hypotension, or cardiac conduction delays.
7. When anticipated survival time is short, consider psychostimulants due to their more immediate onset of effect,[2] but avoid them in the presence of agitation, confusion, insomnia, anxiety, paranoia, or cardiac comorbidity.
8. If life expectancy is 1–3 months, start a psychostimulant and an antidepressant together and then withdraw the stimulant while titrating the antidepressant upwards.

Depression Management Algorithm

Hyperlinks indicate additional information available in guideline sections above:
A = Assessment
M = Management



See also the associated BC Guidelines.ca – *Major Depressive Disorder in Adults – Diagnosis and Management*

Resources

References

1. Lloyd-Williams M, Friedman T. Depression in palliative care patients – a prospective study. Eur J Cancer Care 2001;10:270-4.
2. Fraser Health Authority. Hospice Palliative Care Symptom Guidelines. Depression. c2006. Available from: http://www.fraserhealth.ca/media/08FHSymptomGuidelinesDepression.pdf.
3. Breitbart W, Rosenfeld B, Pessin H, et al. Depression, hopelessness, and desire for hastened death in terminally ill patients with cancer. JAMA 2000;284:2907-11.
4. Chochinov HM, Wilson KG, Enns M, et al. "Are you depressed?" Screening for depression in the terminally ill. Am J Psychiatry 1997;154:674-6.
5. Rodin G, Katz M, Lloyd N, et al. The management of depression in cancer patients: A clinical practice guideline. Cancer Care Ontario. 2006 Oct.

Abbreviations

CHF	congestive heart failure
COPD	chronic obstructive pulmonary disease
DSM-IV	Diagnostic and Statistical Manual of Mental Disorders 4th edition
NaSSA	noradrenergic & specific serotonergic antidepressant
SSRI	selective serotonin reuptake inhibitor
SSNRI	selective serotonin norepinephrine reuptake inhibitor
TCA	tricyclic antidepressant

Appendices

Appendix A – Medications Used in Palliative Care for Depression

Appendix A: Medications Used in Palliative Care for Depression

Tailor dose to each patient; those who are elderly, cachectic, debilitated or with renal or hepatic dysfunction may require reduced dosages; consult most current product monograph for this information: http://www.hc-sc.gc.ca/dhp-mps/prodpharma/databasdon/index-eng.php

ANTIDEPRESSANTS[A, B]						
Generic Name	Trade Name/ Available Dosage Forms	Standard Adult Dose[C] (palliative)	Drug Plan Coverage[D]		Approx. cost per 30 days[E]	Therapeutic Considerations
			Palliative Care	Fair PharmaCare		
NaSSA: Noradrenergic and Specific Serotonergic Antidepressant						
mirtazapine	**Remeron®, G** **Tabs:** 15, 30, 45 mg	**Start:** 7.5 to 15 mg PO at bedtime **Goal:** 15 to 45 mg PO at bedtime **Max:** 60 mg[F] PO at bedtime	Yes, LCA	Yes, LCA	$3–9 (G) $27–80	• Useful for night-time sedation • Rapid dissolve formulation
	Remeron RD® **ODT:** 15, 30, 45 mg		Yes, LCA	Yes, LCA	$3–9 (G) $16–47	
SSNRI: Selective Serotonin Norepinephrine Reuptake Inhibitors						
venlafaxine XR	**Effexor XR®, G** **XR caps:** 37.5, 75, 150 mg	**Start:** 37.5 mg PO qAM **Goal:** 75 to 225 mg PO qAM **Max:** 375 mg[F] PO daily	Yes, LCA	Yes, LCA	$11–32 (G) $64–191	• May cause nausea
duloxetine	**Cymbalta® Caps:** 30 mg, 60 mg	**Start:** 30 mg PO qAM **Goal:** 30 to 60 mg PO qAM **Max:** 120[F] mg PO qAM	No	No	$62–127	• Effective for diabetic neuropathy • Should not be given to individuals with chronic hepatic disease or excessive alcohol consumption
desvenlafaxine	**Pristiq® XR** tabs: 50, 100 mg	**Start:** 50 mg PO once daily **Goal:** 50 to 100 mg PO once daily **Max:** 100 mg PO daily	No	No	$89	• Should not be discontinued abruptly
SSRI: Selective Serotonin Reuptake Inhibitors						
citalopram	**Celexa®, G** **Tabs:** 10, 20, 40 mg	**Start:** 10 mg PO qAM **Goal:** 10 to 40 mg PO qAM **Max:** 60 mg PO qAM	Yes, LCA	Yes, LCA	$5–$8 (G) $22–45	• Least pharmacokinetic drug interactions
escitalopram	**Cipralex®, G** **Tabs:** 10, 20 mg	**Start:** 5 mg PO qAM **Goal:** 5 to 20 mg PO qAM **Max:** 30 mg[F] PO qAM	Yes	Yes	$6–12 (G) $29–62	
	ODT: 10, 20 mg		No	No	$29–62	

ANTIDEPRESSANTS[A, B]						
Generic Name	Trade Name/ Available Dosage Forms	Standard Adult Dose[C] (palliative)	Drug Plan Coverage[D]		Approx. cost per 30 days[E]	Therapeutic Considerations
			Palliative Care	Fair PharmaCare		
TCA: Tricyclic Antidepressants						
desipramine	**G Tabs:** 10, 25, 50, 75, 100 mg	**Start:** 10 to 25 mg PO qAM[G] **Goal:** 50 to 75 mg PO qAM[G] **Max:** 200 mg PO qAM[G]	Yes, LCA	Yes, LCA	$22–29 (G)	• increase dose every 3 to 7 days until goal reached • may help neuropathic pain • useful for night-time sedation • anticholinergic side effects • desipramine and nortriptyline least anticholinergic of TCAs • monitor for postural hypotension
nortriptyline	**Aventyl®, G** **Caps:** 10, 25 mg	**Start:** 10 to 25 mg PO at bedtime **Goal:** 50 to 75 mg PO at bedtime **Max:** 150 mg PO at bedtime	Yes, LCA	Yes, LCA	$33–49 (G) $33–49	

Abbreviations: caps capsules; **G** generics available; **IR** immediate release; **LCA** subject to Low Cost Alternative Program; **max** maximum dose; **ODT** oral disintegrating tablet; **PO** by mouth; **qAM** every morning; **SR** sustained release; **tabs** tablets; **XR** extended release

[A] Refer to guideline and/or algorithm for recommended order of use.
[B] Not a complete list of antidepressants
[C] Start doses listed are recommended starting doses for geriatric patients (half the recommended doses for adults), except for duloxetine
[D] PharmaCare coverage as of October 2016 (subject to revision). Obtain current coverage, eligibility, and coverage information from the online BC PharmaCare Formulary Search page at pharmacareformularysearch.gov.bc.ca
[E] Cost as of October 2016 and does not include retail markups or pharmacy fees. Generic and brand name cost separated as indicated by (G).
[F] This maximum dose used in palliative care, but not approved for marketing by Health Canada
[G] Bedtime dosing may be appropriate for patients experiencing sedation with desipramine

PSYCHOSTIMULANTS[A]						
Generic Name	Trade Name	Available Dosage Forms	Standard Adult Dose (note age specific recommendations)	Drug Plan Coverage[B]		Approx. cost per 30 days[C]
				Palliative Care	Fair PharmaCare	
methylphenidate[D]	Ritalin®, G	**IR tabs:** 5, 10, 20 mg	**Age over 65 years:** Not recommended	Yes, LCA	Yes, LCA	$6–18 (G) $14–41
			Age 18 to 65 years: Start: 5 mg PO bid (AM and noon); use 2.5 mg for frail patients Max: 15 mg PO bid (AM and noon)			
	Biphentin®	**SR caps:** 10, 15, 20, 30 mg	**Once dose stabilized on IR, give equivalent daily dose as SR or XR form once daily in AM**	No	No	$23–59
	Concerta®	**XR tabs:** 18, 27, 36, 54 mg		No	Special Authority[E]	$71–93
	Ritalin-SR®, G	**SR tabs:** 20 mg		No	Yes, LCA	$9 (G) $24
dextro-amphetamine[D]	Dexedrine®, G	**IR tabs:** 5	**Age over 65 years:** Not recommended	No	Yes	$18–134 (G) $24–188
		SR caps: 10, 15 mg	**Age 18 to 65 years:** Start: 2.5 mg PO bid (AM then in 4 to 6 h) Max: 20 mg PO bid (AM then in 4 to 6 h			
			Once dose stabilized on IR, give equivalent daily dose as SR form once daily in AM	No	Yes	$33–135
modafinil[D]	Alertec®, G	**Tabs:** 100 mg	**Age over 65 years:** Start: 100 mg PO qAM Max: 100 mg PO bid (AM and noon)	No	Special Authority[F], LCA	$30–60 (G) $45–90
			Age 18 to 65 years: Start: 100 mg PO bid (AM and noon) Max: 200 mg PO bid (AM and noon)			$60–120 (G) $90–180

Abbreviations: caps capsules; **G** generics; **h** hours; **IR** immediate release; **LCA** subject to Low Cost Alternative Program; **max** maximum dose; **PO** by mouth; **qAM** every morning; **SR** sustained release; **tabs** tablets; **XR** extended release

[A] Refer to guideline and/or algorithm for recommended order of use.
[B] PharmaCare coverage as of October 2016 (subject to revision). Obtain current coverage, eligibility, and coverage information from the online BC PharmaCare Formulary Search page at pharmacareformularysearch.gov.bc.ca
[C] Cost as of October 2016 and does not include retail markups or pharmacy fees. Generic and brand name cost separated as indicated by (G).
[D] This indication (i.e. depression) used in practice, but not approved for marketing by Health Canada
[E] Special authority required to obtain coverage for Concerta® for ADHD as second line treatment
[F] Special authority required to obtain coverage for modafinil for patients with narcolepsy