

GUIDELINES & PROTOCOLS

ADVISORY COMMITTEE

Palliative Care for the Patient with Incurable Cancer or Advanced Disease Part 2: Pain and Symptom Management *Depression*

Effective Date: September 30, 2011

Scope

This section presents assessment and management strategies for dealing with depression occurring in patients with cancer or advanced disease.

Salient Principles in this Section:

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

Included in this Section:

- A – Depression management algorithm
- B – Antidepressant medication reference tables

Depression Management (Refer Appendix A: Depression Management Algorithm)

Assessment

- 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.
- Patients are at high risk of suicide and have an increased desire for hastened death.³
- A useful depression screening question is, "Have you been depressed most of the time for the past two weeks?"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.
- 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.
- Risk factors 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), abrupt onset of menopause (e.g. withdrawal of hormone replacement therapy, use of tamoxifen).

Management Strategies

- Non-pharmacological treatments are the mainstay of treatment for the symptom of depression without a diagnosis of primary affective disorder.
- Treatment of pain and other reversible physical symptoms should occur before initiating antidepressant medication.
- If a diagnosis of primary affective disorder is uncertain in a depressed patient, consider psychiatric referral and a trial of antidepressant medication (refer Appendix B). Consider drug interactions, adverse side effect profiles, and beneficial side effects when choosing an antidepressant.
- In the terminally ill, start with half the usual recommended starting dose of antidepressant.⁵

Palliative Care Part 1: Approach to Care is available at www.bcguidelines.ca/guideline_palliative1.html,

Palliative Care Part 3: Grief and Bereavement is available at www.bcguidelines.ca/guideline_palliative3.html

- First line therapy is with a selective serotonin reuptake inhibitor (SSRI)² or selective serotonin norepinephrine reuptake inhibitor (SSNRI) or noradrenergic and specific serotonergic antidepressant (NaSSA).
- Tricyclic antidepressants (especially nortryptiline and desipramine) can be considered due to their co-analgesic benefit for neuropathic pain (refer Appendix B - Medications Used in Palliative Care for Depression). Avoid with constipation, urinary retention, dry mouth, orthostatic hypotension, or cardiac conduction delays.
- 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.
- If life expectancy is 1-3 months, start a psychostimulant and an antidepressant together and then withdraw the stimulant while titrating the antidepressant upwards.

References

1. Lloyd-Williams M, Friedman T. Depression in palliative care patients – a prospective study. Eur J Cancer Care 2001;10:270-4.
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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. Available at: www.cancercare.on.ca/common/pages/UserFile.aspx?fileid=13930

Abbreviations

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

Appendices

Appendix A – Depression Management Algorithm

Appendix B – Medications Used in Palliative Care for Depression

This guideline is based on scientific evidence current as of the Effective Date.

The guideline was developed by the Family Practice Oncology Network and the Guidelines and Protocols Advisory Committee. The guideline was approved by the British Columbia Medical Association and adopted by the Medical Services Commission.

A mobile version of this and other guidelines is also available at www.BCGuidelines.ca

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

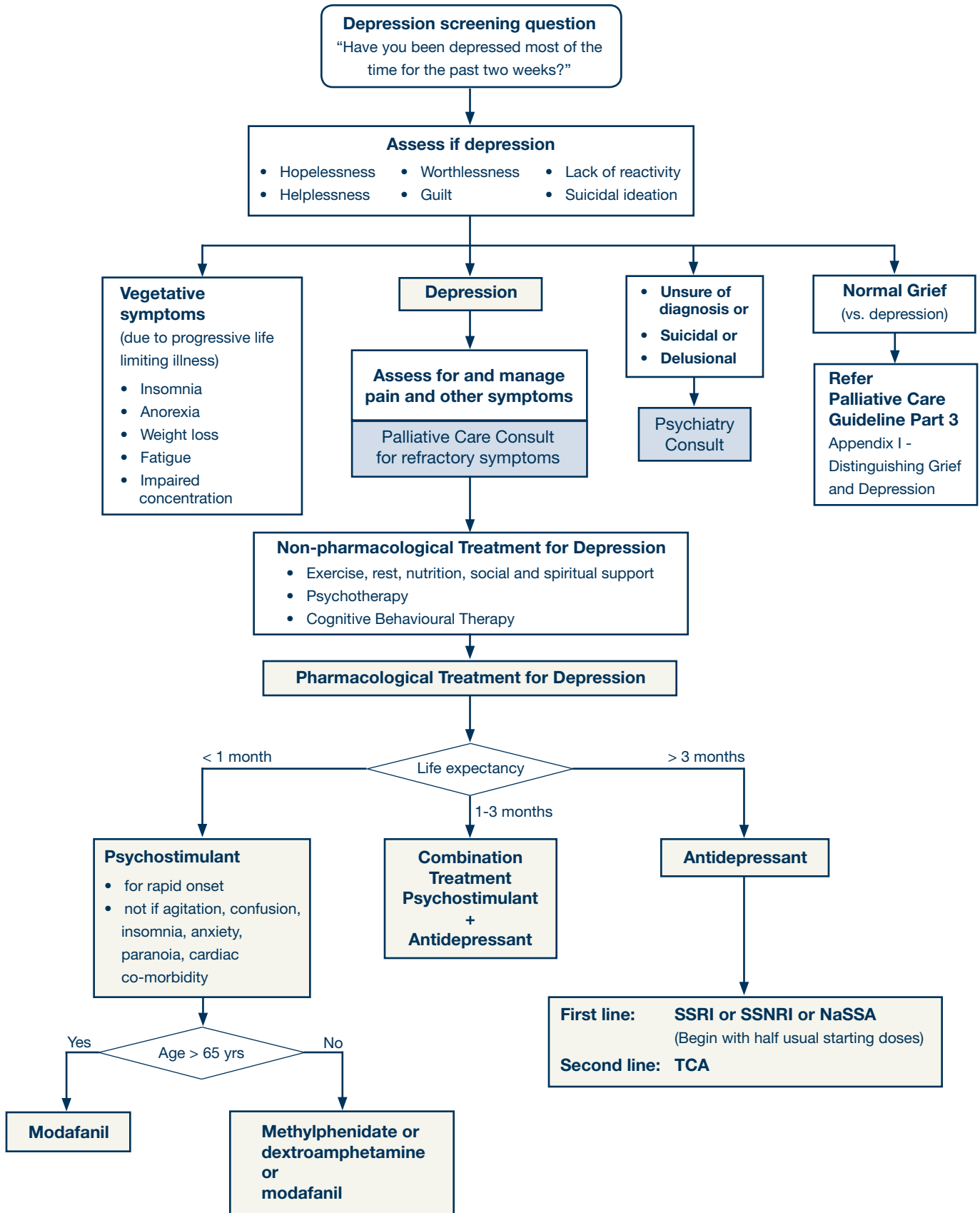
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DISCLAIMER

The Clinical Practice Guidelines (the "Guidelines") have been developed by the Guidelines and Protocols Advisory Committee on behalf of the Medical Services Commission. The Guidelines are intended to give an understanding of a clinical problem and outline one or more preferred approaches to the investigation and management of the problem. The Guidelines are not intended as a substitute for the advice or professional judgment of a health care professional, nor are they intended to be the only approach to the management of clinical problems. **We cannot respond to patients or patient advocates requesting advice on issues related to medical conditions. If you need medical advice, please contact a health care professional.**

Appendix A: Depression Management Algorithm



Appendix B: Medications^a Used in Palliative Care for Depression

^aRefer to guideline and/or algorithm for recommended order of use.

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://webprod.hc-sc.gc.ca/dpd-bdpp/index-eng.jsp>

ANTIDEPRESSANTS ^A						
Generic Name	Trade Name Available Dosage Forms	Standard Adult Dose (palliative) ^B	Drug Plan Coverage ^C		Approx. cost per 30 days	Therapeutic Considerations
			Palliative Care	Fair PharmaCare		
NaSSA: Noradrenergic and Specific Serotonergic Antidepressant						
mirtazapine	Remeron[®], G Remeron RD[®] Tabs: 15, 30, 45 mg RD: 15, 30, 45 mg	Start: 7.5 to 15 mg PO at bedtime Goal: 15 to 45 mg PO at bedtime Max: 60 mg [†] PO at bedtime	Yes, LCA	Yes, LCA	\$6-19 (G) \$20-60	<ul style="list-style-type: none"> Useful for night-time sedation Rapid dissolve formulation
SSNRI: Selective Serotonin Norepinephrine Reuptake Inhibitors						
fuloxetine	Cymbalta[®] Caps: 30 mg, 60 mg	Start: 30 mg PO qAM Goal: 30-60 mg PO qAM Max: 60 mg PO qAM	No	No	\$59-118	<ul style="list-style-type: none"> Effective for diabetic neuropathy Should not be given to individuals with chronic hepatic disease or excessive alcohol consumption
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 [†] PO daily	Yes, LCA	Yes, LCA	\$30-60 (G) \$59-121	<ul style="list-style-type: none"> May cause nausea
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	\$12-\$22 (G) \$27-43	<ul style="list-style-type: none"> Least pharmacokinetic drug interactions
escitalopram	Ciprallex[®] Tabs: 10, 20 mg	Start: 5 mg PO qAM Goal: 5 to 20 mg PO qAM Max: 30 mg [†] PO qAM	Yes	Yes	\$27-\$56	
TCA: Tricyclic Antidepressants						
desipramine	G Tabs: 10, 25, 50, 75, 100 mg	Start: 10 to 25 mg PO qAM ^D Goal: 50 to 75 mg PO qAM ^D Max: 200 mg PO qAM ^D	Yes, LCA	Yes, LCA	\$22-29 (G)	<ul style="list-style-type: none"> 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	\$14-22 (G) \$29-43	

Abbreviations: **caps** capsules; **G** generics available; **IR** immediate release; **LCA** subject to low cost alternative program; **max** maximum dose; **PO** by mouth; **qAM** every morning; **RD** oral disintegrating tablet; **SR** sustained release; **tabs** tablets; **XR** extended release

^A Not a complete list of antidepressants

^B Start doses listed are recommended starting doses for geriatric patients (half the recommended doses for adults), except for duloxetine

^C PharmaCare coverage and cost as of November 2010 (subject to revision). Cost does not include dispensing fee. Generic and brand name cost separated, as indicated by (G). Obtain coverage, eligibility, medication coverage information and explanations here: Information on Provincial Drug Coverage

^D Bedtime dosing may be appropriate for patients experiencing sedation with desipramine

[†] This maximum dose used in palliative care, but not approved for marketing by Health Canada

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://webprod.hc-sc.gc.ca/dpd-bdpp/index-eng.jsp>

PSYCHOSTIMULANTS						
Generic Name	Trade Name	Available Dosage Forms	Standard Adult Dose (note age specific recommendations)	Drug Plan Coverage ^A		Approx. cost per 30 days
				Palliative Care	Fair PharmaCare	
methylphenidate [†]	Ritalin [®] , G	IR tabs: 5, 10, 20 mg	Age over 65 years: Not recommended 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)	Yes, LCA	Yes, LCA	\$6-16 (G) \$11-32
	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	\$21-54
	Concerta [®]	XR tabs: 18, 27, 36, 54 mg		No	Special Authority ^B	\$68 - \$89
	Ritalin [®] SR, G	SR tabs: 20 mg		No	Yes, LCA	\$10 (G) \$20
dextro-amphetamine [†]	Dexedrine [®]	IR tabs: 5 mg	Age over 65 years: Not recommended 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)	No	Yes	\$20 - \$156
		SR caps: 10, 15 mg	Once dose stabilized on IR, give equivalent daily dose as SR form once daily in AM	No	Yes	\$28 - \$112
modafinil [†]	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 ^C , LCA	\$32-60 (G) \$42-83
			Age 18 to 65 years: Start: 100 mg PO bid (AM and noon) Max: 200 mg PO bid (AM and noon)			\$60-120 (G) \$83-167

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 PharmaCare coverage and cost as of November 2010 (subject to revision). Cost does not include dispensing fee. Generic and brand name cost separated, as indicated by (G). Obtain coverage, eligibility, medication coverage information and explanations here: [Information on Provincial Drug Coverage](#)

^B Special authority required to obtain coverage for Concerta[®] for ADHD as second line treatment

^C Special authority required to obtain coverage for modafinil for patients with narcolepsy

[†] This indication (i.e. depression) used in practice, but not approved for marketing by Health Canada

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