CANADIAN STROKE BEST PRACTICE RECOMMENDATIONS

MOOD, COGNITION AND FATIGUE FOLLOWING STROKE

Table 1C: Summary Table for Selected Pharmacotherapy for Post-Stroke Depression

Update 2019

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Table 1C: Summary Table for Selected Pharmacotherapy for Post-Stroke Depression

This table provides a summary of the pharmacotherapeutic properties, side effects, drug interactions and other important information on selected classes of medications available for use in Canada and more commonly recommended for post-stroke depression. This table should be used as a reference guide by health care professionals when selecting an appropriate agent for individual patients. Patient compliance, patient preference and/or past experience, side effects, and drug interactions should all be taken into consideration during decision-making, in addition to other information provided in this table and available elsewhere regarding these medications.

	Selective Serotonin Reuptake Inhibitors (SSRI)	Serotonin–norepinephrine reuptake inhibitors (SNRI)	Other
Medication Generic and Trade Names *recommended	*citalopram – Celexa *escitalopram – Cipralex fluoxetine – Prozac fluvoxamine – Luvox paroxetine – Paxil *sertraline – Zoloft	*duloxetine – Cymbalta *venlafaxine – Effexor	methylphenidate – Ritalin (amphetamine) nortriptyline – Aventyl (tricyclic antidepressant) trazodone – Desyrel (tetracylic antidepressant) *mirtazapine – Remeron (NASSA, noradrenaline and specific serotonin antagonist)
Contra-indications	concurrent monoamine oxidase inhibitor (MAOI) use	concurrent monoamine oxidase inhibitor (MAOI) use	nortriptyline – cardiac conduction abnormalities, uncontrolled narrow angle glaucoma, or concurrent monoamine oxidase inhibitor (MAOI) use
Side Effects	Serotonin syndrome, sedation (fluvoxamine, paroxetine), bleeding, and hyponatremia Fluoxetine, fluvoxamine, paroxetine: interact with certain cardiac medication e.g. clopidogrel and beta-blockers Generally reported: dry mouth, loss of appetite and weight-loss, nausea, dizziness, loss of libido, constipation or diarrhea, insomnia or somnolence, sweating	Increases in heart rate, hypertension (venlafaxine), serotonin syndrome Generally reported: dry mouth, loss of appetite and weight-loss, loss of libido, constipation, nausea, insomnia, dizziness anxiety, sweating	nortriptyline – potential effects on cognition and may increase risk of delirium (anticholinergic); serotonin syndrome, ventricular arrhythmias and orthostatic hypotension Generally reported: dry mouth, loss of appetite and weight-loss, loss of libido, constipation, nausea, dizziness, anxiety, somnolence, sweating
Landmark Trials	citalopram[6,14], fluvoxamine[8] , fluoxetine[1-5] sertraline[7,14] paroxetine[9]	reboxetine[10] , milnacipran[11], venlafaxine[12] , duloxetine[14]	trazodone[15,16] , nortriptyline[17,18] methylphenidate[19]

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Inclusion Criteria & Depression Severity	First ever and recurrent strokes Mild depression[5, 7, 8] Moderate depression[1,2,4,5,6] Severe depression [3, 9, 14]	SNRI: PSD following from first ever stroke. Venlafaxine: moderate depression Duloxetine: severe depression	First ever and recurrent strokes trazodone: mild[15] and moderate[16] depression nortriptyline: mild[17] and moderate[18] depression methylphenidate: moderate depression
Dose Ranges Tested	fluoxetine: 10 - 40mg/day (including variable dose study) citalopram: 10 – 40mg/day[6,10,14,20, 21] Maximum doses: 40mg/day adults, 20mg/day geriatric[22] escitalopram: 10 – 20mg/day Maximum doses: 20 mg/day adults,10 mg/day geriatric[22] sertraline: 50 - 200mg/day[14]	venlafaxine: 75 – 150 mg/day duloxetine: 60 – 120mg/day	trazodone: 200 – 300mg/day mirtazapine: 30mg/day nortriptyline: 20 – 100mg/day
Summary of Findings	Level 1 RCT evidence supports the efficacy of SSRIs fluoxetine and citalopram for treatment of moderate to severe post-stroke depression.	Studies were open-label or uncontrolled; no level 1 RCT evidence available to support efficacy of SNRI for treatment of post-stroke depression.	Level 1 RCT evidence available to support nortriptyline and methylphenidate for treatment of post-stroke depression.
Other Outcomes	Prevention of PSD: fluoxetine, escitalopram and sertraline effective in prophylaxis Mortality & PSD: increased survival of depressed and non-depressed treated with fluoxetine or nortriptyline over placebo in 9-year follow-up[23]. Cognitive function: maintenance of executive function compared to placebo over 21 months	Anxiety in PSD: duloxetine more effective than citalopram in treating anxiety symptoms Alexithymia: venlafaxine results in greater improvement of emotional awareness than fluoxetine	Prevention of PSD: mirtazapine efficacious in preventing PSD[9] Mortality & PSD: increased survival of depressed and non-depressed treated with fluoxetine or nortriptyline over placebo in 9-year follow-up[23] Functional status (ADLs): trazodone treatment resulted in trending improvement

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	follow-up[24]; improvement in verbal and visual memory[25] Sleep: fluvoxamine improved sleep disturbances as measured by peripheral melatonin blood levels. Functional status: **fluoxetine** associated with improved motor recovery (FLAME trial)[25] Other: fluoxetine improved quality of life[2]		
Safety All antidepressants have Health Canada Warnings regarding increased risk of suicidal thinking and behavior (particularly in children, adolescents and young adults)	Discontinuation: Discontinuation of escitalopram may increase post stroke depressive symptoms over 6 months[26] Cerebrovascular AE: rare (<1/1000) in fluoxetine, infrequent to rare (1/100 to 1/1000) for other SSRIs but vigilance required for use in high-risk bleeding & vasoconstrictive stroke.[27] SSRIs lower risk of cardiovascular events but increase bleeding and mortality. [28] Potential risk of hemorrhagic stroke with SSRIs[29] Delirium : anticholinergic effects (paroxetine) may play role in delirium in acute stroke patients[30] QTc prolongation: Health Canada warnings regarding citalopram. Minimal QT effect with escitalopram and sertraline. Fluvoxamine, fluoxetine and paroxetine minimal concern. [31]	QTc prolongation: Among SNRIs, venlafaxine has the greatest risk [31]	Trazodone: serious warning for priapism, associated with increased risk of syncope and falls, particularly in older patients Nortriptyline: special consideration for geriatric population with orthostatic hypotension and anticholinergic effects; caution is advised if used in patients with a personal or family history of cardiovascular disease, arrhythmias or conduction disturbances

	Selective Serotonin Reuptake Inhibitors (SSRI)	Serotonin–norepinephrine reuptake inhibitors (SNRI)	Other
Cost per month/ coverage in Canada	citalopram $0.33/day (regular benefit) escitalopram $1.84 (regular benefit) fluoxetine (20mg) $0.46 (regular benefit) paroxetine – (20mg) $0.45 and (30mg) $0.4796 sertraline - (25mg) $0.20 and ~(100mg) $0.40 fluvoxamine - (50mg) $0.21 and (100mg) $0.38	duloxetine – Cymbalta (30mg) $1.89 and (60mg) $3.79 milnacipran – not available reboxetine - not readily available, not covered by provincial drug coverage plans venlafaxine $0.3469/day (regular benefit)	methylphenidate – $0.28-$4.18 (10-80mg) trazodone ~$0.10/day (regular benefit)

References for Table 1C

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