SECTION III – INFORMATION GUIDE TO ANTIDEPRESSANTS

Latest Revision - March 2009

Antidepressant*	Therapeutic Dose Range (mg/day)	Initial Suggested Dose**	Titration Schedule	Advantages	Disadvantages
Selective Serotonin Reuptake Inhibitors (SSRIs)					
Citalopram (Celexa)	20 – 40	20 mg in morning with food (10 mg in elderly or those with panic disorder)	Maintain initial dose for 4 weeks before dose increase. If no response, increase in 10 mg increments every 7 days as tolerated.	Helpful for anxiety disorders. Few drug interactions. Generic available.	
Escitalopram (Lexapro)	10 – 30	10 mg for escitalopram	Increase to 20 mg if partial response after 4 weeks	More potent s-enantiomer of citalopram, 10 mg dose effective for most. FDA labeling for general anxiety disorder. Reduces all three symptom groups of PTSD.	More expensive than citalopram.
Fluoxetine (Prozac)	10 – 80	20 mg in the morning with food (10 mg in elderly and those with comorbid panic disorder)	Maintain 20 mg for 4-6 weeks and 30 mg for 2-4 weeks before additional dose increases. Increase in 10 mg increments at 7-day intervals. If significant side effects occur within 7 days, lower dose or change medication.	Helpful for anxiety disorders. Long half-life good for poor adherence, missed doses; less frequent discontinuation symptoms. Reduces all three symptom groups of PTSD. Generic available.	Slower to reach steady state and eliminate when discontinued. Sometimes too stimulating. Active metabolite has half-life ~10 days and renal elimination. Inhibitor of cytochrome P450 2D6 and 3A4. Use cautiously in the elderly and others taking multiple medications.
Fluoxetine Weekly (Prozac Weekly)	90	Initiate only after patient stable on 20 mg daily	Start 7 days after last dose of 20 mg.		No generic available.
Paroxetine (Paxil)	10 – 50 (40 in elderly)	20 mg once daily, usually in the morning with food (10 mg in elderly and those with	Maintain 20 mg for 4 weeks before dose increase. Increase in 10 mg increments at intervals of approximately	FDA labeling for most anxiety disorders. Reduces all three symptom groups of PTSD.	Sometimes sedating. Anticholinergic effects can be troublesome. Inhibitor of CYP2D6 (drug

		comorbid panic disorder)	7 days up to maximum dose of 50 mg/day (40 mg elderly)	Generic available.	interactions) Discontinuation/ withdrawal symptoms.
(Paxil CR)	25 – 62.5 (50 in elderly)	25 mg daily (12.5 mg in elderly and those with panic disorder)	Increase by 12.5 mg at weekly intervals, maintain 25 mg for 4 weeks before dose increase.	May cause less nausea and GI distress.	Generic not available.
Sertraline (Zoloft)	25 – 200	50 mg once daily, usually in the morning with food (25 mg for elderly)	Maintain 50 mg for 4 weeks. Increase in 25-50 mg increments at 7-day intervals as tolerated. Maintain 100 mg for 4 weeks before next dose increase.	FDA labeling for anxiety disorders including PTSD. Safety shown post MI. Generic available.	Weak inhibitor of CYP2D6 – drug interactions less likely.
Serotonin and Norepinephrine Antagonist					
Mirtazapine (Remeron)	15 – 45	15 mg at bedtime	Increase in 15 mg increments (7.5 mg in elderly) as tolerated. Maintain 30 mg for 4 weeks before further dose increase.	Few drug interactions. Less or no sexual dysfunction. Less sedation as dose increases. May stimulate appetite. Generic available.	Sedation at low doses only (≤15 mg). Weight gain due to appetite stimulation.
Norepinephrine and Dopamine Reuptake Inhibitor					
Bupropion † (Wellbutrin)	200 – 450	100 mg twice a day (once a day in elderly)	Increase to 100 mg three times a day after 7 days (slower titration for elderly) After 4 weeks, increase to maximum 150 mg three times a day if necessary. Hepatic impairment: 75 mg/day	Can be stimulating. Less or no sexual dysfunction. Generic available.	At higher doses may induce seizures. Contraindicated in persons with seizure disorders or eating disorders. Stimulating effect can increase anxiety or insomnia.
Bupropion SR† (Wellbutrin SR)	200 – 400	150 mg once a day (100 mg in elderly)	Increase to 150 mg twice a day after 7 days (100 bid elderly). Increase to 200 mg twice a day after 4 weeks (150 bid elderly) if insufficient response. Hepatic impairment: 100 mg daily.	Also indicated for smoking cessation (Zyban). Generic available.	Do not split or crush SR or XL products. CYP2B6 inhibitor

Bupropion XL† (Wellbutrin XL)	300 – 450	150 mg once daily (in the morning)	Increase to 300 mg daily after 7 days. Increase to 450 mg per day after 4 weeks if necessary. Hepatic impairment: 150 mg		Generic XL not available.
Serotonin and Norepinephrine Reuptake Inhibitors					
Venlafaxine (Effexor, Effexor XR)	75 – 375	75 mg with food; 37.5 mg if anxious, elderly or debilitated	Immediate release (IR) dose should be divided two or three times a day. For extended release (XR) give 37.5 mg in a.m., then increase to 75 mg in a.m. after 1 week, 150 mg in the a.m. after 2 weeks. If partial response after 4 weeks increase to 225 mg in the a.m. Norepinephrine effect only occurs above 150 mg.	Helpful for anxiety disorders, neuropathic pain, and vasomotor symptoms. XR version should be taken once a day. May reduce all three symptom groups of PTSD. Generic available (IR and XR).	May increase blood pressure at higher doses. Risk for drug interactions similar to fluoxetine. Discontinuation/withdrawal symptoms. Sexual dysfunction.
Desvenlafaxine (Pristiq)	50 – 400	50 mg once daily	No evidence that higher doses are associated with greater effect.	Active metabolite of venlafaxine.	Dose adjustment if CrCl <30 ml/min. Gradually increase dosing interval when discontinuing when taken for $\geq$ 6weeks (taper dose if dose >50 mg/day). Sexual dysfunction. Generic not available.
Duloxetine	40 – 60	40 or 60 mg as a single or divided dose (20 or 40 mg elderly)	Dose can be increased after 1 week. Maximum dose 120 mg/d although doses >60 mg/d have not been shown to be more effective.	Also approved for general anxiety disorder and pain associated with diabetic neuropathy and fibromyalgia.	Dose adjustment if CrCl <30 ml/min. Urinary hesitancy. Sexual dysfunction. Generic not available.
Tricyclic Antidepressants: Secondary Amines					
Desipramine‡ (Norpramin)	100 – 300 (25 – 100 in elderly)	50 mg in the morning (10 or 25 mg elderly)	Increase by 25 to 50 mg every 3 to 7 days to initial target dose of 150 mg (75 or 100 mg elderly) for 4 weeks. Target serum concentration: >115 ng/mL	Effective for diabetic neuropathy and neuropathic pain. Compliance and effective dose can be verified by serum concentration.	Can be stimulating, but sedating to some patients. Anticholinergic, cardiac, and hypotensive (less than tertiary amines); caution in patients with BPH or

				Generic available.	cardiac conduction disorder or CHF.
Nortriptyline‡ (Pamelor)	25 – 100	25 mg (10 mg in elderly) in the evening.	Increase in 10-25 mg increments every 5-7 days as tolerated to 75 mg/day. Obtain serum concentration after 4 weeks; target range: 50-150 ng/mL.	Less orthostatic hypotension than other tricyclics. Compliance and effective dose can be verified by serum concentration. Generic available.	Anticholinergic, cardiac, and hypotensive (less than tertiary amines); caution in patients with BPH or cardiac conduction disorder or CHF.

*There are more antidepressants than those listed in this table. However, this list provides a reasonable variety of drugs that have different side effects and act by different neurotransmitter mechanisms. The January 29, 2009, issue of *The Lancet* includes a meta-analysis and an editorial concluding that sertraline offers the best balance among efficacy, acceptability, and costs compared to 11 other agents.[1,2]

Treatment of Parkinson's disease may include selegiline (Eldepryl), which is a selective monoamine oxidase inhibitor (MAOI), at low doses only. Because the use of many antidepressants is contraindicated in conjunction with a nonselective MAOI, caution with or discontinuation of Eldepryl may be in order. Selegiline is also available as a higher dose and nonselective, transdermal patch (Emsam) approved for the treatment of major depressive disorder.

**For SSRIs, venlafaxine, and the tricyclic antidepressants, start at the beginning of the therapeutic dosing range. If side effects are bothersome, reduce the dose and increase slower. In the elderly, the debilitated or those sensitive to medications, start lower. For all antidepressants, allow four weeks at a therapeutic dose, then assess for response. If only partial or slight response (well tolerated), then increase the dose. If no response, worse symptoms, or intolerable side effects, switch antidepressants.

For treatment of depression in pregnancy, TCAs and SSRIs (particularly fluoxetine) are generally the agents of choice. However, the SSRIs have been associated with persistent newborn pulmonary hypertension with maternal use after 20 weeks of gestation, a slight decrease in gestational age, lower birth weight, and neonatal withdrawal or adaptation syndrome. Paroxetine has been associated with first-trimester cardiovascular malformations (ventricular and atrial septal defects); hence the use of paroxetine should be avoided during the first trimester. TCAs have been associated with neonatal withdrawal symptoms and anticholinergic adverse effects. There are insufficient data about other newer antidepressants, although there may be a link between bupropion and spontaneous abortion.

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[1] Parikh SV. Antidepressants are not all created equal. *The Lancet*. Early Online Publication, Jan 29, 2009. DOI:10.1016/S0140-6736(09)60047-7

[2] Cipriani A, Furukawa TA, Salanti G, Geddes JR, Higgins JPT, Churchill R, Watanabe N, Nakagawa A, Omori IM, McGuire H, Tansella M, Barbui C Comparative efficacy and acceptability of 12 new-generation antidepressants: a multiple-treatments meta-analysis. *The Lancet*, Early Online Publication, 29 January 2009. DOI:10.1016/S0140-6736(09)60046-5

For women planning to breast feed, an antidepressant with the lowest excretion into breast milk, i.e., lowest infant serum concentrations and fewer adverse reactions, should be considered. These include sertraline, paroxetine and nortriptyline. Citalopram and fluoxetine have the highest concentrations in breast milk and more reports of infant adverse effects. A 40% decrease in breast milk concentration can be achieved by switching to escitalopram at 25% of the citalopram dose. Venlafaxine is detectable in the serum and associated with less weight gain in breast-fed infants. Less information is available about burpropion, mirtazepine and trazodone, although the concentrations in breast milk infant serum are low. The TCAs are nearly undetectable in infant plasma concentrations and low concentrations are found in breast milk but have less advantageous side effect profiles.

†Avoid bupropion in patients with a history of seizures, eating disorders, significant central nervous system lesions, or recent head trauma.

‡Tricyclic antidepressants (TCAs) have lower costs but somewhat higher discontinuation rates compared to SSRIs and second generation antidepressants due to side effects. The TCAs are more lethal in overdose than SSRIs. TCAs may be contraindicated in patients with certain physical comorbidities such as recent myocardial infarction, cardiac conduction defects, urinary retention, narrow angle glaucoma, orthostatic hypotension, and cognitive impairment.