Pharmacological Therapies

Disclaimer: This information is believed to be reliable and generally in accord with the accepted standards at the time of its publication. Due to the possibility of human error and changes in medical sciences, use this information as a guide in conjunction with product monographs to be updated continuously as new information becomes available.

ANTIDEPRESSANT GENERIC OPTION	TYPICAL EFFECTIVE DOSE (MG/D)*	MAXIMUM DOSE (MG/D)*	INITIAL SUGGESTED DOSE**	TITRATION SCHEDULE*	ADVANTAGES	DISADVANTAGES
			Selective Serotonin Reuptake Inhibitors (SSRIs)			
Citalopram	20–40	40 (20 in patients >60 years old)	20 mg in a.m. w/food (10 mg in elderly, those w/sensitivity to drug or those w/ panic disorder)	Maintain initial dose as per treatment guide before dose increase. If no response, increase in 10 mg increments q 7 days as tolerated.		
Escitalopram	10–20	20	10 mg	Maintain initial dose as per treatment guide before dose increase. If no response, increase in 5–10 mg increments q 7 days as tolerated.	More potent s-enantiomer of citalopram, 10 mg dose effective for most. FDA approved for GAD.	More expensive than citalopram.
Fluoxetine	20–60	80	20 mg in the a.m. w/food (10 mg in elderly, those w/sensitivity to drug, or those w/comorbid panic disorder)	Maintain initial dose as per treatment guide. Increase in 10 mg increments at 7-day intervals. If significant side effects occur w/in 7 days, lower dose or change med.	Effective in most anxiety and related disorders. Long half-life good for poor adherence, missed doses; less frequent discontinuation syndrome. Reduces all 3 symptom groups of PTSD (studies done as per DSM-IV criteria; dissociative reactions and avoidance were combined in DSM-IV).	Slower to reach steady state and eliminate when discontinued. Sometimes too stimulating. Active metabolite half-life ~10 days, renal elimination. Inhibits cytochrome P450 2D6 and 3A4. Use cautiously in elderly and patients on multiple meds.

*Consult drug monograph if renal, hepatic impairment, or medically ill patient, pregnancy, breastfeeding, and elderly; dose adjustment may be warranted or drug could be contraindicated.

**If initial dose is lower than minimum effective dose (e.g., in elderly), increase to minimum effective dose as tolerated and maintain as per treatment guide. In some disorders (e.g., OCD, PTSD), consider increasing to target dose and then maintain as per treatment guide.

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			Selective Serotonin Reuptake Inhibitors (SSRIs)			
Paroxetine	20–50 (20–40 in elderly)	60	20 mg once daily, usually in the a.m. w/food (10 mg in elderly, those w/sensitivity to drug, or those w/comorbid panic disorder)	Maintain initial dose as per treatment guide before dose increase. Increase in 10 mg increments at intervals of ~7 days up to maximum dose of 60 mg/day (40 mg in elderly).	FDA labeling for most anxiety and related disorders. Reduces all 3 symptom groups of PTSD (studies done as per DSM-IV criteria; dissociative reactions and avoidance were combined in DSM-IV).	Sometimes sedating. Anticholinergic effects can be troublesome. Inhibitor of CYP2D6.
Paroxetine CR	25–62.5 (25–50 in elderly)	75	25 mg daily (12.5 mg in elderly, those w/sensitivity to drug, or those w/panic disorder)	Maintain at initial dose for suggested number of weeks as per treatment guide before dose increase. Increase by 12.5 mg at weekly intervals.	May cause less nausea and GI distress.	More expensive than paroxetine.
Sertraline	50–200	200	50 mg once daily, usually in the a.m. w/food (25 mg for elderly or those w/sensitivity to drug)	Maintain initial dose as per treatment guide before dose increase. Increase in 25–50 mg increments at 7-day intervals as tolerated.	FDA labeling for anxiety and related disorders including PTSD. Safety shown post-MI.	Weak inhibitor of CYP2D6. Drug interactions less likely.
Fluvoxamine	100–300	300	50 mg/day (25 mg/day for elderly or those w/sensitivity to drug)	Maintain initial dose as per treatment guide before dose increase. Increase every 5–7 days by 50 mg/day as tolerated.		Side effects may hinder rapid dose escalation.

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Selective Serotonin Reuptake Inhibitors (SSRIs)						
Fluvoxamine CR	100–300	300	100 mg at bedtime	Maintain initial dose as per treatment guide before dose increase. Increase every 7 days by 50 mg/day as tolerated.	Studies show consistently earlier onset of action than other SSRIs. Allows more aggressive dose titration.	
Noradrenergic and Specific Serotonergic Antidepressants (NaSSAs)						
Mirtazapine	15–45	45	15 mg at bedtime	Maintain initial dose as per treatment guide before dose increase. Increase in 15 mg increments (7.5 mg in elderly) as tolerated.	Few drug interactions. Less sedation as dose increases. May stimulate appetite.	Sedation at low doses only (<15 mg). Weight gain due to appetite stimulation.

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Norepinephrine and Dopamine Reuptake Inhibitor						
Bupropion	200–300	450	100 mg twice a day (100 mg once a day in elderly)	Maintain initial dose as per treatment guide before dose increase. Increase to 100 mg TID as tolerated. Increase to maximum 150 mg TID.	Can be stimulating. Less or no sexual dysfunction. Does not appear to cause weight gain.	Contraindicated in patients w/seizures, CNS lesions, recent head trauma, or eating disorder. Stimulating effect can increase anxiety/insomnia.
Bupropion SR	200–400	400	150 mg once a day (100 mg in elderly)	Maintain initial dose as per treatment guide before dose increase. Increase to 150 mg BID (100 BID in elderly). Increase to a maximum of 200 mg BID (150 BID in elderly).	Dose slowly released in 12 hours. Also indicated for smoking cessation (Zyban). Does not appear to cause weight gain.	Interval of at least 8 hours between successive doses. Do not split or crush SR products.
Bupropion XL	300–450	450	150 mg once daily (in the morning)	Maintain initial dose as per treatment guide before dose increase. Increase to 300 mg daily. Increase to maximum 450 mg once daily.	Dose released for period of 24 hours. Less or no sexual dysfunction. Does not appear to cause weight gain.	Contraindicated in patients w/seizures, CNS lesions, recent head trauma, or eating disorder. Can cause insomnia. Do not split or crush XL products.

XL: Extended release (release of dose for extended period in a day)

SR: Sustained release (slowly released in body throughout the day, maintaining constant drug concentration)

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Serotonin and Norepinephrine Reuptake Inhibitors						
Venlafaxine Venlafaxine XR	75–225	225	75 mg w/food; 37.5 mg if anxious, elderly, panic disorder.	IR: divide dose BID or TID. XR: once daily. If initial dose is 37.5 mg, consider increase to 75 mg in 4–7 days as tolerated. Maintain dose as per treatment guide before dose increase. Increase no sooner than q 4 days by 75 mg to maximum dose of 225 mg.	Helpful also for neuropathic pain and vasomotor symptoms.	May increase BP at higher doses. Greater cardiotoxicity. Risk for drug interactions similar to fluoxetine.
Desvenlafaxine	50	50	50 mg once daily	No evidence that higher doses are associated w/greater effect. Some experts suggest that should it be considered necessary, an escalation to 100 mg/day can be tried.[1]	Active metabolite of venlafaxine.	

IR: Immediate release

1 Warner CH, Warner CM, Appenzeller GN, Hoge CW. Identifying and managing posttraumatic stress disorder. Am Fam Physician. 2013; 88(12):827–834.

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Serotonin and Norepinephrine Reuptake Inhibitors						
Duloxetine	30–120	120	60 mg as a single or divided doses (30–60 mg in elderly)	Dose can be increased after 1 week. Maximum dose 120 mg/day, although doses >60 mg/day not more effective in studies.	Also approved for pain from diabetic neuropathy and fibromyalgia.	May increase BP at higher doses. Greater cardiotoxicity.
Milnacipran	12.5–100	200	12.5 mg	Increase to 12.5 mg twice daily in 2–3 days, then to 50 mg twice daily q 7 days as tolerated. Maintain dose as per treatment guide before dose increase. Increase to maximum 200 mg in divided doses (BID).	Also effective in fibromyalgia.	May increase BP at higher doses. Greater cardiotoxicity.
Serotonin Antagonist and Reuptake Inhibitors						
Trazadone	50–150	400	25–50 mg HS	Increase initial dose to 150 mg/d as tolerated in divided doses (TID). Maintain 150 mg as per treatment guide before dose increase. Increase in 50 mg increments at 4–7-day intervals as tolerated to maximum dose.	Can be helpful for insomnia.	

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Norepinephrine Reuptake Inhibitors						
Atomoxetine	40–100	100	40 (can be OD or divided dose (BID)	Initial dose can be increased after ≥3 days to 80 mg PO OD or in divided doses BID. May be increased to 100 mg if optimal response is not achieved.	Effective for comorbid ADHD.	May only be effective in social anxiety disorder.
Tricyclic Antidepressants: Secondary Amines						
Desipramine	100–200 (25–100 in elderly)	300	25–50 mg in a.m. (10 or 25 mg in elderly)	Increase in 25 to 50 mg increments q 3–7 days to initial target dose of 150 mg (75 or 100 mg in elderly). Target serum concentration: 115–300 ng/mL. Maintain 150 mg as per treatment guide before dose increase. Increase in 25–50 mg increments at 4–7-day intervals as tolerated to maximum dose.	More effect on norepinephrine than serotonin. Effective for diabetic neuropathy and neuropathic pain. Compliance and effective dose can be verified by serum concentration.	May not be helpful for anticipatory anxiety. Can be stimulating, but sedating in some patients. Anticholinergic, cardiac, hypotensive; caution in patients w/BPH, cardiac conduction disorder, or CHF.

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Tricyclic Antidepressants: Secondary Amines						
Nortriptyline	50–150	150	25 mg in p.m. (10 mg in elderly)	Increase initial dose in 10–25 mg increments every 5–7 days as tolerated to initial target dose of 75 mg/day. Obtain serum concentration after 4 wks; target range: 50–150 ng/mL.	Less jitteriness than imipramine. Less orthostatic hypotension than other tricyclics. Compliance and effective dose can be verified by serum concentration.	May not be helpful for anticipatory anxiety. Anticholinergic, cardiac, and hypotensive; caution in patients w/BPH, cardiac conduction disorder, or CHF.
Imipramine	150–250	300	10–25 mg at bedtime	Increase dose 10 mg every day until dose of 50 mg/day reached. Increase 25 mg every third day up to 100 mg. After 1 week, dose can be increased by 25–50 mg as tolerated every third day to maximum dose of 300 mg/day (increments of 10 mg may be required.)	Slowly metabolized; can be taken once daily, usually at bedtime.	May experience more general anxiety the first few days up to 3 weeks.

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Tricyclic Antidepressants: Secondary Amines						
Clomipramine	150–300	300	25 mg in p.m. (10 mg in elderly)	Increase initial dose by 25 mg increments q 3–4 days to 100 mg/day. Maintain 100 mg as per treatment guide before dose increase. Increase in 25 mg increments at 4–7-day intervals as tolerated to maximum dose.	Helps control OCD. Usually taken in 1 dose.	May experience more general anxiety the first few days up to 3 weeks. Can take 4–6 weeks to work.
Mood Stabilizers/Anticonvulsants						
Pregabalin	150–600	600	150 mg in divided doses (BID)	Initial dose may be increased in 75–150 mg increments as tolerated to maximum dose.	No clinically significant laboratory, electrocardiogram, or other treatment-related safety findings.	Weight gain (19–24.4%).[2] Dizziness (12.5%), somnolence, headache, insomnia, balance disorder, tremor, confusional state, coordination abnormal (use with caution in the elderly population). Increased seizure frequency may occur in patients with seizure disorders if rapidly discontinued.

2 Montgomery S, Emir B, Haswell H, Prieto R. Longterm treatment of anxiety disorders with pregabalin: a 1 year open-label study of safety and tolerability. Curr Med Res Opin. 2013; 29(10):1223–1230.

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			Mood Stabilizers/Anticonvulsants			
Gabapentin	900–1800 in divided doses (TID)	3600	300 mg in divided doses (TID)	Initial dose can be increased to 300 mg BID, then TID within 3–7 days. Further increase as tolerated to maximum dose (in divided doses —TID).	Can be effective in concurrent epilepsy, postherpetic neuraldia, and restless leg syndrome.	TID schedule; maximum time between doses should not exceed 12 hours.
			Reversible inhibitor of monoamine oxidase			
Moclobemide	300–600 in divided doses (BID or TID)	600	150 mg after meals	Increase initial dose by increments of 150 mg q 1–2 weeks.	Better tolerated than MAOI; less concern with diet.	Multiple dosing schedule.
			Monoamine Oxidase Inhibitors			
Phenelzine	45–90	90 in divided doses (BID to TID)	15 mg TID; lower initial dose may be required in some patients; e.g., elderly (15 mg OD)	If needed, initial dose can be increased to at least 60 mg/day fairly quickly as tolerated.		Hypertensive crises w/ingestion of foods with a high concentration of tyramine or dopamine.
Tranylcypromine	30–40 in divided doses (BID)	60	10 mg BID; lower initial dose may be required in some patients; e.g., elderly (10 mg OD)	If no response after 2–3 weeks, increase initial dose by increments of 10 mg/day q 1–3 weeks (may need to increase by 5 mg/day in elderly).		Hypertensive crises w/ingestion of foods with high concentration of tyramine or dopamine.

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			Anxiolytics			
Hydroxyzine (antihistamine)	50–100 in divided doses (QID)	100	50 mg in divided doses (may need to start at lower dose of 25 mg in elderly)		Also used in allergic reactions or urticaria.	Higher rates of sleepiness/ drowsiness than benzodiazepines and buspirone. Contraindicated in pregnancy.
			Other			
Agomelatine (melatonin agonist)	25–50 taken at bedtime	50	25 mg HS	After 2 weeks at initial dose, dose may be increased to 50 mg once daily at bedtime.	Usually no adjustment in recommended dose for elderly solely based on age. Limited clinical data on patients >75 years of age; not recommended in this group.	Contraindicated in hepatic disease.
Reboxetine (selective noradrenergic reuptake inhibitor)	6–8	Usually 8 mg in divided doses (BID) May increase to 10 mg as necessary Elderly 2 mg BID	2 mg	Initial dosage can be increased by 2 mg/day weekly to a maximum dosage of 8 mg/day. Can be increased more rapidly if tolerated as soon as 5 days. Elderly may increase to 6 mg/day in divided doses (BID) after 3 weeks.		May not be as effective as paroxetine in addressing panic attacks.

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Other						
Buspirone	20–30	30	7.5 mg BID	Increased every 2–3 days in increments of 2.5 mg twice daily to a maximum of 30 mg twice daily. Divided doses BID and TID can be used.	Approved as second-line monotherapy for GAD.	Significant delay in the onset of clinical activity, which can vary from 2 weeks to much longer.

Note: Black box warning for all antidepressant medications: Increased risks of suicidal thinking and behavior in young adults 18–24 years old during the first 1–2 months of treatment. Scientific data does not show increased risk in adults >24 years of age; adults >65 years of age show decreased risk.