

VA



U.S. Department
of Veterans Affairs

Clinical Pearls for Depression Management

A Quick Reference Guide (2014)

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Key Items to Assess When Treating Depression¹

- Symptom severity (PHQ-9) and risk for suicide
- Tolerability to treatment (adverse effects)
- Adherence to treatment
- Medical problems influencing recovery
- Psychosocial barriers to therapy
- Re-evaluate diagnosis and appropriate treatment

Assess Treatment Response with PHQ-9¹

Onset Response of Treatment	Minimal clinically significant: a change in PHQ-9 score of 25% Response to treatment: improvement in PHQ-9 score of 50% from baseline
Full Remission	PHQ-9 score of 4 or less, maintained for at least 1 month
Recovery	PHQ-9 score of 4 or less, maintained for at least 6 months

PHQ-9 = Patient Health Questionnaire

First-Line Treatment Options for Depression¹

Psychotherapies	Cognitive Behavioral Therapy (CBT) Interpersonal Therapy (IPT) Problem Solving Therapy (PST)	Recommended for patients who: <ol style="list-style-type: none"> 1. Prefer psychological counseling 2. Had a previous good response to psychological counseling 3. Cannot tolerate medications
Pharmacotherapy	SSRIs; SNRIs; Bupropion; Mirtazapine	No evidence that any one medication is better than another. Select based on side effects, cost, and availability

Psychoeducation and Self-Management¹ (Collaboratively Choose 1 or 2 Goals at a Time)

Nutrition	Maintain a balanced diet
Exercise	Strong evidence shows that exercise often has significant antidepressant effects
Bibliotherapy	Use self-help texts
Sleep Hygiene	Education on sleep hygiene should be included for patients exhibiting sleep disturbance
Tobacco Use	Tobacco use has been demonstrated to impact the recovery of depression. Referral or treatment of nicotine dependence should be considered
Caffeine Use	Excessive caffeine use may exacerbate some symptoms of depression
Alcohol Use and Abuse	Even low levels of alcohol use have been demonstrated to impact recovery of depression; patients should be advised to abstain until symptoms remit
Pleasurable Activities	Behavioral activation has been shown to have significant antidepressant effects

Comparison Among Commonly Used Antidepressants^{2,3*}

Class	Drug	Safety						Notes
		Anti-Ach	Sedation	GI	Withdrawal	Drug Interactions	OD risk ^{1,2}	
SSRI	Citalopram**	Less common	Less common	N	Intermediate	Intermediate	Intermediate	May cause QT prolongation
	Sertraline	Less common	Less common	N,D	Intermediate	Intermediate	Less common	May cause diarrhea if dose increased quickly
	Paroxetine	Intermediate	Intermediate	N	More common	More common	Less common	Dosed at bedtime
	Fluoxetine	Less common	Less common	N	Less common	More common	Less common	No need to taper off with discontinuation
	Escitalopram	Less common	Less common	N	Intermediate	Less common	Less common	
SNRI	Venlafaxine	Less common	Less common	N	More common	Intermediate	Intermediate	May increase blood pressure at high doses
	Duloxetine	Less common	Less common	N	More common	Intermediate	Intermediate	Monitor liver function
TCA	Amitriptyline	More common	More common	C	More common	Intermediate	More common	Dosed at bedtime; postural hypotension; weight gain; overdose can cause seizures and cardiac arrhythmia
	Imipramine	More common	More common	C	More common	Intermediate	More common	
	Nortriptyline	+	More common	C	More common	Intermediate	More common	
	Desipramine	+	More common	C	More common	Intermediate	More common	
Other	Bupropion	Less common	Less common	Less common	Less common	Intermediate	Intermediate	Seizure risk
	Mirtazapine	Intermediate	More common	Less common	More common	Intermediate	Less common	Can increase appetite and cause weight gain

*Data taken from package inserts

**If >60 y/o, hepatic impairment, poor 2C19 metabolizes OR on cimetidine → max dose 20 mg

+ These agents may have less anticholinergic, sedating, and hypotensive side effects than other TCAs

C = Constipation, D = Diarrhea, N = Nausea/Vomiting

■ = less common

■ = intermediate

■ = more common

Antidepressant Dosing^{1,4}

Class	Agent	Initial Dose	Titration Schedule	Maximum Dose/Day	Guidance in Special Populations		
					Geriatric (Dosage Range)	Renal	Hepatic
SSRIs	Citalopram	20 mg QD	Weekly	40 mg*	10–20 mg QD	Avoid: CrCl <20 ml/min	Max 20 mg/day
	Escitalopram	10 mg QD	Weekly	40 mg	5–20 mg QD	Avoid: CrCl <20 ml/min	Max 10 mg/day
	Fluoxetine	20 mg QD	2 weeks	80 mg	5–40 mg QD	No change	Dose 50%
	Paroxetine	20 mg QD	Weekly	50 mg	10–40 mg QD	Max 40 mg CrCl <30 ml/min	Max 40 mg/day
	Sertraline	50 mg QD	Weekly	200 mg	25–150 mg QD		↓ Dose 50%
SNRIs	Duloxetine	60 mg QD or divided	NA	60 mg	20–40 mg QD	Avoid: CrCl <30 ml/min	Avoid
	Venlafaxine IR	37.5 mg BID	Weekly	225–375 mg	25–225 mg QD (2 divided doses)	CrCL = 10–70 ml/min, ↓ dose 50%	↓ Dose 50%
	Venlafaxine ER	75 mg QD	Weekly	225 mg	37.5–225 mg QD	CrCL = 10–70 ml/min, ↓ dose 50%	↓ Dose 50%
DNRIs	Bupropion IR	100 mg BID	Weekly	450 mg (3 divided doses)	37.5–75 mg BID	↓ dose	Severe: max dose 75 mg QD
	Bupropion SR	150 QD	Weekly	400 mg (2 divided doses)	↓ dose may be required	↓ dose	Severe: max dose 100 mg QD
	Bupropion XR	150 QD	Weekly	450 mg		↓ dose	Severe: max dose 150 mg QD
NaSSA	Mirtazapine	15 mg QHS	Weekly	45 mg	7.5–45 mg QD	CrCl <40 ml/min use caution	Titrate slowly

*If >60 y/o, hepatic impairment, poor 2C19 metabolizers OR on cimetidine → max dose 20 mg; SSRI = Selective Serotonin reuptake inhibitor; SNRI = Selective Norepinephrine Reuptake Inhibitor; DNRI = Dopamine-Norepinephrine Reuptake Inhibitor; NaSSA = Noradrenergic and Specific Serotonergic Antidepressant.

Suggested Dosing and Treatment Steps Based on PHQ-9 Score

Time	PHQ-9 Score	Citalopram	Sertraline	Fluoxetine	Venlafaxine IR	Bupropion SR	Mirtazapine
Baseline		20 mg QD	50 mg daily x 1 week then increase to 100 mg QD	20 mg QD	37.5 mg BID x 1 week, then 75 mg BID	150 mg daily x 1 week then 150mg BID	15 mg at bedtime x 1 week then increase to 30 mg QHS
4 Weeks	≤4	Continue 20 mg QD	Continue 100 mg QD	Continue 20 mg QD	Continue 75 mg BID	Continue 150 mg BID	Continue 30 mg QHS
	5-10	Continue or increase to 40 mg QD	Continue or increase to 150 mg QD	Continue or increase to 40 mg QD	Continue or increase to 112.5 mg BID	Continue or increase to 200 mg BID	Continue or increase to 45 mg QHS
	>10	Increase to 40 mg*	Increase to 150 mg QD	Increase to 40 mg QD	Increase to 112.5 mg BID	Increase to 200 mg BID	Increase to 45 mg QHS
8 Weeks	≤4	Continue Dose	Continue Dose	Continue Dose	Continue Dose	Continue Dose	Continue Dose
	5-10	Increase to 40 mg QD or add bupropion or mirtazapine	Increase to 200 mg QD or add bupropion or mirtazapine	Increase to 40 mg QD or add bupropion or mirtazapine	Increase to 112.5 mg BID or add bupropion or mirtazapine	Increase to 200 mg BID or add an SSRI, venlafaxine or mirtazapine	Increase to 45 mg QHS or add an SSRI, venlafaxine, or bupropion
	>10	Switch to another SSRI, venlafaxine, mirtazapine or bupropion	Switch to another SSRI, venlafaxine, mirtazapine or bupropion	Switch to another SSRI, venlafaxine, mirtazapine or bupropion	Switch to an SSRI, bupropion or mirtazapine	Switch to an SSRI, mirtazapine or venlafaxine	Switch to an SSRI, bupropion or venlafaxine
12 Weeks	≤4	Continue Dose	Continue Dose	Continue Dose	Continue Dose	Continue Dose	Continue Dose
	>4	Switch to another SSRI, venlafaxine, mirtazapine or bupropion or optimize current therapy	Switch to another SSRI, venlafaxine, mirtazapine or bupropion or optimize current therapy	Switch to another SSRI, venlafaxine, mirtazapine or bupropion or optimize current therapy	Switch to an SSRI or bupropion or add mirtazapine or optimize current therapy	Switch to or add on an SSRI, mirtazapine or venlafaxine or optimize current therapy	Switch to or add an SSRI, bupropion or venlafaxine or optimize current therapy

*If >60 y/o, hepatic impairment, poor 2C19 metabolizes OR on cimetidine → max dose 20 mg; SSRI = Selective Serotonin Reuptake Inhibitor
SNRI = Selective Norepinephrine Reuptake Inhibitor

Switching Antidepressants⁴

Initial medication ↓	Medication Class Switching to:						Equivalent Doses
	SSRIs	SNRIs	Mirtazapine	Bupropion	TCA	MAOIs**	
Citalopram	Yellow	Yellow	Green	Green	Green	Red	20 mg
Escitalopram	Yellow	Yellow	Green	Green	Green	Red	10 mg
Fluoxetine*	Yellow	Yellow	Yellow	Yellow	Green	Red	20 mg
Fluvoxamine*	Yellow	Yellow	Green	Green	Green	Red	100 mg
Paroxetine*	Yellow	Yellow	Green	Green	Green	Red	20 mg
Sertraline	Yellow	Yellow	Green	Green	Green	Red	50–75 mg
Duloxetine*	Green	Yellow	Green	Green	Green	Red	30 mg
Venlafaxine	Green	Yellow	Green	Green	Green	Red	75 mg
Mirtazapine	Green	Green	White	Green	Green	Red	15 mg
Bupropion SA*	Yellow	Green	Green	White	Green	Red	150 mg
TCA	Green	Green	Green	Green	White	Red	
MAOIs	Red	Red	Red	Red	Red	Red	

■ = cross-taper recommended⁺
 ■ = direct switch probably safe
 ■ = washout period advisable

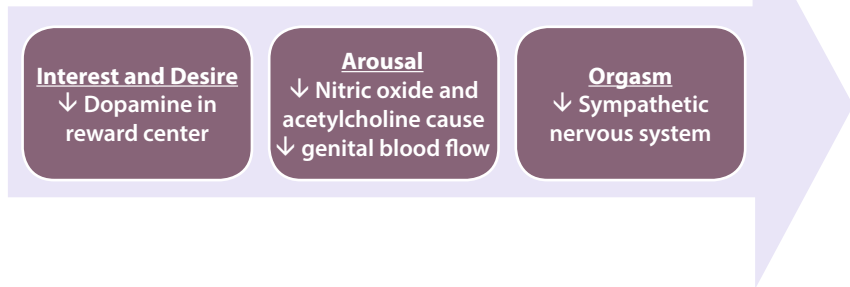
⁺Cross-taper generally takes 1–2 weeks; *May increase serum concentrations of TCAs, SNRIs, and bupropion, thus start at low dose to avoid toxicity; **MAOIs - wait 2 weeks after discontinuation of an MAOI before starting another antidepressant, wait 2 weeks after discontinuing an antidepressant before starting an MAOI, except fluoxetine which needs a washout period of at least 5 weeks; SSRI = Selective Serotonin Reuptake Inhibitor; SNRI = Selective Norepinephrine Reuptake Inhibitor; MAOI = Monoamine Oxidase Inhibitor; TCA = Tricyclic Antidepressant.

Antidepressants and Sexual Dysfunction^{5,6}

- Two times more sexual dysfunction in depressed vs. nondepressed patients (50% vs. 24%).
- 62% of depressed patients receiving pharmacotherapy reported sexual dysfunction vs. 45% of those who were not on medication.
- 50–70% of patients on SSRIs report difficulties in sexual function.
- Medication induced sexual dysfunction can lead to decreased medication adherence.

Risk factors for sexual dysfunction:

- Smoking and alcohol use
- CV disease and diabetes
- Hormone disorders
- Medications
- MDD and other psychiatric diagnoses
- Sexual trauma
- Age (old for men, young for women)



Incidence of Sexual Dysfunction*

	Decreased Libido	Impotence	Abnormal Ejaculation	Anorgasmia
Citalopram	4%	3%	6%	–
Fluoxetine	1–11%	1–7%	2–7%	–
Fluvoxamine	2%	2%	8%	2%
Paroxetine	3–12%	2–8%	2–28%	10%
Sertraline	1–11%	>1%	7–19%	–
Venlafaxine	1–6%	2–6%	2–13%	2–3%
Duloxetine	3%	4–5%	2–3%	2%
Bupropion	3%	3%	<1%	–
Nefazodone	1%	1%	<1%	<1%
Mirtazapine	1%	<1%	<1%	–

*Data taken from package inserts

Treatment Strategies^{5,6}

- **Wait** – within 6 months ~10% of patients report remission of sexual dysfunction and up to 15–20% report symptom improvement
- **Decrease dose** – higher doses have been associated with higher rates of dysfunction; however, decreasing dose may lead to reduced antidepressant effect
- **Switch antidepressants** – bupropion, mirtazapine, and nefazodone are associated with a lower incidence of sexual dysfunction
- **Adjunctive medications**
 - PDE–V inhibitors (sildenafil, vardenafil, tadalafil) used to treat the physiologic aspects of sexual function; will have no effect in the absence of sexual stimulation
 - Bupropion may be effective as adjunctive therapy; however, study results are conflicting

Antidepressants and Hyponatremia

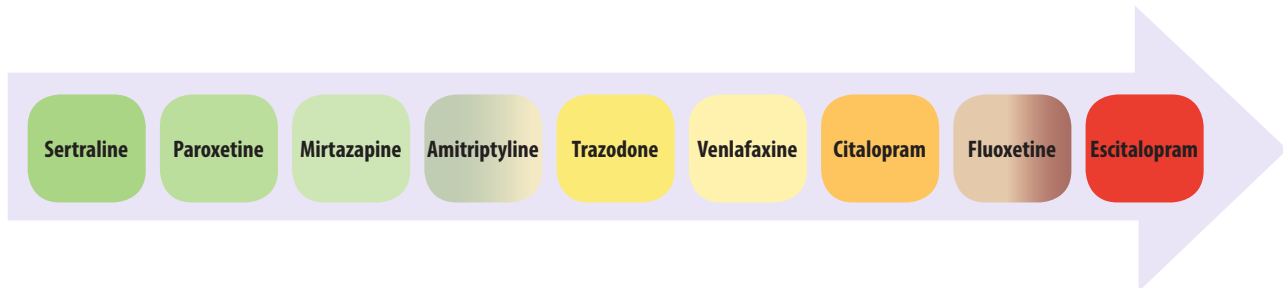
- All antidepressants have been associated with cases of hyponatremia (SSRI's incidence, 0.5–32%)^{4,7,8}
- Onset can be as rapid as 3–4 days after starting medication, but usually occurs within the first few weeks^{7,8,9}
- Not thought to be dose related⁴
- Monitor for hyponatremia especially in higher risk patients⁴
 - Serum electrolyte panel, symptoms (dizziness, nausea, lethargy, confusion, cramps, seizures)
 - Patients don't always report symptoms of hyponatremia
- After discontinuation of the offending antidepressant, hyponatremia typically resolves within 2 weeks^{7,9}

Risk Factors for Hyponatremia^{4,7,8}

History of Hyponatremia	Medical Comorbidities	Medications
Old Age	Diabetes	Trimethoprim
Female	Hypothyroidism	Carbamazepine
Low Baseline Na+	COPD	Antipsychotics
Recent History of Pneumonia	Hypertension and/or CHF	Thiazide Diuretics
GFR <50 mL/min	Head Injury or CVA	NSAIDs and Tramadol
Warm Weather	Various Cancers	Chemotherapy
Low Body Weight		Omeprazole

COPD = Chronic Obstructive Pulmonary Disease; CHF = Congestive Heart Failure; CVA = Cerebrovascular Accident

Antidepressants and Hyponatremia¹⁰



Restarting an Antidepressant After Hyponatremia has Resolved

- Select an agent from a different class – fewer case reports of recurrence of hyponatremia when an agent with a different MOA is selected
 - Paucity of data; however, hyponatremia recurred in 3 of 6 cases when suspected agent was restarted⁸
- Start low, go slow, and monitor serum Na⁺ closely⁴
- Consider long-term maintenance strategies if drug therapy with offending agent is necessary: fluid restriction (250–1000 mL/day), oral sodium chloride (6–82 mg/day) plus a loop diuretic, oral demeclocycline 300–900 mg/day, and/or lithium (last line agent)^{8,11}

Serotonin Reuptake Inhibitors and GI Bleeding

- Serotonin reuptake inhibitors (SRIs) have been associated with a 2x ↑ risk of GI bleed^{12,13,14}
 - Risk is approximately 4x higher in patients on SRI + NSAID and 2–3x higher in patients on SRI + aspirin^{4,12,13,14}
- Risk reduced to almost that of control group with addition of acid-suppressing agent (H2 blocker or PPI)¹²

Risk Factors for Bleeding with SRIs^{4,12}

History of GI bleed	Active peptic ulcer disease
Elderly	Liver disease
Drugs that ↑ risk of bleeding (e.g., warfarin, aspirin)	Surgical procedures
Drugs that cause GI injury (e.g., NSAIDs, steroids)	

Management Strategies

Consider switching to a non-serotonin reuptake inhibitor antidepressant if appropriate

- Risk of bleeding present for as long as the serotonin reuptake inhibitor is present¹²
- Mirtazapine and/or bupropion recommended in patients at risk for bleeding^{9,14}
- Nortriptyline and protriptyline may also be safe alternatives^{9,12,14}

Consider addition of acid-suppressing agents (PPI or H2 blocker) in patients at risk for GI bleed (see Risk Factors table above)^{12,14}

Serotonin Syndrome

Approximately 60% of patients with serotonin syndrome present within 6 hours after initial use of medication or change in dose¹⁵

Signs and Symptoms of Serotonin Syndrome ^{4,15}	
Neurologic	Confusion, Agitation, Ataxia, Akathisia
Neuromuscular	Clonus, Hyperreflexia, Tremor
Autonomic	Sweating, Nausea, Diarrhea, ↑ HR, ↑ BP, ↑ Temp

Medications Associated with Serotonin Syndrome ^{15,16}		
Most antidepressants	Linezolid	Metoclopramide
Lithium	Reserpine	Dextromethorphan
Valproate	Sibutramine	Ginseng
Triptans	Tramadol	St. John's Wort
Buspirone	Fentanyl	Tryptophan

Strategies for Prevention

- When augmenting use non-serotonergic agents if possible (e.g. bupropion)
- Patient education:
 1. Signs and symptoms of serotonin syndrome
 2. Over-the-counter agents may ↑ risk of serotonin syndrome (e.g., dextromethorphan, St. John's Wort)

Treatment After Serotonin Syndrome

If a serotonergic medication is required, restart only after symptoms of serotonin syndrome are no longer present

- o Use low doses and titrate slowly

Augmenting Agents in TRD

Lithium and Triiodothyronine (T3)

- Both lithium and triiodothyronine improve remission rates in patients with MDD when added to SSRIs, TCAs, and MAOIs¹⁷⁻²²

Medication	Initial Dose	Renal Adjustment	Target Dose	Target Level	Side Effects	Monitoring
Lithium	300–450 mg daily or divided BID	≤50 mL/ min requires ↓ dose	N/A	>0.5–1 mEq/L	GI upset, tremor, polyuria, polydipsia, weight gain, hypothyroidism, leukocytosis	EKG, CBC, TFTs, BMP, lithium level
Triiodothyronine (T3)*	25 mcg daily		50 mcg daily	N/A	Hyperthyroidism (anxiety, tremor, palpitations, insomnia, ↑ risk of osteoporosis and/or atrial arrhythmias)	TFTs

EKG = Electrocardiogram, CBC = Complete Blood Count, TFT = Thyroid Function Tests, BMP = Basic Metabolic Panel

Clinical Pearls – Lithium²³

ACE-Is, ARBs, thiazide diuretics, NSAIDs interactions	Can ↑ lithium level up to 4x
Pregnancy Category D	Avoid in 1st trimester due to risk of Ebstein's anomaly
Chronic therapy can result in nephrogenic diabetes insipidus	Usually reversible when lithium d/c
Adequate hydration needed to prevent fluctuations in lithium level	Recommend patients drink 2–3 L water/day

- Due to the ease of use and tolerability, triiodothyronine (T3) may be a more favorable option.

Augmenting Agents in TRD

Antipsychotics

- Antipsychotic augmentation in TRD has been shown to lead to symptom reduction within 1–2 weeks of starting therapy²⁴
 - Long-term use of atypical antipsychotics for TRD is not well supported

Medication	Target Dose	Common Side Effects	Monitoring
Risperidone	0.5–3 mg/day	Hypotension; Hyperprolactinaemia	<ul style="list-style-type: none"> • Assess for initial and continued response • Cardiometabolic monitoring • Monitor for movement disorders <ul style="list-style-type: none"> ◦ Tardive dyskinesia (AIMS) ◦ EPS • Screen for symptoms of hyperprolactinemia • Pregnancy test if applicable
Quetiapine	150–300 mg/day	Sedation; Cardiometabolic changes; Orthostatic hypotension	
Olanzapine + fluoxetine	6–18 mg/day + 25–50 mg/day	High risk weight gain; Cardiometabolic changes	
Aripiprazole	5–20 mg/day	Akathisia; Restlessness	

Buspirone

- Buspirone may be as effective as bupropion when used as an augmentation agent in depression and is considered to be relatively safe and well tolerated¹

Medication	Target Dose	Common Side Effects	Monitoring
Buspirone	40–60 mg/day divided BID-TID	Dizziness, nausea, headache, nervousness	<ul style="list-style-type: none"> • Hepatic impairment may result in a 13x ↑ in steady state AUC

Monoamine Oxidase Inhibitors

Monoamine oxidase inhibitors (MAO-Is) may be effective in patients who do not respond to treatment with other antidepressants

- Requirements for dietary restrictions, adverse effect profile, and propensity for drug interactions limit use¹

Non-Selective MAO Inhibitors*	Initial Dose (mg/day)	Dose Titration Increments (mg)	Dosage Range (mg)	Dosing Schedule
Phenelzine (Nardil)	30	15 per week	60-90	TID-QID
Tranlycypromine (Parnate)	30	10 every 1-3 weeks	30-60	BID
Isocarboxazid (Marplan)	20	10 every 2-3 days	40-60	BID-QID
MAO-B Selective Inhibitors				
Selegiline ⁺	6	3 every 2 weeks Increase above 6 mg may not be necessary	6-12	Every 24 hours

*Inhibit MAO-A & B; ⁺6 mg/day patch, ≤9 mg/day oral, ≤2.5 mg/day ODT

MAO-Is and Tyramine

Because MAO inhibition also occurs in the gut, ingestion of tyramine can cause a life-threatening hypertensive crisis.

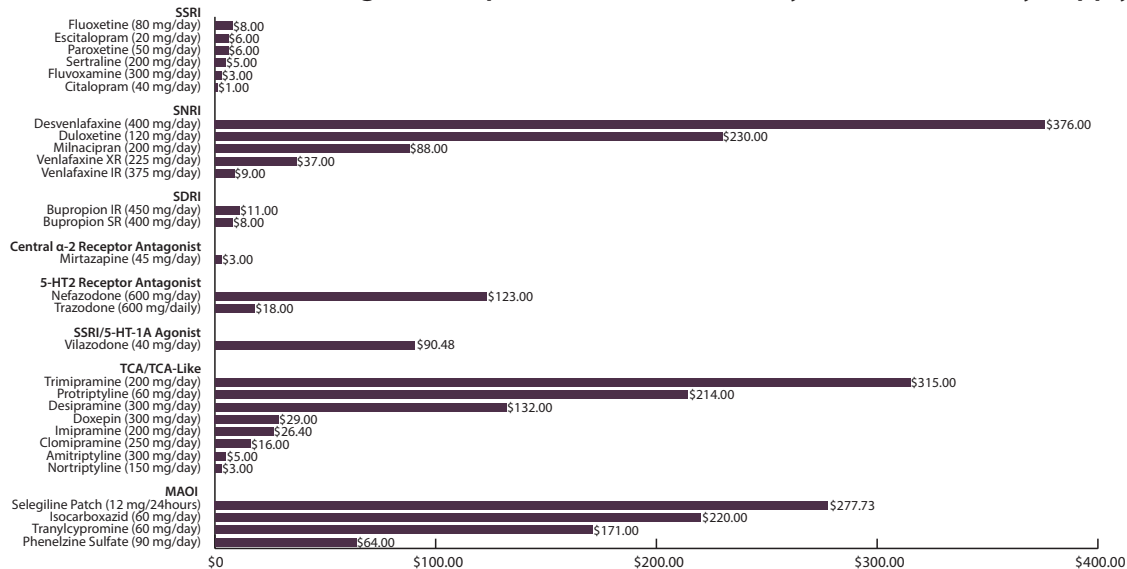
Selected Foods with High Tyramine Content²³

Tap beers Red wine	Smoked meat or fish	Soybeans
Aged cheese	Sauerkraut	Dried meats (eg. salami)

Selected MAO-I Mental Health Drug Interactions²³

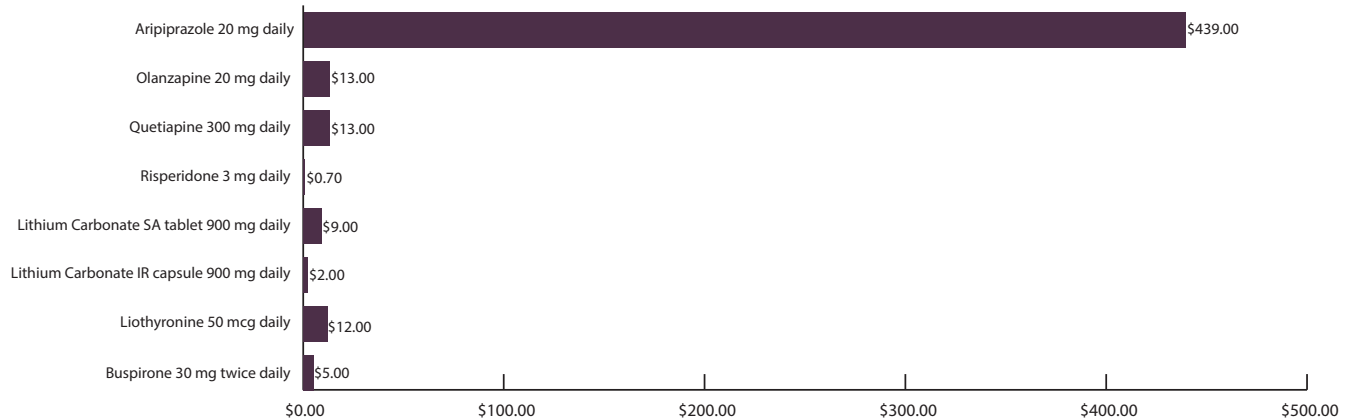
Amphetamines	↑ risk of HTN episode
Atomoxetine	↑ risk of HTN episode
Bupropion	↑ risk of neurotoxic effects
Serotonergic meds	↑ risk of serotonin syndrome

National Average Antidepressant Maximum Daily Dose Cost/30 Day Supply



Cost data is subject to change based on updated contracts, shortages, and transitions of drugs from brand to generic. The prices reported are based on VA pricing from August 2014.

National Average Augmentation Cost/30 day Supply



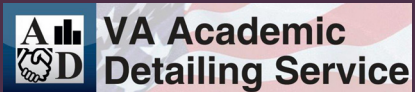
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References

1. Management of Major Depressive Disorder. Washington, DC: Office of Quality and Performance and the Veterans Affairs and Department of Defense Development Work Group, Veterans Health Administration, Department of Veterans Affairs; May 2009.
2. Taylor D, Paton C, Kapur S. (2010). The Maudsley Prescribing Guidelines. 10th ed. London, England: Informa Healthcare.
3. Poisindex® Managements. Thomson Micromedex. Greenwood Village, CO. <http://www.thomsonhc.com>. Accessed September 2, 2010.
4. Taylor D, Paton C, Kapur S. (2012). The Maudsley Prescribing Guidelines in Psychiatry, 11th ed. West Sussex, UK: Wiley–Blackwell.
5. Taylor MJ, et al. *J Affect Disord* 2005; 88:241–254.
6. Worsham J, et al. *JCPNP* 2007.
7. Liamis G, Milionis H, Elisaf M. A review of drug–induced hyponatremia. *Am J Kidney Dis* 2008; 52:144–53.
8. Jacob S, Spinler SA. Hyponatremia associated with selective serotonin–reuptake inhibitors in older adults. *Ann Pharmacother* 2006; 40:1618–22.
9. Perry PJ, et al. (1997). *Psychotropic Drug Handbook*, 8th ed. Baltimore, MD: Lippincott Williams & Wilkins.
10. Coupland C, et al. Antidepressant use and risk of adverse outcomes in older people: population based cohort study. *BMJ* 2011; 343:d4551.
11. Guay DRP. Hyponatremia associated with selective serotonin reuptake inhibitors. *Consult Pharm* 2000; 15:160–77.
12. Andrade C, Sandarsh S, Chethan KB, Nagesh KS. Serotonin reuptake inhibitor antidepressants and abnormal bleeding: a review for clinicians and a reconsideration of mechanisms. *J Clin Psychiatry* 2010; 71(12):1565–1575.
13. Dalton SO, et al. Use of selective serotonin reuptake inhibitors and risk of upper gastrointestinal tract bleeding. *Arch Intern Med* 2003; 163:59–64.

References

14. De Abajo FJ, Garcia-Rodríguez LA. Risk of upper gastrointestinal tract bleeding associated with selective serotonin reuptake inhibitors and venlafaxine therapy. *Arch Gen Psychiatry* 2008; 65(7):795–803.
15. Boyer EW, Shannon M. The Serotonin Syndrome. *N Engl J Med* 2005; 352:1112–20.
16. McAllen KJ, Schwartz DR. Adverse drug reactions resulting in hyperthermia in the intensive care unit. *Crit Care Med* 2010; 38:S244–52.
17. Bauer M, Dopfmer S. Lithium augmentation in treatment-resistant depression: meta-analysis of placebo-controlled studies. *J Clin Psychopharmacol* 1999; 19:427–434.
18. Joffe RT, Singer W, Levitt AJ et al. A placebo-controlled comparison of lithium and triiodothyronine augmentation of tricyclic antidepressants in unipolar Refractory Depression. *Arch Gen Psychiatry* 1993; 50:387–393.
19. Nierenberg AA, Fava M, Trivedi MH, et al. A Comparison of Lithium and T3 Augmentation Following Two Failed Medication Treatments for Depression: A STAR*D Report. *Am J Psychiatry* 2006; 163:1519–1530.
20. Lojko D, Rybakowski JK. L-thyroxine augmentation of serotonergic antidepressants in female patients with refractory depression. *Journal of Affective Disorders* 2007; 103:253–256.
21. Thase ME, Kupfer DJ, Jarrett DB. Treatment of imipramine-resistant recurrent depression: an open clinical trial of adjunctive L-triiodothyronine. *J Clin Psychiatry* 1989; 50:385–388.
22. Abraham G, Milev R, Lawson JS. T3 augmentation of SSRI resistant depression. *Journal of Affective Disorders* 2006; 91:211–215.
23. Fuller MA, Sajatovic M. (Eds). *Drug Information Handbook for Psychiatry* (7th ed.). Hudson, OH: Lexi-Comp.
24. Chen J. et al. Second-generation antipsychotics in major depressive disorder: update and clinical perspective. *Curr Opin Psychiatry* 2011; 24:10–17.



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This reference guide was created to be used as a tool available for VA facilities to use from SharePoint. These are general recommendations only; specific clinical decisions should be made by the treating physician based on an individual patient's clinical condition.

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