

Pharmacologic Treatment of Depression

General Principles of Pharmacotherapy

- No agent has been proven to be superior to another in efficacy or time to response.
- Use what has worked for the patient in the past.
- The most common cause of treatment failure is an inadequate medication trial.
- If no response at 4-6 weeks, consider switching, combining or augmenting the pharmacotherapy.
- SSRIs are agents of first choice due to ease of use, more tolerable side effects and safety in overdose.
- Counsel pregnant women and those considering pregnancy. The potential risks and benefits of pharmacotherapy must be weighed.

Managing Medication Side Effects

- Insomnia - Consider Diphenhydramine at HS or a brief trial of a short-acting non-addictive BZ receptor-binding agent, then reassess.
- Akathisia - Associated with newer antidepressants. Consider adding a small dose of clonazepam (0.5 mg q HS) or propranolol (10-20 mg bid/tid).
- Sexual dysfunction - Common with all SSRIs and others. Bupropion is least likely to produce this side effect.

Strategies for Refractory Depression

- If partial response to one antidepressant, can add tri-iodothyronine (T3), 25-50 micrograms in one daily dose. Baseline T4 or TSH are not

predictive of response but useful to monitor TSH suppression during T3 therapy.

- Lithium carbonate, 600-900 mg daily can be added to the existing medication with serum lithium levels monitored
- Trazodone, 50 to 100 mg at night may improve sleep, particularly in conjunction with an SSRI.
- Bupropion may be used with SSRIs, especially for fatigue or sexual dysfunction.
- Anticonvulsants (e.g. carbamazepine) may be added to antidepressants, especially with multiple depressive episodes in one year or prominent impulsivity, irritability or anxiety.
- Change of antidepressant class.
- ECT may be used but should be followed by maintenance treatment with antidepressant or ECT.

Medications That Can Cause Depression

Evidence

QE	SR	Drug/Drug Class
I	B	Amphetamine withdrawal, Anabolic Steroids, Digitalis, Glucocorticoids
I	C	Cocaine withdrawal
II-1	C	Reserpine
II-2	A	Gonadotropin-releasing agonists, Pimozide
II-2	B	Propranolol (Beta Blockers)
II-2	C	ACE inhibitors, Antihyperlipidemics, Benzodiazepines, Cimetidine, Ranitidine, Clonidine, Cycloserine, Interferons, Levodopa, Methylodopa, Metoclopramide, Oral contraceptives, Topiramate, Verapamil (Calcium channel Blockers)

VA/DoD Clinical Practice Guideline for Management of Major Depressive Disorder in Adults: Inpatient

POCKET GUIDE

Evaluate & treat/stabilize emergency condition

Suicidal risk, violent behavior, unstable medical condition, comorbid substance abuse



Conduct comprehensive evaluation

Hx, MSE, PE, laboratory
Meets criteria for inpatient admission?
DSM-IV diagnosis of depression



Initiate treatment for depression

Antidepressant Tx in adequate dose & duration
(SSRI first line medication)
ECT if primary indication present (psychotic feature, catatonic stupor, severe suicidality, other)



Evaluate treatment for depression

Reevaluate daily. If sub-optimal response, consider additional strategy for refractory depression Tx. Change antidepressant class, T3, Li, Co3, trazodone, bupropion, anticonvulsant, ECT.
If depressive symptoms have responded to initial Tx, evaluate for step down to less restrictive environment (stabilization/improvement of symptoms; level of function adequate to less restrictive setting; no acute manifestation of intent to harm self or others; support level allows active participation in aftercare)



If discharge criteria met, ensure appropriate level & continuity of aftercare & discharge to appropriate setting

VA access to full guidelines: <http://www.oqp.med.va.gov/cpg/cpg.htm>

DoD access to full guidelines: <http://www.cs.amedd.army.mil/Qmo>

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Medical Conditions Related to Depression

Pathology	Disease
Cardio/vascular	Coronary artery disease, Congestive heart failure, Uncontrolled hypertension, Anemia, Stroke, Vascular Dementias
Chronic Pain Syndrome	Fibromyalgia, Reflex sympathetic dystrophy, Low back pain (LBP), Chronic pelvic pain, Bone or disease related pain
Degenerative	Presbyopia, Presbycusis, Alzheimer's disease, Parkinson's disease, Huntington's disease, Other Neurodegenerative diseases
Immune	HIV (both primary and infection-related), Multiple Sclerosis, Systemic Lupus Erythematosus (SLE), Sarcoidosis
Infection	Systemic Inflammatory Response Syndrome (SIRS), Meningitis
Metabolic/Endocrine Conditions (include renal and pulmonary)	Malnutrition, Vitamin deficiencies, Hypo/Hyperthyroidism, Addison's Disease, Diabetes Mellitus, Hepatic disease (cirrhosis), Electrolyte disturbances, Acidbase disturbances, Chronic Obstructive Pulmonary Disease (COPD) or Asthma, Hypoxia
Neoplasm	Of any kind, especially pancreatic or central nervous system (CNS)

ANTIDEPRESSANT MEDICATION TABLE – Refer to pharmaceutical manufacturer's literature for full prescribing information

SEROTONIN SELECTIVE REUPTAKE INHIBITORS (SSRIs)								
GENERIC	BRAND NAME	ADULT STARTING DOSE	MAX	EXCEPTION	SAFETY MARGIN	TOLERABILITY	EFFICACY	SIMPLICITY
Citalopram	Celexa	20 mg	60 mg	Reduce dose for the elderly & those with renal or hepatic failure	No serious systemic toxicity even after substantial overdose. Drug interactions may include tricyclic antidepressants, carbamazepine & warfarin.	Nausea, insomnia, sedation, headache, fatigue, dizziness, sexual dysfunction, anorexia, weight loss, sweating, GI distress, tremor, restlessness, agitation, anxiety.	Response rate = 2 - 4 wks	AM daily dosing. Can be started at an effective dose immediately.
Fluoxetine	Prozac	20 mg	80 mg					
Paroxetine	Paxil	20 mg	50 mg					
Sertraline	Zoloft	50 mg	200 mg					
<p style="text-align: center;">First Line Antidepressant Medication</p> <p>Drugs of this class differ substantially in safety, tolerability and simplicity when used in patients on other medications. Can work in TCA nonresponders. Useful in several anxiety disorders. Taper gradually when discontinuing these medications. Fluoxetine has the longer half-life.</p>								
SEROTONIN and NOREPINEPHRINE REUPTAKE INHIBITORS (SSRIs)								
GENERIC	BRAND NAME	ADULT STARTING DOSE	MAX	EXCEPTION	SAFETY MARGIN	TOLERABILITY	EFFICACY	SIMPLICITY
Venlafaxine IR	Effexor IR	75 mg	375 mg	Information Not Available	No serious systemic toxicity. Downtaper slowly to prevent clinically significant withdrawal syndrome. Few drug interactions.	Comparable to SSRIs at low dose. Nausea, dry mouth, insomnia, somnolence, dizziness, anxiety, abnormal ejaculation, head-ache, asthenia, sweating.	Response rate = 2 - 4 wks (4 - 7 days at ~ 300 mg/day)	BID or TID dosing with IR. Daily dosing with XR. Can be started at an effective dose (75 mg) immediately.
Venlafaxine XR	Effexor XR	75 mg	375 mg					
<p>Dual action drug that predominantly acts like a Serotonin Selective Reuptake inhibitor at low doses and adds the effect of an Norepinephrine Selective Reuptake Inhibitor at high doses. Possible efficacy in cases not responsive to TCAs or SSRIs. Taper dose prior to discontinuation.</p>								
SEROTONIN (5-H2A) RECEPTOR ANTAGONIST and WEAK SEROTONIN REUPTAKE INHIBITORS								
GENERIC	BRAND NAME	ADULT STARTING DOSE	MAX	EXCEPTION	SAFETY MARGIN	TOLERABILITY	EFFICACY	SIMPLICITY
Nefazodone	Serzone	200 mg	600 mg	Reduce dose for the elderly & those with renal or hepatic failure	No serious systemic toxicity from OD. Can interact with agents that decrease arousal/impair cognitive performance and interact with adrenergic agents that regulate blood pressure.	Somnolence, dizziness, fatigue, dry mouth, nausea, headache, constipation, impaired vision. Unlikely to cause sexual dysfunction.	Response rate = 2 - 4 wks	BID dosing. Requires dose titration.
Trazodone	Desyrel	150 mg	600 mg					
<p>Corrects sleep disturbance and reduces anxiety in about one week.</p>								
DOPAMINE and NOREPINEPHRINE REUPTAKE INHIBITORS (DNRIs)								
GENERIC	BRAND NAME	ADULT STARTING DOSE	MAX	EXCEPTION	SAFETY MARGIN	TOLERABILITY	EFFICACY	SIMPLICITY
Bupropion - IR	Wellbutrin - IR	200 mg	450 mg	Reduce dose for the elderly & those with renal or hepatic failure	Seizure risk at doses higher than max. Drug/drug interactions uncommon.	Rarely causes sexual dysfunction.	Response rate = 2 - 4 wks	BID/TID dosing. Requires dose titration.
Bupropion - SR	Wellbutrin - SR	150 mg	400 mg					
<p>Least likely antidepressant to result in a pt becoming manic. Do not use if there is a history of seizure disorder, head trauma, bulimia or anorexia. Can work in TCA nonresponders.</p>								
TRICYCLIC ANTIDEPRESSANTS (TCAs) – Mainly Serotonin Reuptake Inhibitors								
GENERIC	BRAND NAME	ADULT STARTING DOSE	MAX	EXCEPTION	SAFETY MARGIN	TOLERABILITY	EFFICACY	SIMPLICITY
Amitriptyline *	Elavil, Endep *	50 - 100 mg	300 mg	Reduce dose for those with renal or hepatic failure	Serious toxicity can result from OD. Slow system clearance. Can cause multiple drug/drug interactions.	Sedation, increased anticholinergic effects, orthostatic hypotension, cardiac conduction disturbances, arrhythmia & wt gain, dizziness, sexual dysfunction.	Response rate = 2 - 4 wks Therapeutic Levels: Imipramine 200-350 ng/ml	Can be given QD. Monitor serum level after one week of treatment
Imipramine *	Tofranil *	75 mg	300 mg					
Doxepin *	Sinequan *	75 mg	300 mg					
<p>These antidepressants are not recommended for use in the elderly. Highest response rates. TATCAs useful in chronic pain, migraine headaches & insomnia. * Tertiary Amine Tricyclic Antidepressants (TATCAs).</p>								
TRICYCLE ANTIDEPRESSANTS (TCAs) – Mainly Norepinephrine Reuptake Inhibitors								
GENERIC	BRAND NAME	ADULT STARTING DOSE	MAX	EXCEPTION	SAFETY MARGIN	TOLERABILITY	EFFICACY	SIMPLICITY
Desipramine *	Norpramin *	75 - 200 mg	300 mg	Reduce dose for the elderly & those with renal or hepatic failure	Serious toxicity can result from OD. Reserve Maprotiline as a second-line agent due to risk of seizures at therapeutic & nontherapeutic doses.	Generally Good	Response rate = 2 - 4 wks Therapeutic Levels: Desipramine 125-300 ng/mL Nortriptyline 50-150 ng/mL	Can be given QD. Can start effective dose immediately. Monitor serum level after one week of treatment.
Nortriptyline *	Aventyl/Pamelor	50 mg	150 mg					
<p>Consider Desipramine or Nortriptyline first in the elderly if TCAs are necessary. * Secondary Amine Tricyclic Antidepressants (SATCAs)</p>								