Medications for Depression

Antidepressants alter the concentrations of one or more key neurotransmitters in the brain, namely norepinephrine, serotonin, and dopamine. As depression may be a presenting symptom of a mixed manic episode, it is important to adequately screen patients with depressive symptoms to determine if they are at risk of bipolar disorder. All patients should also be monitored with regards to mental status for depression, suicidal ideation, anxiety, social functioning, mania, panic attacks, or other unusual changes in behavior. All antidepressants carry a black box warning of increased risk of suicidal thinking and behavior in children and adolescents, particularly in the first few months of therapy. MAOIs are contraindicated with all other classes of antidepressants and should not be used in combination. Common side effects often improve within the first two weeks of treatment. A low starting dose might help increase tolerance and adherence.

DRUG CATEGORY	MEDICATION	COMMON SIDE EFFECTS	MONITORING PARAMETERS	ADDITIONAL COMMENTS
Selective Serotonin Reuptake Inhibitors (SSRIs)	▪Citalopram (IR, Liq)* ▪Escitalopram (IR, Liq) ▪Fluoxetine (IR, Liq) ▪Fluvoxamine† (IR, ER) ▪Paroxetine (IR, ER, Liq) ▪Sertraline (IR, Liq)	▪**GI:** effects are common (nausea, xerostomia, diarrhea) ▪**Sexual dysfunction:** in both men & women ▪**Hematologic:** Impaired platelet aggregation/bleeding ▪**CNS:** drowsiness, headache ▪**Cardiovascular:** QT interval prolongation, specifically in ▪citalopram, escitalopram, fluoxetine, and sertraline	▪Weight and BMI ▪Signs/symptoms of serotonin syndrome ▪Electrolytes, especially in older patients, due to potential for hyponatremia ▪ECG in patients at increased risk for QT interval prolongation	▪Comparable to TCAs in efficacy, but are markedly safer and better tolerated ▪SSRIs differ from each other with respect to their degree of selectivity for the serotonin transporter, but share most indications, and are comparable in efficacy ▪Fluoxetine has the longest half-life, paroxetine has the shortest half-life ▪Paroxetine is pregnancy category D ▪Select SSRIs are approved for treating anxiety disorders including: OCD, PTSD, GAD, panic disorder, and social anxiety disorder ▪Select SSRIs may be used for PMDD, hot flashes, and premature ejaculation
Serotonin and Norepinephrine Reuptake Inhibitors (SNRIs)	▪Desvenlafaxine (ER) ▪Duloxetine (IR) ▪Levomilnacipran (ER) ▪Venlafaxine (IR, ER)	▪**GI**: effects are common. Nausea is the most common, then xerostomia, diarrhea, constipation, and vomiting ▪**Sexual dysfunction**: more so in men ▪**Hematologic:** Impaired platelet aggregation/bleeding ▪**CNS:** drowsiness, headache ▪**Cardiovascular:** elevated blood pressure (notably venlafaxine, but all SNRIs have been associated with this) ▪**Dermatologic:** hyperhidrosis ▪**Hepatic:** increased LFTs	▪Weight and BMI ▪Blood pressure ▪Signs/symptoms of serotonin syndrome ▪Electrolytes, especially in older patients, due to potential for hyponatremia serum cholesterol in venlafaxine/desvenlafaxine	▪SNRIs appear to provide similar response rates to SSRIs in the treatment of MDD ▪Like TCAs, which also have combined serotonin and norepinephrine activity, SNRIs are useful in the treatment of chronic pain ▪Duloxetine should not be used in patients with hepatic impairment or risk factors for hepatic impairment ▪Duloxetine has proven efficacy and safety in the treatment of fibromyalgia, and is also indicated for diabetic neuropathy, GAD, musculoskeletal pain, and osteoarthritis ▪Venlafaxine is additionally indicated for GAD, panic disorder, and social phobia
Norepinephrine/ Dopamine Reuptake Inhibitor (NDRI)	▪Bupropion (IR, ER)	▪**GI:** nausea, constipation, xerostomia ▪**CNS:** agitation, anxiety, headache, insomnia ▪**Cardiovascular:** tachycardia ▪**Endocrine:** weight loss ▪**Dermatologic:** hyperhidrosis	▪Weight and BMI ▪Heart rate and blood pressure	▪Contraindicated in history of seizures, bulimia, and/or anorexia ▪Also indicated for seasonal affective disorder (SAD) and tobacco cessation ▪Used off-label for multiple neurological/psychological uses, including ADHD and neuropathic pain
Tricyclic Antidepressants (TCAs)	▪Amitriptyline (IR) ▪Amoxapine (IR) ▪Clomipramine†(IR) ▪Desipramine (IR) ▪Doxepin (IR, Liq) ▪Imipramine (IR) ▪Maprotiline‡ (IR, liq) ▪Nortriptyline (IR, liq) ▪Protriptyline (IR) ▪Trimipramine (IR)	▪**Anticholinergic:** are the most common (xerostomia, constipation, urinary hesitancy, blurred vision) ▪**Sexual dysfunction** ▪**CNS:** sedation, drowsiness ▪**Cardiovascular:** orthostatic hypotension (most often with amitriptyline), ECG changes ▪**Endocrine:** weight gain ▪**Ocular:** increase in ocular pressure	▪Weight and BMI ▪Signs/symptoms of serotonin syndrome ▪Blood pressure, ECG, heart rate ▪LFTs ▪Blood levels are useful for therapeutic monitoring for select TCAs	▪Generally second-line agents for MDD because of their inferior safety and tolerability profile compared with SSRIs, SNRIs, and bupropion ▪TCAs are first-line agents for several types of neuropathic pain ▪TCAs have a wide range of indications, including MDD, dysthymic disorder, neuropathic pain, and migraine or tension-type headache. ▪Lowering of seizure threshold is a rare complication of TCA therapy ▪TCAs are potentially fatal in overdose, and are second only to analgesics in terms of the number of fatalities associated with overdose
Tetracyclic Antidepressants	▪Mirtazapine (IR, ODT)	▪**GI:** constipation, xerostomia ▪**Hematologic:** severe neutropenia ▪**CNS:** drowsiness (most common side effect), dizziness ▪**Endocrine:** weight gain, appetite stimulation ▪**Lipids:** hypercholesterolemia	▪Weight and BMI ▪Signs/symptoms of serotonin syndrome ▪LFTs ▪CBC with differential ▪Renal function	▪Possesses an anxiolytic effect that may be useful in depressed adult patients who have a coexisting anxiety disorder. It has also been shown to improve sleep patterns ▪Women have a longer elimination half-life (37 hours) than men (26 hours) ▪Clearance is reduced in hepatic dysfunction, renal dysfunction, and in elderly
Monoamine Oxidase Inhibitors (MAOIs)	▪Isocarboxazid (IR) ▪Phenelzine (IR) ▪Selegiline Transdermal[i] ▪Tranylcypromine (IR)	▪**Sexual dysfunction** ▪**CNS:** dizziness, sleep disturbances/insomnia; may aggravate anxiety and agitation (Tranylcypromine and isocarboxazid) ▪**Cardiovascular:** fluctuations in blood pressure, hypertensive crisis, orthostatic hypotension ▪**Endocrine:** weight gain	▪Weight and BMI ▪Blood pressure, heart rate ▪LFTs ▪Renal function ▪Use tranylcypromine and isocarboxazid cautiously in hyperthyroid patients	▪Rarely first line agents due to adverse effects, dietary restrictions and interactions ▪Used primarily for atypical depression or MDD that is refractory to treatment with other antidepressants ▪Patients must avoid foods with high tyramine, dopamine, or tryptophan content ▪Not to be used concomitantly with other antidepressants, must be spaced 14 days apart
Mixed Serotonergic Agents	▪Nefazodone (IR) ▪Trazodone (IR, ER) ▪Vortioxetine (IR) ▪Vilazodone (IR)	▪Nefazodone/trazodone: headache, drowsiness, dizziness, insomnia, xerostomia, nausea, constipation, and orthostatic hypotension Vortioxetine: sexual dysfunction, diarrhea, and nausea ▪Vilazodone: diarrhea, nausea	▪Weight and BMI ▪Signs/symptoms of serotonin syndrome ▪LFTs (nefazodone in particular as it has a black box warning for hepatotoxicity)	▪Trazodone is also used in the treatment of GAD and insomnia ▪Nefazodone is structurally similar to trazodone; however it causes less sedation. It is as effective as other antidepressants, but lacks the risk of cardiovascular toxicity. ▪Vortioxetine is the only drug with a combination of reuptake inhibition at the 5-HT transporter and agonist, partial agonist, or antagonist effects at serotonin receptors ▪Vilazodone enhances serotonergic activity via a novel dual mechanism

†only FDA indicated for OCD; off-label, recommended for use depression; ‡Maprotiline is a tetracyclic antidepressant, but has a very similar clinical profile as the TCAs; i = only the transdermal formulation of selegiline is FDA indicated for depression

***Dosage Forms Available**: IR = Immediate Release Oral Formulation, ER= Extended Release Oral Formulation, Liq= Oral Liquid, ODT= Orally Disintegrating Tablet

Facts and Comparisons [database online]. St. Louis, MO: Wolters Kluwer Health, Inc; 2017. Accessed May 8, 2019
Clinical Pharmacology powered by ClinicalKey. Tampa (FL): Elsevier. c2018- [cited 2019 May 8]. Available from: http://www.clinicalkey.com