MDD Treatment: A List of Medications Commonly Prescribed for Depression

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Major depressive disorder (MDD) is a mood disorder characterized by persistent low mood, loss of interest in activities one previously enjoyed, and feelings of hopelessness.[1] In addition to nonpharmacological interventions such as psychotherapy, clinical guidelines typically recommend treatment with antidepressant medications. A depression medication list of commonly prescribed MDD treatments will include selective serotonin reuptake inhibitors (SSRIs), serotonin-norepinephrine reuptake inhibitors (SNRIs), and tricyclic antidepressants (TCAs).

Serotonin-norepinephrine reuptake inhibitors are typically first-line medications due to their high efficacy and lower risk for adverse effects compared with other antidepressants, while SNRIs are generally used for patients whose depression does not improve with SSRIs.[2] As an older class of antidepressants, TCAs are used less often than SSRIs and SNRIs but may be a good option for patients with certain comorbidities.

This article describes the mechanism of action, indications/contraindications, dosages, and adverse effects of the SSRIs, SNRIs, and TCAs most commonly prescribed for treating MDD. Many of these medications are also Food and Drug Administration (FDA)-approved for the treatment of other conditions, but this review focuses only on their use for MDD.

Selective Serotonin Reuptake Inhibitors for Major Depressive Disorder

Researchers believe that the neurotransmitters serotonin (5-hydroxytryptamine; 5-HT) and norepinephrine (NE) are central to the regulation of mood.[2] By binding to 5-HT transporters, SSRIs inhibit the reuptake of serotonin, thereby increasing the concentration of serotonin in the extracellular space. This increases the activity of the 5-HT receptor and enhances the postsynaptic response. Researchers believe that at low doses SSRIs bind primarily to 5-HT transporters but at higher doses these medications also bind to NE transporters.[2]

The SSRIs most commonly prescribed for MDD are fluoxetine, sertraline, paroxetine, citalopram, and escitalopram (Table 1[3-8]).

Table 1. Selective Serotonin Reuptake Inhibitors for Major Depressive Disorder

Medication	Dosages	Warnings/Adverse Effects
Fluoxetine	20 mg/d to 80 mg/d	Serious: Serotonin syndrome, abnormal bleeding, mania/hypomania, rash, seizures, QT prolongation, hyponatremia, angle closure glaucoma Common: Nausea, diarrhea, dry mouth, decreased appetite, somnolence, insomnia, nervousness, anxiety, sexual dysfunction
Sertraline	50 mg/d to 200 mg/d	
Paroxetine	20 mg/d to 50 mg/d	
Citalopram	20 mg/d to 40 mg/d	
Escitalopram	10 mg/d to 20 mg/d	

Fluoxetine

Fluoxetine is FDA-approved for acute and maintenance treatment of MDD in patients aged 8 to 18 years.[3] It also is approved for use in combination with olanzapine in adult patients with treatment-resistance depression (depression that does not respond to 2 distinct trials of different antidepressants of adequate dose and duration).[4]

For adults, the recommended initial dosage of fluoxetine is 20 mg/d administered in the morning.[3] If the patient's symptoms do not respond to 20 mg/d, the dose can be increased up to 80 mg/d as need. Dosages greater than 20 mg/d can be administered once a day, or twice a day in divided doses.[3]

Lower or less frequent fluoxetine dosing should be considered for patients aged 65 and older, individuals with hepatic impairment, and patients with comorbid illnesses or who are taking multiple concomitant medications.[3]

The use of fluoxetine is contraindicated with concurrent use of the following medications[3]:

- Monoamine oxidase inhibitors (MOAIs; risk for serotonin syndrome);
- Thioridazine (risk for QT prolongation or elevated plasma thioridazine concentrations); and
- Pimozide (risk for QT prolongation and drug interaction).

In addition, fluoxetine should not be used within 14 days of stopping an MAOI.[3]

Sertraline

Sertraline is FDA-approved for the management of MDD in adults. The recommended initial dosage is 50 mg/d. If the patient's response to 50 mg/d is not adequate, the dosage can be increased once a week in increments of 25 mg/d to 50 mg/d, up to a maximum of 200 mg/d.[5]

For patients with mild hepatic impairment, the recommended initial dosage of sertraline is 25 mg/d and the recommended maximum dosage is 100 mg/d.[5] Sertraline is not recommended for patients with moderate or severe hepatic impairment.

Sertraline is contraindicated in patients taking pimozide or MAOIs, and within 14 days of stopping an MAOI.[5] Because the oral solution of sertraline contains alcohol, the use of this formulation is contraindicated in patients taking disulfiram because the combination may result in a disulfiram-alcohol reaction.[5]

Paroxetine

Paroxetine is FDA-approved for the treatment of MDD in adults. It should be administered once daily in the morning, with or without food. The recommended initial dose is 20 mg/d. For patients who do not respond to 20 mg/d, the dose may be increased once a week in 10 mg/d increments, up to a maximum of 50 mg/d.[6] For older adults and patients with severe renal or hepatic impairment, the recommended initial dosage is 10 mg/d and the maximum dosage is 40 mg/d.[6]

The use of paroxetine is contraindicated in patients taking pimozide or thioridazine, and in those taking or within 14 days of stopping an MAOI.[6]

Citalopram

Citalopram is FDA-approved for MDD in adults. The recommended initial dosage is 20 mg/d, which can be titrated in 20-mg increments as needed up to 40 mg/d.[7] For older patients (aged >60 years), individuals with hepatic impairment, and CYP2C19 poor metabolizers, the recommended maximum dosage is 20 mg/d.[7]

Citalopram is contraindicated in patients taking pimozide or an MAOI, as well as within 14 days of discontinuing an MAOI.[7]

Escitalopram

Escitalopram is FDA-approved for the acute and maintenance management of MDD in adults and adolescents aged 12 to 17. The recommended initial dosage is 10 mg/d with or without food.[8] The maximum dosage is 20 mg/d, and the dosage should only

be increased to that point after a minimum of 3 weeks in adolescents or 1 week in adults.[8]

The recommended dosage for older patients and patients with hepatic impairment is 10 mg/d. No dosage adjustment is required for patients with mild or moderate renal impairment, but escitalopram should be used with caution in patients with severe renal impairment.[8]

Escitalopram should not be prescribed to patients taking pimozide or an MAOI, or within 14 days of discontinuing an MAOI.[8]

SNRIs for Major Depressive Disorder

Selective serotonin norepinephrine reuptake inhibitors (SNRI) are generally a second-line therapeutic option for patients with MDD who don't respond or only partially respond to SSRIs.[2] The SNRIs most commonly used treat MDD are venlafaxine, its active metabolite desvenlafaxine, and duloxetine (Table 2[9-11]). Venlafaxine and desvenlafaxine inhibit the 5-HT reuptake transporter and the NE reuptake transporter in a dose-dependent manner. At low doses they act as SSRIs but at higher concentrations they increase extracellular NE levels. Duloxetine also inhibits 5-HT and NE reuptake.[2]

Table 2. Serotonin-Norepinephrine Reuptake Inhibitors for Major Depressive Disorder

Medication	Dosages	Adverse effects
Venlafaxine	75 mg/d to 225 mg/d	Serious: Serotonin syndrome, elevated blood pressure, increased risk of bleeding, mania/hypomania, rash, seizures, QT prolongation, hyponatremia, angle closure glaucoma, interstitial lung disease and eosinophilic pneumonia For duloxetine: hepatotoxicity Common: Nausea, dry mouth, sweating, decreased appetite, dizziness, constipation, somnolence, insomnia, nervousness, anxiety, sexual dysfunction
Desvenlafaxine	50 mg/d	
Duloxetine	40 mg/d to 120 mg/d	

Venlafaxine

Venlafaxine is available as an immediate-release or an extended-release (XR) formulation.[9] It is FDA-approved for the treatment of MDD in adults.

Venlafaxine XR should be administered once a day with food in the morning or evening at approximately the same time. Each capsule should be swallowed whole and not divided, crushed, or chewed.[9] Venlafaxine XR also can be taken by sprinkling the contents of the capsule on a spoonful of applesauce, swallowing it without chewing, and immediately drinking a glass of water. The recommended initial dosage is 75 mg/d. Alternately, it can be started at 37.5 mg/d for 4 to 7 days to allow the patient to adjust to the medication before increasing the dosage to 75 mg/d. In patients who do not achieve a sufficient response from 75 mg/d, the dosage can be increased to a maximum of 225 mg/d. The dosage can be increased in increments of up to 75 mg/d but not more often than once every 4 days.[9]

The total daily dose should be reduced by 50% in patients with mild to moderate hepatic impairment and by at least 50% in individuals with severe hepatic impairment or cirrhosis.[9] The total daily dose should be reduced by 25% to 50% in patients with mild to moderate renal impairment and by at least 50% in those with severe renal impairment or those who are undergoing hemodialysis. When discontinuing treatment, the dosage of venlafaxine should be reduced gradually by 75 mg/d not more often than once a week.[9]

Venlafaxine is contraindicated in patients taking an MAOI, or within 14 days of stopping an MAOI.[9]

Desvenlafaxine

Desvenlafaxine is available as an extended-release formulation.[10] It is FDA-approved for the treatment of MDD in adults. The recommended initial and therapeutic dosage is 50 mg once a day at approximately the same time with or without food. In clinical trials no additional benefits were observed with dosages greater than 50 mg/d.[10] The tablet must be swallowed whole and not divided, crushed, chewed, or dissolved.[10]

No dose adjustment is required in patients with mild to moderate renal impairment, but patients with severe renal impairment or end-stage renal disease (ESRD) should receive 50 mg every other day. The doses of desvenlafaxine should not be escalated in patients with moderate or severe renal impairment or ESRD. For older patients, the possibility of reduced renal clearance of desvenlafaxine should be considered. In patients with hepatic impairment dose escalation above 100 mg/day is not recommended.[10]

Desvenlafaxine is contraindicated in in patients taking an MAOI, or within 14 days of stopping an MAOI.[10]

Duloxetine

Available as an extended-release formulation, duloxetine is FDA-approved for the treatment of MDD in adults.[11] The recommended starting dosages and target dosages for acute treatment are 40 mg/d (given as 20 mg twice daily) to 60 mg/d (given once daily or as 30 mg twice daily). In this case, duloxetine should be administered at a total dose of 60 mg once daily.[11] For maintenance treatment, the recommended dosage is 60 mg/d. The maximum recommended dosage is 120 mg/d.

Duloxetine should not be administered to patients with chronic liver disease or cirrhosis and is not recommended for patients with severe renal impairment.[11]

Duloxetine is contraindicated in patients taking an MAOI and within 14 days of stopping an MAOI.[11]

Tricyclic Antidepressants for Treat Major Depressive Disorder

Tricyclic antidepressants are an older class of medications that work by inhibiting 5-HT and NE reuptake transporters, thereby blocking the reuptake of 5-HT and NE from the extracellular space.[2] Commonly used TCAs include imipramine, amitriptyline, nortriptyline, protriptyline, desipramine, and clomipramine. Compared to other classes of antidepressants, TCAs have a broader adverse effects profile because they are able to bind to channels and receptors in addition to their therapeutic targets.[2] Although TCAs generally have more adverse effects than newer antidepressants, they are useful for treating pain and may be a preferred option for patients with MDD and pain syndromes such as migraine headaches, neuropathic pain, somatic pain disorders, and chronic fatigue syndrome.[2,12]

Adverse Effectives and Drug Interactions

Increased suicidality and discontinuation syndrome are potential adverse effects of many classes of antidepressants, including SSRIs, SNRIs, and TCAs. The FDA requires all antidepressants to include in their labeling a black-box warning about the increased the risk of suicidal ideation and behavior in children, adolescents, and young adults. All patients being treated with antidepressants should be evaluated for suicidal thoughts

and behaviors, especially during the first few months of treatment and during dosage changes.[3-11]

Discontinuation syndrome is associated with the abrupt withdrawal of SSRIs, SNRIs, and TCAs. This condition is characterized by irritability, agitation, dizziness, sensory disturbances, anxiety, confusion, headache, lethargy, emotional lability, insomnia, hypomania, and gastrointestinal flu-like symptoms.[3-11] When an antidepressant needs to be discontinued, a gradual tapering regimen is recommended to avoid triggering this syndrome.

Adverse Effects of SSRIs and SNRIs

The adverse effects associated with SSRIs and SNRIs are summarized in Table 1[3-8] and Table 2,[9-11] respectively. Both classes can disrupt sexual function, often decreasing libido.[3-11] Gastrointestinal distress, including nausea, diarrhea, dry mouth, and decreased appetite, is common. The use SSRIs and SNRIs increases the risk of serotonin syndrome, a rare but serious increase in 5-HT levels that can cause the following[3-11]:

- Mental status changes (agitation, hallucinations, delirium, and coma);
- Autonomic instability (tachycardia, labile blood pressure, dizziness, diaphoresis, flushing, hyperthermia);
- Neuromuscular symptoms (tremor, rigidity, myoclonus, hyperreflexia, incoordination);
- Seizures; and/or
- Gastrointestinal symptoms (nausea, vomiting, diarrhea).

The risk of serotonin syndrome is increased not only when an SSRI or SNRI is used with other serotonergic agents (such as triptans, TCAs, fentanyl, lithium, tramadol, tryptophan, buspirone, amphetamines and St. John's Wort) or drugs that impair serotonin metabolism (such as an MAOI), but also when used alone.[3-11]

The use of SSRIs and SNRIs in the third trimester of pregnancy may increase the risk of neonatal complications requiring prolonged hospitalization, respiratory support, and tube feeding, and/or persistent pulmonary hypertension of the newborn.[3-11]

Selective serotonin reuptake inhibitors are contraindicated with concomitant use of the antipsychotic pimozide due to the risk of drug interaction or QT_c prolongation.[3-8]

Adverse Effects of Tricyclic Antidepressants

The most serious adverse effects of TCAs are cardiovascular effects, particularly conduction delays such as first-degree atrioventricular and bundle branch blocks, which can be fatal.[2] Electrocardiogram should be used to rule out conduction system disease before starting a TCA.[2]

Because 10 to 20 mg/kg of a TCA can cause potentially lethal toxicity, overdose risk is a concern.[12] Patients should be assessed for a history of overdose or suicidal behavior before being prescribed a TCA, and patients should be given only a limited supply.[12]

Tricyclic antidepressants can also have anticholinergic, antihistaminergic, and antiadrenergic effects as follows[2]:

- Anticholinergic: nausea, vomiting, anorexia, dry mouth, blurred vision, altered mental status, constipation, tachycardia, and urinary retention;
- Antihistaminergic: sedation, weight gain, and confusion (in older patients); and
- Antiadrenergic: orthostatic hypotension (which is of particular significance in older patients), reflex tachycardia, drowsiness, and dizziness.

Serotonin syndrome is a potential risk with clomipramine and imipramine; other TCAs are weaker inhibitors and are unlikely to cause toxicity.[13]

For a full list of references, please visit:
https://www.neurologyadvisor.com/factsheets/depression-medication-list/