ANTİDEPRESSANTS

What Is Depression?

Depression (major depressive disorder) is a common and serious medical illness that negatively affects how you feel, the way you think and how you act. Fortunately, it is also treatable. Depression causes feelings of sadness and/or a loss of interest in activities once enjoyed. It can lead to a variety of emotional and physical problems and can decrease a person's ability to function at work and at home.

Depression symptoms can vary from mild to severe and can include:

-Feeling sad or having a depressed mood

-Loss of interest or pleasure in activities once enjoyed

-Changes in appetite — weight loss or gain unrelated to dieting

-Trouble sleeping or sleeping too much

-Loss of energy or increased fatigue

Increase in purposeless physical activity (e.g., hand-wringing or pacing) or slowed movements and speech (actions observable by others)

-Feeling worthless or guilty

-Difficulty thinking, concentrating or making decisions

-Thoughts of death or suicide

Symptoms must last at least two weeks for a diagnosis of depression. Also, medical conditions (e.g., thyroid problems, a brain tumor or vitamin deficiency) can mimic symptoms of depression so it is important to rule out general medical causes.Depression affects an estimated one in 15 adults (6.7%) in any given year. And one in six people (16.6%) will experience depression at some time in their life. Depression can strike at any time, but on average, first appears during the late teens to mid-20s. Women are more likely than men to experience depression. Some studies show that one-third of women will experience a major depressive episode in their lifetime.

Depression Is Different From Sadness or Grief/Bereavement

The death of a loved one, loss of a job or the ending of a relationship are difficult experiences for a person to endure. It is normal for feelings of sadness or grief to develop in response to such situations. Those experiencing loss often might describe themselves as being "depressed."

But being sad is not the same as having depression. The grieving process is natural and unique to each individual and shares some of the same features of depression. Both grief and

depression may involve intense sadness and withdrawal from usual activities. They are also different in important ways:

In grief, painful feelings come in waves, often intermixed with positive memories of the deceased. In major depression, mood and/or interest (pleasure) are decreased for most of two weeks.

In grief, self-esteem is usually maintained. In major depression, feelings of worthlessness and self-loathing are common.

For some people, the death of a loved one can bring on major depression. Losing a job or being a victim of a physical assault or a major disaster can lead to depression for some people. When grief and depression co-exist, the grief is more severe and lasts longer than grief without depression. Despite some overlap between grief and depression, they are different. Distinguishing between them can help people get the help, support or treatment they need.

How Is Depression Treated?

Depression is among the most treatable of mental disorders. Between 80 percent and 90 percent of people with depression eventually respond well to treatment. Almost all patients gain some relief from their symptoms.

Medication: Brain chemistry may contribute to an individual's depression and may factor into their treatment. For this reason, antidepressants might be prescribed to help modify one's brain chemistry. These medications are not sedatives, "uppers" or tranquilizers. They are not habit-forming. Generally antidepressant medications have no stimulating effect on people not experiencing depression.

Psychotherapy: Psychotherapy, or "talk therapy," is sometimes used alone for treatment of mild depression; for moderate to severe depression, psychotherapy is often used in along with antidepressant medications. Cognitive behavioral therapy (CBT) has been found to be effective in treating depression. CBT is a form of therapy focused on the present and problem solving. CBT helps a person to recognize distorted thinking and then change behaviors and thinking.

Electroconvulsive Therapy (ECT) is a medical treatment most commonly used for patients with severe major depression or bipolar disorder who have not responded to other treatments. It involves a brief electrical stimulation of the brain while the patient is under anesthesia. A patient typically receives ECT two to three times a week for a total of six to 12 treatments. ECT has been used since the 1940s, and many years of research have led to major improvements. It is usually managed by a team of trained medical professionals including a psychiatrist, an anesthesiologist and a nurse or physician assistant.

Self-help and Coping There are a number of things people can do to help reduce the symptoms of depression. For many people, regular exercise helps create positive feeling and improve mood. Getting enough quality sleep on a regular basis, eating a healthy diet and avoiding alcohol (a depressant) can also help reduce symptoms of depression.

Overview on Drugs

Depression is a mental health issue that starts most often in early adulthood. It's also more common in women. However, anyone at any age may deal with depression.

Depression affects your brain, so drugs that work in your brain may prove beneficial. Common antidepressants may help ease your symptoms, but there are many other options as well. Each drug used to treat depression works by balancing certain chemicals in your brain called neurotransmitters. These drugs work in slightly different ways to ease your depression symptoms.

Many common drugs fall into the following drug classes:

1. Selective serotonin reuptake inhibitors (SSRIs)
2. Serotonin and norepinephrine reuptake inhibitors (SNRIs)
3. Tricyclic antidepressants (TCAs)
4. Tetracyclic antidepressant
5. Dopamine reuptake blocker
6. 5-HT1A receptor antagonist
7. 5-HT2 receptor antagonists
8. 5-HT3 receptor antagonist
9. Monoamine oxidase inhibitors (MAOIs)
10. Noradrenergic antagonist
11. Atypical antidepressants,

1. Selective serotonin reuptake inhibitors (SSRIs)

SSRIs are the most commonly prescribed class of antidepressants. An imbalance of serotonin may play a role in depression. These drugs fight depression symptoms by decreasing serotonin reuptake in your brain. This effect leaves more serotonin available to work in your brain. SSRIs ease depression by increasing levels of serotonin in the brain. Serotonin is one of the chemical messengers (neurotransmitters) that carry signals between brain cells. SSRIs block the reabsorption (reuptake) of serotonin in the brain, making more serotonin available. SSRIs are called selective because they seem to primarily affect serotonin, not other neurotransmitters.

SSRIs include:

sertraline

fluoxetine

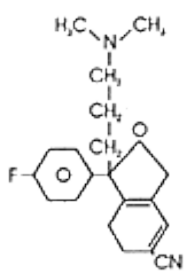
citalopram

escitalopram

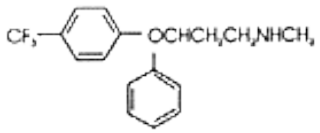
paroxetine

fluvoxamine

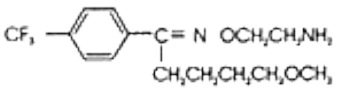
Citalopram



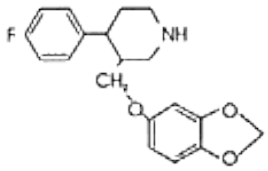
Fluoxetine



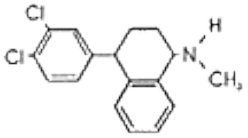
Fluvoxamine



Paroxetine



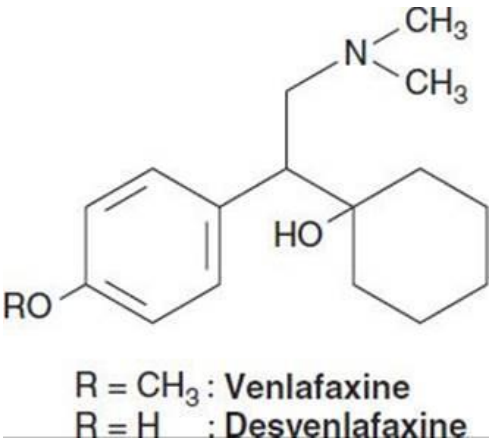
Sertraline

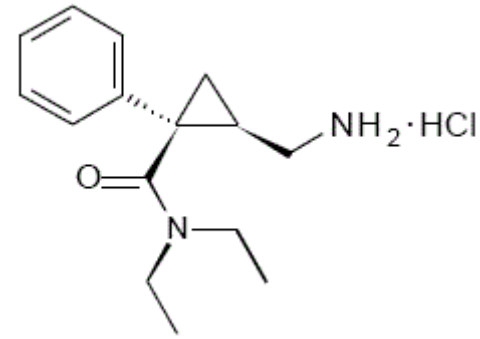


Common side effects of SSRIs include:

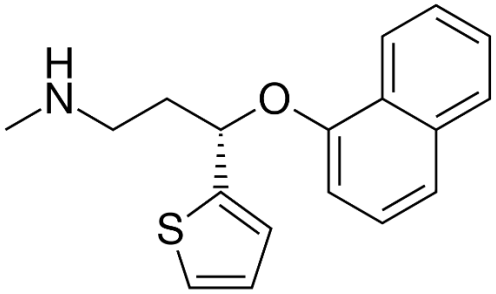
Nausea, trouble sleeping, nervousness, tremors, sexual problems

2. Serotonin and norepinephrine reuptake inhibitors (SNRIs)





Levomilnacipran



Duloxetine

SNRIs help improve serotonin and norepinephrine levels in your brain. This may reduce depression symptoms. SNRIs ease depression by impacting chemical messengers (neurotransmitters) used to communicate between brain cells. Like most antidepressants, SNRIs work by ultimately effecting changes in brain chemistry and communication in brain nerve cell circuitry known to regulate mood, to help relieve depression. SNRIs block the reabsorption (reuptake) of the neurotransmitters serotonin and norepinephrine in the brain.

These drugs include:

desvenlafaxine

duloxetine

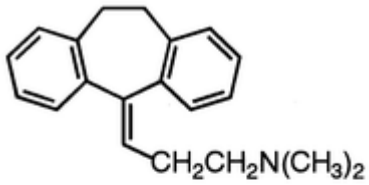
levomilnacipran

venlafaxine

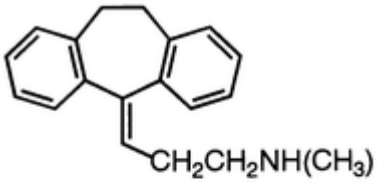
In addition to treating depression, duloxetine may also relieve pain. This is important because chronic pain can lead to depression or make it worse. In some cases, people with depression become more aware of aches and pains. A drug that treats both depression and pain, such as duloxetine, can be helpful to these people.

Common side effects of SNRIs include: nausea, drowsiness, fatigue, constipation, dry mouth,

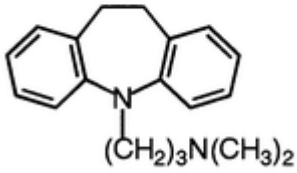
3. Tricyclic antidepressants (TCAs)



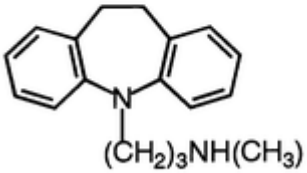
amitriptyline



nortriptyline



imipramine



desipramine

TCAs are often prescribed when SSRIs or other antidepressants don't work. It isn't fully understood how these drugs work to treat depression. Cyclic antidepressants ease depression by impacting chemical messengers (neurotransmitters) used to communicate between brain cells. Like most antidepressants, cyclic antidepressants work by ultimately effecting changes in brain chemistry and communication in brain nerve cell circuitry known to regulate mood, to help relieve depression. Cyclic antidepressants block the absorption (reuptake) of the neurotransmitters serotonin and norepinephrine increasing the levels of these two neurotransmitters in the brain. Cyclic antidepressants also affect other chemical messengers, which can lead to a number of side effects.

TCAs include:

amitriptyline

amoxapine

clomipramine

desipramine

doxepin

imipramine

nortriptyline

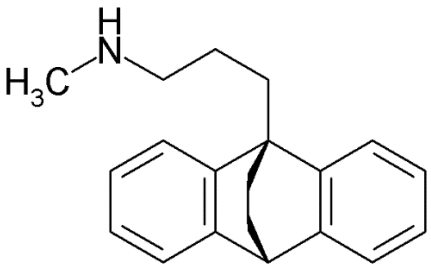
protriptyline

trimipramine

Common side effects of TCAs can include: constipation, dry mouth, fatigue, The more serious side effects of these drugs include: low blood pressure, irregular heart rate, seizures

4. Tetracyclic antidepressant

Maprotiline is used to treat depression and anxiety. It also works by balancing neurotransmitters to ease symptoms of depression. Maprotiline hydrochloride, USP is a tetracyclic antidepressant, available as 25 mg, 50 mg and 75 mg tablets for oral administration. Its chemical name is N-methyl-9,10-ethanoanthracene-9(10H)-propylamine hydrochloride. The mechanism of action of Maprotiline is not precisely known. It does not act primarily by stimulation of the central nervous system and is not a monoamine oxidase inhibitor. The postulated mechanism of Maprotiline is that it acts primarily by potentiation of central adrenergic synapses by blocking reuptake of norepinephrine at nerve endings. This pharmacologic action is thought to be responsible for the drug's antidepressant and anxiolytic effects.



Common side effects of this drug include: drowsiness, weakness, lightheadedness, headache, blurry vision, dry mouth

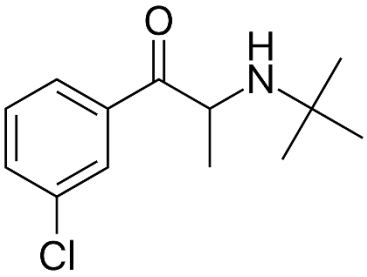
5. Dopamine reuptake blocker

Bupropion (Wellbutrin, Forfivo, Aplenzin) is a mild dopamine and norepinephrine reuptake blocker. It's used for depression and seasonal affective disorder. It's also used in smoking cessation. The exact mechanism of action of bupropion is not fully understood.

What is known is that bupropion enhances both noradrenergic and dopaminergic neurotransmission via reuptake inhibition of the norepinephrine transporter and the dopamine transporter. In addition, its mechanism of action may involve the presynaptic release of norepinephrine and dopamine.

In contrast to what was described in animal studies, human in vivo research suggests that bupropion effects on dopamine are relatively modest.

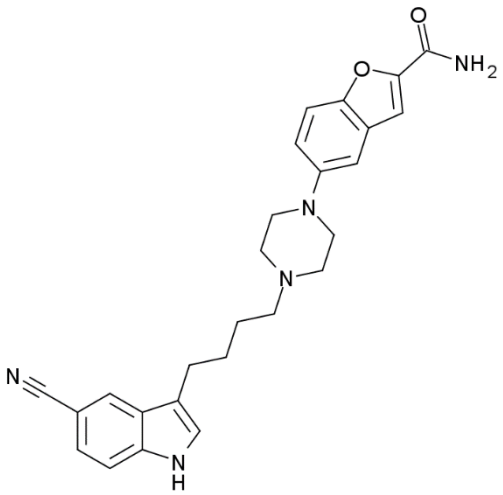
A more recently discovered pharmacological property of bupropion is its affinity for nicotinic receptors. Bupropion is a non competitive antagonist of nicotinic acetylcholine receptors. This is thought to contribute to its antidepressant effects, as well as to its effectiveness as smoking cessation drug.



Common side effects include: nausea, vomiting, constipation, dizziness, blurry vision

6. 5-HT1A receptor antagonist

The drug in this class that's used to treat depression is called vilazodone (Viibryd). It works by balancing serotonin levels and other neurotransmitters. Vilazodone is a novel compound with combined high affinity and selectivity for the 5-hydroxytryptamine (5-HT) transporter and 5-HT(1A) receptors. It has been shown to be equally efficacious as other antidepressants with similar gastrointestinal side effects and possibly with reduced sexual side effects and weight gain. Vilazodone is an antidepressant agent that can used as an alternative for patients who cannot tolerate therapy with other antidepressant classes such as selective serotonin reuptake inhibitors or serotonin norepinephrine reuptake inhibitors. Treatment should be titrated towards the target dose, which is 40mg per day.



This drug is rarely used as a first-line treatment for depression. That means it's usually only prescribed when other medications didn't work for you or caused bothersome side effects.

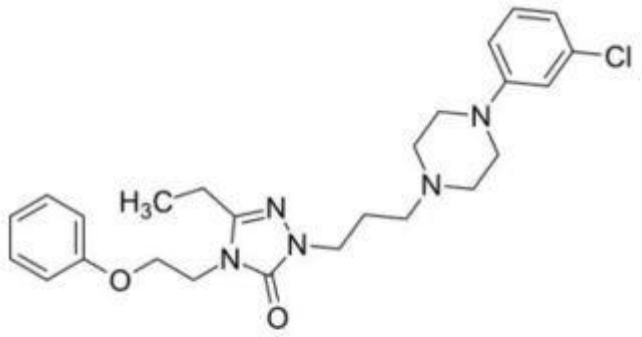
Side effects can include: nausea, vomiting, trouble sleeping

7. 5-HT2 receptor antagonists

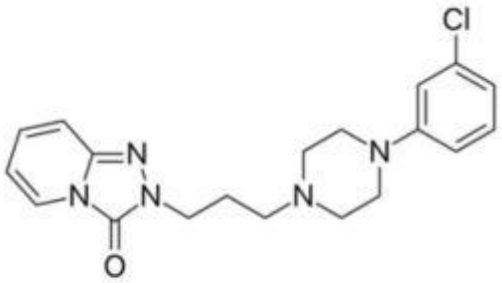
Two 5-HT2 receptor antagonists, nefazodone and trazodone (Oleptro), are used to treat depression. These are older drugs. They alter chemicals in your brain to help depression.

Nefazodone, an antidepressant synthetically derived phenylpiperazine, is used to treat major depression. Although it is structurally similar to trazodone, nefazodone has a mechanism of action different from other antidepressants and, hence, lacks the risk for major cardiovascular toxicity seen with tricyclics and insomnia and inhibition of REM sleep seen with the selective serotonin reuptake inhibitors. Within the serotonergic system, nefazodone acts as an antagonist at type 2 serotonin ($5\text{-}HT_2$) post-synaptic receptors and, like fluoxetine-type antidepressants, inhibits pre-synaptic serotonin (5-HT) reuptake. These mechanisms increase the amount of serotonin available to interact with 5-HT receptors. Within the noradrenergic system, nefazodone inhibits norepinephrine uptake minimally. Nefazodone also antagonizes alpha(1)-adrenergic receptors, producing sedation, muscle relaxation, and a variety of cardiovascular effects. Nefazodone's affinity for benzodiazepine, cholinergic, dopaminergic, histaminic, and beta or alpha(2)-adrenergic receptors is not significant.

Trazodone is an antidepressant and hypnotic chemically unrelated to tricyclic, tetracyclic, or other known antidepressant agents. The mechanism of trazodone's antidepressant action in man is not fully understood. In animals, trazodone selectively inhibits serotonin uptake by brain synaptosomes and potentiates the behavioral changes induced by the serotonin precursor, 5-hydroxytryptophan. Cardiac conduction effects of trazodone in the anesthetized dog are qualitatively dissimilar and quantitatively less pronounced than those seen with tricyclic antidepressants. Trazodone is not a monoamine oxidase inhibitor and, unlike amphetamine-type drugs, does not stimulate the central nervous system. In man, trazodone is well absorbed after oral administration without selective localization in any tissue. Since the clearance of trazodone from the body is sufficiently variable, in some patients trazodone may accumulate in the plasma. Trazodone binds at 5-HT2 receptor, it acts as a serotonin agonist at high doses and a serotonin antagonist at low doses. Like fluoxetine, trazodone's antidepressant activity likely results from blockage of serotonin reuptake by inhibiting serotonin reuptake pump at the presynaptic neuronal membrane. If used for long time periods, postsynaptic neuronal receptor binding sites may also be affected. The sedative effect of trazodone is likely the result of alpha-adrenergic blocking action and modest histamine blockade at H1 receptor. It weakly blocks presynaptic alpha2-adrenergic receptors and strongly inhibits postsynaptic alpha1 receptors. Trazodone does not affect the reuptake of norepinephrine or dopamine within the CNS.



Nefazodone

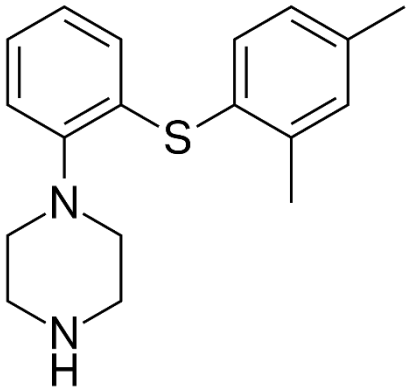


Trazodone

Common side effects include: drowsiness, dizziness, dry mouth,

8. 5-HT3 receptor antagonist

The 5-HT3 receptor antagonist vortioxetine (Brintellix) treats depression by affecting the activity of brain chemicals. Vortioxetine is an atypical antipsychotic and antidepressant indicated for the treatment of major depressive disorder (MDD). It is classified as a serotonin modulator and simulator (SMS) as it has a multimodal mechanism of action towards the serotonin neurotransmitter system whereby it simultaneously modulates one or more serotonin receptors and inhibits the reuptake of serotonin. More specifically, vortioxetine acts via the following biological mechanisms: as a serotonin reuptake inhibitor (SRI) through inhibition of the serotonin transporter, as a partial agonist of the 5-HT1B receptor, an agonist of 5-HT1A, and an antagonist of the 5-HT3, 5-HT1D, and 5-HT7 receptors. SMSs were developed because there are many different subtypes of serotonin receptors, however, not all of these receptors appear to be involved in the antidepressant effects of SRIs. Some serotonin receptors seem to play a relatively neutral or insignificant role in the regulation of mood, but others, such as 5-HT1A autoreceptors and 5-HT7 receptors, appear to play an oppositional role in the efficacy of SRIs in treating depression.



Common side effects include: sexual problems, nausea,

9. Monoamine oxidase inhibitors (MAOIs)

MAOIs are older drugs that treat depression. They work by stopping the breakdown of norepinephrine, dopamine, and serotonin. They're more difficult for people to take than most other antidepressants because they interact with prescription drugs, nonprescription drugs, and some foods. They also can't be combined with stimulants or other antidepressants.

Monoamine oxidase inhibitors block the actions of monoamine oxidase enzymes. Monoamine oxidase enzymes are responsible for breaking down neurotransmitters such as dopamine, norepinephrine, and serotonin in the brain. Low levels of these three neurotransmitters have been linked with **depression** and **anxiety**. By blocking the effects of monoamine oxidase enzymes, MAOIs increase the concentration of these three neurotransmitters, and are useful at relieving depression and/or anxiety.

MAOIs are typically only used when other antidepressants have proven ineffective, because they have a higher risk of drug interactions than standard antidepressants and can also interact with certain types of food such as aged cheeses and cured meats. They also tend to have more side effects than standard antidepressants, and may cause a withdrawal syndrome on discontinuation.

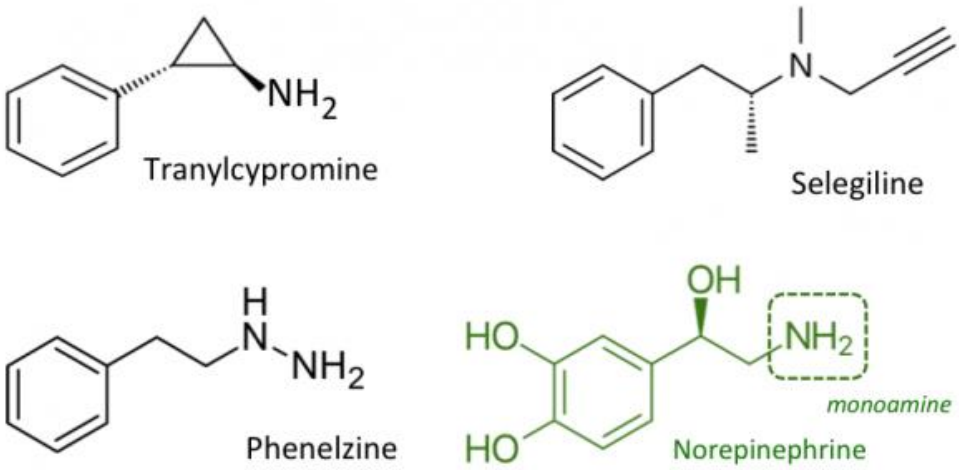
MAOIs include:

isocarboxazid (Marplan)

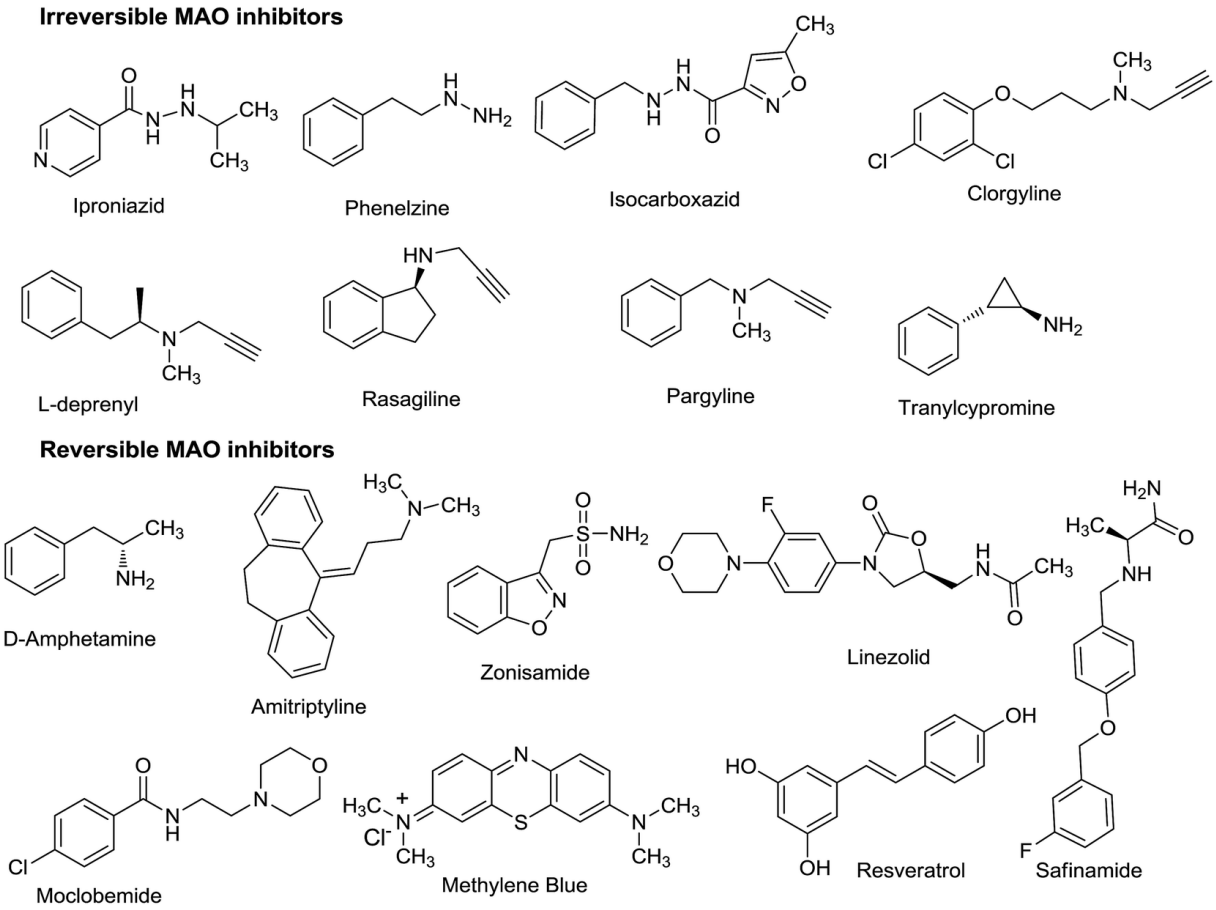
phenelzine (Nardil)

selegiline (Emsam), which comes as a transdermal patch

tranylcypromine (Parnate)

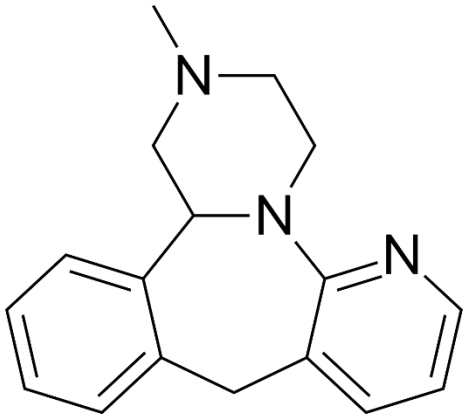


MAOIs also have many side effects. These can include: nausea, dizziness, drowsiness, trouble, sleeping, restlessness



10. Noradrenergic antagonist

Mirtazapine (Remeron) is used primarily for depression. It alters certain chemicals in your brain to ease depression symptoms. Mirtazapine acts as an antagonist at central pre-synaptic alpha(2)-receptors, inhibiting negative feedback to the presynaptic nerve and causing an increase in NE release. Blockade of heteroreceptors, alpha(2)-receptors contained in serotenergic neurons, enhances the release of 5-HT, increasing the interactions between 5-HT and 5-HT_1 receptors and contributing to the anxiolytic effects of mirtazapine. Mirtazapine also acts as a weak antagonist at 5-HT_1 receptors and as a potent antagonist at 5-HT_2 (particularly subtypes 2A and 2C) and 5-HT_3 receptors. Blockade of these receptors may explain the lower incidence of adverse effects such as anxiety, insomnia, and nausea. Mirtazapine also exhibits significant antagonism at H1-receptors, resulting in sedation. Mirtazapine has no effects on the reuptake of either NE or 5-HT and has only minimal activity at dopaminergic and muscarinic receptors.



Common side effects include: drowsiness, dizziness, weight gain

11. Atypical antidepressants

Atypical antidepressants are not typical — they don't fit into other classes of antidepressants. They are each unique medications that work in different ways from one another.

Atypical antidepressants ease depression by affecting chemical messengers (neurotransmitters) used to communicate between brain cells. Like most antidepressants, atypical antidepressants work by ultimately effecting changes in brain chemistry and communication in brain nerve cell circuitry known to regulate mood, to help relieve depression.

Atypical antidepressants change the levels of one or more neurotransmitters, such as dopamine, serotonin or norepinephrine.