

# Tricyclic (TCAs) and Heterocyclic Antidepressants For Depression

**An article about cyclic antidepressants: how they work, how to take them, and what side effects to expect.**

"What I remember most about being depressed was always being exhausted. I could never get to sleep at night, and when I did, I had nightmares. Then I'd wake up in the morning and have to drag myself to work. And in all that time -- four or five years, I guess -- I never once enjoyed anything. I was actually planning my own suicide when my doctor referred me to a psychiatrist who put me on imipramine. For the first time in years, I finally began to get some pleasure out of life."

-- Sam, 43

Before Prozac, tricyclics were the first line of defense against encroaching depression, and had been ever since imipramine's release in 1958 under the brand name Tofranil. Today, tricyclics are a less popular choice than the new generation of antidepressants, but they're still an important weapon in the antidepressant arsenal for a subset of people who don't respond to anything else. This type of medication is used to help relieve the symptoms of major depression.

## **Common Cyclic Antidepressants (Lower doses are used with elderly patients)**

<b>Drug</b>	<b>Usual Effective Daily Dose</b>
Amitriptyline (Elavil, Endep, Emitrip, Enovil)	150-300 mg
Amoxapine (Asendin)	150-400 mg
Clomipramine (Anafranil)	100-150 mg
Desipramine (Norpramin, Pertofrane)	100-300 mg
Doxepin (Adapin, Sinequan)	75-300 mg
Imipramine (Janimine, Tipramine, Tofranil, Tofranil-PM)	150-300 mg
Maprotiline	75-150 mg

(Ludiomil)

Nortriptyline                      50-150 mg  
(Pamelor, Aventyl)

Protriptyline                      15-60 mg  
(Vivactil)

Before tricyclics were developed, psychiatrists treating severely depressed clients had only two real choices: amphetamines or electroshock therapy. Imipramine was discovered by Swiss scientists searching for a successful schizophrenia treatment; it turned out that imipramine didn't do much for schizophrenia at all. What it did do very well was perk up depressed patients.

With the discovery of imipramine, doctors finally had a drug that relieved a person's underlying depression. And when scientists realized how effective imipramine was -- about 70 percent of depressed patients responded to this drug -- they flocked to the laboratories in search of similar drugs based on imipramine's three-ring ("tricyclic") antihistaminic chemical structure. Before long, laboratories all over the country began churning out tricyclic clones, each one a little different from, but none any better than, imipramine itself. A later-developed drug in this class, maprotiline (Ludiomil), had four rings and was therefore called "tetracyclic." Taken together, the tricyclics and tetracyclics are known as "heterocyclics" or "cyclics."

But while all these cyclics were effective, not one provided the perfect solution to depression for which scientists had been searching.

## **How They Work**

The cyclic antidepressants work by beefing up the brain's supply of norepinephrine and serotonin levels -- chemicals that are abnormally low in depressed patients. This allows the flow of nerve impulses to return to normal. The cyclics do not act by stimulating the central nervous system or by blocking monoamine oxidase.

The problem with cyclics is that they don't stop there. They go on to interfere with a range of other neurotransmitter systems and a variety of brain cell receptors, affecting nerve cell communication all over the brain in the process. And the more neurotransmitter systems and receptors you affect, the more side effects a patient will have.

## SSRIs

1. [Celexa \(citalopram\)](#)
2. [Lexapro \(escitalopram oxalate\)](#)
3. [Luvox \(fluvoxamine\)](#)
4. [Paxil \(paroxetine\)](#)
5. [Prozac \(fluoxetine\)](#)
6. [Zoloft \(sertraline\)](#)

# Selective Serotonin Reuptake Inhibitors (SSRIs)

## General information about the SSRIs, their relative merits, and their side effects.

### Prime Candidates

The SSRIs are particularly helpful in heading off depression in the early stages, before it becomes deeply rooted. Some studies suggest that SSRIs are ideal for those people with minor depressive illness -- much better than tricyclics, such as imipramine, or the complication-prone MAOIs. The SSRIs are effective for major depression, too.

"Before taking Zoloft, I had a bad case of the blahs. Everything just seemed colorless. But now, sometimes I'll just lie in bed and rub the blanket between my fingers," says Sharon, 38. "It's not sexual, but my sensitivity is heightened. The feel-goodness goes right down into my bones."

Research seems to suggest that you can head off serious full-blown illness by taking an SSRI during the early stages of depression.

This doesn't mean that SSRIs are the only worthwhile antidepressant, of course. There is still a place for the older drugs. Research has shown that the older tablets (Tricyclics) are just as effective as the newer ones (SSRIs) but, on the whole, the newer ones seem to have fewer side-effects. A major advantage of the SSRIs is that they are not so dangerous if someone takes an overdose.

Researchers also note that the SSRIs don't work for 20 percent to 40 percent of depressed or anxious people who try them -- the same failure rate as for the older antidepressants.

### How SSRI's work

Serotonin is a brain neurotransmitter, which is felt to be heavily involved in the cause of depression. As a result drugs which specifically affect this neurotransmitter have been developed. As such they have the advantage of fewer side effects than older drugs. SSRIs relieve depression in most people who take them. There is some evidence that they may be more effective than other medications at treating people with uncommon symptoms of depression, such as eating or sleeping too much or being overly sensitive to rejection.

## Which SSRI Is Best?

Most experts agree that no single SSRI is better than the rest, despite Prozac's image as a miracle drug that not only cures depression but can make many healthy people "better than well". Each drug has a certain profile of its own particular side effects; some have markedly similar side effects, while others vary widely.

For example, Zoloft and Paxil don't last as long in the body as Prozac; the half-life of Zoloft is about 26 hours, and the half-life of Paxil is about 21 hours. ("Half-life" is the time it takes for a drug in the blood to decrease by half of its original dose.)

It's important to understand that all the SSRIs may cause nausea, headache, anxiety, dry mouth, insomnia, and a variety of sexual dysfunctions. But as mentioned, what makes Prozac less desirable is that it lingers in the body much longer than other SSRIs; up to six weeks after you stop taking the drug, traces of Prozac and its metabolites can still be found in your body. If you have a bad reaction to Zoloft or Paxil, symptoms last for a week or two. But side effects while taking Prozac can last for up to six weeks before all traces of the drug leave your body.

Of course, none of the SSRIs are any sort of wonder drug. They all have some side effects, although they are less severe than those of other antidepressants.

One of the biggest problems with these drugs is their cost. All of them are much more expensive than the generic versions of older drugs like MAOIs or tricyclics. Generic versions of the older drugs are available because their patents have expired.

No matter how wonderful a drug may be, if you can't afford it, it's not going to do you much good. The high cost of the SSRIs can be a real hardship for someone with no insurance, or whose insurance doesn't cover drugs. At about \$2 to \$3 per pill, the pharmacy bill can be overwhelming.

It's a problem for Mary, 28, whose health insurance covers all drugs except medications for mental health problems. "My psychiatrist is very aware of this problem," Mary explains. "He doesn't give me Zoloft alone because it would be too expensive. So he prescribes a smaller amount of Zoloft with desipramine (a less-expensive tricyclic)." The desipramine boosts the effects of Zoloft, and the combination costs less than a full dose of Zoloft alone.

## SSRI Antidepressants, Suicidal Feelings and Young People

There is evidence of increased suicidal thoughts and behaviors and other side effects in young people taking antidepressants. So SSRI antidepressants, with the exception of Prozac, are not approved by the FDA for use in people under 18.

In fact, in 2004, the FDA ordered the strongest safety warning possible:

Antidepressants increase the risk of suicidal thinking and behavior (suicidality) in children and adolescents with major depressive disorder (MDD) and other psychiatric disorders. Anyone considering the use of [Drug Name] or any other antidepressant in a child or adolescent must balance this risk with the clinical need.

There is no clear evidence of an increased risk of self-harm and suicidal thoughts in adults - age 18 years or over. But, individuals mature at different rates. Young adults are more likely to commit suicide than older adults, so a young adult should be particularly closely monitored if he or she takes an SSRI antidepressant.

## Medical Cautions

Severe kidney or liver disease could result in higher-than-normal blood levels of the SSRIs. In addition, the SSRIs may not be the best choice in the treatment of patients with mania, or in those with a history of seizures.

## Side Effects

The side effects of SSRIs are usually mild and manageable, although once in a while a sensitive person gets a severe reaction. Like most antidepressants, SSRIs may cause nausea, dizziness, or dry mouth, not to mention a range of sexual-function side effects, including decreased sexual interest (in men), increased sexual interest (in women), ejaculation problems, impotence, or menstrual changes.

During the first couple of weeks of taking them, you may feel sick and more anxious. Some of these tablets can produce nasty indigestion, but you can usually stop this by taking them with food. More seriously, as noted above, they may interfere with your sexual function. There have been reports of episodes of aggression, although these are rare.

The list of side effects looks worrying - there is even more information about these on the [leaflets that come with the medication](#). However, most people get a small number of mild side-effects (if any). The side effects usually wear off over a couple of weeks as your body gets used to the medication. It is important to have this whole list, though, so you can recognize side effects if they happen. You can then talk them over with your doctor. The more serious ones - problems with urinating, difficulty in remembering, falls, confusion - are uncommon in healthy, younger or middle-aged people.

The most common side effects with Zoloft, launched in 1991, and Paxil, introduced in 1993, are insomnia, diarrhea, tremor, and drowsiness. If you get side effects while taking either of these, your doctor may switch you to Wellbutrin, as long as you don't have any of the conditions that might make you vulnerable to seizures with this drug (such as previous severe head injury or epilepsy). And like Prozac, Zoloft, Paxil, Celexa, Lexapro and other SSRIs, it can produce mild mania in some people with a genetic tendency in that direction.

Sexual dysfunction may occur in SSRI users from one to five percent according to the drug companies (although actual incidence of the problem may be much higher, critics charge -- as high as 40 percent).

It is common, if you are depressed, to think of harming or killing yourself. Tell your doctor - suicidal thoughts should pass once the depression starts to lift.