

# Tricyclics

The tricyclics were among the first antidepressants and remain among the most effective. They work well when other antidepressants have not.

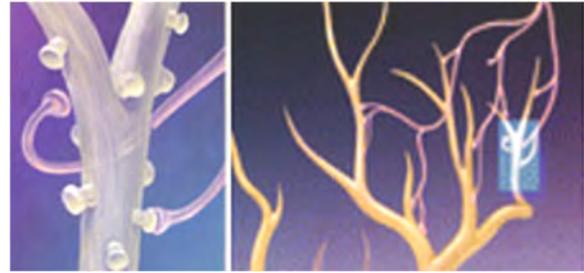
Besides depression, this class of medication has also been used to treat:

- Anxiety and OCD
- Insomnia
- Chronic pain, migraines
- Irritable bowel syndrome
- Nocturnal enuresis (bedwetting)

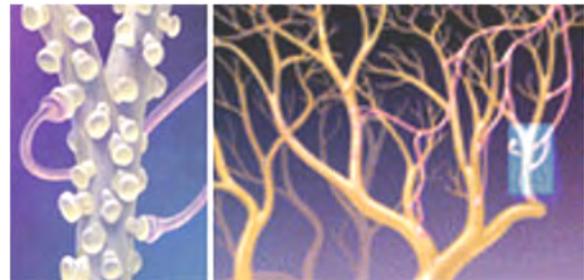
The tricyclics are particularly effective for melancholic depression. In this type of depression people often worry and ruminate over guilty or negative thoughts and have a low, non-reactive mood all day. They often have low appetite, early morning awakening, and slowing or agitation of the muscles.

## How they work

Tricyclic antidepressants enhance the transmission of serotonin and norepinephrine in the brain. Both of these neurotransmitters are involved in depression. Serotonin also relieves anxiety, and norepinephrine can improve energy and reduce physical pain. These medicines also enhance brain growth in the hippocampus and amygdala, which are involved in mood and memory:



*Before treatment:* the effects of depression and stress have caused this nerve cell to shrink back like a tree with few branches.



*After treatment:* Antidepressant treatment has strengthened the roots and connections of the brain cell. The result is better communication within the brain and better stress management.

## How should I take them?

Most people find them sedating and take them before bedtime. Tricyclics can be taken with or without food.

## What if I forget a dose?

Take the missed dose as soon as you remember it. However, if it is almost time for the next dose, skip the missed dose and continue your regular dosing schedule. Do not take a double dose to make up for a missed one.

## How long do I need to take it?

In general, the medicine should be taken at least 6-12 months after the symptoms resolve in order to prevent the problem from returning. That gives the brain time to build up habits of stability. Some people may need to take the medication longer to prevent the return of depression, especially if they have had three or more episodes of depression in their life.

## What happens if I stop it?

Tricyclics usually have no withdrawal symptoms, and can be stopped all at once if you have only been on them a few weeks and are not tolerating them. If you have been taking them longer it is best to stop them gradually to prevent withdrawal symptoms. These are flu-like symptoms that are unpleasant but not dangerous; examples include:

> Dizziness, nausea, lethargy, sensory changes (numbness, tingling, shock-like feelings), blurred vision, headache, vivid dreams, anxiety.

You cannot become addicted to tricyclics. In other words, if you stop the medicine, you will not crave it or be more likely to have depression or anxiety than before. Instead, treatment helps the brain rebuild connections in ways that help prevent future symptoms.

## Side effects

*These side effects tend to improve with time (3-4 weeks) or by lowering the dose:*

Dizziness (this can improve by standing up slowly), drowsiness, concentration problems ("spacey", slowed-down, forgetful).

Dry mouth and skin, blurred vision, constipation (may improve by increasing fiber or taking colace), and difficulty urinating.

Weight gain (worse with amitriptyline, nortriptyline, and doxepin). Sexual difficulties.

As you are starting a tricyclic, use caution when driving or performing tasks that require alertness. This should not be a problem once you have adjusted to the medicine and know how it affects you.

*The following side effects indicate that the medicine may need to be stopped; call me if they occur:*

Agitation, intense mood swings, racing thoughts, insomnia, restless feelings like you can't stop moving, worsening of suicidal thoughts.

## Medical Risks

Falls from low blood pressure (orthostatic hypotension).

Slowing of heart-conduction (arrhythmia).

Tricyclics can be dangerous if you have certain health problems including: narrow-angle glaucoma, heart disease or seizures.

*Serotonin syndrome:* this condition is very rare with tricyclics. The risk is greatest with clomipramine or if tricyclics are taken with other antidepressants or with lithium, tryptophan, buspar, or St. John's Wort. Symptoms include fever, muscle jerks, diarrhea, sweats, racing heart, stomach pain, confusion and mood swings. If this occurs, stop the medication and call me or go to your local emergency room.

*Liver:* very rarely, toxicity of the liver (hepatitis) has been reported with certain tricyclics

*Blood count:* very rarely, decreases in blood count have occurred on tricyclics.

*Pregnancy:* Tricyclics have not been adequately evaluated during pregnancy. They pass through breast milk and may cause irritability, jitteriness, and rare seizures in newborns.

## Overdose

Tricyclics are extremely lethal in acute overdoses, particularly in children. Overdoses often result in death. A person who appears to

have overdosed should be brought to the emergency room (call 911) with their medication bottle.

### **Interactions**

Drug interactions are important with tricyclics, as high ledifferent with each tricyclic. The web sites below help you check for drug interactions. You should talk with us about the information you find as many drug interactions have only a mild effect:

[www.webmd.com/interaction-checker](http://www.webmd.com/interaction-checker)  
[reference.medscape.com/drug-interactionchecker](http://reference.medscape.com/drug-interactionchecker)

### **How to store and dispose of medication**

- Keep out of the reach of children.
- Store away from heat, direct light and damp places.
- To safely dispose of unwanted pills: Do not pour in the toilet or sink (it will enter the water supply). To prevent children or pets from eating it, mix unwanted pills in a bag with a little water and inedible trash (such as coffee grounds or kitty litter) and throw in the trash.

### **Cost and insurance coverage**

The tricyclics are available as generics. If paying out of pocket, you'll find the lowest price at [www.goodrx.com](http://www.goodrx.com).

—Chris Aiken, MD, updated 6/23/2025

## Tricyclic Antidepressants

Generic (brand)	Sizes	FDA Approval, Typical doses
Amitriptyline (Elavil) <i>Released 5/20/1983</i>	Tabs: 10, 25, 50, 75, 100, 150mg	Depression (25-300mg/d)
Clomipramine (Anafranil) <i>Released 12/29/1989</i>	Caps 25, 50, 75mg	Obsessive Compulsive Disorder (OCD) (25-250mg/d)
Doxepin (Sinequan, Silenor) <i>Released 3/11/1974</i>	Caps: 10, 25, 50, 75, 100, 150mg Liquid: 10mg/ml	Depression (10-300mg/d) Insomnia (the Silenor brand is used for insomnia, in 3 and 6mg doses)
Imipramine (Tofranil) <i>Released 7/15/1987</i>	Caps: 75, 100, 150mg Tabs: 10, 25, 50mg	Depression (10-200mg/d) Childhood enuresis (bedwetting) (2.5 mg/kg/day)
Nortriptyline (Pamelor) <i>Released 11/6/1964</i>	Caps: 10, 25, 50, 75mg Liquid 10mg/5ml	Depression (25-150mg/d)
Protriptyline (Vivactil) <i>Released 9/27/1967</i>	Tabs: 5, 10mg	Depression (10-60mg/d)
Trimipramine (Sumontil) <i>Released 6/12/1979</i>	Caps: 25, 50, 100mg	Depression (25-300mg/d)
Desipramine (Norpramin) <i>Released 11/20/1964</i>	Tabs: 10, 25, 50, 75, 100, 150mg	Depression (10-300mg/d)
Maprotiline (Ludomil) <i>Released 12/1/1980</i>	Tabs: 25, 50, 75mg	Depression, anxiety (25-225mg/d)
Amoxapine (Ascendin) <i>Released 9/22/1980</i>	Tabs: 25, 50, 100, 150mg	Depression (25-600mg/d)

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