



Norpramin (desipramine)

Generic name: Desipramine

Available strengths: 10 mg, 25 mg, 50 mg, 75 mg,
100 mg, 150 mg tablets

Available in generic: Yes

Drug class: Tricyclic antidepressant

General Information

Norpramin (desipramine) exerts its antidepressant action principally by inhibiting the reuptake of **norepinephrine** and, to a lesser extent, **serotonin**, two important neurotransmitters in the central nervous system, and thereby boosting neurotransmission. Norpramin also has other pharmacologic effects, which are associated with its side effects. Depression and other mental disorders may be due to abnormally low levels of certain neurotransmitters in the brain. This abnormality may in turn produce changes in affected areas of the brain, resulting in psychiatric symptoms such as depression or anxiety. Norpramin exerts its antidepressant action presumably by boosting the levels of serotonin and norepinephrine. There is usually a time lag of 3–4 weeks for antidepressants to achieve their optimal effect, which may be the time needed for the brain to restore normal functioning before reducing the symptoms of the illness.

Norpramin was approved by the U.S. Food and Drug Administration (FDA) for the treatment of depression. The use of a medication for its approved indication is called *labeled use*. In clinical practice, however, physicians often prescribe medications for *unlabeled* (“off-label”) uses when published clinical studies, case reports, or their own clinical experiences support the efficacy and safety for those treatments. Unlabeled uses of Norpramin include treatment of chronic pain syndromes (e.g., migraine, diabetic neuropathy, cancer pain), eating disorders (bulimia nervosa), panic disorder, premenstrual dysphoric disorder, posttraumatic stress disorder, and insomnia, and facilitation of cocaine withdrawal. Physicians may also use Norpramin in combination with another antidepressant, such as a **selective serotonin reuptake inhibitor** (SSRI), to augment the antidepressant effect. This augmentation strategy is often successful in treating refractory depression when response to a single antidepressant is inadequate.

Dosing Information

The recommended starting dose is 75 mg, taken once a day, preferably at bedtime. The dosage is increased by 25–50 mg weekly, depending on tolerability, to 100–200 mg/day, which may be taken in a single bedtime

dose or in divided doses. If depressive symptoms persist after 8 weeks, the physician may further increase the dosage up to a maximum of 300 mg/day or switch the patient's medication to another antidepressant. Seniors and adolescents generally require lower dosages of 25–100 mg/day, and dosages greater than 150 mg/day are not recommended for those patients.

Common Side Effects

Because the tricyclic and tetracyclic antidepressants inhibit **cholinergic neurons** in the nervous system, they frequently produce a cluster of symptoms called **anticholinergic** side effects, which include dry mouth and skin, blurred vision, constipation, and difficulty urinating. Usually, individuals become tolerant to these side effects, but excessive anticholinergic effects may lead to confusion and a psychiatric disorder called delirium if not monitored closely. Sometimes the physician may prescribe another medication to counteract the anticholinergic action of the antidepressant. For example, a physician may prescribe a 1% pilocarpine eye drop to treat blurred vision and bethanechol (e.g., Urecholine), a cholinergic agent, to treat urinary difficulties. For constipation, an over-the-counter stool softener such as Colace (docusate) is usually helpful.

Individuals may experience dizziness from tricyclic and tetracyclic antidepressants. Dizziness may be caused by the drugs' effect in momentarily dropping blood pressure; they block the body's compensatory response to maintain a stable blood pressure when a person moves from lying down to a sitting position or from sitting to standing. This reaction is known in medical terms as **orthostatic hypotension**. Seniors and those taking other medications to lower blood pressure may be more susceptible to orthostatic hypotension from these antidepressants.

Weight gain is also another common problem. Most individuals gain several pounds while taking TCAs, including Norpramin. If the individual's weight does not stabilize, the physician may switch the patient's medication to one of the newer, weight-neutral antidepressants such as an SSRI.

Norpramin may also produce sexual difficulties, including impotence and ejaculatory difficulty in men and decreased sexual drive in both men and women. If this is a problem, the physician may switch the patient's medication to another antidepressant, such as bupropion (Wellbutrin-SR or -XR), that does not interfere with sexual functioning.

Adverse Reactions and Precautions

Norpramin may cause significant drowsiness and blurred vision in some people. Patients should not drive, operate machinery, or perform other potentially hazardous tasks until they are certain that their vision, alertness, or coordination is not affected by the medication. Patients with a known allergy to Norpramin or who have experienced a severe reaction after taking it should not take Norpramin.

Norpramin may affect cardiac conduction by slowing the electrical impulses that travel across cardiac tissues, leading to a disturbance in heart rhythms called an arrhythmia. This side effect is common in seniors and in people with a history of arrhythmias or cardiovascular disease. Therefore, patients over 65 years of age and those with a history of heart disease should obtain a pretreatment electrocardiogram and periodic checks (at least annually).

As previously stated, seniors and individuals taking medications to lower blood pressure may be particularly susceptible to Norpramin-induced orthostatic hypotension. In such susceptible individuals, the sudden drop in blood pressure from rising too rapidly may cause fainting. To prevent this from occurring, the individual should rise slowly, allowing blood pressure to adjust gradually.

Use in Pregnancy and Breastfeeding: Pregnancy Category C

Norpramin has not been tested in women to determine its safety in pregnancy. Tricyclic antidepressants are not recommended during pregnancy, especially during the first 3 months. The anticholinergic side effects

induced by these drugs may also affect the baby, known as **fetal anticholinergic effects**. Thus, use during pregnancy must be clearly weighed against the potential risk of the medication to the fetus. Women who are pregnant or may become pregnant should discuss this with their physician. Some women may experience a recurrence of their depression when they stop their antidepressant. In these circumstances it may be necessary to restart the medication or seek an alternative medication or treatment.

Nursing mothers should not take Norpramin, because small amounts will pass into breast milk and be ingested by the baby. If stopping the antidepressant is not an alternative, breastfeeding should not be started or should be discontinued.

Possible Drug Interactions

The combined use of Norpramin with certain medications may result in adverse drug interactions, because one medication may alter the blood levels of the other. The significant drug interactions with Norpramin are summarized in the table below.

Selective serotonin reuptake inhibitors (SSRIs)	The combination of Norpramin with an SSRI may significantly increase the level of Norpramin, resulting in adverse or toxic reactions.
Tegretol (carbamazepine)	This combination may result in decreased levels of Norpramin and lower its positive pharmacologic effects; the combination may also increase Tegretol levels, resulting in more side effects and increased toxicity.
Coumadin (warfarin)	Norpramin may increase Coumadin levels and its anti-coagulant effect, resulting in bleeding.
Catapres (clonidine)	This combination may result in dangerous elevation of blood pressure and should be avoided.
Quinidine	The combination of Norpramin and quinidine, an antiarrhythmia medication, may increase the risk of arrhythmias and should be avoided.
Depakote, Depakote-ER, or Depakene	This combination may elevate Norpramin levels, which may increase side effects.
Anticholinergic agents (e.g., Cogentin, Benadryl)	Anticholinergic side effects may increase when Norpramin is combined with an anticholinergic agent or another medication with anticholinergic side effects.

Antidepressants known as **monoamine oxidase inhibitors (MAOIs)** should not be taken together with Norpramin, because the combination may potentially produce a toxic reaction that includes elevated temperature, high blood pressure, and extreme excitation and agitation. Patients should consult their physician or pharmacist before taking any new medications, including over-the-counter medications and herbal supplements, with Norpramin.

Patients taking Norpramin should avoid alcohol or should consume it in moderation because the combination may worsen depression.

Overdose

Norpramin, like other tricyclic and tetracyclic antidepressants, is extremely lethal in acute overdose, especially in children. Overdoses may result in death, especially when the antidepressant is combined with other medications or alcohol. Disturbance of cardiac rhythm is usually the leading cause of death.

Any suspected overdose should be treated as an emergency. The person should be taken to the emergency department for observation and treatment. The prescription bottle of medication (and any other medication suspected in the overdose) should be brought as well, because the information on the prescription label can be helpful to the treating physician in determining the number of pills ingested.

Special Considerations

Most cases of major depression can be treated successfully, usually with medication, psychotherapy, or both. The combination of psychotherapy and antidepressants is very effective in treating moderate to severe depression. The medications improve mood, sleep, energy, and appetite, while therapy strengthens coping skills, deals with possible underlying issues, and improves thought patterns and behavior.

In general, antidepressants alone help about 60%–70% of those taking them. Although a few individuals may experience some improvement from antidepressants by the end of the first week, most people do not see significant benefits from their antidepressants until after 3–4 weeks, and it can sometimes take as long as 8 weeks for the medication to produce its full effects. Thus it is critical that patients continue to take their antidepressant long enough for the medication to be beneficial and that patients not get discouraged and stop their medication prematurely if they do not feel better immediately.

The controversial issue of suicide and antidepressants has prompted the FDA to ask manufacturers of some antidepressants, particularly the SSRIs, to provide warnings in their package insert that the risk of suicide may be increased in depressed individuals (especially children) during the first several weeks after beginning an antidepressant. However, studies have found that when more people in a community are taking antidepressants, the suicide rate is lower. The risk of suicide is inherent in depression and may persist until the individual responds to treatment. Depressed individuals who are at risk for suicide should be closely watched at the outset of therapy, and any signs of suicidal or violent behavior should be immediately reported to the physician or a mental health provider.

- **Warning:** Always let your physician or a family member know if you have suicidal thoughts. Notify your psychiatrist or your family physician whenever your depressive symptoms worsen or whenever you feel unable to control suicidal urges or thoughts.
- Do not discontinue your medication without consulting with your physician. Norpramin should not be stopped abruptly, but gradually tapered down before discontinuation. Abrupt discontinuation of Norpramin may cause nausea, headache, and malaise.
- If you miss a dose, take it as soon as possible. If it is close to your next scheduled dose, skip the missed dose and continue on your regular dosing schedule, but do not take double doses.
- Norpramin may cause significant drowsiness. Until you are certain that your alertness and coordination are not affected by your medication, you should avoid driving and operating machinery.
- If you experience blurred vision, you should avoid driving, operating machinery, or performing potentially hazardous tasks. Consult your physician if you experience blurred vision.
- Do not take Norpramin if you have a known allergy to Norpramin or have experienced a severe reaction to it.
- Store the medication in its originally labeled, light-resistant container, away from heat and moisture. Heat and moisture may precipitate breakdown of your medication.
- Keep your medication out of reach of children. Tricyclic antidepressants are extremely dangerous in acute overdose in young children.

If you have any questions about your medication, consult your physician or pharmacist.

