

# Remeron (mirtazapine)

Available strengths: 15 mg, 30 mg, 45 mg tablets; 15 mg, 30 mg, 45 mg quick-dissolving tablets (Remeron SolTab)

Available in generic: Yes, except Remeron SolTab

Drug class: Norepinephrine-serotonin modulator antidepressant

## General Information

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Remeron (mirtazapine) exerts its antidepressant action principally through antagonism of certain types of receptors, thereby altering neurotransmission of serotonin and norepinephrine in the brain. Neurotransmitters, such as serotonin and norepinephrine, are chemicals produced by brain cells called neurons that enable them to communicate with each other. The neurotransmitters are released by one neuron into the space between that neuron and the next neuron. The neurotransmitters come into contact on specific sites on the surface membrane of neurons called receptors. From there, the chemical signal is transformed into an electrical impulse and travels down the neuron, causing further release of neurotransmitters. This process of neurotransmission is repeated along a chain of neurons.

Depression and other psychiatric disorders may be caused by 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. When levels of the neurotransmitter are elevated by the antidepressant, the affected areas that were previously altered by the low neurotransmitter levels are restored to normal functioning. Presumably, Remeron works by blocking presynaptic  $\alpha_2$ -adrenergic receptors, which affect serotonin and norepinephrine neurotransmission, thereby boosting the levels of both of these neurotransmitters. In addition, Remeron antagonizes postsynaptic 5-HT<sub>2A</sub>, 5-HT<sub>3</sub>, and H<sub>1</sub> receptors. For these reasons, Remeron is referred to as a norepinephrine-serotonin modulator. 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 make the changes to restore previously affected areas to normal functioning, hence reducing or eliminating the symptoms of the illness.

Remeron was approved by the U.S. Food and Drug Administration (FDA) for the treatment of major depressive disorder. The use of a medication for its approved indication is called its 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 of these medications for these unapproved indications. Unlabeled uses of Remeron include treatment of anxiety disorders with or without depression, posttraumatic stress disorder, and insomnia.

Physicians may use Remeron in combination with a selective serotonin reuptake inhibitor (SSRI) such as Zoloft (sertraline) or Lexapro (escitalopram) to augment the antidepressant effect. This augmentation strategy may be successful in treating refractory depression for which the response to a single antidepressant was inadequate.

## Dosing Information

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The recommended starting dose is 15 mg, taken once a day, preferably in the evening prior to bedtime. After 1–2 weeks, the dosage may be increased in increments of 15 mg/day at intervals of 1–2 weeks up to a maximum of 45 mg/day. Remeron also comes in quick-dissolving tablets (Remeron SolTab) for ease of swallowing.

## Common Side Effects

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Remeron is usually well tolerated, and only infrequently is the medication stopped because of intolerable side effects. The most common side effects are dry mouth, drowsiness, sedation, and weight gain. Daytime sleepiness may be managed by taking a single dose close to bedtime.

For some patients taking Remeron, increased appetite and weight gain may be problematic. About 20% of patients taking Remeron gain weight with long-term use. In addition, Remeron may have effects on cholesterol and triglycerides. Cholesterol may significantly increase in about 15%, and triglycerides in about 6%, of the patients taking Remeron. Management of weight gain is usually accomplished by controlling appetite and diet and through exercise. Cholesterol and triglyceride levels should be checked before and periodically (at least annually) during treatment with Remeron. Any patient with Remeron-induced weight gain should be monitored closely, especially if at risk for diabetes and heart disease.

Unlike SSRIs, Remeron rarely induces sexual dysfunction. It is a useful alternative to other antidepressants that produce sexual dysfunction.

## Adverse Reactions and Precautions

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Remeron may cause drowsiness in some people. Patients should not drive or operate machinery until they are certain that their alertness or coordination is not affected by the medication. Patients with a known allergy to Remeron or who have experienced a severe reaction after taking it should not take Remeron.

## Use in Pregnancy and Breastfeeding: Pregnancy Category C

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Remeron has not been tested in women to determine its safety in pregnancy. The effects of the

medication on the developing fetus in pregnant women are unknown. In animal studies, there was no evidence of harm to the fetus due to Remeron. However, animal studies are not always predictive of effects in humans. 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 Remeron 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

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Like many other medications, Remeron is metabolized in the liver. The combined use of Remeron with some medications may result in adverse drug interactions, because one medication may alter the blood levels of the other. Fortunately, there are few drug interactions with Remeron. The significant drug interactions that have been reported with Remeron are summarized in the table below.

Tagamet (cimetidine)	Tagamet may increase the blood levels of Remeron, potentially causing side effects.
Tegretol (carbamazepine)	Tegretol reduces the blood levels of Remeron, possibly decreasing antidepressant effect.
Luvox (fluvoxamine)	Luvox may significantly increase the blood levels of Remeron to toxic levels when the two medications are combined.

Other medications, including herbal supplements (such as St. John's wort), that boost serotonin can result in excessive levels of the neurotransmitter serotonin when combined with Remeron and produce a toxic syndrome known as serotonin syndrome. The early signs of serotonin syndrome are restlessness, confusion, tremors, flushing, and involuntary muscle jerks. If the medications are not stopped, the individual may develop more life-threatening complications resulting in muscle disorders, high fever, respiratory problems, clotting problems, and destruction of red blood cells that can lead to acute renal failure. Hence, patients taking Remeron should be alert to the possible signs of serotonin syndrome, which require immediate medical attention and discontinuation of the serotonin-boosting medications.

Antidepressants known as monoamine oxidase inhibitors (MAOIs) should not be taken together with Remeron, 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 Remeron.

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

## Overdose

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Compared with some other antidepressants, such as tricyclic antidepressants, Remeron is relatively safe in overdose. However, when multiple medications are involved in overdose, the other medications may increase the risk of more serious complications.

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

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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.
- 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.
- Remeron may be taken with or without food.
- 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.