



Wellbutrin/Wellbutrin-SR/ Wellbutrin-XL (bupropion)

Generic name: Bupropion

Available strengths: 75 mg, 100 mg immediate-release tablets;
100 mg, 150 mg, 200 mg sustained-release tablets
(Wellbutrin-SR); 150 mg, 300 mg extended-release tablets
(Wellbutrin-XL)

Available in generic: Yes, except extended-release tablets

Drug class: Dopamine-norepinephrine reuptake inhibitor
antidepressant

General Information

Unlike the **selective serotonin reuptake inhibitors** (SSRIs) such as Prozac (fluoxetine), **Wellbutrin (bupropion)** has more than one mechanism of action. Presumably, it works primarily by altering the neurotransmission of **dopamine** and **norepinephrine** in the brain. *Neurotransmitters*, such as dopamine 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 member of the neuron 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. Wellbutrin works in the brain by inhibiting dopamine and norepinephrine from going back into the neurons where they were originally produced; therefore the antidepressant increases levels of the neurotransmitters. Consequently, Wellbutrin is classified as a *dopamine-norepinephrine reuptake inhibitor* (DNRI).

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 antidepressants, the affected areas of the brain that were previously altered by the low neurotransmitter levels are restored to normal functioning. 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.

Wellbutrin was approved by the U.S. Food and Drug Administration (FDA) for the treatment of major depressive disorder and smoking cessation (with the sustained-release tablet, which is marketed under the brand **Zyban**). The use of a medication for its approved indications 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. A common unlabeled use of Wellbutrin is for the treatment of attention-deficit/hyperactive disorder in both children and adults. It is a safe alternative to stimulants such as Ritalin (methylphenidate) or Dexedrine (dextroamphetamine).

Physicians may use Wellbutrin in combination with another antidepressant, such as an **SSRI** (e.g., Zoloft, Lexapro, Paxil) to augment the antidepressant effect. This augmentation strategy may be successful in treating refractory depression for which response to a single antidepressant was inadequate. Because Wellbutrin is associated with few or no sexual side effects, it is a good alternative for individuals who have had sexual dysfunction from other antidepressants such as SSRIs or Effexor. Wellbutrin generally has not been effective in the treatment of anxiety disorders, such as panic disorder, in part because Wellbutrin is activating and anxious patients prefer other agents, such as an SSRI, over Wellbutrin.

Dosing Information

Wellbutrin is available in three formulations: immediate-release (Wellbutrin), sustained-release (Wellbutrin-SR), and extended-release (Wellbutrin-XL) tablets. All three contain the same active ingredient, but the rate in which they are absorbed from the stomach and intestines into the blood stream varies. Immediate-release Wellbutrin is more quickly absorbed and eliminated and usually needs to be taken three times a day. Wellbutrin-SR tablets have a slower release and can be taken twice daily. Wellbutrin-XL requires only once-daily dosing. Because of the convenience of the sustained- and extended-release tablets, they have largely replaced the earlier immediate-release formulation; they also are associated with fewer side effects. Both the immediate-release and sustained-release tablets are available in generic forms, but the extended-release tablet is not.

The usual starting dose of Wellbutrin-SR or Wellbutrin-XL is 150 mg, taken once a day, for 1 week. Generally, the target dosage for treatment of depression is 300 mg/day. The dosage may be increased after 1 week, to 150 mg twice a day with Wellbutrin-SR or 300 mg once a day with Wellbutrin-XL. The maximum recommended dosage is 400 mg/day for the sustained-release (in divided doses) and 450 mg/day (in a single dose) for the extended-release formulation.

Common Side Effects

Wellbutrin-SR and Wellbutrin-XL are usually well tolerated, and only infrequently is the medication stopped because of intolerable side effects. The most common side effects of Wellbutrin-SR and -XL are dry mouth, nervousness, tremors, and insomnia. Insomnia may be managed by taking the daily dose of Wellbutrin-XL early in the morning or by taking the second dose of Wellbutrin-SR early in the evening, with a separation of 6–8 hours between the morning and evening doses.

Other antidepressants, such as **monoamine oxidase inhibitors** (MAOIs), **tricyclic antidepressants** (TCAs), and SSRIs frequently induce sexual dysfunction. In contrast, patients taking Wellbutrin generally do not encounter this problem. Moreover, Wellbutrin does not induce weight gain and is a useful alternative for patients who experience excessive weight gain from other antidepressants.

Adverse Reactions and Precautions

A concern with Wellbutrin is the potential for developing seizures at higher dosages. This adverse reaction was evident in patients when they exceeded 150 mg in a single dose or a total daily dosage of 400 mg. Seizures occurred mainly with the immediate-release form of Wellbutrin, and the risk of seizures has significantly decreased with the introduction of the sustained-release and extended-release formulations. To reduce the

risk of seizures, the manufacturer recommends limiting a single dose to a maximum of 200 mg for Wellbutrin-SR and 150 mg for Wellbutrin; the maximum total daily dosage of either formulation should not exceed 400 mg/day. With the recent advance formulation of Wellbutrin-XL, a single daily dose is safe up to 300 mg, but the maximum total dosage should not exceed 450 mg/day. The concurrent use of stimulants, alcohol, and cocaine with Wellbutrin may increase the risk of seizures. In patients with head injury or an eating disorder such as bulimia nervosa and anorexia nervosa, the risk of seizures is apparently increased when taking Wellbutrin. In patients with a seizure disorder, Wellbutrin should be avoided.

Wellbutrin must be used with caution in patients with liver impairment, and the dosage may need to be reduced.

Use in Pregnancy and Breastfeeding: Pregnancy Category B

Wellbutrin 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 when exposed to Wellbutrin. Animal studies, however, 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 Wellbutrin 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

Like many other medications, Wellbutrin is metabolized in the liver. The combined use of Wellbutrin 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 Wellbutrin. The significant drug interactions reported with Wellbutrin are summarized in the table below.

Tegretol (carbamazepine)	Tegretol reduces the blood levels of Wellbutrin, possibly decreasing its antidepressant effects.
Antiparkinson agents (e.g., levodopa, Sinemet)	If Wellbutrin is combined with antiparkinson medications to treat Parkinson’s disease, dopamine levels in the brain may be elevated, increasing the probability of side effects such as hallucinations.
Norvir (ritonavir)	The AIDS medication Norvir may increase blood levels of Wellbutrin, increasing the risk of Wellbutrin toxicity and adverse effects, especially seizures in high-risk individuals.

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

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

Overdose

Compared with some other antidepressants, such as TCAs, Wellbutrin is safe in overdose. In most cases of Wellbutrin overdose, the most serious reaction was seizures, but patients generally recovered without significant sequelae. 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

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) 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.
- 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.
- Do not crush or cut the sustained-release or extended-release tablets; swallow them whole.
- Wellbutrin may be taken with or without food.
- Be aware that Wellbutrin is also prescribed for smoking cessation under the brand name Zyban, which contains sustained-release Wellbutrin. To prevent the co-administration of Wellbutrin and Zyban, inform your physician if you are taking a Wellbutrin medication.
- 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.

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

