



Effexor/Effexor XR (venlafaxine)

Generic name: Venlafaxine

Available strengths: 25 mg, 37.5 mg, 50 mg, 75 mg,
100 mg immediate-release tablets; 37.5 mg, 75 mg,
150 mg controlled-release capsules (Effexor-XR)

Available in generic: No

Drug class: Serotonin-norepinephrine reuptake
inhibitor antidepressant

General Information

Unlike the selective-serotonin reuptake inhibitors (SSRIs) such as Prozac (fluoxetine), which are relatively **serotonin**-specific antidepressants, **Effexor (venlafaxine)** has a dual mechanism of action. Presumably, it works by altering the neurotransmission of both **serotonin** and **norepinephrine**, two important neurotransmitters in the brain.

During neurotransmission, *neurotransmitters* are released by one neuron into the space between that neuron and the next neuron. The neurotransmitters come into contact with specific sites on the surface membrane of neurons called receptors. From there, the chemical is transformed into an electrical impulse that travels down the neuron, causing further release of neurotransmitters. This process of neurotransmission is repeated along a chain of neurons. During neurotransmission, after neurotransmitters are released and the chemical signal is transferred to neurons, the neurotransmitters are recaptured back into brain cells by a process known as *reuptake*. By blocking the neurotransmitters from going back into the neurons from where they were released, the antidepressant can amplify the effects of the neurotransmitter.

Effexor exerts its antidepressant effect principally by blocking the reuptake of serotonin and norepinephrine. This action is similar to that of the SSRIs, but notably different in that Effexor also inhibits the reuptake of norepinephrine. Through reuptake inhibition, Effexor boosts serotonin and norepinephrine neurotransmission. For this reason, Effexor is called a *serotonin-norepinephrine reuptake inhibitor* (SNRI). Depression and other mental disorders may be caused by abnormally low levels (or abnormal neurotransmission) of serotonin, norepinephrine, or both. This abnormality may in turn produce changes in affected areas of the brain, resulting in psychiatric symptoms such as depression or anxiety. When neurotransmission is improved by the antidepressant, the affected areas of the brain are restored to normal functioning, reducing the symptoms of the illness.

Effexor was approved by the U.S. Food and Drug Administration for the treatment of major depressive disorder, generalized anxiety disorder, and social anxiety disorder. The use of a medication for its approved

indications is called its *labeled use*. In clinical practice, 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. Physicians often prescribe Effexor to treat panic disorder and posttraumatic stress disorder, attention-deficit/hyperactivity disorder, neuropathic pain, fibromyalgia, and other chronic pain conditions. Effexor has also proved useful in treating more seriously depressed patients with melancholic depression, which may not respond as well to other antidepressants.

Dosing Information

Effexor comes in two formulations: immediate-release tablets (Effexor-IR) and extended-release capsules (Effexor-XR). In general, physicians prefer to prescribe Effexor in the extended-release form because it offers the convenience of once-daily dosing and because the slow-release form may be better tolerated over the immediate-release tablet.

The recommended starting dosage is 75 mg/day, taken in two or three divided doses in the immediate-release tablets or once a day in the extended-release capsule. For some patients, especially for seniors and those with chronic medical problems, a starting dosage of 37.5 mg/day of Effexor-XR may be better tolerated, with subsequent increases in dosage to 75 mg/day. The dosage then may be increased after another week or two, depending on tolerability and clinical response, to 150 mg/day. If needed, further dosage increases are made gradually. For outpatient treatment of moderate depression, the dosage range for Effexor-XR is usually between 75 mg/day and 225 mg/day. For more severe depression and depression refractory to other treatments, higher dosages may be needed. The usual maximum dosage for Effexor-IR is 375 mg/day and for Effexor-XR is 225 mg/day.

Common Side Effects

The most common side effects from taking Effexor are nausea, vomiting, dry mouth, nervousness, anxiety, dizziness, headaches, and insomnia. Side effects generally occur after starting the medication or when increasing the dose. If side effects become intolerable, the physician may decrease the dosage to allow the individual to adjust to the medication before increasing it again slowly.

Sexual side effects, including delayed orgasm in women and retarded ejaculation in men, occur at about the same rate with Effexor as with the other SNRI antidepressant Cymbalta, but less than the 50%–60% incidence reported with the SSRIs.

Adverse Reactions and Precautions

In about 5% of patients taking normal dosages of Effexor, mild elevation of blood pressure (hypertension) may occur. At higher dosages, the incidence of Effexor-induced hypertension may be higher. The increase in blood pressure is usually modest, and very few patients have to discontinue Effexor because of hypertension. Generally, lowering the dosage will normalize blood pressure. For this reason, patients' blood pressure should be checked before starting Effexor and routinely during therapy as a precautionary measure, especially for individuals with preexisting hypertension or those with a history of heart disease.

Effexor 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 Effexor or who have experienced a severe reaction after taking it should not take Effexor.

Use in Pregnancy and Breastfeeding: Pregnancy Category C

Effexor has not been tested in women to determine its safety in pregnancy. The effects of the medication on the developing fetus are unknown. 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 Effexor 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

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

Tagamet (cimetidine)	Tagamet may inhibit the metabolism of Effexor. This can result in elevated levels of Effexor, potentially increasing adverse side effects. Blood pressure should be monitored closely with this combination.
Selective serotonin reuptake inhibitors (SSRIs)	SSRIs, particularly Paxil, may inhibit the metabolism of Effexor and elevate blood levels. When this combination is used for treatment of refractory depression, blood pressure should be monitored closely. Patients should also be monitored for signs of serotonin syndrome.
Tricyclic antidepressants (TCAs)	Effexor may increase levels of TCAs when this combination is used, potentially increasing adverse side effects from the TCA. Patients should also be monitored for signs and symptoms of serotonin syndrome.
Haldol (haloperidol)	Effexor can decrease the clearance of Haldol and increase its blood levels, potentially increasing adverse side effects of the antipsychotic medication.

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 Effexor 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 Effexor 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 Effexor, 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 Effexor.

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

Overdose

In contrast to tricyclic and MAOI antidepressants, overdose with Effexor is generally much less dangerous, especially when taken alone, than the older antidepressants. Patients more often overdose with multiple medications, and other medications may increase the risk of more serious complications. The combination of central nervous depressants (e.g., alcohol, narcotics, benzodiazepines) and Effexor can be lethal, and death is usually from respiratory depression.

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. Effexor may also be very beneficial for treating anxiety.

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 physicians whenever your depressive symptoms worsen or whenever you feel unable to control suicidal urges or thoughts.
- Do not discontinue Effexor abruptly. To prevent unpleasant discontinuation symptoms, Effexor requires gradual tapering before completely stopping the medication.

