



Lithium

(Eskalith, Eskalith-CR, Lithium Citrate, Lithobid, Lithotab)

Brand names: Eskalith, Eskalith-CR,
Lithium citrate, Lithobid, Lithotab

Available strengths: 150 mg, 300 mg, 600 mg capsules;
300 mg tablet (Eskalith);
450 mg controlled-release tablet (Eskalith-CR);
8 mEq/5 mL or 300 mg/5 mL syrup (Lithium citrate)
300 mg slow-release tablet (Lithobid);
300 mg tablet (Lithotab)

Available in generic: Yes

Drug class: Mood stabilizer

General Information

Lithium has been the standard of treatment for bipolar disorder for a number of years and was one of the first mood stabilizers used in the treatment of mood disorders. Over several decades of clinical experience, it has become evident that lithium is effective not only in treating mania but also in preventing relapse of mania and depression in bipolar disorder. Lithium is also used to augment antidepressant therapy when treatment of depression is unsuccessful with antidepressants alone. This augmentation of an antidepressant with lithium is often effective for treating refractory depression as well as preventing depressive relapse.

Lithium is a simple ion, not unlike sodium found in table salt (sodium chloride). It is available in the salt form as lithium carbonate and in a liquid preparation as lithium citrate. Lithium carbonate is also available in controlled-release preparations (Lithobid and Eskalith-CR), which may help reduce many of the gastrointestinal side effects associated with lithium.

It is interesting how a simple ion like lithium has such complex action in the brain. Lithium's actions in mood stabilization are probably the result of complex actions on different neurotransmitter systems in the

brain. Lithium appears to stabilize the balance between excitatory and inhibitory effects of different neurons and their neurotransmitters. Bipolar disorder may be conceptualized as overactivation of neurons and neuronal systems. Mania may be the result of the excitatory neuronal system being overactivated, and conversely, overactivation of the inhibitory neural system may result in depression. Lithium's ability to dampen these neural systems may explain its effectiveness in mania and depression.

Dosing Information

Lithium therapy must be carefully monitored with laboratory tests because of its potential for toxicity. Before starting therapy, it is important for the patient's renal function to be determined, because the kidneys primarily eliminate lithium. The dosage must be adjusted for individuals with reduced renal function. Lithium levels are measured routinely to determine if adequate plasma levels are achieved with the specific dosage. When clinical response is achieved, lithium levels are generally in the range of 0.7–1.2 mEq/L (milliequivalents per liter). However, lithium has a narrow therapeutic window, and when serum levels exceed 1.5 mEq/L, lithium toxicity is a concern.

In acute mania, higher dosages are usually necessary for optimal response. One strategy is starting with 300 mg twice a day and increasing by 300 mg/day every 3–5 days until manic symptoms abate and if lithium has not reached toxic levels. Dosages may vary from 600 to 1,800 mg/day depending on the patient's size, age, and kidney function. Once the patient's mania is in remission, the goal is to prevent relapse with maintenance therapy. The maintenance dosage may be lowered so that the patient may better tolerate the medication and continue to take lithium on a long-term basis.

Common Side Effects

Gastrointestinal side effects are the most frequent side effects associated with taking lithium, including dry mouth, nausea, vomiting, abdominal cramping, indigestion, bloated feeling, and excessive salivation. Stomach upset may be avoided by taking lithium immediately after meals or with food. Other side effects related to lithium therapy include drowsiness and mental sluggishness, fine tremors of fingers, drying and thinning of hair, skin rash, exacerbation of acne and psoriasis, frequent urination, thirst, and weight gain. Generally, many of these side effects subside as the patient develops tolerance to lithium, or the side effect may be managed by lowering the dosage.

Adverse Reactions and Precautions

Lithium may cause drowsiness and impair alertness, especially at the start of therapy. Patients should use caution when driving or performing tasks that require alertness.

Lithium Toxicity

There is a narrow margin between the therapeutic and toxic levels of lithium. Close monitoring of lithium levels is important. Early symptoms of lithium toxicity include drowsiness, diarrhea, vomiting, nausea, muscular weakness, and impaired coordination. At higher lithium levels, toxic symptoms include dizziness, ringing in the ears (**tinnitus**), slurred speech, increasing confusion, blurred vision, inability to coordinate movements (**ataxia**), and twitching of facial muscles and limbs. At very toxic levels, there is danger of death resulting from seizures, arrhythmias, and delirium. Thus, early recognition and intervention are important to reverse lithium toxicity. When the aforementioned symptoms develop, the patient should interrupt lithium therapy and contact his or her physician as soon as possible.

It is important to keep in mind that the kidneys excrete lithium, and interference with its elimination may increase lithium to toxic levels. In patients with renal disease, excretion of lithium may be significantly compromised. The dosage must be adjusted lower to compensate for reduced renal function. With dehydration, a low-salt diet, or taking lithium with thiazide diuretics, the kidneys reabsorb lithium back into the body more intensely, which results in high lithium levels and frequently causes toxicity. Dehydration can result from inadequate fluid intake, especially on hot days with excessive physical exertion and from fever and diarrhea.

Hypothyroidism

Long-term lithium therapy may affect the thyroid glands and diminish thyroid function (**hypothyroidism**). A common laboratory test used to measure thyroid function is to obtain a **thyroid stimulating hormone (TSH)** level. TSH is a hormone that stimulates the function of the thyroid glands. An elevated TSH level in the presence of clinical symptoms is indicative of hypothyroidism. Clinical signs and symptoms of hypothyroidism may include enlarged thyroid glands, tiredness, intolerance to cold, low energy, and depression. Lithium-induced hypothyroidism may be reversed when the medication is discontinued or if the patient receives supplemental thyroid hormone.

Abnormal Electrocardiogram

Lithium may affect the electrical conduction in the heart and thus the rhythm of the heart. It may induce changes that show up on the electrocardiogram. Although most people taking lithium experience no change in cardiac function, the physician may order a pre-treatment electrocardiogram for seniors or for those who have a history of cardiovascular disease.

Impairment of Kidneys to Concentrate Urine

Infrequently, chronic lithium administration is associated with impairment of the concentrating ability of the kidneys (**nephrogenic diabetes insipidus**). As a result, the individual is unusually thirsty and must drink copious amounts of water, which is lost through frequent urination because the kidneys cannot reabsorb and conserve the body's water. Fortunately, this disorder can be reversed when lithium is decreased or discontinued.

Use in Pregnancy and Breastfeeding: Pregnancy Category D

Lithium crosses the placenta and may cause harm to the fetus. Cases of newborns with cardiac abnormalities have been reported in women who took lithium during pregnancy. The risk appears to be highest when lithium is taken in the first trimester. The use of lithium should be avoided in pregnancy whenever possible, especially in the first trimester. However, when lithium is stopped, reoccurrence of mania may be harmful for the mother and unborn child. In these circumstances, the physician may discuss the need to restart lithium after the first trimester or seek an alternative medication or treatment.

Nursing mothers should not take lithium, because it is excreted in breast milk and may be harmful to the baby when ingested. If stopping the medication is not an alternative, breastfeeding should not be started or should be discontinued.

Possible Drug Interactions

Some medications when taken concomitantly with lithium may result in drug interactions that alter their levels, which may produce undesired reactions. The clinically significant drug interactions reported with lithium are summarized in the table on the next page.

Thiazide diuretics	Thiazide diuretics (e.g., hydrochlorothiazide, Zaroxolyn) may increase lithium serum levels and induce toxicity.
Haldol (haloperidol)	The combination of Haldol and lithium may increase neurotoxic effects despite normal lithium and Haldol levels.
Loop diuretics (e.g., Lasix)	Loop diuretics such as Lasix (furosemide) may increase levels of lithium and induce toxicity. This interaction is less likely with loop diuretics than with thiazides diuretics.
Potassium iodide	Concurrent use of potassium iodide (used as an expectorant) and lithium may increase the risk of hypothyroidism.

Patients taking lithium should not consume alcohol because the combination may make some side effects worse. For example, drinking excessive alcohol can cause dehydration, and this may increase lithium to toxic blood levels. Moreover, the sedative effects of alcohol can act as a depressant, obscuring the therapeutic effects of lithium and complicating treatment.

Overdose

Lithium overdose is extremely hazardous, and the severity of toxic symptoms increases with increasing lithium levels. When serum lithium levels are between 1.5 and 2.0 mEq/L, common symptoms include diarrhea, nausea, vomiting, dizziness, muscle weakness, and impaired coordination. As the levels increase greater than 2.0 mEq/L, symptoms may include blurred vision, increased confusion and disorientation, muscle twitches, and urinary and fecal incontinence. When levels reach 3.0 mEq/L and higher, complications may include seizures, acute renal failure, cardiac arrhythmias, low blood pressure, and cardiovascular collapse, with a high risk of mortality.

Any suspected overdose should be treated as an emergency. The person should be taken to the emergency department for observation and treatment. In severe cases, hemodialysis may be indicated. 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

- It is important understand that after your manic symptoms abate, you will need to continue taking your medication to prevent relapse.
- If you miss a dose, take it as soon as possible, within 2–3 hours of the scheduled dosing. 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.
- Take lithium immediately after meals or with food to decrease stomach upset.
- Drink plenty of water or liquid to prevent dehydration, especially from prolonged exposure to hot weather.
- Contact your physician if you have fever or diarrhea.

