PRODUCT MONOGRAPH

INCLUDING PATIENT MEDICATION INFORMATION

[Pr] LITHANE

Lithium carbonate capsules USP

Capsules, 150 and 300 mg, Oral

Antimanic agent

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RECENT MAJOR LABEL CHANGES

7 Warnings and Precautions, Skin	06/2022

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Sections or subsections that are not applicable at the time of authorization are not listed.

PART I: HEALTH PROFESSIONAL INFORMATION

1 INDICATIONS

LITHANE (lithium carbonate) is indicated for:

- the treatment of acute manic episodes in patients with manic-depressive disorders.

Maintenance therapy has been found useful in preventing or diminishing the frequency of subsequent relapses in bipolar manic-depressive patients (with a strong history of mania).

1.1 Pediatrics

Pediatrics (<18 years of age): Health Canada has not authorized an indication for pediatric use (see 7.1.3 Pediatrics).

1.2 Geriatrics

Evidence from clinical studies and experience suggests that use in the geriatric population is associated with differences in safety or effectiveness (see 7.1.4 Geriatrics).

2 CONTRAINDICATIONS

LITHANE (lithium carbonate) is contraindicated in patients with:

- who are hypersensitive to this drug or to any ingredient in the formulation, including any non-medicinal ingredient, or component of the container. For a complete listing, see 6 Dosage forms, strengths, composition and packaging.
- significant cardiovascular or renal disease;
- evidence of severe debilitation;
- evidence of severe dehydration;
- sodium depletion;
- brain damage;
- conditions requiring low sodium intake.

3 SERIOUS WARNINGS AND PRECAUTIONS BOX

Serious Warnings and Precautions

- **Therapy with LITHANE (lithium carbonate) requires reaching plasma levels of lithium which are relatively close to the toxic level. Lithium toxicity is closely related to serum lithium concentrations (should usually not exceed 1.5 mmol/L), and can occur at doses close to therapeutic concentrations. Facilities for prompt and accurate serum lithium determinations should be available before initiating therapy since frequent serum determinations are required especially during the initial period of treatment.**

- **Since lithium is excreted primarily by the kidney, adequate renal function and adequate salt and fluid intake (2500 to 3000 mL) are essential in order to avoid lithium accumulation and intoxication. A decision to initiate lithium therapy should be preceded by a thorough clinical examination and evaluation of each patient, including laboratory determinations, electrocardiogram (ECG), and a very careful assessment of renal function.**

- **Outpatients and their families should be warned that patients must discontinue LITHANE therapy and contact their physician immediately if clinical signs of lithium toxicity such as diarrhea, vomiting, tremor, mild ataxia, drowsiness, fatigue or muscular weakness occur.**

- **There is evidence of decreased tolerance to lithium once the acute manic episode breaks. Therefore, when the acute attack subsides, the dosage should be reduced rapidly in order to produce serum lithium levels no higher than between 0.6 and 1.2 mmol/L.**

4 DOSAGE AND ADMINISTRATION

4.1 Dosing Considerations

- Selection of patients and approach to lithium therapy: since lithium acts without the production of "sedation", some prefer it to neuroleptics or use these to supplement lithium therapy and obtain rapid control of overt manic behaviour. Lithium also has a useful indication in those cases that fail to respond to neuroleptics. The results of lithium therapy depend largely on the nature and course of the illness itself, rather than on the symptoms. The selection of patients for long-term treatment requires a clear-cut diagnosis of primary affective disorder, the condition for which the stabilizing effects of lithium have been found useful. The variables that have been more consistently associated with response to lithium therapy in patients with a primary affective disorder are: the good quality of remissions with good function and no significant symptomatology during the free intervals between previous episodes of illness; low frequency of episodes, typically 1 or 2 (and not more than 3 or 4) per year; and symptomatology during the acute episodes that meet strict criteria for a primary affective disorder (DSM-III: Research Diagnostic Criteria).

- Screening for lithium candidates should include at least: a medical history and physical examination with emphasis on the CNS, urinary, cardiovascular, gastrointestinal and endocrine systems and the skin. It should also include: routine 24 hour urine volume, serum creatinine, record of weight, an ECG, possibly electrolytes and TSH, and for long-term treatment, creatinine clearance and a urine concentration test. Other examinations and tests should be used when indicated.

- Monitoring lithium treatment should include, for each visit: mental status, physical examination, weight, 12 hour serum lithium and a check for lithium side effects and compliance. It should also include serum creatinine every 2 months, plasma thyroid hormone and TSH every 6 to 12 months, particularly in female patients, and attention to renal and thyroid function should be maintained throughout, with tests used for baseline screening repeated as required. Also, consider serum calcium level before onset of treatment, after 6 months, and yearly thereafter in long-term treatment.

- The first objective of treatment is to establish an effective and safe daily dosage of lithium with the aid of standardized 12 hour serum lithium levels maintained within the therapeutic range, as high as necessary for efficacy, and with the patient as much as possible free of significant side effects. Three daily doses should be used initially, at least until the daily dosage is established. The next aim

is to move to an optimal dose, which should be as low as possible, consistent with protection against relapse. During follow-up, an adjustment to lower dosages may be required to minimize adverse effects, and a change in the lithium preparation used and/or the frequency of dosing, either towards multiple doses or towards a single dose, may be necessary to handle absorption-related adverse effects or concern over possible renal toxicity. Intermittent lithium treatment in carefully selected patients has been recommended by some lithium experts, but should not be undertaken without careful planning and great caution. The cooperation of patients and relatives is required throughout.

- Before deciding on the institution of long-term treatment, it is essential to establish that the patient has clearly responded to a course of stabilizing lithium therapy and that the risk of such therapy is acceptable. Maintaining a patient with a lithium non-responsive condition on long-term therapy poses an unacceptable risk. A decision with regards to long-term therapy can be made during a time-limited trial of lithium therapy with frequent reassessment of outcome. The following are among the factors to be reassessed before a decision is made: careful reconfirmation of the diagnosis of primary affective disorder; the health status of the patient; the side effects of lithium therapy experienced by the patient; and the response to treatment. Assessment of response to treatment is based strictly on firm evidence of relapse prevention during a reasonable trial period, but can be assisted by consideration of the predictors of response outlined above. Great pains should be taken to exclude false responders and false non-responders. It should also be borne in mind that non-responders are more susceptible to the adverse effects of lithium.

4.2 Recommended Dose and Dosage Adjustment

Acute Mania

The therapeutic dose of LITHANE (lithium carbonate) for the treatment of acute mania should be based primarily on the patient's clinical condition. It must be individualized for each patient according to blood levels and clinical response. Manic patients usually require serum lithium levels in excess of 1 mmol/L and the dosage should be adjusted to obtain serum levels between 1 and 1.5 mmol/L (in blood samples drawn before the patient has had his first lithium dose of the day; see Note below Table 1).

In properly screened adult patients, the suggested daily dosage for acute mania is 1800 mg (approximately 50 mmol), divided into three doses. In view of the large variability of renal lithium excretion between individuals, it is suggested that lithium treatment be started at a dose between 600 and 900 mg/day, reaching a level of 1200 to 1800 mg in divided doses on the second day (Table 1). Depending on the patient's clinical condition, the initial dosage should be adjusted to produce the desired serum lithium level. The weight of the patient should also influence the choice of the initial dose.

LITHANE should be used cautiously and in reduced doses in the elderly patient, usually in the range of 600 to 1200 mg/day. Serum lithium levels should be monitored frequently and kept below 1.5 mmol/L (Table 1).

Long-Term Control

After the acute manic episode subsides, usually within a week, the dosage of LITHANE should be rapidly reduced to achieve serum levels between 0.6 and 1.2 mmol/L (with the level kept below 1.5 mmol/L) (Table 1), since there is evidence at this time of a decreased tolerance to lithium. The average suggested dosage at this stage is 900 mg/day (approximately 25 mmol), divided into three doses, with a range usually between 600 and 1200 mg/day (Table 1). If a satisfactory response is not obtained in 14 days, lithium therapy should be discontinued. When the manic attack is controlled, lithium

administration should be maintained during the expected duration of the manic phase, since early withdrawal might lead to relapse. It is essential to maintain clinical supervision of the patient and monitor lithium levels as required during treatment (see 7 WARNINGS AND PRECAUTIONS, General).

Lithium may be used concomitantly with neuroleptic drugs (See 7 WARNINGS AND PRECAUTIONS, Neurologic and 9 DRUG INTERACTIONS).

Serum lithium levels in uncomplicated cases receiving maintenance therapy during remission should be monitored at least every 2 months.

Patients abnormally sensitive to lithium may exhibit toxic signs at serum levels of 1.0 to 1.4 mmol/L. Elderly patients often respond to reduced dosage and may exhibit signs of toxicity at serum levels ordinarily tolerated by other patients.

Table 1. Lithium Dosing

	Acute Mania		**Long-Term Control (usually within a week of manic episode subsides)**
	Treatment Initiation	**Day 2 and onward**	
Adults	600-900 mg/day in divided doses	1200 to 1800 mg in divided doses (serum lithium concentration reaching 1 to 1.5 mmol/L)	600-1200 mg/day with a suggested dose of 900 mg/day in divided doses (serum lithium concentration of 0.6 to 1.2 mmol/L
Elderly		600 to 1200 mg/day (serum lithium concentration below 1.5 mmol/L)	

NOTE: Blood samples for serum lithium determinations should be drawn immediately prior to the next dose when lithium concentrations are relatively stable (i.e. 8-12 hours after the previous dose). Total reliance must not be placed on serum levels alone. Accurate patient evaluation requires both clinical and laboratory analysis.

Discontinuation of Therapy

The majority of patients do not experience withdrawal symptoms or rebound phenomenon upon cessation of long-term lithium therapy. In view of the occasional reports of sudden relapses occurring with abrupt discontinuation, gradual discontinuation is recommended unless abrupt withdrawal is necessary because of toxicity.

4.5 Missed Dose

In case of missed dose, the next dose should be taken as scheduled. A double dose should not be taken.

5 OVERDOSAGE

Symptoms

Lithium toxicity is closely related to the concentration of lithium in the blood and is usually associated with serum levels in excess of 2 mmol/L. Early signs of toxicity which may occur at lower serum levels are described under section 8

ADVERSE REACTIONS and usually respond to reduction of dosage. Lithium intoxication has been preceded by the appearance or aggravation of the following symptoms: sluggishness, drowsiness, lethargy, coarse tremors or muscle twitching, loss of appetite, vomiting and diarrhea. Occurrence of these symptoms requires immediate cessation of medication and careful clinical reassessment and management.

In eight cases of lithium poisoning, the patients frequently developed muscle rigidity with hyperactive deep reflexes, generalized muscle tremors or fasciculations, attacks of hyperextension of the limbs with gasping and wide opening of the eyes, and sometimes epileptic seizures and various neurological dysfunction. There was progressive impairment of consciousness and in some patient's coma. Electroencephalography (EEG) changes in some patients consisted of decrease of alpha activity and increase of theta and delta activity, the latter at times paroxysmal with maximal activity frontally. Periods of beta activity with sharp waves were also observed. The kidney function was probably impaired in several patients. Three of these patients died, all of pulmonary complications.

Treatment

No specific antidote for lithium poisoning is known. The treatment of lithium poisoning is symptomatic. Early symptoms of lithium toxicity can usually be treated by reduction or cessation of dosage of the drug and resumption of treatment at a lower dose after 24 to 48 hours. In severe cases of lithium poisoning, the first and foremost goal of treatment consists of elimination of this ion from the organism. Treatment of lithium poisoning is 1) lavage, 2) correction of fluid and electrolyte imbalance, and 3) regulation of kidney function. Sodium depletion in particular must be corrected. However, administration of large amounts of sodium in the absence of depletion of this electrolyte has not been very successful in many as a means of speeding lithium excretion. Lithium excretion may be facilitated by the judicious use of intravenous urea, sodium bicarbonate, acetazolamide or aminophylline. Hemodialysis is an effective and rapid means of removing the ion from the severely toxic patient or in the presence of impaired renal function. Infection prophylaxis, regular chest X-rays and preservation of adequate respiration are essential.

For management of a suspected drug overdose, contact your regional poison control centre.

6 DOSAGE FORMS, STRENGTHS, COMPOSITION AND PACKAGING

Table 2 – Dosage Forms, Strengths, Composition and Packaging

Route of Administration	Dosage Form / Strength/Composition	Non-medicinal Ingredients
Oral	Capsules 150 mg, 300 mg	Gelatin (from capsules)

Description

LITHANE (lithium carbonate) is available as capsules containing 150 and 300 mg of lithium carbonate. LITHANE capsules contain pure lithium carbonate with no excipient.

The 300 mg green and ivory #1 capsules are available in opaque plastic bottles (HDPE) of 1000 capsules. The 150 mg ivory #3 capsules are available in opaque plastic bottles of 100 and 1000 capsules.

7 WARNINGS AND PRECAUTIONS

Please see 3 SERIOUS WARNINGS AND PRECAUTIONS BOX.

General

Periodic review and monitoring of kidney and cardiovascular function is advisable during therapy with lithium carbonate. Other laboratory tests should be performed as indicated by the patient's clinical condition. The appearance of signs of toxicity or a rise in the blood level of lithium after the dosage is stabilized should alert the physician to determine the reasons for lithium accumulation.

Therapy with LITHANE (lithium carbonate) requires reaching plasma levels of lithium which are relatively close to the toxic level. Since lithium is excreted primarily by the kidney, adequate renal function and adequate salt and fluid intake (2500 to 3000 mL) are essential in order to avoid lithium accumulation and intoxication. Thus, a decision to initiate lithium therapy should be preceded by a thorough clinical examination and evaluation of each patient, including laboratory determinations, ECG, and a very careful assessment of renal function.

Means of obtaining accurate determination of serum lithium levels should be available, since frequent serum determinations are required especially during the initial period of treatment. Lithium toxicity is closely related to serum lithium levels and during treatment they should usually not exceed 1.5 mmol/L, if serious adverse reactions and lithium intoxication are to be avoided. This lithium level refers to a blood sample drawn before the patient has had his/her first lithium dose of the day, therefore, 9 - 12 hours after his/her last dose of drug. Serum lithium levels should usually be monitored three times weekly during the initial period of administration and periodically as required thereafter. If lithium levels exceed 1.5 - 2 mmol/L, the drug should be discontinued and, if appropriate, administration resumed at a lower level after 24 hours. Prodromal toxic signs such as fatigue, muscular weakness, incoordination, drowsiness, coarse tremors, diarrhea and vomiting, provide a sensitive warning of lithium intoxication.

In view of the limited dosage range of lithium compared to other psychotropic agents, particular care is required for the patient to receive exactly the prescribed number of LITHANE capsules.

Cardiovascular

Patients with underlying cardiovascular disease should be observed carefully for signs of arrhythmias.

Dependence/Tolerance

After the acute manic episode subsides, usually within a week, the dosage of LITHANE should be rapidly reduced since there is evidence at this time of a decreased tolerance to lithium; see 4.2 Recommended Dose and Dosage Adjustment.

Endocrine and Metabolism

Since the formation of non-toxic goiters has been reported during lithium therapy, the thyroid gland should be examined before treatment and appropriate thyroid function tests performed. Non-toxic

goiters reported during prolonged lithium therapy have disappeared following discontinuation of the medication. Treatment with small doses of thyroxin or desiccated thyroid in patients who develop a diffuse non-toxic goiter may stop further growth or lead to shrinkage of the gland.

A systematic review and meta-analysis indicates that about 10% of patients on long-term lithium therapy may develop hypercalcemia with or without hyperparathyroidism. Screening of serum calcium level and if necessary serum parathormone level need to be considered.

Infectious Disease

In addition to sweating and diarrhea, concomitant infection with elevated temperatures may necessitate a temporary reduction or cessation of medication.

Neurologic

An encephalopathic syndrome (characterized by weakness, lethargy, fever, tremulousness and confusion, extrapyramidal symptoms, leucocytosis, elevated serum enzymes, BUN and FBS) followed by irreversible brain damage has occurred in a few patients treated with lithium plus haloperidol. A causal relationship between these events and the concomitant administration of lithium and haloperidol has not been established; however, patients receiving such combined therapy should be monitored closely for early evidence of neurologic toxicity and treatment discontinued promptly if such signs appear (see 9 DRUG INTERACTIONS). The possibility of similar adverse interactions with other antipsychotic medication exists (see 9 DRUG INTERACTIONS).

Renal

Good kidney function and adequate salt and fluid intake are essential to maintain lithium excretion. When sodium intake is lowered, lithium excretion is reduced. Diminished intake or excessive loss of salt and fluids, as a result of vomiting, diarrhea, perspiration or use of diuretics will also increase lithium retention. Thus, lithium should not be given to patients on a salt-free diet and sodium depletion must be carefully avoided. Therefore, it is essential for the patient to maintain a normal diet including adequate salt and fluid intake during lithium therapy. Salt supplements and additional fluids may be required if excessive losses occur. LITHANE should generally not be given to patients receiving diuretics, since the risk of lithium toxicity is very high in such patients. If diuretics are used during lithium therapy the serum lithium concentration must be closely monitored (see 9 DRUG INTERACTIONS).

Chronic lithium therapy may be associated with diminution of renal concentrating ability, occasionally presenting as nephrogenic diabetes insipidus, with polyuria and polydipsia. Such patients should be carefully managed to avoid dehydration with resulting lithium retention and toxicity. This condition is usually reversible when lithium is discontinued.

Morphologic changes with glomerular and interstitial fibrosis and nephron atrophy have been reported in patients on chronic lithium therapy. Morphological changes have also been seen in manic depressive patients never exposed to lithium. The relationship between renal functional and morphologic changes and their association with lithium therapy have not been established.

When kidney function is assessed for baseline data prior to starting lithium therapy or thereafter, routine urinalysis and other tests may be used to evaluate tubular function (e.g. urine specific gravity or osmolality following a period of water deprivation, or 24 hour urine volume) and glomerular function (e.g. serum creatinine or creatinine clearance). During lithium therapy, progressive or sudden changes in renal function, even within the normal range, indicate the need for re-evaluation of treatment.

Reproductive Health: Female and Male Potential

Refer to section 7.1.1 Pregnant Women and 16 NON-CLINICAL TOXICOLOGY, Reproductive and Developmental Toxicology; consider contraception for both females and males.

- **Fertility**

  Lithium decreases the fertility of male rats and is spermicidal in vitro for human and animal spermatozoa 16 NON-CLINICAL TOXICOLOGY, Reproductive and Developmental Toxicology.

Skin

Cases of Drug Reaction with Eosinophilia and Systemic Symptoms (DRESS) for which lithium carbonate was suspected to have contributed were reported.

7.1 Special Populations

7.1.1 Pregnant Women

Lithium should not be used during pregnancy or in women of child-bearing potential unless it cannot be substituted by other appropriate therapy and in the opinion of the physician the expected benefits outweigh the possible hazards to the fetus.

In various animal species, lithium affects reproduction and has been noted to have teratogenic effects (see 16 NON-CLINICAL TOXICOLOGY, Reproductive and Developmental Toxicology). A group of spontaneous reports concerning 37 mothers who received lithium during pregnancy included two who gave birth to infants with congenital malformations. Data from lithium birth registries suggests that the drug may increase the incidence of cardiac and other anomalies, especially Ebstein's anomaly.

When possible, lithium should be withdrawn for at least the first trimester unless it is determined that this would seriously endanger the mother.

If this drug is used during pregnancy, or if the patient becomes pregnant while taking the drug, the patient should be appraised for the potential hazards to the fetus.

When lithium is used during pregnancy, serum lithium concentrations should be carefully monitored and dosage adjusted if necessary since renal clearance of the drug and distribution of the drug into erythrocytes may be increased during pregnancy. Pregnant women receiving lithium may have sub therapeutic serum lithium concentrations if dosage of the drug is not increased during pregnancy. Immediately postpartum, renal clearance of lithium may decrease to pre-pregnancy levels; therefore, to decrease the risk of postpartum lithium intoxication, dosage of the drug should be reduced from 1 week before parturition.

7.1.2 Breast-feeding

Lithium is excreted in human milk (concentrations of 33-50% of those in the mother's serum). Nursing should not be undertaken during lithium therapy except in rare and unusual circumstances where, in the opinion of the physician, the potential benefits to the mother outweighs possible hazards to the child.

7.1.3 Pediatrics

Pediatrics (<18 years old): Health Canada has not authorized an indication for pediatric use.

There has been a report of a transient syndrome of acute dystonia and hyperreflexia occurring in a 15 kg child who ingested 300 mg of lithium carbonate.

7.1.4 Geriatrics

Geriatric patients appear to be more susceptible to adverse effects even when lithium levels are therapeutic.

8 ADVERSE REACTIONS

8.1 Adverse Reaction Overview

Adverse reactions may be encountered with LITHANE (lithium carbonate) even when serum lithium values remain below 1 mmol/L. The most frequent adverse reactions are the initial postabsorptive symptoms, believed to be associated with a rapid rise in serum lithium levels. They include, gastrointestinal (GI) discomfort, nausea, vertigo, muscle weakness and a dazed feeling, and frequently disappear after stabilization of therapy. The more common and persistent adverse reactions are: fine tremor of the hands, and, at times, fatigue, thirst, and polyuria. These do not necessarily require reduction of dosage.

Mild to moderate toxic reactions may occur at lithium levels from 1.5 - 2 mmol/L, and moderate to severe reactions at levels above 2 mmol/L.

A number of patients may experience lithium accumulation during initial therapy, increasing to toxic levels and requiring immediate discontinuation of the drug. Some elderly patients with lower renal clearances for lithium may also experience different degrees of lithium toxicity, requiring reduction or temporary withdrawal of medication. However, in patients with normal renal clearance the toxic manifestations appear to occur in a fairly regular sequence related to serum lithium levels.

The usually transient GI symptoms are the earliest adverse reactions to occur. A mild degree of fine tremor of the hands may persist throughout therapy. Thirst and polyuria may be followed by increased drowsiness, ataxia, tinnitus and blurred vision, indicating early intoxication. As intoxication progresses the following manifestations may be encountered: confusion, increasing disorientation, muscle twitching, hyperreflexia, nystagmus, seizures, diarrhea, vomiting, and eventually coma and death.

8.5 Post-Market Adverse Reactions

The following adverse reactions have been reported and are usually related to serum lithium levels:

Allergy: Allergic vasculitis

Autonomic Nervous System: Blurred vision, dry mouth.

Cardiovascular: Arrhythmia, hypotension, peripheral circulatory failure, cardiac collapse, and peripheral edema.

ECG Changes: Reversible flattening, isoelectricity or inversion of T-waves.

Central and Peripheral Nervous System: tremor, muscle hyperirritability (fasciculation, twitching, especially of facial muscles and clonic movements of the limbs), hypertonicity, ataxia, choreoathetotic movement, hyperactive deep tendon reflexes, extrapyramidal symptoms including acute dystonia and parkinsonism, general muscle weakness, urinary and fecal incontinence, slurred speech, blackout spells, seizures, cranial nerve involvement, psychomotor retardation, somnolence, dizziness, toxic

confusional states, restlessness, stupor, coma, tinnitus, hallucinations, poor memory, slowed intellectual functioning, startled response, worsening of organic brain syndromes, myasthenic syndromes (rarely).

Cases of pseudotumor cerebri (increased intracranial pressure and papilledema) have been reported with lithium use. If undetected, this condition may result in enlargement of the blind spot, constriction of visual fields and eventual blindness due to optic atrophy. Lithium should be discontinued, if clinically possible, if this syndrome occurs.

EEG Changes: Diffuse slowing, widening of frequency spectrum, potentiation and disorganization of background rhythm. Sensitivity to hyperventilation and paroxysmal bilateral synchronous delta activity have also been described.

Dermatologic: drying and thinning of hair, anesthesia of skin, chronic folliculitis, xerosis cutis, alopecia, exacerbation of psoriasis, rash, and pruritus, and drug reaction with eosinophilia and systemic symptoms (DRESS).

Gastrointestinal: Anorexia, nausea, vomiting, diarrhea, abdominal pain, and weight loss.

General: General fatigue, leg ulcers, metallic taste, and slight elevation of plasma magnesium.

Genitourinary: Albuminuria, oliguria, polyuria, and glycosuria.

Hematopoietic and Lymphatic: Anemia, leukopenia, leukocytosis.

Metabolic and Nutritional Disorders: Thirst, hyperglycemia, and dehydration.

Miscellaneous Reactions Unrelated to Dosage: Excessive weight gain, edematous swelling of ankles or wrists. A single report has been received of the development of painful discoloration of fingers and toes and coldness of the extremities within one day of the starting of treatment of lithium. The mechanism through which these symptoms (resembling Raynaud's Syndrome) developed is not known. Recovery followed discontinuance.

Thyroid Abnormalities: Euthyroid goiter and/or hypothyroidism (including myxedema) accompanied by lower T_3 and T_4. I^{131} iodine uptake may be elevated. Rare cases of hyperthyroidism have been reported.

Serious reactions to long-term therapy: In addition to other possible adverse reactions, the main concern during chronic lithium therapy centers on kidney function, the thyroid, parathyroid, the bones and skin.

9 DRUG INTERACTIONS

9.4 Drug-Drug Interactions

The drugs listed in this table are based on either drug interaction case reports or studies, or potential interactions due to the expected magnitude and seriousness of the interaction (i.e., those identified as contraindicated).

Table 3 - Established or Potential Drug-Drug Interactions

Drug class / name	Source of Evidence	Effect	Clinical comment
Diuretics or Angiotensin Converting Enzyme (ACE) Inhibitors	T	Caution should be exercised when lithium and diuretics or ACE inhibitors are used concomitantly because sodium loss may reduce the renal clearance of lithium and increase serum lithium levels with risk of lithium toxicity.	When such combinations are used, the lithium dosage may need to be decreased, and more frequent monitoring of lithium plasma levels is recommended (see also 7 WARNINGS AND PRECAUTIONS, Renal).
Haloperidol	T	It has been proposed that haloperidol and lithium could have a combined inhibitory effect on striatal adenylate cyclase.	If haloperidol and lithium are used concomitantly, careful attention should be given to the dose of both agents as well as to early detection of neurotoxicity, particularly in the presence of one or more predisposing factors which include large doses of one or both drugs, the presence of acute mania, failure to discontinue drugs when adverse effects occur, pre-existing brain damage, a history of extrapyramidal symptoms with neuroleptic therapy alone, the concurrent use of anticholinergic antiparkinsonian drugs, and the presence of other physiologic disturbances such as infection, fever, or dehydration (see also 7 WARNINGS AND PRECAUTIONS, Neurologic).
Phenothiazines	C	Both pharmacokinetic interactions and clinical toxicity with the combined use of phenothiazines and lithium have been described. Lithium-induced reductions in plasma chlorpromazine levels, phenothiazine-induced increases in red	Clinicians should be alert for altered response to either drug when used in combination and when either drug is withdrawn.

Drug class / name	Source of Evidence	Effect	Clinical comment
		cell uptake of lithium and chlorpromazine-induced increases in renal lithium excretion have been reported. Clinically, occasional cases of neurotoxicity have been reported and may be more likely to occur with thioridazine than other phenothiazines, when combined with lithium.	
Non-Steroidal Anti-Inflammatory Drugs (NSAID)s	C	NSAIDs have been reported to increase significantly, steady state plasma lithium levels. In some cases lithium toxicity has resulted from such interactions.	In a patient stabilized on lithium and NSAIDs, discontinuation of the NSAIDs may result in inadequate serum lithium concentrations. When such combinations are used, more frequent plasma lithium level monitoring is recommended.
Selective Serotonin Reuptake Inhibitors (SSRI) Drugs (including fluvoxamine, fluoxetine, and sertraline)	C and CT	Lithium may enhance the serotonergic effects of SSRI drugs. Co-administration of lithium with SSRI drugs may lead to a higher incidence of serotonin associated side effects (serotonin syndrome) and lithium toxicity. *Fluvoxamine*: Several cases of adverse reactions including convulsions have been reported in patients receiving concomitant lithium and fluvoxamine. *Fluoxetine*: There have been reports of both increased and decreased lithium levels when lithium was used concomitantly with	Combined use of lithium and SSRI drugs should be carried out with caution. Lithium levels should be monitored when these drugs are administered concomitantly, so that appropriate adjustments to the lithium dose may be made if necessary. Monitor patients for signs and symptoms of serotonin syndrome, particularly during lithium initiation. If serotonin syndrome occurs, consider discontinuation of lithium and/or concomitant serotonergic drugs.

Drug class / name	Source of Evidence	Effect	Clinical comment
		fluoxetine. Cases of lithium toxicity have been reported with co-administration of fluoxetine and lithium. *Sertraline*: In placebo-controlled study in normal volunteers sertraline did not alter steady-state concentrations or renal clearance of lithium. However, there was a high incidence of apparently treatment-related side effects with the combination in this study, tremors being the most frequently observed. There is no clinical experience with lithium in sertraline treated patients.	
Carbamazepine	C	Several cases of neurotoxicity (in the absence of toxic serum lithium concentrations) have been reported in patients receiving lithium and carbamazepine, but the combination has also been used to advantage in some manic patients.	Patients should be monitored for evidence of lithium toxicity when carbamazepine is given concurrently. It is not yet established whether plasma lithium concentrations are useful in monitoring this interaction since the carbamazepine might increase the effect of lithium without increasing plasma lithium concentrations.
Neuromuscular Blocking Agents	T	In patients receiving chronic lithium therapy, the action of neuromuscular blocking agents (e.g., succinylcholine, pancuronium) may be prolonged.	Monitor for prolonged paralysis.
Theophylline	CT	Theophylline enhances	When initiating lithium therapy

Drug class / name	Source of Evidence	Effect	Clinical comment
		the renal clearance of lithium in most patients, thus tending to reduce serum lithium concentrations.	in a patient on chronic theophylline, lithium dosage requirements may be higher than anticipated. When initiating theophylline therapy in a patient on chronic lithium, there may be reduced lithium response. Discontinuation of theophylline in a patient on chronic lithium may result in excessive lithium response. Monitoring of serum lithium concentration is recommended.
Calcium Channel Blockers (CCBs)	T	The addition of verapamil or diltiazem to patients stabilized on lithium therapy may result in neurotoxicity. The CCB effects may be additive to that of lithium on transmitter secretion in the nervous system.	The use of CCBs in the treatment of patients with bipolar disorders receiving lithium should be commenced carefully with observation for neurotoxic effects. The therapeutic range of lithium may need to be toward the lower end when a CCB is co-administered.
Propranolol	C	Limited clinical data suggests that propranolol may increase lithium serum concentrations, and its co-administration with lithium may produce bradycardia.	Pending further data, patients maintained on lithium should be monitored for changed lithium serum concentrations or exaggerated beta-blocker effects.
Tricyclic Antidepressants	T	Both lithium and tricyclic antidepressants lower the seizure threshold. An additive effect is possible.	
Potassium Iodide	T	The hypothyroidic and goitrogenic effects of lithium carbonate and potassium iodide (and possibly other iodides) may be additive if the two drugs are used concurrently.	Monitor patients for signs or symptoms of hypothyroidism and goiter.
Diazepam	C	An isolated case has been reported of serious	Since hypothermia is potentially fatal if it occurs and its general

Drug class / name	Source of Evidence	Effect	Clinical comment
		hypothermia during concurrent treatment with lithium and diazepam.	incidence is not known, it would be prudent to watch for this interaction during concurrent treatment.
Sodium Bicarbonate	T	Concomitant use can lower serum lithium concentrations by increasing urinary lithium excretion.	Patients on combined sodium bicarbonate and lithium therapy should be monitored for decreased lithium effects. Lithium blood levels may be helpful in assessing this interaction.
Urea	C	Limited clinical experience indicates that urea may enhance the renal excretion of lithium resulting in reduced lithium serum concentrations.	More frequent serum lithium concentration monitoring.
Other	C	Isolated cases of lithium toxicity have been reported to be induced by concomitant administration of mazindol, methyldopa and phenytoin.	Monitor patients closely for adverse reactions of methyldopa and phenytoin.

Legend: C = Case Study; CT = Clinical Trial; T = Theoretical

9.5 Drug-Food Interactions

Patients on salt-restricted diets who receive lithium are prone to developing symptoms of lithium toxicity. In contrast, increased sodium intake has been associated with reduced therapeutic response to lithium. Extremely large or small intakes of sodium chloride should be avoided in patients receiving lithium (see also 7 WARNINGS AND PRECAUTIONS, Renal).

10 CLINICAL PHARMACOLOGY

10.1 Mechanism of Action

Although lithium is useful for its antimanic effect and in preventing relapses in patients with a clearcut diagnosis of bipolar affective disorder, it has very little, if any, direct effect on moods, normal or abnormal.

Lithium alters sodium transport in nerve and muscle cells, affects a shift toward intraneuronal metabolism of catecholamines and has an inhibitory action on the intracellular formation of cyclic AMP.

However, the specific biochemical mechanism of action of lithium in mania is still largely unknown.

Lithium is inactive in most screening psychopharmacological tests but it produces marked potentiation of amphetamine hyperactivity in animals. It does not appear to protect against the action of stimulant and convulsive drugs and produces only slight potentiation of CNS depressants.

10.2 Pharmacodynamics

ECG changes with lithium have been reported in both animals and human.

10.3 Pharmacokinetics

Lithium ions are rapidly absorbed from the gastrointestinal (GI) tract following oral administration of LITHANE (lithium carbonate). Peak plasma lithium concentrations are reached 2-4 hours after LITHANE administration. The distribution of lithium in the body approximates that of total body water, but its passage across the blood-brain barrier is slow and at equilibration the CSF lithium level reaches only approximately half the plasma concentration.

Lithium is excreted primarily in urine with less than 1% being eliminated with the feces. Lithium is filtered by the glomeruli and 80% of the filtered lithium is reabsorbed in the tubules, probably by the same mechanism responsible for sodium reabsorption. The renal clearance of lithium is proportional to its plasma concentration. The half-life of elimination of lithium is approximately 24 hours. A low salt intake resulting in low tubular concentration of sodium will increase lithium reabsorption and might result in retention or intoxication (see 7 WARNINGS AND PRECAUTIONS, Renal).

Renal lithium clearance is, under ordinary circumstances, remarkably constant in the same individual but decreases with age and falls when sodium intake in lowered. The dose necessary to maintain a given concentration of serum lithium depends on the ability of the kidney to excrete lithium. However, renal lithium excretion may vary greatly between individuals and lithium dosage must, therefore, be adjusted individually. In clinical reports, it has been noted that serum lithium may rise an average of 0.2 - 0.4 mmol/L after intake of 300 mg and 0.3-0.6 mmol/L after intake of 600 mg of lithium carbonate. It has been suggested that manic patients retain larger amounts of lithium during the active manic phase, but studies have been unable to confirm a clear difference in excretion patterns. However, patients in a manic state seem to have an increased tolerance to lithium.

Balance studies indicate that lithium may produce a transitory diuresis with increase in sodium and potassium excretion. A period of equilibrium or slight retention may follow, but persistent polyuria may occur in some patients. There is evidence that therapeutic doses of lithium decrease the 24-hour exchangeable sodium. Longitudinal metabolic studies have demonstrated cumulative lithium retention in some patients without undue rise in plasma lithium values, indicating a possible intracellular retention of lithium. There is some evidence that lithium may affect the metabolism of potassium, magnesium and calcium.

11 STORAGE, STABILITY AND DISPOSAL

Store at 15-30°C. Keep out of reach and sight of children.

12 SPECIAL HANDLING INSTRUCTIONS

Not applicable.

PART II: SCIENTIFIC INFORMATION

13 PHARMACEUTICAL INFORMATION

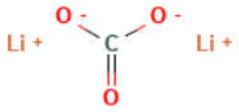
Drug Substance

Proper name: Lithium Carbonate

Chemical name: Lithium Carbonate

Molecular formula and molecular mass: Li_2CO_3 - 73.89 g/mol

Structural formula:



Physicochemical properties: Lithium is a monovalent cation which belongs to the group of alkali metals together with sodium, potassium and other elements with which it shares some of its properties.

Lithium carbonate is a white, odourless, amorphous or microcrystalline powder. One gram of lithium carbonate corresponds to 27 mmol of lithium and one 300 mg LITHANE (lithium carbonate) Capsule contains approximately 8.1 mmol of lithium.

14 CLINICAL TRIALS

The clinical trial data on which the original indication was authorized is not available.

15 MICROBIOLOGY

No microbiological information is required for this drug product.

16 NON-CLINICAL TOXICOLOGY

General Toxicology

Acute Toxicity (Mice and Rats)

The oral LD_{50} of lithium carbonate in the rat is 635 mg/kg, and in the mouse 650 mg/kg.

Subacute Toxicity

Subacute toxicity studies indicate that lithium accumulates faster and death occurs earlier in rats and dogs fed low sodium diets. Dogs given 20 mg/kg/day of lithium chloride showed no signs of toxicity when fed a normal salt diet, but died in 2-4 weeks when fed a low sodium diet. Similar results occurred in rats. The signs of toxicity consisted of tremors, lethargy, salivation, vomiting, diuresis, bloody diarrhea, anorexia, emaciation and coma. ECG changes similar to those produced by potassium intoxication, were observed. Animals protected by a high sodium intake developed only polyuria.

Serum lithium rose gradually in the animals developing signs of toxicity, while serum potassium levels remained fairly constant. In the final stages, serum lithium values rose rapidly as a result of irreversible renal damage and in the terminal stages hyperkalemia and azotemia were recorded.

The principal toxic effects of lithium are on the kidney with lesions in the distal convoluted tubule of dogs and in the proximal convoluted tubules of rats. The primary toxic effects in man appear to be on the central nervous system.

Long-Term Toxicity

The long-term toxicity of lithium has not been tested in animal studies.

Reproductive and Developmental Toxicology

Lithium salts influenced the embryonal development of sea urchins, mollusks, amphibians, and chicken embryos.

Adverse effects on reproduction have also been reported in mammalian species. Adverse effects on the number of corpora lutea, percentage of resorption, embryonal viability and weaning weights in rats, the number of implantation sites in rabbits, and the birth weights in monkeys, have been produced in lithium studies. Cleft palates occurred in the offspring of treated mice and rats, in the latter species together with ocular and auricular defects, with lithium doses producing blood levels similar to those obtained with therapeutic doses in man.

Lithium decreases the fertility of male rats and is spermicidal in vitro for human and animal spermatozoa.

PATIENT MEDICATION INFORMATION

READ THIS FOR SAFE AND EFFECTIVE USE OF YOUR MEDICINE

[Pr]LITHANE

Lithium Carbonate Capsules USP

Read this carefully before you start taking **LITHANE** and each time you get a refill. This leaflet is a summary and will not tell you everything about this drug. Talk to your healthcare professional about your medical condition and treatment and ask if there is any new information about **LITHANE**.

Serious Warnings and Precautions

- LITHANE is a medicine for which small increases in dose or blood concentration can lead to lithium toxicity. It is also known as a lithium overdose. This means that toxic side effects can occur at doses close to the prescribed dose. Your healthcare professional will need to monitor your blood levels of lithium to find the best dose for you.
- Certain medical conditions can increase your risk of lithium toxicity. Your healthcare professional will decide if LITHANE is right for you by carefully assessing your medical condition. This includes body weight checks, electrocardiogram (ECG), blood and/or urine tests.
- After a manic episode, usually within a week, your healthcare professional may rapidly decrease your dose of LITHANE. This is because your lithium tolerance may decrease after a manic episode and taking your usual dose may lead to lithium toxicity.
- Stop taking LITHANE and seek **immediate** medical help if you think you have taken too much LITHANE or if you experience the following symptoms of lithium toxicity:
  - lack of muscle control, diarrhea, vomiting, shaking, muscle weakness, lack of energy or sleepiness.
- You may find it helpful to tell a relative or close friend that you are taking LITHANE. Ask them to:
  - read this leaflet; and
  - tell you if they notice any signs of lithium toxicity while you are taking LITHANE.

What is LITHANE used for?

LITHANE is used to treat manic episodes in adults who suffer from manic-depressive disorders (bipolar disorder). A manic episode includes symptoms such as:

- feeling invincible or an all-powerful inflated self-esteem,
- having racing thoughts, easily losing train of thought,
- overreacting to what you see or hear,
- speeding-up your activities,
- talking very quickly, too loudly, or more than usual,
- needing less sleep,
- having poor judgment,
- severe irritability.

LITHANE is also used as a long-term treatment in adults with bipolar disorder (with a strong history of mania) to prevent or reduce further episodes of mania and depression.

How does LITHANE work?

LITHANE belongs to a group of medicines called antimanic agents. LITHANE modifies the transport of sodium in nerves and muscle cells. Exactly how LITHANE works is unknown. However, it seems to treat manic episodes and prevent the symptoms of mania and depression in people with manic-depressive disorders.

What are the ingredients in LITHANE?

Medicinal ingredients: Lithium carbonate

Non-medicinal ingredients: Gelatin

LITHANE comes in the following dosage forms:

Capsules: 150 mg and 300 mg

Do not use LITHANE if:

- you are allergic to lithium or any other ingredients in LITHANE or its packaging.
- you have severe heart or kidney problems.
- you have a condition that causes severe weakness or frailty.
- you are severely dehydrated.
- you have low blood sodium, or have a condition that requires you to have a diet low in sodium.
- you have or have had brain damage.

To help avoid side effects and ensure proper use, talk to your healthcare professional before you take LITHANE. Talk about any health conditions or problems you may have, including if you:

- have an infection with fever.
- have or have had heart problems, including an abnormal heart beat.
- have or have had thyroid problems.
- have been told you have low blood calcium.
- suffer from excessive vomiting, diarrhea, or sweating.
- take haloperidol or other antipsychotic medicines (used to treat serious mental and emotional disorders, including schizophrenia and other psychotic disorders).
- take diuretics, also known as “water pills” (used to treat high blood pressure and other heart problems).
- are pregnant, think you might be pregnant, or plan to become pregnant.
- are breastfeeding.

Other warnings you should know about:

LITHANE may cause serious side effects, including:

- **Thyroid problems**: The thyroid is a butterfly-shaped gland located at the front of your neck. LITHANE can cause an enlarged thyroid, also known as a goiter. Tell your healthcare professional if you notice your thyroid getting bigger while taking LITHANE. They may prescribe you small doses of thyroid hormones to help stop further growth or shrink your thyroid. If you have taken LITHANE for a long time, the goiter may disappear on its own after you stop taking LITHANE.

- **Hypercalcemia** (high blood calcium): Taking LITHANE for a long time may cause high levels of calcium in the blood. This can also be accompanied with a hormone disorder known as hyperparathyroidism. This is a condition where your parathyroid glands, which are located behind the thyroid, create too much parathyroid hormone in the blood. This can lead to other medical problems.

- **Encephalopathic syndrome** (a rare neurological disorder): Rare cases of encephalopathic syndrome have been reported in patients taking lithium with haloperidol, an antipsychotic medicine. This syndrome can lead to permanent brain damage. Your healthcare professional will closely monitor you if you take lithium with an antipsychotic medicine.

- **Kidney problems**: LITHANE may cause frequent urination, and other kidney problems that may affect how the kidney work. This may occur in patients taking LITHANE for a long time.

See the **Serious side effects and what to do about them** table for more information on these and other serious side effects.

Diet and hydration:

- While taking LITHANE:
  - do not make sudden changes to your salt (sodium) intake. Discuss any changes to your salt intake with your healthcare professional before making them.
  - drink plenty of fluids, especially during periods of prolonged or intense exercise.

  This is to ensure your body is able to properly get rid of the lithium in your blood.
- Low-sodium diets and dehydration may affect the level of lithium in your blood, leaving you at risk for lithium toxicity. If you have been suffering from excessive vomiting, sweating or diarrhea, you may need more salt and fluids. Talk to your healthcare professional if this happens.

Pregnancy and birth control:

- You should use a highly effective birth control method while taking LITHANE (males and females).
- LITHANE should not be taken during pregnancy or by women who could become pregnant unless:
  - no other appropriate therapy exists; and
  - your healthcare professional has determined the expected benefits outweigh the possible risks to your baby.

- Tell your healthcare professional right away if you become pregnant or think you might be pregnant while taking LITHANE. They will discuss the specific risks with you and decide if you should continue taking LITHANE, or use other treatments instead.

Breast-feeding: LITHANE can pass into breast milk and harm a breastfed baby. LITHANE should not be taken during breast-feeding unless your healthcare professional has determined the expected benefits outweigh the possible risks to your baby.

Adults (65 years of age or older): You may be more susceptible to side effects while taking LITHANE, even at prescribed doses.

Check-ups and testing: Your healthcare professional may do check-ups and tests before you start LITHANE and during your treatment. These tests may include:

- blood tests to monitor:
  - the amount of lithium in your blood
  - the health of your kidneys, thyroid and parathyroid glands
  - the amount of electrolytes (sodium and calcium) in your blood
- urine tests to monitor:
  - your hydration level
  - the health of your kidneys
- electrocardiogram (ECG) tests to monitor the health of your heart.
- body weight checks to monitor any weight gain.
- mental status checks to monitor your mental health.

Tell your healthcare professional about all the medicines you take, including any drugs, vitamins, minerals, natural supplements or alternative medicines.

The following may interact with LITHANE:

- medicines used to treat high blood pressure or other heart problems such as:
  - diuretics, also known as “water pills”.
  - Angiotensin Converting Enzyme (ACE) inhibitors (e.g., benazepril, captopril, enalapril or lisinopril).
  - calcium channel blockers (e.g., verapamil, diltiazem, amlodipine, felodipine, nifedipine).
  - a beta blocker called propranolol.
  - methyldopa.
- medicines used to treat serious mental and emotional disorders, including schizophrenia and other psychotic disorders. These include:
  - haloperidol.
  - phenothiazines (e.g., prochlorperazine, chlorpromazine, thioridazine, perphenazine, fluphenazine).
- medicines used to treat seizures (e.g., carbamazepine, phenytoin).
- medicines used to cause short-term paralysis during surgery (e.g., succinylcholine, pancuronium).

- medicines used to treat depression (e.g., selective serotonin reuptake inhibitors (SSRI) such as fluvoxamine, fluoxetine, citalopram and sertraline; tricyclic antidepressants).
- Non-steroidal anti-inflammatory Drugs (NSAIDs), used to relieve pain and reduce inflammation (e.g., ibuprofen, naproxen, diclofenac, celecoxib).
- theophylline, used to treat asthma and other lung diseases.
- potassium iodide, used to treat an overactive thyroid and to protect the thyroid gland from the effects of radiation.
- diazepam, used to treat anxiety, alcohol withdrawal and seizures.
- sodium bicarbonate, used to reduce stomach acid and treat heartburn.
- urea, used to treat low blood sodium.
- mazindol, used to suppress the appetite.
- low-sodium diets.

How to take LITHANE:

- Take LITHANE by mouth. Swallow capsules with a glass of water, if needed.
- Take LITHANE exactly as your healthcare professional has told you. Your healthcare professional will prescribe you the lowest dose possible needed for your treatment.
- Never take more than you are told. This may cause you serious harm or even death.

Usual dose:

- The dose prescribed to you will depend on your medical condition. Your healthcare professional will tell you how much and how often to take LITHANE.
- During your treatment, your healthcare professional will check if LITHANE is working for you and if it is causing you any unwanted effects. They may change your dose depending on the amount of lithium in your blood and how your respond to LITHANE.
- After a manic episode, usually within a week, your healthcare professional may rapidly decrease your dose. This is to avoid unwanted effects.

Overdose:

Signs of an overdose with LITHANE may include:

- lack of coordination or muscle control, shaking, muscle weakness or twitching,
- feeling sluggish, lack of energy,
- sleepiness,
- loss of appetite, vomiting,
- diarrhea.

If these signs occur, stop taking LITHANE and get **immediate** medical help.

If you think you, or a person you are caring for, have taken too much LITHANE, contact a healthcare professional, hospital emergency department, or regional poison control centre immediately, even if there are no symptoms.

Missed Dose:

If you miss a dose, skip it and take your next dose as scheduled. **Do not take two doses at once to make up for the missed dose.**

What are possible side effects from using LITHANE?

These are not all the possible side effects you may have when taking LITHANE. If you experience any side effects not listed here, tell your healthcare professional.

- upset stomach
- nausea
- muscle weakness
- vertigo (feeling like you are spinning)
- feeling dazed
- shaky hands
- sleepiness
- feeling thirsty or dehydrated
- need to urinate more often than usual
- dry mouth
- swelling of the hands, wrists, ankles or feet
- loss of bladder control
- inability to control bowel movements
- slurred speech
- feeling restless
- abdominal pain
- weight changes
- dehydration
- drying and thinning of hair, hair loss
- itchy or dry skin
- worsening of psoriasis (a skin condition)

Serious side effects and what to do about them			
Symptom / effect	**Talk to your healthcare professional**		**Stop taking drug and get immediate medical help**
	Only if severe	**In all cases**	
UNKNOWN FREQUENCY			
Arrhythmia (abnormal heart rhythms): fast, slow or irregular heartbeat.		✓	
Drug reaction with eosinophilia and systemic symptoms (DRESS) (serious skin reaction that may affect one or more organs): fever,			✓

Serious side effects and what to do about them			
Symptom / effect	**Talk to your healthcare professional**		**Stop taking drug and get immediate medical help**
	Only if severe	**In all cases**	
severe rash, peeling skin, swollen lymph glands, swelling of face or legs, flu-like feeling, yellow skin or eyes, shortness of breath, dry cough, chest pain or discomfort, feeling thirsty, urinate less often, less urine or dark urine.			
Encephalopathic syndrome (a rare neurological disorder): feeling weak, extreme sleepiness, fever, trembling, confusion, inability to sit still, involuntary muscle contraction or facial movements, shaking, or stiff muscles.			✓
Hypercalcemia (high blood calcium): constipation, weight loss, nausea, vomiting, abdominal pain, loss of appetite. Can be accompanied with body aches, sleepiness or difficulty sleeping, bone pain, memory loss, poor concentration, depression, or headache.		✓	
Hypotension (low blood pressure): dizziness, fainting, light-headedness.		✓	
Kidney problems: need to urinate more often, feeling thirsty, dehydration.	✓		
Lithium toxicity (lithium overdose): upset stomach, diarrhea, vomiting, feeling thirsty, lack of coordination, muscle control or energy, shaking, muscle weakness, sleepiness, ringing in the ears, blurry vision, confusion, feeling disoriented, muscle twitching, lack of reflexes, involuntary eye movements (side-to-side, up and down, or circular motion of the eyes), seizures, coma, death.			✓

Serious side effects and what to do about them			
Symptom / effect	**Talk to your healthcare professional**		**Stop taking drug and get immediate medical help**
	Only if severe	**In all cases**	
Pseudotumor cerebri (increased pressure in the skull): severe headache, ringing in the ears, blurred vision, double vision or brief periods of blindness.		✓	
Thyroid problems: enlarged thyroid gland, weight changes, tiredness, anxiety or nervousness, hair loss, muscle weakness, feeling cold, dry skin, constipation or frequent and loose bowel movements, shortness of breath, puffy face, heavier than normal or irregular menstrual periods, feeling hot and possibly feelings of having rapid, fluttering or pounding heart.		✓	

If you have a troublesome symptom or side effect that is not listed here or becomes bad enough to interfere with your daily activities, tell your healthcare professional.

Reporting Side Effects

You can report any suspected side effects associated with the use of health products to Health Canada by:

- Visiting the Web page on Adverse Reaction Reporting (https://www.canada.ca/en/health-canada/services/drugs-health-products/medeffect-canada/adverse-reaction-reporting.html) for information on how to report online, by mail or by fax; or
- Calling toll-free at 1-866-234-2345.

NOTE: Contact your health professional if you need information about how to manage your side effects. The Canada Vigilance Program does not provide medical advice.

Storage:

- Store between 15°C and 30°C.
- Keep out of reach and sight of children.

If you want more information about LITHANE:

- Talk to your healthcare professional
- Find the full product monograph that is prepared for healthcare professionals and includes this Patient Medication Information by visiting the Health Canada website: (https://www.canada.ca/en/health-canada/services/drugs-health-products/drug-products/drug-product-database.html); the manufacturer's websitewww.searchlightpharma.ca, or by calling 1-647-945-9762.

This leaflet was prepared by Searchlight Pharma Inc.

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