Front

Size: 210 x 240 mm

210 mm

240 mm

LITHIUM CARBONATE

MICROLIT

300 mg Tablet

MOOD STABILIZER

PRODUCT NAME: Microlit

NAME AND STRENGTH:
Lithium Carbonate tablets 300 mg

PHARMACOLOGIC CATEGORY: Anti psychotic

PRODUCT DESCRIPTION:
White, flat, circular, beveledged uncoated tablets with a breakline on one surface and MICRO embossing on other surface.

FORMULATION/COMPOSITION:
Each uncoated tablet contains:
Lithium Carbonate BP..... 300 mg

PHARMACODYNAMICS/PHARMACOKINETICS:
Pharmacodynamics:
Lithium is an alkali metal available for medical use as lithium carbonate or lithium citrate. The exact mechanism of action of lithium in the treatment of bipolar disorders is not known.
The mode of action of lithium is still not fully understood. However, lithium modifies the production and turnover of certain neurotransmitters, particularly serotonin, and it may also block dopamine receptors.
It modifies concentrations of some electrolytes, particularly calcium and magnesium, and it may reduce thyroid activity.

Pharmacokinetics:
Lithium is readily absorbed from the gastrointestinal tract, and is distributed throughout the body over a period of several hours. Lithium is excreted almost exclusively in the kidneys but can also be detected in sweat and saliva. It is not bound to plasma proteins. It crosses the placenta, and is excreted in breast milk. The half-life of non-sustained lithium varies considerably, but generally is considered to be about 12 to 24 hours following a single dose. It is however increased for example in those with renal impairment and with age, and may increase significantly during long-term therapy.

INDICATIONS:
- In the management of acute manic or hypomanic episodes.
- In the management of episodes of recurrent depressive disorders where treatment with other antidepressants has been unsuccessful.
- In the prophylaxis against bipolar affective disorders.
- Control of aggressive behaviour or intentional self harm.

DOSAGE AND MODEL ROUTE OF ADMINISTRATION:
Acute Mania
Optimal patient response to Lithium Carbonate Tablets usually can be established and maintained with
600 mg t.i.d. Such doses will normally produce an effective serum lithium level ranging between 1 and
1.5 mEq/L. Dosage must be individualized according to serum levels and clinical response. Regular monitoring of the patient's clinical state and of serum lithium levels is necessary. Serum levels should be determined twice per week during the acute phase, and until the serum level and clinical condition of the patient have been stabilized.
Long-Term Control
The desirable serum lithium levels are 0.6 to 1.2 mEq/L. Dosage will vary from one individual to another, but usually 300 mg of Lithium Carbonate t.i.d. or q.i.d. will maintain this level. Serum lithium levels in uncomplicated cases receiving maintenance therapy during remission should be monitored at least every two months.
Patients abnormally sensitive to lithium may exhibit toxic signs at serum levels of 1 to 1.5 mEq/L. Elderly patients often respond to reduced dosage, and may exhibit signs of toxicity at serum levels ordinarily tolerated by other patients.
N.B.
Blood samples for serum lithium determination 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.

CONTRAINDICATIONS &PRECAUTION(S), WARNING(S)
- Hypersensitivity to lithium or to any of the excipients.
- Cardiac disease.
- Cardiac insufficiency.
- Severe renal impairment.
- Untreated hypothyroidism.
- Breast-feeding.
- Patients with low body sodium levels, including for example dehydrated patients or those on low sodium diets.
- Addison's disease.
- Brugada syndrome or family history of Brugada syndrome.

PRECAUTIONS & WARNINGS:
General
When considering Lithium Carbonate therapy, it is necessary to ascertain whether patients are receiving lithium in any other form. If so, check serum levels before proceeding.
The minimum clinically effective dose of lithium should always be used. Clear instructions regarding the symptoms of impending toxicity should be given by the physician to patients receiving long-term lithium therapy. They should be warned of the urgency of immediate action should these symptoms appear, and also of the need to maintain a constant and adequate salt and water intake. At the first sign of toxicity, the patient should consult a physician and lithium levels should be checked. Treatment should be discontinued immediately on the first signs of toxicity.
Monitoring recommendations
Before starting treatment with lithium, renal function, cardiac function and thyroid function should be evaluated. Patients should be euthyroid before initiation of lithium therapy. Lithium therapy is contraindicated in patients with severe renal insufficiency or cardiac insufficiency.
Renal, cardiac and thyroid functions should be re-assessed regularly during treatment with lithium.
For monitoring recommendations of lithium serum levels.
Renal Impairment
Since lithium is primarily excreted via the renal route, significant accumulation of lithium may occur in patients with renal insufficiency. Therefore, if patients with mild or moderate renal impairment are being treated with lithium, serum lithium levels should be closely monitored and the dose should be adjusted accordingly. If very regular and close monitoring of serum lithium levels and plasma creatinine levels is not possible, lithium should not be prescribed in this population. Lithium is contraindicated in patients with severe renal insufficiency
The possibility of hypothyroidism and renal dysfunction arising during prolonged treatment should be borne in mind and periodic assessments made.
Patients should be warned to report if polyuria or polydipsia develops. In patients who develop polyuria and/or polydipsia.
renal function should be monitored in addition to the routine serum lithium assessment.
Renal tumours: Cases of microcysts, oncocytomas and collecting duct renal carcinoma have been reported in patients with severe renal impairment who received lithium for more than 10 years
Fluid/electrolyte balance
If episodes of nausea, vomiting, diarrhoea, excessive sweating, and/or other conditions leading to salt/water depletion (including severe dieting) occur, lithium dosage should be closely monitored and dosage adjustments made as necessary. Drugs likely to upset electrolyte balance such as diuretics should also be reported. Indeed, sodium depletion increases the lithium plasma concentration (due to competitive reabsorption at the renal level). In these cases, lithium dosage should be closely monitored and reduction of dosage may be necessary.
Caution should be exercised to ensure that diet and fluid intake are normal in order to maintain a stable electrolyte balance. This may be of special importance in very hot weather or work environment. Infectious diseases including colds, influenza, gastro-enteritis and urinary infections may alter fluid balance and thus affect serum lithium levels. Treatment discontinuation should be considered during any intercurrent infection.
Risk of convulsions
The risk of convulsions may be increased in case of co-administration of lithium with drugs that lower the epileptic threshold, or in epileptic patients
Benign intracranial hypertension
There have been case reports of benign intracranial hypertension. Patients should be warned to report persistent headache and/or visual disturbances.
QT prolongation
As a precautionary measure, lithium should be avoided in patients with congenital long QT syndrome, and caution should be exercised in patients with risk factors such as QT interval prolongation (e.g. uncorrected hypokalemia, bradycardia), and in patients concomitantly treated with drugs that are known to prolong the QT interval.
Brugada syndrome
Lithium may unmask or aggravate Brugada syndrome, a hereditary disease of the cardiac sodium channel with characteristic electrocardiographic changes (right bundle branch block and ST segment elevation in right precordial leads), which may lead to cardiac arrest or sudden death. Lithium should not be administered to patients with Brugada Syndrome or a family history of Brugada Syndrome. Caution is advised in patients with a family history of cardiac arrest or sudden death.
Elderly patients
Elderly patients are particularly liable to lithium toxicity and may exhibit adverse reactions at serum levels ordinarily tolerated by younger patients. Caution is also advised since lithium excretion may be reduced in the elderly due to age related disease in renal function.
Children
The use in children is not recommended.

PREGNANCY AND LACTATION:
Pregnancy: Lithium therapy should not be used during pregnancy, especially during the first trimester, unless considered essential. There is epidemiological evidence that it may be harmful to the foetus in human pregnancy. Lithium crosses the placental barrier. In animal studies lithium has been reported to interfere with fertility, gestation and foetal development. Cardiac especially Ebstein anomaly, and other malformations have been reported. Therefore, a pre-natal diagnosis such as ultrasound and electrocardiogram examination is strongly recommended. In certain cases where a severe risk to the patient could exist if treatment were stopped, lithium has been continued during pregnancy.
If it is considered essential to maintain lithium treatment during pregnancy, serum lithium levels should be closely monitored and measured frequently since renal function changes gradually during pregnancy and suddenly at parturition. Dosage adjustments are required. It is recommended that lithium be discontinued shortly before delivery and reinitiated a few days *post-partum*.
Neonates may show signs of lithium toxicity including symptoms such as lethargy, flaccid muscle tone, or hypotonia. Careful clinical observation of the neonate exposed to lithium during pregnancy is recommended and lithium levels may need to be monitored as necessary.
Women of child-bearing potential: Women of child-bearing potential should use effective contraceptive methods during treatment with lithium.
Lactation: Lithium is secreted in breast milk and there have been case reports of neonates showing signs of lithium toxicity. Therefore lithium should not be used during breast-feeding. A decision should be made whether to discontinue lithium therapy or to discontinue breast-feeding, taking into account the importance of the drug to the mother and the importance of breast-feeding to the infant.

INTERACTIONS:
Interactions which increase lithium concentrations:
Serum lithium levels may be increased if one of the following drugs is co-administered. When appropriate, either lithium dosage should be adjusted or concomitant treatment stopped.
- Metronidazole may reduce lithium renal clearance.
- Non-steroidal anti-inflammatory drugs, including cyclo-oxygenase (COX) 2 inhibitors (monitor serum lithium concentrations more frequently if NSAID therapy is initiated or discontinued).
- Angiotensin-converting enzyme (ACE) inhibitors.
- Angiotensin II receptor antagonists.
- Diuretics (thiazides show a paradoxical antidiuretics effect resulting in possible water retention and lithium intoxication). If a thiazide diuretic has to be prescribed for lithium-treated patient, lithium dosage should first be reduced and the patient re-stabilized with frequent monitoring. Similar precautions should be exercised on diuretic withdrawal. Loop diuretics seem less likely to increase lithium levels.
- Other drugs affecting electrolyte balance, e.g. steroids, may alter lithium excretion and should therefore be avoided.
- Tetracyclines.

Interactions which decrease serum lithium concentrations:
Serum lithium levels may be decreased due to an increase in lithium renal clearance in case of concomitant administration of one of the following drugs:
- Xanthines (theophylline, caffeine).

- Sodium bicarbonate containing products.
- Diuretics (osmotic and carbonic anhydrase inhibitors).
- Urea
- Calcitonin

Interactions causing neurotoxicity:
Co-administration of the following drugs may increase the risk of neurotoxicity:

- Antipsychotics (particularly haloperidol at higher dosages), flupentixol, diazepam, thioridazine, fluphenazine, chlorpromazine and clozapine may lead in rare cases to severe neurotoxicity with symptoms such as confusion, disorientation, lethargy, tremor, extra-pyramidal symptoms and myoclonus. Increased lithium levels were present in some of the reported cases. Co-administration of antipsychotics and lithium may increase the risk of Neuroleptic Malignant Syndrome, which may be fatal. Discontinuation of both drugs is recommended at the first signs of neurotoxicity.
- Methyldopa.
- Triptan derivatives and/or serotonergic antidepressants such as Selective Serotonin Re-uptake Inhibitors (e.g. fluvoxamine and fluoxetine) as this combination may precipitate a serotoninergic syndrome*, which justifies immediate discontinuation of treatment.
- Calcium channel blockers may lead to neurotoxicity with symptoms such as ataxia, confusion and somnolence. Lithium concentrations may be increased.
- Carbamazepine may lead to dizziness, somnolence, confusion and cerebellar symptoms such as ataxia.

Other
Caution is advised if lithium is co-administered with other drugs that prolong the QT interval, e.g. Class IA (e.g. quinidine, disopyramide), or Class III (e.g. amiodarone) antiarrhythmic agents, cisapride, antibiotics such as erythromycin, antipsychotics such as thioridazine or Amisulpride. The list is not comprehensive.
Caution is advised if lithium is co-administered with drugs that lower the epileptic threshold, e.g. antidepressants such as SSRIs, tricyclic antidepressants, antipsychotics, anaesthetics, and theophylline. The list is not comprehensive
Lithium may prolong the effects of neuromuscular blocking agents. There have been reports of interaction between lithium and phenytoin, indomethacin and other prostaglandin-synthetase inhibitors.
*Serotonin syndrome
Serotonin syndrome is a potentially life-threatening adverse reaction, with is caused by an excess of serotonin (e.g. from overdose or concomitant use of serotonergic drugs), necessitating hospitalization and even causing death.
Symptoms may include:
- Mental status changes (agitation, confusion, hypomania, eventually coma)
- Neuromuscular abnormalities (myoclonus, tremor, hyperreflexia, rigidity, akathisia)
- Autonomic hyperactivity (hypo or hypertonia, tachycardia, shivering, hyperthermia, diaphoresis)
- Gastrointestinal symptoms (diarrhoea)

Strict adherence to the recommended doses is an essential factor for the prevention of the occurrence of this syndrome

ADVERSE EFFECTS:
Side effects are usually related to serum lithium concentration and are less common in patients with plasma lithium concentrations below 1.0 mmol/l. The adverse reactions usually subside with a temporary reduction or discontinuation of lithium treatment. Mild gastrointestinal effects such as nausea, a general discomfort and vertigo, may occur initially, but frequently disappear after the first few days of lithium administration. Fine hand tremors, polyuria and mild thirst may persist.
• Blood and lymphatic system disorders
Leukocytosis
• Endocrine disorders
Long-term adverse effects may include thyroid function disturbances such as euthyroid goiter and/or hypothyroidism and thyrotoxicosis. Lithium-induced hypothyroidism may be managed successfully with concurrent thyroxine.
Hypercalcaemia, hypermagnesaemia, hyperparathyroidism have been reported.
• Metabolism and nutrition disorders
Weight increase, Hyperglycaemia
• Psychiatric disorders
Confusion, delirium
• Nervous system disorders
Ataxia, hyperactive deep tendon reflexes, slurred speech, dizziness, stupor, coma, myasthenia gravis, giddiness, dazed feeling, memory impairment.
Tremor, especially fine hand tremors, dysarthria, myoclonus, benign intracranial hypertension
Vertigo, impaired consciousness, abnormal reflexes, convulsions, extrapyramidal disorders, encephalopathy, cerebellar syndrome (usually reversible), nystagmus
The above symptoms may result in fall.
Peripheral neuropathy may occur on long-term treatment and is usually reversible at cessation of lithium.
• Cardiac disorders
Cardiac arrhythmia, mainly bradycardia, sinus node dysfunction, peripheral circulatory collapse, hypotension, ECG changes such as reversible flattening or inversion of T-waves and QT prolongation, AV block, cardiomyopathy.
• Gastrointestinal disorders
Abdominal discomfort, taste disorder, nausea, vomiting, diarrhoea, gastritis, salivary hypersecretion, dry mouth, anorexia.
• Skin and subcutaneous tissue disorders
Follicultis, pruritus, papular skin disorders, acne or acneiform eruptions, aggravation or occurrence of psoriasis, allergic rashes, alopecia, cutaneous ulcers
• Musculoskeletal and connective tissue disorders
Muscle weakness, rhabdomyolysis
• Renal and urinary disorders
Polydipsia and/or polyuria and nephrogenic diabetes insipidus, histological renal changes with interstitial fibrosis after long term treatment have been reported. This is usually reversible on lithium withdrawal.
Long-term treatment with lithium may result in permanent changes in kidney histology, and impairment of renal function.
High serum concentrations of lithium including episodes of acute lithium toxicity may aggravate these changes.
Rare cases of nephrotic syndrome have been reported.
Frequency unknown: Microcysts, oncocytomas and collecting duct renal carcinoma (in long-term therapy)
• General disorders and administration site conditions
Peripheral oedema
Urticaria and angioedema, attributed to some excipients such as acacia powder (or Arabic gum)
• Reproductive
Sexual dysfunction
• Senses
Dysgeusia, blurred vision, scotomata
If any of the above symptoms appear, treatment should be stopped immediately and arrangements made for serum lithium measurement.

OVERDOSAGE AND TREATMENT:
In patients with a raised lithium concentration, the risk of toxicity is greater in those with the following underlying medical conditions: hypertension, diabetes, congestive heart failure, chronic renal failure, schizophrenia, Addison's disease.
Acute
A single acute overdose usually carries low risk and patients tend to show mild symptoms only, irrespective of their serum lithium concentration. However more severe symptoms may occur after a delay if lithium elimination is reduced because of renal impairment, particularly if a slow-release preparation has been taken. The fatal dose, in a single overdose, is probably over 5g.
If an acute overdose has been taken by a patient on chronic lithium therapy, this can lead to serious toxicity occurring even after a modest overdose as the extravascular tissues are already saturated with lithium.
Chronic
Lithium toxicity can also occur in chronic accumulation for the following reasons: Acute or chronic overdo sage; dehydration e.g. due to intercurrent illness, deteriorating renal function, drug interactions, most commonly involving a thiazide diuretic or a non-steroidal anti-inflammatory drug (NSAID).
Symptoms
The onset of symptoms may be delayed, with peak effects not occurring for as long as 24 hours, especially in patients who are not receiving chronic lithium therapy or following the use of a sustained release preparation.
Symptoms of lithium intoxication include:
Mild: Nausea, diarrhoea, blurred vision, polyuria, light headedness, fine resting tremor, muscular weakness and drowsiness.
Moderate: Increasing confusion, blackouts, fasciculation and increased deep tendon reflexes, myoclonic twitches and jerks, choreoathetosis movements, urinary or faecal incontinence, increasing restlessness followed by stupor. Hypernatremia
Severe: Coma, convulsions, cerebellar signs, cardiac dysrhythmias including sinoatrial block, sinus and junctional bradycardia and first degree heart block. Hypotension or rarely hypertension, circulatory collapse and renal failure
Others:
Gastrointestinal disorders: increasing anorexia and vomiting.
Nervous system disorders: Encephalopathy, cerebellar syndrome with symptoms such as muscle weakness, lack of coordination, drowsiness or lethargy, giddiness, ataxia, nystagmus, coarse tremor. Tinnitus, dysarthria, twitching, myoclonus, extrapyramidal disorders
ECG changes (flat or inverted T waves, QT prolongation), AV block, dehydration and electrolyte disturbances
At blood levels above 2-3 mmol/l, there may be a large output of dilute urine and renal insufficiency, with increasing confusion, convulsions, coma and death.

Management
There is no specific antidote to lithium. In the event of lithium overdose, lithium should be discontinued and lithium serum levels monitored closely.
Supportive treatment should be initiated, which includes correction of fluid and electrolyte balance, if necessary.
Diuretics should not be used. All patients should be observed for a minimum of 24 hours. ECG should be monitored in symptomatic patients. Steps should be taken to correct hypotension.
Consider gastric lavage for non-sustained-release preparations if more than 4 g has been ingested by an adult within 1 hour or definite ingestion of a significant amount by a child. Slow-release tablets do not disintegrate in the stomach and most are too large to pass up a lavage tube. Gut decontamination is not useful for chronic accumulation. Activated charcoal does not adsorb lithium.
Hemodialysis is the treatment of choice for severe lithium intoxication (especially in patients manifesting with severe nervous system disorders), or in cases of overdose accompanied by renal impairment.
Hemodialysis should be continued until there is no lithium in the serum or dialysis fluid. Serum lithium levels should be monitored for at least another week to take account of any possible rebound in serum lithium levels as a result of delayed diffusion from the body tissues.
In cases of acute on chronic overdose or in cases of chronic lithium toxicity if the lithium concentration is >4.0 mmol/l, discuss with your local poisons service.
Clinical improvement generally takes longer than reduction of serum lithium concentrations regardless of the method used.

STORAGE CONDITION:
Store at temperatures not exceeding 30°C.

DOSAGE FORMS AND PACKAGING AVAILABLE:
Alu/ PVC (Clear) Blister Pack of 10's (Box of 50's)

INSTRUCTIONS AND SPECIAL PRECAUTIONS FOR HANDLING AND DISPOSAL (IF APPLICABLE):
Not Applicable

NAME AND ADDRESS OF MARKETING AUTHORIZATION HOLDER:
Marketing Authorization Holder
Brown & Burk Philippines Inc
U-501, 5/F., SEDCCO 1 Bldg., 120 Rada cor.,
Legaspi Sts., Legaspi Village, Makati City, Philippines

NAME AND ADDRESS OF MANUFACTURER:
MICRO LABS LIMITED
92, Sipcot Industrial Complex,
Hosur – 635126, India.

CAUTION STATEMENT:
FOODS, DRUGS, DEVICES, AND COSMETICS ACT PROHIBITS DISPENSING WITHOUT PRESCRIPTION.

ADR REPORTING STATEMENT:
"FOR SUSPECTED ADVERSE DRUG REACTION, REPORT TO THE FDA: www.fda.gov.ph
Seek medical attention immediately at the first sigh of Adverse Drug Reaction.

REGISTRATION NUMBER:
DR No. : XY42242

DATE OF FIRST AUTHORIZATION:
18 JUL 2013.

DATE OF REVISION OF PACKAGE INSERT:
Apr. 2018

EXG-ML01I-1101/A

MICRO LABS LIMITED, BANGALORE, INDIA			
1	Product Name	Microlit	Colours Used
2	Strength	300 mg	BLACK
3	Component	Leaflet	
4	Category	Export - Philippines	
5	Dimension	210 x 240 mm	
6	Artwork Code	EXG-ML01I-1101/A	
7	Pharma Code	N/A	
8	Reason for Change	New Regulation	

	Prepared by (DTP)	Checked by (PD)	Approved by			
			Head CQA	Head Production/ Packing (Site)	Head QC (Site)	Head QA (Site)
Sign	Kantharaju L.					
Date	17-01-2020					