1. NAME OF THE MEDICINAL PRODUCT

Li-Liquid 1018mg/5ml Oral Syrup

2. QUALITATIVE AND QUANTITATIVE COMPOSITION

Lithium Citrate Tetrahydrate 1018mg/5ml
equivalent to lithium ion 10.8mmol
equivalent to Lithium Carbonate 400mg

Excipient(s) with known effect:
Methyl hydroxybenzoate (E218)- 6mg/5ml
Propyl hydroxybenzoate (E216)- 1.5mg/5ml
Propylene Glycol (E1520)- 155.6mg/5ml
Sorbitol (E420)- 272.8mg/5ml
Glucose- 1.7g/5ml
Ethanol- 4.4mg/5ml
Sunset Yellow (E110)- 0.1mg/5ml

For the full list of excipients, see section 6.1

3 PHARMACEUTICAL FORM

Solution for oral administration

4 CLINICAL PARTICULARS

4.1 Therapeutic indications

- Treatment of mania and hypomania
- Treatment of recurrent bipolar depression, where the use of alternative anti-depressants has been ineffective
- Prophylactic treatment of recurrent affective disorders
- Control of aggressive or self mutilating behaviour

Treatment should be directed to stabilise manic depressive illness rather than to establish early control of acute episodes.

4.2. Posology and Method of Administration

Dosage must be individualised depending on serum lithium levels and clinical response. The dosage necessary to maintain serum lithium levels within the therapeutic range varies from patient to patient. The minimum effective dose should be sought and maintained.

For oral administration only.

A simple treatment schedule has been evolved which except for some minor variations should be followed whether using Li-Liquid therapeutically or prophylactically. The minor variations to this schedule depend on the elements of the illness being treated and these are described later.

Adults:
1. In patients of average weight (70 kg) an initial total daily dose of 1018 – 3054mg Lithium citrate (equivalent to 400 - 1200mg Lithium carbonate which is 5-15ml of liquid) should be given in divided doses, in the morning and in the evening.

When changing between lithium preparations, serum lithium levels should first be checked, then Li-liquid therapy commenced at a daily dose as close as possible to that of the other form of lithium. As bioavailability varies from product to product (particularly with regard to slow release preparations) a change of product should be regarded as initiation of new treatment.

2. Four to a maximum of seven days after starting treatment serum lithium levels should be measured. Optimal maintenance serum levels may vary from patient to patient.

3. The objective is to adjust the Li-liquid dose so as to maintain the serum lithium level permanently within the diurnal range of 0.5 - 1.0mmol/L. Blood samples for measurement of serum lithium concentration should be taken before a dose is due and not less than 12 hours after the previous dose. 'Target' serum lithium concentration at 12 hours should be 0.5 - 0.8 mmol/L. Serum lithium levels should be monitored weekly until stabilisation is achieved. Levels of more than 1.5mmol/L must be avoided.
The liquid should be taken at the same time every day. A double dose to make up for a dose that has been missed should not be taken.

4. Lithium therapy should not be initiated unless adequate facilities for routine monitoring of serum concentrations are available. Following stabilisation of serum lithium levels, the period between subsequent estimations can be increased gradually but should not normally exceed two to three months. Additional measurements should be made following alteration of dosage, on development of intercurrent disease, signs of manic or depressive relapse, following significant changes in sodium or fluid intake, or if signs of lithium toxicity occur.

5. Whilst a high proportion of acutely ill patients may respond within three to seven days after the commencement of therapy with Li-Liquid, it should be continued through any recurrence of the affective disturbance. This is important as

the full prophylactic effect may not occur for 6 to 12 months after the initiation of therapy.

6. In patients who show a positive response to therapy with Li-Liquid, treatment is likely to be long term. Careful clinical appraisal of the patient should be exercised throughout medication (see precautions).

7. If lithium is to be discontinued, particularly in cases of high doses, the dose should be reduced gradually.

Prophylactic treatment of recurrent affective disorders: It is recommended that the described treatment schedule is followed.

Treatment of acute mania, hypomania and recurrent bipolar depression: It is likely that a higher than normal intake of Li-Liquid may be necessary during an acute phase. As a general rule the monitoring should maintain serum levels at 0.8 – 1.2 mmol/l until acute symptoms have been controlled. In all other details the described treatment schedule is recommended. The dosage needed may vary from patient to patient. Serum lithium levels should be monitored (see above) and should not exceed 1.5 mmol/l. As soon as control of mania or depression is achieved, the serum lithium level should be determined and it may be necessary, dependent on the results, to lower the dose of Li-Liquid and to re-stabilise serum lithium levels to the prophylactic dose.

Elderly: In elderly patients or those below 50 kg in weight, it is recommended that a starting dose of 509mg lithium citrate (equivalent to 200mg lithium carbonate which is 2.5ml of liquid) is taken in divided doses, in the morning and in the evening. Elderly patients may be more sensitive to undesirable effects of lithium and may also require lower doses in order to maintain normal serum lithium levels. It follows therefore that long term patients often require a reduction in dosage over a period of years.

Children and adolescents: Not recommended.

Renal impairment
In patients with mild and moderate renal insufficiency treated with lithium, serum lithium levels must be closely monitored and the dose should be adjusted accordingly to maintain serum lithium levels within the recommended range (see Section 4.4).

Lithium is contraindicated in patients with severe renal insufficiency (see Section 4.3).

4.3. Contraindications

Do not use in patients with a history of hypersensitivity to lithium or to any of the excipients listed in section 6.1, severe renal insufficiency, cardiac disease, cardiovascular insufficiency and untreated hypothyroidism.

Lithium should not be given to patients with low body sodium levels, including, for example, dehydrated patients, those on low sodium diets those with Addison's disease those with Brugada syndrome or family history of Brugada syndrome.

Do not use in patients who are breastfeeding.

4.4. Special warnings and precautions for use

General
When considering Li-Liquid 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 (see Section 4.2). Clear instructions regarding the symptoms of impending toxicity should be given by the physician to patients receiving long-term lithium therapy (see Section 4.9). 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 (see Section 4.9).

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 (see Section 4.3).
Renal, cardiac and thyroid functions should be re-assessed regularly during treatment with lithium.
For monitoring recommendations of lithium serum levels see Section 4.2.

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 (see Section 4.2) 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 (see Section 4.3).
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 develop. In patients who develop polyuria and/or polydipsia (see Section 4.8), 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 (see Section 4.8).

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 (see sections 4.5 and 4.8).

Benign intracranial hypertension
There have been case reports of benign intracranial hypertension (see Section 4.8). 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 hypokalaemia, bradycardia), and in patients concomitantly treated with drugs that are known to prolong the QT interval (see Sections 4.5 and 4.8).

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 (see

Section 4.3). Caution is advised in patients with a family history of cardiac arrest or sudden death.

Bariatric surgery
A lower maintenance dosage of lithium may be required for patients who have undergone bariatric surgery because of decreased glomerular filtration following marked weight loss. Also, drug levels should be monitored closely in connection with bariatric surgery due to the risk of lithium toxicity.

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 (see Sections 4.2 and 5.2).

Children
The use in children is not recommended.

Excipients in the formulation

Li -lithium 1018mg/5ml Oral Syrup contains:

- Methyl (E218) and propyl hydroxybenzoates (E216) (preservatives) which may cause allergic reactions (possibly delayed).
- propylene glycol (E1520). This medicine contains 155.6mg propylene glycol in each 5ml.
- Glucose. The medicine contains 1.7g of glucose in each 5ml. Patients with rare glucose-galactose malabsorption should not take this medicine.
- Sorbitol. This product also contains 272.8 mg of sorbitol in each 5ml. The additive effect of concomitantly administered products containing sorbitol (or fructose) and dietary intake of sorbitol (or fructose) should be taken into account. The content of sorbitol in medicinal products for oral use may affect the bioavailability of other medicinal products for oral use administered concomitantly. Patients with hereditary fructose intolerance (HFI) should not take/be given this medicinal product.
- This medicine contains less than 1 mmol sodium (23 mg) per 5ml, that is to say essentially ‘sodium-free’.
- Ethanol This medicine contains 4.4 mg of alcohol (ethanol) in each 5ml.The amount in 5ml of this medicine is equivalent to less than 1 ml beer or 1 ml wine. The small amount of alcohol in this medicine will not have any noticeable effects
- Sunset yellow (E110). It also contains sunset yellow colouring agent which can cause allergic reactions.

4.5. Interaction with other Medicinal Products and other forms of Interaction

If one of the following drugs is initiated, lithium dosage should either be adjusted or concomitant treatment stopped, as appropriate.

Interactions which increase lithium concentrations

- Metronidazole may reduce lithium renal clearance.
- Non-steroidal anti-inflammatory drugs including selective cyclo-oxygenase (COX) 2 inhibitors (monitor serum lithium concentrations more frequently if NSAID therapy is initiated or discontinued)
- ACE inhibitors
- Angiotensin II receptor antagonists
- Diuretics (thiazides show a paradoxical antidiuretic effect resulting in possible water retention and lithium intoxication). Should be prescribed with extreme caution and careful monitoring. Similar precautions should be exercised on diuretic withdrawal. Note that thiazides show a paradoxical antidiuretic effect resulting in possible water retention and lithium intoxication. If a thiazide diuretic has to be prescribed for a lithium-treated patient, lithium dosage should first be reduced and the patient re-stabilised 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 therefore should 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:

- urea
- xanthines (such as caffeine and theophylline)
- sodium bicarbonate containing products
- Diuretics (osmotic and carbonic anhydrase inhibitors)
- Calcitonin

Co-administration of the following drug with lithium may lead to decreased lithium concentrations and a risk of loss of efficacy:

- empagliflozin
- dapagliflozin.

Interactions causing neurotoxicity

- Neuroleptics (particularly haloperidol at higher dosages), flupentixol, risperidone, diazepam, thioridazine, fluphenazin, chlorpromazine and clozapine may lead in rare cases to neurotoxicity in the form of confusion, disorientation, lethargy, tremor, extrapyramidal symptoms and myoclonus. Co-administration of lithium with neuroleptics increases the risk of Neuroleptic Malignant Syndrome (NMS), 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 serotonergic syndrome, which justifies immediate discontinuation of treatment.
- Calcium channel blockers may lead to a risk of neurotoxicity in the form of ataxia, confusion and somnolence, reversible after discontinuation of the drug. Lithium concentrations may be increased.
- Carbamazepine may lead to dizziness, somnolence, confusion and cerebellar symptoms such as ataxia.
- Tri-cyclic antidepressants.

Other
Caution is advised if lithium is co-administered with other drugs that prolong the QT interval (see Sections 4.4 and 4.8), 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 (see Section 4.4), e.g. antidepressants such as SSRIs, tricyclic antidepressants, antipsychotics, anaesthetics, 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, indometacin and other prostaglandin-synthetase inhibitors.

Raised plasma levels of ADH may occur during treatment.

Serotonin syndrome
Serotonin syndrome is a potentially life-threatening adverse reaction, which is caused by an excess of serotonin (e.g. from overdose or concomitant use of serotonergic drugs), necessitating hospitalisation 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.

4.6. Fertility, 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 lithium 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. An increase in cardiac and other abnormalities, especially Ebstein anomaly, 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.

It is strongly recommended that lithium be discontinued before a planned pregnancy. If it is considered essential to maintain treatment with Li-Liquid during pregnancy, serum lithium levels should be monitored closely since renal function changes gradually during pregnancy and suddenly at parturition, requiring dosage adjustments. It is recommended that administration of Li-Liquid be discontinued shortly before delivery and recommenced 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
It is advisable that women treated with lithium should adopt adequate contraceptive methods.

Lactation
Lithium is secreted in breast milk, therefore bottle feeding is recommended. (See section 4.3 Contraindications).

There have been case reports of neonates showing signs of lithium toxicity (see Pregnancy). Therefore lithium should not be used during breast-feeding (see Section 4.3). 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.

Fertility
Published studies in rats exposed to lithium have reported spermatogenesis abnormalities that may lead to impairment of fertility.
This risk may also potentially apply to humans.

4.7. Effects on Ability to Drive and Use Machines

Lithium may cause disturbances of the CNS. Since lithium may slow reaction time, and considering the adverse reactions profile of lithium (see Section 4.8),

patients should be warned of the possible hazards when driving or operating machinery.

4.8. Undesirable 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.

System Organ Class	Adverse event
Blood and lymphatic system disorders	Leucocytosis.
Endocrine disorders	Long-term adverse effects may include thyroid function disturbances such as euthyroid goitre and/or hypothyroidism and thyrotoxicosis. Lithium-induced hypothyroidism may be managed successfully with concurrent thyroxine. Hypercalcaemia, hypermagnesemia, hyperparathyroidism have been reported.
Metabolism and nutrition disorders	Weight increase, hyperglycaemia, thirst.
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 (see Section 4.4). • Vertigo, impaired consciousness, abnormal reflexes, convulsions (see Sections 4.4 and 4.5), extrapyramidal disorders, encephalopathy, cerebellar syndrome (usually reversible), nystagmus. The above symptoms may result in falls. • Peripheral neuropathy may occur on long-term treatment and is

	usually reversible at cessation of lithium. • Dysgeusia • Serotonin syndrome • Neuroleptic malignant syndrome.
Eye disorders	Blurred vision, scotoma.
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 (see Sections 4.4 and 4.5), AV block, cardiomyopathy.
Gastrointestinal disorders	Abdominal discomfort, taste disorder, nausea, vomiting, diarrhoea, gastritis, salivary hypersecretion, dry mouth, anorexia.
Skin and subcutaneous tissue disorders	Folliculitis, pruritus, papular skin disorders, acne or acneform eruptions, aggravation or occurrence of psoriasis, allergic rashes, alopecia, cutaneous ulcers Frequency unknown: lichenoid drug reaction.
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 (see Section 4.4). 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. The minimum clinically effective dose of lithium should always be used. In patients who develop polyuria and/or polydipsia, renal function should be monitored, e.g. with measurement of blood urea, serum creatinine and urinary protein levels in addition to the routine

	serum lithium assessment. • *Rare cases* of nephrotic syndrome have been reported. • Frequency unknown: Microcysts, oncocytoma and collecting duct renal carcinoma (in long-term therapy) (see Section 4.4).
Reproductive system and breast disorders	Sexual dysfunction.
General disorders and administration site conditions	• Peripheral oedema. • Urticaria and angioedema, attributed to some excipients.

If any of the above symptoms appear, treatment should be stopped immediately and arrangements made for serum lithium measurement.

Reporting of suspected adverse reactions
Reporting suspected adverse reactions after authorisation of the medicinal product is important. It allows continued monitoring of the benefit/risk balance of the medicinal product. Healthcare professionals are asked to report any suspected adverse reactions via the Yellow Card Scheme at www.mhra.gov.uk/yellowcard or search for MHRA Yellow Card in the Google Play or Apple App Store.

4.9. Overdose

Any overdose in a patient who has been taking chronic lithium therapy should be regarded as potentially serious.

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 overdosage:
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, choreoathetoid movements, urinary or faecal incontinence, increasing restlessness followed by stupor.
Hypernatraemia.
Severe: Coma, convulsions, cerebellar signs, cardiac dysrhythmias including sino-atrial 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 serum levels monitored closely . Diuretics should not be used (see section 4.5).

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. Supportive treatment should be initiated, which includes correction of fluid and electrolyte balance, if necessary.

Consider gastric lavage for non-sustained-release preparations if more than 4 g has been ingested by an adult within one 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.

Haemodialysis 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. Haemodialysis should be continued until there is no lithium in the serum or dialysis fluid.

Serum lithium levels should be monitored for at least a further 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.

5. PHARMACOLOGICAL PROPERTIES

5.1. Pharmacodynamic Properties

Mood-stabilising agent

Pharmacotherapeutic group: Psycholeptics; Lithium, ATC code: N05AN01

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.

5.2. Pharmacokinetic Properties

Lithium is rapidly and completely absorbed from the gastrointestinal tract when taken in solution as one of its salts.

Peak plasma concentrations are obtained about 0.75 hours after ingestion of Li-Liquid. Lithium is reported to have a plasma half-life of about 7 to 20 hours during the daytime. Lithium is excreted by the kidneys. There is a narrow margin between the therapeutic and the toxic plasma concentration. Therefore, not only is individual titration of lithium dosage essential to ensure constant plasma concentrations for the patient involved, but the conditions under which the blood samples are taken for monitoring must be carefully controlled. .

Special populations
Elimination half-life may be increased in elderly patients due to age related decrease in renal function and also in patients with renal impairment (see Sections 4.2 and 4.4).

5.3 Preclinical safety data

There is epidemiological evidence that lithium may be harmful to the foetus in human pregnancy. Therefore it is recommended that lithium be discontinued or if the lithium is necessary, the levels in the patient should be monitored closely.

Lithium is a drug on which extensive clinical experience has been obtained. Relevant information for the prescriber is provided elsewhere in the Summary of Product Characteristics.

6. PHARMACEUTICAL PARTICULARS

6.1. List of excipients

Citric acid monohydrate, saccharin sodium, sorbitol solution(E420), syrup liquid glucose, propylene glycol (E1520), methyl (E218) and propyl hydroxybenzoate (E216), sunset yellow (E110), cherry flavour (containing ethanol and propylene glycol (E1520)) and purified water

6.2 Incompatibilities

None known

6.3 Shelf life

24 months

6 months opened

6.4 Special precautions for storage

Store above 4°C and protect from light.

6.5. Nature and Contents of Container

Bottles: Amber (Type III) glass bottles with capacity of 150ml.

Closures: HDPE EPE wadded, tamper evident, child resistant.

6.6. Special Precautions for Disposal and Other Handling

Keep out of the sight and reach of children.

7 MARKETING AUTHORISATION HOLDER

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8 MARKETING AUTHORISATION NUMBER(S)

PL 00427/0075

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