SUMMARY OF PRODUCT CHARACTERISTICS

1 NAME OF THE MEDICINAL PRODUCT

Priadel 400mg prolonged release tablets.

2 QUALITATIVE AND QUANTITATIVE COMPOSITION

Each prolonged-release tablet contains 400 mg lithium carbonate.

For the full list of excipients, see section 6.1.

3 PHARMACEUTICAL FORM

Prolonged-release tablet.

White, circular, bi-convex tablets engraved PRIADEL on one side, scored on the other side, in a prolonged-release formulation.

The tablet can be divided into equal doses.

4 CLINICAL PARTICULARS

4.1 Therapeutic indications

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

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.
As a general rule, the following dosing schedule is recommended. Please refer also to the specific recommendations for the different indications as listed below:

1. In patients of average weight (70 kg) an initial dose of 400-1,200 mg of Priadel may be given as a single daily dose in the morning or on retiring. Alternatively, the dose may be divided and given morning and evening. hen changing between lithium preparations serum lithium levels should first be checked, then Priadel therapy started at a daily dose as close as possible to the dose of the other form of lithium. As bioavailability varies from product to product (particularly with regard to retard or 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. Blood samples should be taken 12 or 24 hours after the previous dose of lithium, just before the next dose is due, to measure the serum lithium level at its trough. The serum level should not exceed 1.5 mmol/l.

   The objective is to adjust the Priadel dose so as to maintain the "Target" serum lithium concentrations at 12 and 24 hours as shown in the table below.

"Target" serum lithium concentration (mmol/l)		
	At 12 hours	At 24 hours
Once daily dosage	0.7 – 1.0	0.5 – 0.8
Twice daily dosage	0.5 – 0.8	

   Serum lithium levels should be monitored weekly until stabilisation is achieved. The serum level should not exceed 1.5 mmol/l.

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 measurements 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 change in sodium or fluid intake, or if signs of lithium toxicity occur (see section 4.9).

5. Whilst a high proportion of acutely ill patients may respond within three to seven days of the commencement of Priadel therapy, Priadel 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 Priadel therapy, 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 bipolar affective disorders and control of aggressive behaviour or intentional self-harm:
It is recommended that the described treatment schedule is followed. The dosage needed may vary from patient to patient. As a general rule, serum lithium levels should be maintained within the range of 0.5 to 1.0 mmol/L, and should not exceed 1.5 mmol/L. Optimal maintenance serum lithium levels may vary from patient to patient.

Treatment of acute manic or hypomanic episodes and recurrent depressive disorders:
It is likely that a higher than normal Priadel intake may be necessary during an acute phase and divided doses would be required here. 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. Once clinical control is achieved, dosage should be reduced to the prophylactic dose.

Elderly:
Elderly patients or those below 50 kg in weight, often require lower lithium dosage to achieve therapeutic serum lithium levels. Starting doses of 200 mg to 400 mg are recommended. Dosage increments of 200 to 400 mg every 3 to 5 days are usual. Total daily doses of 800 to 1800 mg may be necessary to achieve effective blood lithium levels of 0.8 to 1.0 mmol/l. For prophylaxis, the dosage necessary to reach a blood lithium level of 0.4 to 0.8 mmol/l is generally in the range of 600 to 1200 mg/day.

***Paediatric population*:**
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).

Method of administration
The prolonged-release tablets should not be crushed or chewed. The prolonged-release tablets 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.
The tablets have break lines and therefore they can be divided accurately to provide dosage requirements as small as 200 mg.

4.3 Contraindications

- Hypersensitivity to the active substance or to any of the excipients listed in

section 6.1.

- 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.

4.4 Special warnings and precautions for use

- **General**

When considering Priadel 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 ECG changes (right bundle branch block and ST segment elevation in right precordial leads), which may lead to cardiac arrest or sudden death. Lithium is not recommended in patients with known Brugada syndrome or a family history of Brugada syndrome. Caution is advised in patients with a family history of cardiac arrest or sudden death.

- **Bariatric surgery**

In patients who have undergone bariatric surgery, a lower maintenance dose of lithium may be required. Lithium levels should be closely monitored due to the risk of lithium toxicity until weight has stabilized.

- **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).

- **Paediatric population**

The use in children is not recommended.

- **Excipients**

This medicine contains less than 1 mmol sodium (23 mg) per tablet, that is to say essentially 'sodium-free'.

4.5 Interaction with other medicinal products and other forms of interaction

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 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 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
- Empagliflozin
- Dapagliflozin

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 (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, 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 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.

Topiramate: In healthy volunteers, there was an observed reduction (18% for AUC) in systemic exposure for lithium during concomitant administration with topiramate 200 mg/day. In patients with bipolar disorder, the pharmacokinetics of lithium were unaffected during treatment with topiramate at doses of 200 mg/day; however, there was an observed increase in systemic exposure (26% for AUC) following topiramate doses of up to 600 mg/day. There have been reports on lithium toxicity when concurrently administered with topiramate. Lithium levels should be closely monitored when co-administered with topiramate.

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 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.

Breast-feeding

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 (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. Fine hand tremors, polyuria and mild thirst may persist.

Tabulated list of adverse reactions

System Organ Class	Adverse reactions
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. • Hypermagnesaemia has been reported. • Very frequent: Hypercalcaemia • Frequency not known: Hyperparathyroidism, parathyroid adenoma, parathyroid hyperplasia
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 (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 fall. • 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. Frequency not known: Brugada syndrome (Unmasking/aggravation)
Gastrointestinal disorders	Abdominal discomfort, taste disorder, nausea, vomiting, diarrhoea, gastritis, salivary hypersecretion, dry mouth, anorexia.
Skin and subcutaneous tissue disorder	Folliculitis, pruritus, papular skin disorders, acne or acneform eruptions, aggravation or occurrence of psoriasis, allergic rashes, alopecia, cutaneous ulcers Frequency unknown: lichenoid drug reaction. Frequency not known: Drug reaction with eosinophilia and systemic symptoms (DRESS)
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. • *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 such as acacia powder (or Arabic gum).

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

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 5 g.
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 dysrythmias 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 (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.

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.

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 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.

5 PHARMACOLOGICAL PROPERTIES

5.1 Pharmacodynamic properties

Pharmacotherapeutic group: Psycholeptics; Lithium, ATC code: N05AN01

Mood-stabilising agent

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

Time to peak serum level for prolonged release Priadel tablets is about 2 hours and approximately 90% bioavailability would be expected.

Absorption
Lithium is rapidly absorbed from the gastrointestinal tract.
Steady-state lithium levels may not be obtained until 4-6 days.

Distribution
Lithium has a low volume of distribution (0.7 to 0.9 L/kg).
It is not bound to plasma proteins.
Lithium crosses the placenta and is excreted in breast milk.

Biotransformation
Lithium is not metabolised in the liver.

Elimination
Lithium is primarily excreted by the kidneys (>95% of the dose).
Elimination half-life ranges from 18 to 36 hours.
Lithium can be eliminated by haemodialysis.

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

Nothing of therapeutic relevance.

6 PHARMACEUTICAL PARTICULARS

6.1 List of excipients

Glycerol distearate
Mannitol (E421)
Acacia spray dried
Sodium laurilsulfate (E487)

Magnesium stearate
Maize starch
Sodium starch glycolate (Type A)

6.2 Incompatibilities

Not applicable.

6.3 Shelf life

3 years.

6.4 Special precautions for storage

Store below 25ºC. Store in the original package in order to protect from moisture.

6.5 Nature and contents of container

Securitainers: 1000, 100 or 50 tablets
Blister packs: 100 tablets
Hospital packs: 100 tablets

Not all pack sizes may be marketed.

6.6 Special precautions for disposal

No special requirements.

7 MARKETING AUTHORISATION HOLDER

Essential Pharma Ltd,
Vision Exchange Building
Triq it-Territorjals, Zone 1,
Central Business District,
Birkirkara, CBD 1070,
Malta

8 MARKETING AUTHORISATION NUMBER(S)

PL 50301/0002

9 DATE OF FIRST AUTHORISATION/RENEWAL OF THE AUTHORISATION

Date of first authorisation: 15 August 1985

10 DATE OF REVISION OF THE TEXT

12/09/2024