SHARED PRESCRIBING GUIDELINE

DRUG: PRESCRIBING OF LITHIUM FOR ADULTS

Introduction	**Licensed Indications** 1. In the management of acute mania 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 behaviours of intentional self-harm. **Background:** Lithium salts have a narrow therapeutic/toxicity ratio and regular monitoring is required. Prescribing is by brand name and Lancashire and South Cumbria NHS Foundation Trust (LSCFT) prescribes Priadel ® when initiating patients on lithium. Information in the Priadel Summary of product characteristics (SPC) notes the following target serum lithium concentration ranges in 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
Formulation	Tablets as brand Priadel 200mg and 400mg **(Please note:** Priadel liquid is lithium **citrate** not carbonate and is given twice a day)
Dose and administration	**Treatment and Prophylaxis** **Dosing information for Priadel® preparations only** – for other lithium preparations please refer to the current version of the BNF or individual product SPC: **Priadel® - By mouth** **For Adult (body-weight up to 50 kg)** Initially 200–400 mg daily, dose adjusted according to serum-lithium concentration, doses are initially divided throughout the day, but once daily administration is preferred when serum-lithium concentration stabilised. **For Adult (body-weight 50 kg and above)** Initially 0.4–1.2 g once daily, alternatively initially 0.4–1.2 g daily in 2 divided doses, dose adjusted according to serum-lithium concentration, doses are initially divided throughout the day, but once daily administration is preferred when serum-lithium concentration stabilised. **For Elderly (over the age of 60 – definition confirmed with the manufacturer of Priadel®)** Initially 200–400 mg daily, dose adjusted according to serum-lithium concentration, doses are initially divided throughout the day, but once daily administration is preferred when serum-lithium concentration stabilised. The dose should be adjusted following lithium levels. Lithium levels should be checked 4-7 days following initiation, then weekly until the desired therapeutic range is achieved.
Responsibilities	**Secondary Care Responsibilities are:** 1. Lithium therapy will be instigated in secondary care for patients who meet the diagnostic criteria listed above. 2. Before commencing treatment baseline monitoring will be undertaken in secondary care as listed below. 3. Patients and carers will be provided with both written and verbal information to facilitate concordance 4. Women of childbearing age should be advised of the risk of teratogenic effects and the need for effective contraception while taking lithium. 5. Patients will be provided with the NPSA lithium pack including the purple lithium level record book. 6. Patients and carers will be advised of risk situations 7. Patients will be advised that erratic compliance or rapid discontinuation may increase the risk of a manic relapse 8. To initiate treatment

	9. To monitor until steady state lithium levels are obtained 10. Older adults will be monitored carefully for symptoms of lithium toxicity because they may develop high levels of lithium at doses in the normal range and lithium toxicity is possible at moderate serum levels. 11. Urea and creatinine levels become elevated, closer monitoring of lithium levels and dose will be undertaken and an assessment made of the rate of deterioration of renal function. Prescribers will consider seeking advice from a renal specialist regarding ongoing treatment. 12. Treatment will be stopped if considered to be no longer appropriate. Lithium should be stopped over at least 4 weeks but preferably over a three month period particularly if there is a history of manic relapse Following initiation and stabilisation of the drug the patient will be maintained on lithium for a minimum period of three months to establish response and tolerability. During this period the medication will be prescribed by secondary care. After this period the patient will be reassessed in secondary care and if: • The illness has stabilised • The side effects are manageable • The target serum lithium level has been achieved • Adherence to the regime is established Then a shared prescribing agreement between primary and secondary care to manage the patient should be progressed as follows: 1. A referral letter will be sent to the patient's general practitioner (GP) asking them to consider the prescribing of lithium under shared prescribing arrangements. This will state if the indication is off label. 2. The shared prescribing guidance will be included with the letter 3. The GP will be informed of the target therapeutic serum lithium level for each individual patient 4. Test results will be communicated to the GP (complete the "copy to" section on the blood form) 5. The patient will be provided with a further 28 days supply of medication during this period to ensure continuity of care 6. The patient will be informed of the process 7. The patients response will reviewed at regular intervals(to be agreed with the LCFT prescriber) 8. The patient will be reviewed promptly where the GP when undertaking shared care indicates that there are signs of renal impairment, unacceptable side effects or deterioration in mental state. Where the GP indicates possible signs of toxicity the patient will depending on the clinical picture and/or lithium level results, be reviewed the same day by secondary care services or where emergency management is indicated be sent to accident and emergency or the medical assessment unit for immediate intervention. Once all if the above are in place and the GP has agreed to participate in shared care arrangements a record will be made in the patients notes and the patient will be informed that their next supply of medication will be obtained from their GP.
Monitoring undertaken by Secondary Care	**Baseline monitoring to be completed prior to initiating lithium**
	Full Blood Count Blood glucose Lipid profile Urea and Electrolytes including calcium eGFR Liver Function (LFT) Thyroid Function (TFT) – patients should be euthyroid before commencing lithium therapy Blood Pressure (BP) ECG if there are risk factors for or evidence of existing cardiovascular disease as assessed by the clinician 24 hour creatinine clearance if history of renal infection or problems Weight* (BMI) Height* ***For children and adolescents weight and height should be monitored monthly for six months, then every six months**
	Continuation monitoring
	Lithium levels: Obtain lithium levels 12 hours post dose and should always be taken at the same time to give consistent results **7 days after initiation and 7 days after dose increase, then weekly until desired target range is obtained**. **Target range**: 0.4 mmol/L 1.0 mmol/L (to be identified by secondary care prescriber) Once stabilised, obtain lithium levels every 3 months for the first year. Maintain 3 monthly monitoring for the following patient groups: • Elderly, • Poor adherence • On Interacting Drugs • Impaired renal or thyroid function • Poor Symptom control

	• Previous level over 0.8 mmol/L After the first year, If patient remains stable the monitoring frequency can extend to 6 monthly thereafter. (NICE **CG** 185) After initiation patient should be maintained on Lithium for at least three months to establish response and ensure tolerability. • For new starters consider maintaining plasma levels between 0.6 -0.8 mmol/L • For patients previously on Lithium that have relapsed or with subthreshold symptoms plus functional impairment- consider maintaining levels between 0.8 -1.0 mmol/L for at least 6 months. • TFTs, U&E plus Calcium, EGFR should be checked every 6 months. Monitoring frequency should increase if clinical signs of deterioration present or taking interacting drugs like NSAIDS, ACE Inhibitors, and Diuretics. • Lipid profile annually if over 40 years. • Once stable, TFTs, Blood Glucose, Weight, Blood pressure annually. • Weight should be measured more frequently if rapid weight gain occurs Monitor the person at every appointment for symptoms of neurotoxicity, including paraesthesia, ataxia, tremor and cognitive impairment, which can occur at therapeutic levels of lithium – see 'monitoring required in primary care' also.
Primary Care Responsibilities	**Primary care responsibilities are:** 1. To undertake monitoring as set out below under monitoring in primary care 2. To undertake continuation monitoring as set out and take appropriate action if these tests are abnormal 3. To reduce or discontinue treatment in serious diarrhoea, vomiting or intercurrent infection (especially if sweating profusely). Consideration should be given to stopping lithium for up to seven days if the patient becomes acutely and severely unwell with a metabolic or respiratory disturbance of any cause. 4. To stop lithium if signs of toxicity occur and contact the consultant psychiatrist for advice on treatment and future management 5. To refer back to secondary care for specialist advice if the treatment is ineffective or if the patient develops unacceptable side effects. This is particularly important where patients develop signs of renal impairment. 6. To review the patient in accordance with NICE guidance and advice from LCFT 7. To provide the patient with repeat prescriptions specifying the brand on the prescription. Incorrect dosing can occur if the patient changes preparation. 8. To make a clear statement in the primary care notes showing where the monitoring is being carried out
Monitoring required in primary care	1. To take serum lithium levels at three monthly intervals and after any dose changes, change of preparation, during an acute UTI, or changes in other medication which may affect lithium levels. Samples must be taken at least 12 hours post dose, and the time of the sample, total daily dose and the time of the previous dose noted on the sample. In the event of a twice daily dosing regimen, the morning dose should be omitted until after the blood sample has been taken. After the first year, If patient remains stable the monitoring frequency can extend to 6 monthly unless they fulfilling criteria for more frequent monitoring as outlined below. (NICE CG 185) 2. Maintain more frequent (three monthly monitoring) for the following patient groups: • Elderly (over the age of sixty) • Poor adherence • On interacting drugs • Impaired renal or thyroid function • Poor symptom control • Previous level over 0.8mmol/l 3. Target range: 0.4 mmol/L- 1.0 mmol/L, however any patient specific target range will be communicated to primary care by secondary care prescribers For new starters consider maintaining plasma levels between 0.6 -0.8 mmol/L For patients previously on Lithium that have relapsed or with subthreshold symptoms plus functional impairment- consider maintaining levels between 0.8 -1.0 mmol/L for at least 6 months. 4. TFTs, U&E plus Calcium, EGFR should be checked every 6 months. Monitoring frequency should increase if clinical signs of deterioration present or taking interacting drugs like NSAIDS, ACE Inhibitors, and Diuretics.

	5. Once stable, TFTs, Blood Glucose, Weight, Blood pressure checks can be conducted annually for patients who are clinically stable and not prescribed interacting drugs 6. Lipid profile annually if over 40 years. 7. To check patients for side effects and signs of lithium toxicity at each appointment. Toxicity can occur without apparent increase in serum level, and it is important to "treat the patient not the level". Signs of neurotoxicity which can occur at therapeutic levels include paraesthesia, ataxia, tremor and cognitive impairment. 8. Results should be shared with secondary care. **9.** To record results in patient's lithium monitoring booklet
Adverse effects	Thirst, polyuria, GI upset, Diabetes insipidus – may inhibit ADH (must maintain fluid intake), Acne, Cardiac arrhythmias, Weight gain, oedema, Hypothyroidism, Lethargy, feeling cold, vertigo. **Please refer to the current version of the BNF or individual product SPCs for a complete list of adverse effects.** **Signs of Lithium Toxicity** 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. **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. 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. **Action to be taken if level over target range** 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. 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.
Drug 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, **should be avoided** • 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. 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, 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.
Contraindications	Hypersensitivity to lithium or it's excipients, breast feeding, severe renal impairment (may be given if closely monitored in mild to moderate renal impairment), untreated hypothyroidism, cardiac disease or insufficiency, hyponatraemia, Addison's disease, Brigade syndrome or family history of Brugada Syndrome Lithium should not be used in pregnancy, especially the first trimester, unless considered essential

Contact details	As per correspondence from LSCFT
This guidance does not replace the SPC's which should be read in conjunction [1] [2]	

Bibliography

[1] Royal Pharmaceutical Society, British National Formulary, London: Pharmaceutical Press, 2023. Acessed via www.bnf.nice.org.uk [accessed online 1st February 2023].

[2] Essential Pharma Ltd, "Priadel 200mg prolonged release tablets," Datapharm, 3rd October September 2022. [Online]. Available: https://www.medicines.org.uk/emc/product/13162/smpc [Accessed 1st February 2023].

Appendix 1

Optional Shared Care Agreement form

Request by Specialist Clinician for the patient's GP to enter into a shared care agreement

PLEASE NOTE: The use of this form is not compulsory, but the same information must be communicated between the specialist service and primary care in advance of entering into a shared-care agreement.

Part 1 - To be signed by Consultant / Associate Specialist / Speciality Trainee or Specialist Nurse (who must be a prescriber)

Dear Doctor:	Click or tap here to enter text.
Name of Patient:	Click or tap here to enter text.
Address:	Click or tap here to enter text.
	Click or tap here to enter text.
	Click or tap here to enter text.
Date:	Click or tap to enter a date.
Patient NHS Number:	Click or tap here to enter text.
Patient Hospital Number:	Click or tap here to enter text.
Diagnosed Condition:	Click or tap here to enter text.

I request that you prescribe:

(1) Click or tap here to enter text.
(2) Click or tap here to enter text.
(3) Click or tap here to enter text.
(4) Click or tap here to enter text.

for the above patient in accordance with the LMMG shared care guideline(s) (Available on the LMMG website).

Last Prescription Issued:	Click or tap to enter a date.
Next Supply Due:	Click or tap to enter a date.
Date of last blood test (if applicable):	Click or tap to enter a date.
Date of next blood test (if applicable:	Click or tap to enter a date.
Frequency of blood test (if applicable:	Click or tap here to enter text.

I confirm that the patient has been stabilised and reviewed on the above regime in accordance with the Shared Care guideline.

If this is a Shared Care Agreement for a drug indication which is unlicensed or off label, I confirm that informed consent has been received from the patient.

I will accept referral for reassessment at your request. The medical staff of the department are available if required to give you advice.

Details of Specialist Clinicians

Name:	Click or tap here to enter text.
Date:	Click or tap to enter a date.
Position:	Choose an item.
Signature:	Click or tap here to enter text.

(An email from the specialist clinician will be taken as the authorised signature)

In all cases, please also provide the name and contact details of the Consultant.

When the request for shared care is made by a Specialist Nurse, it is the supervising consultant who takes medicolegal responsibility for the agreement.

Consultant	Click or tap here to enter text.

Contact Details	
Telephone Number	Click or tap here to enter text.
Extension	Click or tap here to enter text.
Email Address	Click or tap here to enter text.

Part 2 - To be completed by Primary Care Clinician (GP)

I agree to prescribe and monitor Click or tap here to enter text. for the above patient in accordance with the LMMG shared care guideline(s) commencing from the date of next supply / monitoring (as stated in Part 1 of the agreement form).

Name:	Click or tap here to enter text.
Date:	Click or tap to enter a date.
Signature:	Click or tap here to enter text.

*Please sign and return a copy **within 14 calendar days** to the address above* **OR**

If you **do not** agree to prescribe, please sign below and provide any supporting information as appropriate:

I **DO NOT** agree to enter in to a shared care agreement on this occasion.

Name:	Click or tap here to enter text.
Date:	Click or tap to enter a date.
Signature:	Click or tap here to enter text.
Further information:	Click or tap here to enter text.