Shared Care Guideline

This guidance reinforces responsibilities and behaviours expected of all healthcare professionals involved with the prescribing, monitoring and care of the patient. The purpose of this guideline is to provide seamless transfer of care between specialist and primary services.

Medicine Name: **Lithium**

NOTES to the Primary Care Prescriber
Medicines like Lithium require specialist (consultant psychiatrist) initiation and/or dose titration and specific ongoing monitoring. The initiation includes the prescribing, monitoring and dose stabilization and this should be executed by a consultant psychiatrist until the patient is stabilized (usually for a minimum 3 months), after which the Primary Care Prescriber may be asked to agree to shared care of the patient, through the use of shared care guidelines.

The expectation is that this guideline should provide sufficient information to enable Primary Care Prescribers to be confident to take clinical and legal responsibility for prescribing this medication and continuing care in the community.

The questions below will help you confirm this:

1. Is the patient currently under your care? (e.g. shared care should not be agreed if the patient is currently in intermediate care following hospital discharge.)
2. Do you have the relevant knowledge, skills and access to equipment to allow you to monitor treatment as indicated in this shared care agreement?
3. Have you been provided with relevant clinical details including monitoring data?

If you can answer YES to all these questions (after reading this shared care guideline), then it is appropriate for you to accept prescribing responsibility.

If the answer is NO to any of these questions, you should not accept prescribing responsibility. You should write to the consultant psychiatrist within 14 days, outlining your reasons for NOT accepting shared care and the prescribing of lithium for this patient.

The patient's best interests are always paramount

This Guideline was prepared using information available at the time of preparation, users should always refer to the manufacturer's current edition of summary of product characteristics (Data Sheet) for more details. Prescribers should also refer to the New Zealand Formulary, section 4.2.3. Drugs for bipolar disorder and Lithium monograph.

General Information

For product information
[Lithium (Priadel) Consumer information leaflet]
[Health Navigator]

This information sheet does not replace the product data information provided by the manufacturer, which should be read in conjunction with this guideline.

Links to the relevant Data sheet website:
Priadel® Lithium 400mg prolonged release tablets
Lithium Carbonate 250 mg Capsule

Indication/s, including license status:
- Management of acute manic or hypomanic episodes – licensed indication.
- Management of episodes of recurrent depressive disorders – licensed indication.
- Prophylaxis against bipolar affective disorders – licensed indication.
- Control of aggressive behavior or intentional self-harm – unlicensed indication

General

The minimum clinically effective dose of lithium should always be used. Clear instructions regarding the symptoms of impending toxicity should be given by the doctor to patients receiving long-term lithium therapy.
Patients 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 doctor and lithium levels should be checked.

Treatment should be discontinued immediately on the first signs of toxicity.

Dose & administration:
Lithium prescribing is brand specific. Two formulations are currently funded for lithium in New Zealand - 400 mg modified release tablets and 250 mg immediate release capsules. Bioavailability varies therefore formulations are not interchangeable. A change of product should be regarded as initiation of new treatment, and adequate monitoring should occur.

Target serum lithium concentration (mmol/L) will vary depending on the diagnosis and past response to treatment. The lower end of the therapeutic range being 0.4 mmol/L and the higher end 1.0 mmol/L.

Swallowing difficulties, there are no liquid preparations for lithium in NZ. Please consult with Hospital Pharmacy and Psychiatrist if patient is unable to swallow the tablets or capsules whole.

Contraindications:

- 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 cardiac arrest and sudden death

Adverse effects: (see also product data sheet for details)
Adverse effects are directly related to blood levels and their **frequency increases dramatically at plasma levels above 1.0 mmol/L**

Note

Periods of fever, infection, dehydration, gastric illness with diarrhoea or vomiting may result in salt and water depletion, this can lead to an increase in lithium levels. Closer monitoring is required.

Adverse effects Vs Toxicity:

Adverse Effects	Toxic Effects
Dry Mouth / metallic taste	Severe shaking / tremor
Thirst (polydipsia)	Blurred vision
Increased urination (polyuria)	Unsteadiness of their feet
Dizziness	Muscle twitches
Mild shaking or tremor of hand(s)	Muscle weakness
Exacerbation of psoriasis	Confusion
Weight gain	Difficulty speaking / slurring of words
Oedema	Clumsiness
Mental dulling	
Hypokalaemia	
Raised antidiuretic hormone concentration	
Thyroid function disturbances	

Toxicity can occur AT ANY LEVEL even within the therapeutic range
Levels above 0.8mmol/l are associated with higher risk of renal toxicity levels of > 1.0 mmol/L but especially >1.5 mmol/L are reliably associated with toxicity and require urgent action.
Levels above 2.0 mmol/L are considered dangerous and **require urgent admission to hospital. Increased disorientation and seizures may lead to coma and death.**

Medicine Interactions: (add table from inpatient guideline

- Diuretics (esp. thiazides) can lead to increased lithium levels
- ACE-Inhibitors & Angiotensin Receptor Blockers can lead to increase lithium levels
- Non-Steroidal Anti-Inflammatory Drugs can lead to increase lithium levels
- SSRIs: may increase CNS toxicity, (although lithium levels may not be raised, increased monitoring should be considered)
- Many other interactions are possible – refer to NZF interaction checker

Potentially hazardous interactions. Combined administration should be avoided or only undertaken with caution and appropriate monitoring.

DRUG	INTERACTION
ACE inhibitors e.g. enalapril, Angiotensin-II antagonists e.g.losartan	• Lithium excretion reduced, Increased plasma concentration • May cause toxicity • Monitor closely for signs of lithium toxicity, and consider taking lithium levels • Be alert for the need to reduce the lithium dose
Anti-inflammatories (NSAIDs) e.g. diclofenac, ibuprofen, aspirin	• Excretion of lithium reduced • Increased risk of toxicity • Avoid concomitant use *Note - paracetamol is safer to use with lithium*
Anti-arrhythmics e.g. amiodarone	• Risk of ventricular arrhythmias • Avoid concomitant use
Diuretics (thiazides, potassium-sparing and loop diuretics)	• Lithium excretion reduced • Increased plasma concentration and risk of toxicity • Loop diuretics are safer than thiazides
Methyldopa	• Neurotoxicity may occur without increasing plasma concentrationof lithium • Avoid concurrent use whenever possible

Less significant interactions – usually without serious consequences

Acetazolamide	• Excretion of lithium is reduced
Antacids e.g. Sodium bicarbonate	• Excretion increased • Reduced plasma concentration
Antiepileptics e.g. carbamazepine, phenytoin, topiramate	• Neurotoxicity may occur without increased lithium plasmaconcentrations
Antidepressants eg. SSRIs,tricyclics, venlafaxine	• Increased serotonergic effects seen and an increased risk of CNS effects as well as risk of lithium toxicity reported • All canincrease lithium toxicity without affecting lithium levels
Antipsychotics	• Increased risk of extrapyramidal side effects and possibleneurotoxicity • Monitor for risk of QTc prolongation
Calcium channel blockers	• Neurotoxicity may occur with diltiazem or verapramil withoutincreasing the plasma concentration of lithium
Metronidazole	• Increased risk of lithium toxicity
Muscle Relaxants - orphenadrine	• Lithium enhances the effect of muscle relaxants • Hyperkinesiscaused by lithium is aggravated by baclofen
Parasympathomimetics	• Lithium antagonises the effects of neostigmine and Pyridostigmine
Theophylline/ aminophylline	• Increased excretion of lithium • Reduced plasma lithium concentration • Depressive and manic relapse may occur if the dosage of lithium is not raised when theophylline is given • Lithiumlevels should be monitored if theophylline (or aminophylline) is stopped, started or altered

Criteria for use:
Lithium treatment should only be continued if the patient is properly monitored against the criteria set out below:

Routine monitoring:
Results of routine monitoring should be recorded in a patient held lithium monitoring booklet. If the patient does not hold one, a copy should be provided for the patient and the importance of carrying the booklet for healthcare professionals to refer to should be stressed.

Monitoring recommendations

	Baseline	Monitoring frequency	Comments
Height	✓	Annually	
Weight /BMI	✓	3 – 6 monthly	
Pregnancy	✓		If childbearing potential contraception advised
Lithium blood level		3 monthly	3 monthly elderly or ill
Urea and electrolytes	✓	3 - 6 monthly	3 monthly elderly or ill
eGFR	✓	3 - 6 monthly	3 monthly if elderly or complicating factors
TSH	✓	6 monthly	If TSH raised recheck 4 – 6 weekly
Corrected Calcium	✓	Annually	
ECG	If appropriate		
Full blood count	If appropriate		
Physical Health Check • Lipid levels • Plasma glucose level • Blood pressure • Smoking and alcohol use	✓	Annually	

- Before starting treatment with lithium, renal function, cardiac function and thyroid function would have been 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 see Monitoring table above

Approaching Lithium blood results
Always check the timing of the last dose prior to the blood sample.

The desired level depends on the indication the lithium has been prescribed for and the clinical response:

- 0.4 - 1.0 mmol/L may be effective for recurrent depressive disorder,
- 0.6 - 1.0 mmol/L may be effective in bipolar affective disorder, depressive disorder,
- 0.8 – 1.0 mmol/L may be effective in difficult to treat bipolar affective disorder, manic episodes

If the level is low (typically <0.4 mmol/L)

a. If the patient is well and the levels are consistently low but consistent within a particular range, do not alter dose.
b. If the patient is unwell and the levels have been on the low end of the range for the treatment indication:
    i. Assess compliance
    ii. Consult psychiatrist regarding potential to increase dose and expected monitoring requirements
    iii. Recheck blood plasma lithium levels at 5 days after dose adjustments
c. If levels are low and inconsistent with a trend;
    i. Assess compliance
    ii. Consider other factors, e.g. drug interactions, excess fluid intake, inconsistent brands used
    iii. Recheck level after 5 days and if still low and inconsistent trend consult psychiatrist

If the level is within therapeutic range and

a. patient is well do not alter anything, if patient requests stopping medicines – this should be discussed with consultant psychiatrist
b. patient is well but complaining of adverse effects e.g. polyuria, polydipsia, this could indicate that a dose reduction may be needed:
    i. review patient's diet and salt intake
    ii. review other medicines for interactions
    iii. consult clinical psychiatrist regarding dose reduction
c. patient is mentally and clinically unwell – liaise further with consultant psychiatrist.

If the level is high (>1.0 mmol/L) with no signs of toxicity

a. Consider withholding Lithium for 48-72 hours, increasing fluid intake and reviewing diet, resume current dose and review Li level and eGFR 5 days after the withholding

doses and then again after another 5days.

b. Review concurrent medicines for drug interactions
c. If level returns to normal 10 days after withholding doses, then continue therapy as normal.
d. If level >1.0mmol/L after 5 or 10 days of withholding the dose then contact consult psychiatrist regarding dose reduction.

Further information

- Different brands of lithium are not bio-equivalent; hence lithium therapy **must** be prescribed by brand name.
- If a product brand change of lithium occurs then the same precautions should be followed as when starting treatment.
- Lithium levels can be affected by many other medicines. See 'Medicine Interactions' above for further guidance.
- Temporary dose reduction or suspension may be necessary in diarrhoea, vomiting or concurrent infection.
- Patients need to be made aware of what they should do if they become ill or find themselves in a situation that results in profuse sweating

Stopping Lithium

The consultant psychiatrist should be contacted if Lithium therapy is to be discontinued. Abrupt cessation of lithium therapy can lead to further complication.

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.

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.

- Medicines likely to disturb electrolyte balance such as diuretics should also be reviewed and discussed with the prescriber. 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 stable in order to maintain a stable electrolyte balance. This may be of special importance in very hot weather or work environment, or those wanting to lose weight drastically. Infectious diseases including colds, influenza, gastro-enteritis and urinary infections may alter fluid balance and thus affect serum lithium levels. Closer monitoring of lithium levels should occur.

Risk of convulsions

- The risk of convulsions may be increased in cases of co-administration of lithium with other medicines 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 hypokalaemia, 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 decrease in renal function.

Pregnancy

- Prescribers should discuss the potential risks lithium poses during pregnancy. Contraception options should be offered, and a plan elicited if such contraception method fails. Consultant psychiatrist should be consulted if a patient does become pregnant.

Ultrasound and cardiac echo are recommended at 6 weeks of gestation.

Breastfeeding

- Lithium passes into the breastmilk, leading to the risk of toxicity occurring in the infant. Breastfeeding is not recommended. Seek consultant psychiatrist and pharmacist advise if the patient is wanting to breastfeed while on lithium.

Children

- Lithium is not approved in NZ for use in children

RESPONSIBILITIES and ROLES

Consultant Psychiatrist responsibilities:

1. To discuss fully the aims, benefits, risks and side effects of treatment with the patient and/or carer and for written information about lithium to be supplied to and discussed with the patient and/or carer.
2. To explain their role and provide written information as necessary
3. Explain the treatment plan to the patient and/or carer including the dosing schedule
4. Undertake baseline monitoring as required (specific to the medicine)
5. Ensure a patient is issued with a Lithium Monitoring Record booklet and the benefits of tracking in this booklet.
6. To provide the patient and/ carer with printed advice including a lithium monitoring & information booklet and initiation instructions.
7. To initiate treatment and monitor lithium levels until the dosage is stabilized - by prescribing usually for a minimum of 3 months. A copy of the lithium levels should be available / sent to the GP.
8. While prescribing for this patient to monitor and evaluate response to treatment with the patient and/or carer, including adverse drug reactions, and to continue / discontinue treatment in line with the agreed treatment plan
9. Discuss the possibility of shared care with the patient and/or carer and ensure that they understand the plan for their subsequent treatment. Ensure they are aware of importance of blood monitoring and attending the GP visits at agreed timeframes to get repeat prescriptions.
10. Supply GP with a summary of the patient's review (including anticipated length of treatment) and a link to the shared care guideline when requesting transfer of prescribing to GP or Primary Care Prescribers
11. To ensure that all parties (GP, CNS, Keyworker, Psychiatrist, Patient, Carer) are in agreement regarding on-going responsibility for taking blood and monitoring lithium levels.
12. To provide the GP with target serum levels of lithium and to advise on actions to take when the serum level is outside the range.
13. To document any changes and/or results in the patient's Lithium Treatment - Monitoring booklet
14. To advise on dose alterations, abnormal results and concurrent medicines.
15. To review the patient at least every 2 years and when requested to by the GP to assess response, the benefits of continued treatment and which treatment is most appropriate.
16. Advise GP if treatment is to discontinue at any point
17. Inform GP if patient does not attend any planned follow-up with the consultant psychiatrist

GP or Primary Care Prescribers Responsibilities:

1. Continue prescribing of lithium at the dose recommended after stabilisation
2. Inform the Consultant Psychiatrist of any issues that may arise
3. To undertake routine blood / lithium level monitoring once dosage is stabilised and act upon the results
4. To document any changes and/or results in the patient's Lithium Treatment - Monitoring booklet.
5. Monitor for adverse effects throughout treatment and check for medicine interactions on initiating new treatments
6. To report adverse drug reactions to the consultant psychiatrist and complete a CARM report if serious.
7. To keep the key worker/mental health team informed, e.g. any change of medicine(s) prescribed for any indication.
8. To monitor the patient's overall health and well being
9. Ensure that if care of the patient is transferred to another prescriber, that the new prescriber is made aware of the shared care guideline.

Monitoring Requirements – See monitoring table on page 6

If lithium levels are outside the target range, consider contacting the consultant psychiatrist for advice. If **above 1.2 to 1.5 mmol/L** then doses should be suspended and additional serum levels taken until back within range. A discussion with the psychiatrist is recommended. The reasons for the rise in serum level should be investigated with the patient/carer, e.g. change in lifestyle, over the counter medicine (s), adherence problems. Advice on future dosages must also be obtained from the consultant psychiatrist.

If serum levels are **above 2 mmol/L the patient should be admitted urgently** into an acute hospital.
GPs should request a copy of any test results go to the consultant psychiatrist for information. Results should be provided to the patient so their lithium monitoring booklet can be updated.

MHS Key Worker Role :

To assist in the transition to Shared care

1. To advocate and assist the patient in their Lithium treatment.
2. Understand the treatment plan of the patient.
3. Ensure that there is a shared guideline in place for the patient.
4. Understand the basic pharmacology of Lithium including the adverse effects, toxicity signs and symptoms and common drug interactions.
5. Able to provide patient education around lithium including missed doses.
6. Advocate and communicate to the GP, Consultant Psychiatrist or pharmacist regarding any concerns or difficulties of Lithium therapy.
7. Assist the patient with compliance issues and communicate this to the multidisciplinary team.
8. Assess the patient for risk of toxicity at each visit by reviewing the monitoring booklet.

Patient's/Carer's Role:

1. Ask the consultant psychiatrist or GP or Primary Care Prescriber for information, if he or she does not have a clear understanding of the treatment
2. To take lithium as prescribed.
3. Share any concerns in relation to treatment with lithium
4. Tell the consultant psychiatrist or GP or Primary Care Prescriber of any other medicine(s) being taken, including over-the-counter products.
5. Read the patient information leaflet included with your medicine and report any side effects or concerns you have to the consultant psychiatrist or GP or Primary Care Prescriber.
6. Attend the follow up appointments with the consultant psychiatrist or GP for monitoring
7. To attend appointments for monitoring blood tests.
8. To inform the GP if health problems arise.
9. To be aware of side effects, situations that could affect their lithium levels and report any relevant symptoms.

To carry their Lithium Treatment-Monitoring booklet whenever consulting a healthcare professional.

SHARED CARE AGREEMENT
MEDICINE NAME: Lithium

Indication:

Agreement for transfer of prescribing to General Practice or Primary Care Prescriber

Patient details:

Name:	
NHI:	
DoB:	
Address:	

Medicine name and strength:

The following tests and investigations have been carried out:

Date treatment initiated:

Patient is now stabilised on a dose of:

I confirm the following:

- At last review the patient's symptoms were well controlled and the medicine is providing benefit
- The patient has been given written information about their medication.
- The patient understands that this medicine is being prescribed under a shared care agreement between their GP and consultant psychiatrist and that they also have responsibilities under the agreement.
- The patient has been informed that their GP can opt-out of taking on prescribing responsibility if they do not feel clinically able to prescribe or if the patient does not attend for treatment monitoring.
- I will arrange to review this patient 2 yearly. Date of next clinic appointment:

Consultant signature_____ Date_____

If the Primary Care Prescriber wishes to decline shared care, the named consultant must be informed within 14 days of receipt of this request.

	Name / position	Telephone	Email
Consultant Psychiatrist			
Key Worker			
Out of hours:	TDHB on-call Psychiatrist	06 753 6139	
Hospital Pharmacy	TDHB Pharmacy	06 753 6139	

References:

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3. Maudsley Prescribing Guidelines 13th edition, 2018, pg190-192
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