Therapeutics Advisory Group

Improving lives together
Norfolk and Waveney Integrated Care System

# NORFOLK AND WAVENEY STP THERAPEUTICS ADVISORY GROUP (TAG)

# SHARED CARE AGREEMENT FRAMEWORK

## Shared care guidelines for Lithium for patients within adult services

**AMB 1 - Prescribe the drug and perform a higher level of monitoring, e.g. 6-monthly**

### Generic and Proprietary/Brand Name

- **Lithium carbonate:** Priadel® 200mg and 400mg prolonged-release tablets, Camcolit® 400 mg controlled release tablets, Liskonum® 450mg controlled release tablets, Lithium carbonate Essential Pharma: 250 mg film-coated tablets (immediate release)
- **Lithium citrate:** Priadel® Liquid: 520mg/5 mL strength sugar-free, pineapple flavoured syrup, Li-Liquid®: 509mg/5 mL and 1,018mg/5 mL strength cherry flavoured syrup

### Indications for shared care

Treatment and prophylaxis of mania, bipolar disorder, mania and recurrent depression; aggressive or self-harming behaviour

| Specialist Prescribing and Monitoring Responsibilities | GP / Community Team - Primary Care Prescribing and Monitoring Responsibilities |
|---|---|
| 1. Assess patient, confirm diagnosis, and discuss benefits and risks of treatment with the patient and/or their carer using shared decision-making approach and provide appropriate counselling.<br>2. Obtain and document patient consent and **register on lithium database** SystemTDM®.<br>3. Perform pre-treatment assessments and monitoring as detailed on pages 8&9.<br>4. Initiate, titrate and stabilise patient on treatment with drug in line with Nice Guidance 185. Prescribe the maintenance treatment for at least 4 weeks and until optimised. Prescribers should familiarise themselves with the drug indication, dose, administration, contra-indications, cautions, side-effects, interactions and preparation by referring to the current version of the Summary of Product Characteristics (SPC) or the BNF.<br>5. Provide an appropriate patient information leaflet and means for the patient to keep a record of their serum plasma lithium levels, such as the purple lithium pack and details on how to obtain a log-in to the lithium database (New user registration here). Advise patient to carry the **'Lithium Alert Card'** at all times whilst on treatment. National Patient Safety Agency purple lithium pack: Supplies of the booklets can be ordered from nhsforms@mmm.com.<br>6. Lithium is a teratogen. Women of childbearing age should be advised to use a reliable form of contraception. | 1. Review request from the specialist to participate in the SCA.<br>2. **Respond to the specialist as soon as possible (within 14 days)** if **NOT** willing to participate in the SCA (stating the reason for not participating).<br><br>**If willing to participate in the SCA, the GP will:**<br>3. Make a record in the patient's primary care notes that treatment is being given as part of an SCA.<br>4. **Prescribe oral lithium (by the brand name)** in accordance with the specialist prescribing and treatment plan. Prescribers should familiarise themselves with the drug indication, dose, administration, contra-indications, cautions, side-effects, interactions and preparation by referring to the current version of the SPC or the BNF.<br>5. Assess for interactions with lithium when starting new medications.<br>6. Report any adverse effects to the specialist and to the MHRA via the Yellow Card Scheme.<br>7. Follow advice from the specialist regarding any changes required to treatment.<br>8. Perform on-going monitoring as advised by the specialist and detailed on page 10. Communicate any abnormal results to the specialist.<br>9. Refer to the specialist if the patient's clinical condition deteriorates, if intolerance to treatment develops, or if contra- |

7. Inform patient to maintain adequate fluid intake, avoid dietary changes and to inform community pharmacy when purchase medicine over the counter
8. Discuss proposed SCA with the patient and explain that their GP may or may not wish to participate.
9. **Send a letter to the patient's GP to request participation in the SCA. Include**
   - **Contact information.**
   - **SCA or link**
   - **Diagnosis, prescribing and treatment plan**
   - **The target lithium range**
10. **GPs are invited to participate in the agreement but are under no obligation to do so**. The GP must respond to the specialist **within 14 days if they are NOT willing to participate**.
11. Full clinical responsibility for the patient and the prescribed treatment will remain with the specialist if the GP declines to participate.

**If the GP is willing to participate in the SCA, the specialist will:**

12. Make a record in the patient's secondary care notes that treatment is being given as part of an SCA.
13. Inform the patient of the aspects of care that will be provided by the specialist and by the GP.
14. Give at least 1 months' notice to the GP before prescribing is transferred. Prescribe sufficient medication to enable transfer to primary care, including where there are unforeseen delays to transfer of care
15. Ask the patient to report any adverse effects about their treatment to the specialist or GP. Adverse events should be reported by the specialist or GP to the MHRA via the Yellow Card Scheme.
16. Review the patient regularly and inform the GP of any changes to treatment. Inform the GP of how frequently specialist review of the patient will be carried out.
17. Advise the GP of the on-going treatment monitoring required as detailed on page 10.
18. Advise the GP of when and how to discontinue treatment (if necessary).
19. Ensure clear arrangements exist for GPs to obtain advice and support.
20. Reassume prescribing responsibilities if a woman becomes or wishes to become pregnant.

indications/cautions arise that prevent continued prescribing.

10. If toxicity is suspected, withhold lithium and discuss urgently with the specialist. Plasma lithium levels should be acquired immediately to aid interpretation and facilitate specialist advice
11. If plasma lithium levels are above the specified range, check the dose, adherence, and timing of the sample (repeating if necessary). Determine whether toxicity is present and discuss with the specialist with an urgency determined by clinical judgement.
12. Refer the management back to the specialist if the patient becomes or plans to become pregnant.
13. Discontinue treatment (if necessary) on the advice of the specialist.
14. Contact the specialist for any necessary advice and support via the telephone helpline numbers provided.

## Patient and/or carer responsibilities and information

- Take lithium as prescribed and avoid abrupt withdrawal unless advised by their prescriber.
- Attend regularly for monitoring and review appointments with primary care and specialist and bring their purple lithium pack to keep a record of lithium levels or use their online access to the database. Alternatively apps are available for apple and android, respectively, at: https://itunes.apple.com/us/app/nhs-physical-health-monitor/id1040946243?mt=8 https://play.google.com/store/apps/details?id=com.incentivated.nhs.HealthMonitor
- Keep contact details up to date with both prescribers. Be aware that medicines may be stopped if they do not attend.
- Report adverse effects to their primary care prescriber. Seek immediate medical attention if they develop any symptoms as detailed in in **Patient Information** below.

- Report the use of any over the counter medications to their primary care prescriber and be aware they should discuss the use of lithium with their pharmacist before purchasing any over-the-counter medicines.
- Moderate their alcohol intake to no more than 14 units per week. Avoid recreational drugs.
- Not to drive or operate heavy machinery if lithium affects their ability to do so safely.
- Use an appropriate form of contraception, as agreed with their doctor/nurse/sexual health service. Patients of childbearing potential should take a pregnancy test if they think they could be pregnant and inform the specialist or GP immediately if they become pregnant or wish to become pregnant.

**The patient should be advised to report any of the following signs or symptoms to their GP without delay:**

- Lithium toxicity (diarrhoea, vomiting, loss of appetite, muscle weakness or twitching, clumsiness or poor coordination, dizziness, confusion, tinnitus, blurred vision, coarse tremor, writhing movements, change in speech, lethargy and/or drowsiness, incontinence, restlessness, confusion, seizures/fits).
- Signs of hypothyroidism (e.g. fatigue, cold intolerance, weight gain, constipation and depression), renal dysfunction (including polyuria and polydipsia), and benign intracranial hypertension (persistent headache and visual disturbance).

**Additional advice for patients/carers:**

- Patients should notify their primary care prescriber straight away if there is any change in their health, e.g. an infection, or significant weight loss. Additional lithium monitoring may be required.
- The same brand of lithium should always be taken unless otherwise instructed. Patients should become familiar with their brand and check they have received the correct one before taking.
- Changes in hydration and sodium balance can affect plasma lithium levels. Patients should maintain adequate fluid intake, particularly in hot weather or when activity levels change (such as increases in exercise or immobility). Large changes in dietary sodium should be avoided – changing dietary regime may inadvertently alter sodium intake.
- Substantial changes in plasma lithium levels can occur if patients develop diarrhoea or vomiting, or if they become acutely ill for any reason. Patients should seek medical advice in such instances.
- Excessive alcohol consumption should be avoided as it can lead to dehydration, increasing plasma lithium levels and so risk of toxicity.
- Patients should be warned about common drug interactions and advised to present their 'Lithium alert card' whenever they redeem a new prescription. They should specifically be advised not to take OTC NSAIDs as these can increase plasma lithium levels and so risk toxicity.
- Lithium may impair performance of skilled tasks (e.g. driving, operating machinery). Patients with a diagnosis of bipolar disorder must notify the Driver and Vehicle Licensing Agency (DVLA); see https://www.gov.uk/bipolar-disorder-and-driving.
- Patients of childbearing potential should be advised that lithium carries additional risks in pregnancy and is a potential teratogen. They should be aware of the need to use reliable contraception. If they become pregnant while taking lithium they should not stop taking it, but should tell their doctor straight away if they become pregnant while taking lithium. Breastfeeding should be avoided during treatment with lithium.
- For acute indications such as mania or augmentation, patients may respond within days to weeks of starting lithium. Depending on episode frequency, it may take months or even years to determine whether lithium has proven effective for relapse prevention.

**Patient information on this medicine can be found at the following links:**

- NHS: https://www.nhs.uk/medicines/lithium/
- MIND: https://www.mind.org.uk/information-support/drugs-and-treatments/lithium-and-other-mood-stabilisers/lithium/
- Choice and Medication: https://www.choiceandmedication.org/nsft/medication/lithium-carbonate-and-citrate/

## Specialist Contact Details

Please contact the **initiating specialist or prescriber** via the **Hellesdon Hospital Switchboard on 01603 421421**.

For urgent clinical matters, queries should be directed to the relevant prescriber directly in first instance. Alternatively, primary care prescribers can access support via the **Midlands and East Medicines Advice Service (MEMAS)** — a fully funded service available to all primary care colleagues:
0300 770 8564 or MEMAS.enquiries1@nhs.net

## GENERAL PRINCIPLES FOR SHARED CARE PRESCRIBING

- Shared Care is only appropriate if it provides the optimum solution for the patient.
- GPs are **invited** to participate. If GPs are not confident to undertake these roles, they are under no obligation to do so. In such an event, the total clinical responsibility for the patient for the diagnosed condition remains with the specialist.
- **If a specialist asks the GP to prescribe this drug, the GP should reply to this request as soon as practicable if they are unwilling to do so.**
- Prescribing responsibility will only be transferred when it is agreed by the consultant and the patient's GP and when the patient's condition is stable or predictable.
- Safe prescribing must be accompanied by effective monitoring.
- **The doctor who prescribes the medication legally assumes clinical responsibility for the drug and the consequences of its use.**

### Background to Treatment

Lithium is licensed for the treatment and prevention of mania, bipolar depression, recurrent depression (unipolar) and aggressive/self-mutilating behaviour. Not all patients respond to lithium, so the benefits and risks should be regularly and individually assessed. Lithium treatment should not be stopped suddenly, as this can cause relapse.

Lithium has a narrow therapeutic window of between 0.4 and 0.8 mmol/L for most indications, although a narrower range is usually specified on an individual patient. Higher target plasma levels (0.8–1 mmol/L) are occasionally recommended for acute episodes of mania, for patients who have previously relapsed or when subthreshold symptoms of illness are associated with functional impairment. **The specialist service will determine the target range for each patient and advise the primary care prescriber accordingly.**

Lithium has numerous mild side effects but can be toxic if the dose is too high. Toxicity usually occurs with levels above 1.5 mmol/L but can emerge at lower levels in susceptible patients such as the elderly or those with renal impairment. Toxicity can also occur when levels are in the 'therapeutic range'. Excluding excessive ingestion, toxicity most commonly arises due to a reduced elimination of lithium. Elimination of lithium is almost exclusively renal and is sensitive to the handling of sodium by the kidneys. Lithium toxicity can itself impair renal function, so rapid escalations in plasma lithium levels may occur. With long-term use, lithium can have adverse effects on the kidneys, the thyroid, and the parathyroid glands.

**Lithium should always be prescribed by brand and form**; tablets and liquids are not interchangeable. Extra care must be taken when prescribing liquid forms, with clarity over the name and strength of the preparation. Patients should be involved in treatment decisions and understand the importance of lithium monitoring.

This shared care protocol applies to all adults aged 18 and older.

### Licenced use and agreed local off-label use

**Indications:**

- Treatment and prophylaxis of mania
- Treatment and prophylaxis of bipolar disorder
- Treatment and prophylaxis of recurrent depression. NB: lithium should not be used as a sole agent to prevent recurrence, see NICE Guideline NG222: Depression in adults: treatment and management
- Treatment and prophylaxis of aggressive or self-harming behaviour
- Augmentation of antidepressants ǂ See NICE Guideline NG222: Depression in adults: treatment and management

ǂ Off-label indications. (Please note licensed indications vary by manufacturer).

**Locally agreed off-label use to be agreed and completed locally (include supporting information)**

## Criteria for Patient Selection

Aged over 18

**Diagnosis:**

- Treatment and prophylaxis of mania,
- Bipolar disorder,
- Mania and recurrent depression
- Aggressive or self-harming behaviour

## Form and strength of preparation

**Lithium is available as**

- lithium carbonate (tablet formulations) and
- lithium citrate (liquid formulations).

The patient should be maintained on the same brand and formulation of lithium. If a switch in brand or formulation is considered, refer to the specialist team.
**Note: Lithium tablets and liquids are not interchangeable.**

**Lithium Carbonate:**

- Priadel® 200mg and 400mg prolonged-release tablets
- Camcolit® 400mg controlled release tablets
- Liskonum® 450mg controlled release tablets
- Lithium carbonate Essential Pharma: 250mg film-coated tablets (immediate release)

**Lithium Citrate:**

- Priadel® Liquid: 520mg/5 mL strength sugar-free, pineapple flavoured syrup
- Li-Liquid®: 509mg/5 mL and 1,018mg/5 mL strength cherry flavoured syrup

Extra care must be taken when prescribing lithium in liquid form, as some offer different strengths (mg/ml) under the same brand name (Li-liquid®) and some brand names (Priadel®) are used for the liquid and tablet forms.

**Always prescribe lithium by brand name. Switching preparation (either between brands of the same form or changing between tablets and liquid) requires additional monitoring to ensure that the 12-hour plasma lithium level remains in the desired range.**
**Particular care should be taken if prescribing liquid preparations; lack of clarity may lead to the patient receiving a sub-therapeutic or toxic dose.**

## Side Effects

BNF - https://bnf.nice.org.uk/

SPC - https://www.medicines.org.uk/emc

**For all lithium salts**

**Rare or very rare**

Nephropathy

**Frequency not known**

Abdominal discomfort; alopecia; angioedema; appetite decreased; arrhythmias; atrioventricular block; cardiomyopathy; cerebellar syndrome; circulatory collapse; coma; delirium; diarrhoea; dizziness; dry mouth; electrolyte imbalance; encephalopathy; folliculitis; gastritis; goitre; hyperglycaemia; hyperparathyroidism; hypersalivation; hypotension; hypothyroidism; idiopathic intracranial hypertension; leucocytosis; memory loss; movement disorders; muscle weakness; myasthenia gravis; nausea; neoplasms; nystagmus; peripheral neuropathy; peripheral oedema; polyuria; QT interval prolongation; reflexes abnormal; renal disorders; renal impairment; rhabdomyolysis; seizure; sexual

dysfunction; skin reactions; skin ulcer; speech impairment; taste altered; thyrotoxicosis; tremor; vertigo; vision disorders; vomiting; weight increased

## Drug Interactions

**The following medicines must not be prescribed without consultation with specialists:**

- **Medicines that may increase plasma lithium concentrations** (by reducing renal elimination) and so risk toxicity:
  - NSAIDs (including cyclo-oxygenase 2 inhibitors). If NSAID use is unavoidable, a dose reduction of lithium may be required, and levels should be monitored more frequently; discuss with specialist team. 'As required' use of NSAIDs should be avoided since it may cause fluctuations in lithium levels and makes monitoring levels challenging.
  - Diuretics, particularly thiazide diuretics
  - Angiotensin converting enzyme (ACE) inhibitors and angiotensin II receptor antagonists
  - Other drugs which alter electrolyte balance with the potential to alter lithium clearance e.g. steroids.
  - Certain antibiotics including metronidazole and tetracyclines
- **Medicines that may decrease plasma lithium concentrations** (by increasing renal elimination) and so risk loss of efficacy:
  - Theophylline
  - Products which contain sodium bicarbonate e.g. antacids
- **Medicines that may increase risk of neurotoxicity** when co-administered with lithium:
  - Calcium channel blockers with cardiac effects (e.g. verapamil, diltiazem)
  - Antipsychotics (e.g. haloperidol, olanzapine, clozapine, flupentixol, chlorpromazine)
  - Antidepressants with a serotonergic action (e.g. SSRIs, tricyclic antidepressants, venlafaxine, duloxetine)
  - Carbamazepine
- **Medicines associated with QT prolongation** (e.g. amiodarone, macrolides, tricyclic antidepressants) – potential for additive effects when co-administered with lithium.
- **Medicines that lower seizure threshold** (e.g. SSRIs, tricyclic antidepressants, antipsychotics) – increased risk of seizures

**Care should be taken on initiation, dose adjustment or discontinuation of any interacting medicines. The onset and degree of the interaction can vary and additional lithium monitoring is likely to be indicated, with doses adjusted accordingly. Discuss with specialist team.**

## Cautions and Contraindications

This information does not replace the Summary of Product Characteristics (SPC) and should be read in conjunction with it. Please see BNF & SPC for comprehensive information.

Contraindications:

- Hypersensitivity to lithium or any of the excipients
- Addison's disease
- Cardiac disease associated with rhythm disorder
- Cardiac insufficiency
- Family or personal history of Brugada syndrome
- Patients with abnormal sodium levels, including dehydrated patients or those on low sodium diets
- Untreated hypothyroidism
- Severe renal impairment
- Pregnancy (especially the first trimester), unless considered essential
- Breastfeeding

Cautions:

- Mild to moderate renal impairment
- Use in elderly patients

- Adequate and stable sodium and fluid intake should be maintained. This may be of special importance in hot weather, or during infectious diseases, including influenza, gastro-enteritis or urinary infections, when dose reduction may be required.
- Review lithium dose if diarrhoea and/or vomiting present and in cases where the patient has an infection and/or profuse sweating. Adjustments may be required.
- Risk of seizures may be increased if co-administered with drugs that lower the seizure threshold, or in patients with epilepsy.
- Cardiac disease
- May exacerbate psoriasis
- Surgery: discontinue 24 hours prior to major surgery and re-commence post-operatively once kidney function and fluid-electrolyte balance is normalised. Discontinuation is not required prior to minor surgery, providing fluids and electrolytes are carefully monitored.

## Initiation of therapy

**Initiation and ongoing dose regimen**

- Transfer of monitoring and prescribing to primary care is normally after at least 12 weeks, and when the patient's dose has been optimised and with satisfactory investigation results for at least 4 weeks.
- The duration of treatment & frequency of review will be determined by the specialist, based on clinical response and tolerability.
- All dose or formulation adjustments will be the responsibility of the initiating specialist unless directions have been discussed and agreed with the primary care clinician.
- Termination of treatment will be the responsibility of the specialist.

## Initial dose and method of administration and supply

**Initial stabilisation:**

**Lithium carbonate**

Typically, 400mg once daily, then adjusted according to patient response and 12-hour plasma levels. In some scenarios, such as acute mania, a higher starting dose may be preferable. The BNF outlines the typical starting doses by indication and brand.
Doses may initially be divided throughout the day, but once-daily administration is preferred when plasma lithium concentration is stabilised in the target range (specified by specialist team).
Lithium carbonate tablets should be prescribed unless there is a specific problem with swallowing difficulties.

**Lithium citrate**

Typically 509mg or 520mg twice daily (depending on brand), in the morning and evening, then adjusted according to patient response and 12-hour plasma levels.
Liquid formulations contain lithium citrate and doses are not equivalent to lithium carbonate; bioavailability is significantly different. If a switch in formulation is considered, discuss with the specialist team.
Extra care must be taken when prescribing lithium in liquid form, as some offer different strengths under the same brand names, and some brands are used for the liquid and tablet forms.

**The initial period must be prescribed by the initiating specialist.**

## Maintenance Dose and Administration

**Maintenance dose (following initial stabilisation):**

Individualised, to achieve plasma lithium levels in the range specified for the patient.

**The initial maintenance dose must be prescribed by the initiating specialist.**

## Duration of therapy / How the treatment will be reviewed and if appropriate, stopped

**Conditions requiring dose adjustment:**

Lower doses may be required in older or physically frail/low body weight patients, in mild to moderate renal impairment and electrolyte imbalance. Dose adjustments may also be required in patients prescribed interacting medicines.

**Stopping lithium treatment**

The decision to stop treatment will be the responsibility of the specialist. Clinicians, patients, and carers should be aware that abrupt discontinuation of lithium increases the risk of relapse. If lithium is to be stopped, the dose should gradually be reduced over a period of at least four weeks but preferably over a period of up to three months.

## Initial monitoring / baseline assessment – by Specialist

**Monitoring at baseline and during initiation is the responsibility of the specialist; only once the patient is optimised on the chosen medication with no anticipated further changes expected in immediate future will prescribing and monitoring be transferred to primary care.**

Monitoring at baseline and during initiation is the responsibility of the specialist. Recent and relevant investigation results must be documented in the corresponding letter from specialist

Baseline (all indications):

- Urea and electrolytes (U&Es), including estimated glomerular filtration rate (eGFR)
- Calcium
- Thyroid function tests (TFTs)
- Electrocardiogram (ECG) recommended for patients with existing cardiovascular disease (CVD) or risk factors
- Full blood count (FBC)
- Height, weight and body mass index (BMI)
- Exclude pregnancy

Additional baseline investigations (bipolar disorder):

- Cardiovascular status including pulse and blood pressure (BP)
- Metabolic status including fasting blood glucose, glycosylated haemoglobin (HbA1c) and blood lipid profile.
- Liver function tests (LFTs).

Initial monitoring:

- 12-hour plasma lithium levels one week after initiation and one week after any change in dose or formulation; lithium levels take 4-7 days to reach steady state concentrations. Typically, this means levels will be monitored weekly until the desired level and clinical effect is achieved. Following a dose, levels fluctuate during absorption/distribution, so measurements are made 12 hours post-dose for monitoring purposes.

Ongoing monitoring:

- Review patient at least every 12 months to assess their mental health, effectiveness of treatment and the ongoing need for lithium.

| **GP / Community Team or other Primary Care monitoring responsibilities –**<br><br>**See Summary in Appendix 1** | |
|---|---|
| **Monitoring – all indications** | **Frequency** |
| **Plasma lithium level taken 10-14 hours post-dose. NB: samples should be taken as close to 12-hours post-dose as possible.**<br>• Record results in the patient's record as well as patient-held purple lithium pack, or other suitable recording mechanism.<br>• It is advisable to document the actual time interval between the last dose and the blood sample | **At least every 12 weeks for the first year, then every 6 months.**<br>More frequent long-term monitoring may be advised by the specialist team in some circumstances (e.g. elderly, renal impairment, altered laboratory parameters, poor symptom control or adherence, concurrent interacting medicines) or if most recent 12-hour plasma lithium level is at the threshold of target range.<br>**Consider additional monitoring whenever there is a change in the patient's circumstances, e.g. intercurrent illness.** |
| • **U&Es, including eGFR**<br>• **Calcium**<br>• **TFTs**<br>• **Height, weight, and BMI.** | **Every 6 months.**<br>More frequent monitoring (particularly renal function) may be advised by the specialist team in some circumstances (e.g. elderly, renal impairment, altered TFTs, concurrent interacting medicines). |
| **Signs of toxicity**<br>Enquire about and document signs and symptoms which might indicate toxicity, e.g. paraesthesia, ataxia, tremor, cognitive impairment. | **At every consultation with the prescriber regarding lithium treatment** |
| **Additional monitoring – bipolar disorder** | **Frequency** |
| **Diet, nutritional status and level of physical activity.**<br>**Cardiovascular status including pulse and BP.**<br>**Metabolic status including fasting blood glucose, $HbA_{1c}$ and blood lipid profile.**<br>**LFTs.** | Annually as part of physical health check recommended in NICE CG185 Bipolar disorder: assessment and management. |
| **(If relevant) If monitoring results are forwarded to the specialist team, please include clear clinical information on the reason for sending, to inform action to be taken by secondary care.** | |

**Adverse effects and other management in primary care – See Summary in Appendix 1**

**As well as responding to absolute values in laboratory tests, a rapid change or a consistent trend in any value should prompt caution and extra vigilance.**

**Further information**

Consistency is paramount in lithium treatment and monitoring. Doses should be taken regularly, at the same time every day. Lithium carbonate tablets should not be crushed or chewed.

Priadel® 200mg and 400mg tablets have score lines and can be divided accurately to provide dosage requirements as small as 100mg within product license.

Liskonum® 450mg tablets are licensed to be halved for the purposes of dose adjustment.

Other brands may be scored to facilitate breaking for ease of swallowing, but not to divide into equal doses. Breaking these tablets is not expected to alter their release properties but the accuracy of the division is not established

If a dose is missed, then the next scheduled dose should be taken as usual; a double dose should not be taken to make up for a missed dose.

For a given total daily dose, 12-hour plasma lithium levels will differ for once versus twice daily dosing schedules. The schedule should be determined by the specialist and not altered without their advice

**Pregnancy, paternal exposure and breast feeding**

It is the responsibility of the specialist to provide advice on the need for contraception to **male and female patients** on initiation and at each review, but the ongoing responsibility for providing this advice rests with both the primary care prescriber and the specialist.

All patients should be informed of the risks and benefits of taking this medicine during pregnancy and breastfeeding.

**Pregnancy:**
If a patient becomes pregnant whilst on lithium, the specialist team should be informed immediately **(but do not stop the lithium)**.

Lithium should not be used during pregnancy where possible, especially in the first trimester (risk of teratogenicity, including cardiac abnormalities). In certain cases where a severe risk to the patient could exist if treatment were stopped, lithium has been continued during pregnancy; under these circumstances prescribing is the responsibility of the specialist team.

There is a risk of relapse of bipolar disorder if lithium is withdrawn, particularly in the postnatal period.

- **Information for healthcare professionals:** https://www.medicinesinpregnancy.org/bumps/monographs/USE-OF-LITHIUM-IN-PREGNANCY/
- **Information for patients and carers:** https://www.medicinesinpregnancy.org/Medicine--pregnancy/Lithium/

**Breastfeeding:**
Lithium is secreted in breast milk and there have been case reports of neonates showing signs of lithium toxicity. Breastfeeding should be avoided during treatment with lithium.
Information for healthcare professionals: https://www.sps.nhs.uk/medicines/lithium/

**Paternal exposure:**
- Animal studies have reported spermatogenesis abnormalities that may lead to impairment of fertility. It is unknown if this risk applies to humans.

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|---|---|
| **Author(s) and Organisation** | Adapted for local use from RMOC national shared care protocol. Adapted for local use by NWICB Medicines Optimisation Team and NSFT |
| **Date of Approval** | June 2025 |
| **Reviewed by** | Supported by NSFT and TAG. Ratified by Medicines Optimisation Programme Board |
| **Last review date** | N/A – new agreement |
| **Date of next review** | June 2027 |

**Document History**

| Version | Date | Author / Editor | Status | Comment |
|---|---|---|---|---|
| 1.0 | June 2025 | MO Team, NWICB and Clinicians from NSFT | Final | New SCA supported by NSFT MOG, TAG and ratified by MOPB |
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**Appendix 1: Shared Specialist & GP Responsibilities: Monitoring**
**Ongoing monitoring will be transferred from the specialist to GP after stabilisation**

| Parameter | Frequency | Result | Action for Primary Care |
|---|---|---|---|
| **As well as responding to absolute values in laboratory tests, a rapid change or a consistent trend in any value should prompt caution and extra vigilance.** | | | |
| **Plasma lithium level taken 10-14 hours post-dose. NB: samples should be taken as close to 12-hours post-dose as possible.**<br>• Record results in the patient's record as well as patient-held purple lithium pack, or other suitable recording mechanism.<br>It is advisable to document the actual time interval between the last dose and the blood sample | **At least every 12 weeks for the first year, then every 6 months.**<br>More frequent long-term monitoring may be advised by the specialist team in some circumstances (e.g. elderly, renal impairment, altered laboratory parameters, poor symptom control or adherence, concurrent interacting medicines) or if most recent 12-hour plasma lithium level is at the threshold of target range.<br>**Consider additional monitoring whenever there is a change in the patient's circumstances, e.g. intercurrent illness.** | **12-hour plasma lithium level. Below target range**<br>NB: range for each patient to be determined by the specialist team. Note that local reference ranges may vary | Assess adherence, including discussion with patient and check of GP clinical systems. Offer advice on adherence if appropriate (e.g. daily routines, reminders). Ensure level was taken 12 hours after lithium dose.<br>**Contact specialist team for advice** if suspected that the dose is too low. |
| | | **Above target range**<br>NB: range for each patient to be determined by the specialist team. Note that local reference ranges may vary | Ensure level was taken 12 hours after lithium dose and that the correct dose has been prescribed and taken. Check for interactions, hydration, patient's physical and mental status, and features of toxicity. Repeat level if necessary.<br>**Withhold lithium if there are features of toxicity.** Contact specialist team for advice in all cases.<br>If ≥2.0mmol/L – consider sending patient to A&E, based on clinical presentation (e.g. features of toxicity) and inform specialist team. |
| | | **Within target range but toxicity suspected**<br>NB: range for each patient to be determined by the specialist team. Note that local reference ranges may vary | **Contact specialist team for advice.**<br>Referral to secondary care may be required depending on the severity of symptoms and the certainty of toxicity. Use clinical judgement to determine the urgency of referral. |
| | | **Within target range but marked change since last level (and there has been no dose change)**<br>NB: range for each patient to be determined by the specialist team. Note that local reference ranges may vary | Establish whether level was taken 12 hours after lithium dose. Repeat level with an urgency determined by clinical judgement. Assess adherence, including discussion with patient and check of GP clinical systems. Offer advice on adherence if appropriate (e.g. daily routines, reminders).<br>**More frequent monitoring may be required.** |
| • **TFTs** | **Every 6 months.**<br>More frequent monitoring (particularly renal function) may be advised by the specialist team in some circumstances (e.g. elderly, renal impairment, altered TFTs, concurrent interacting medicines). | **Thyroid function**<br>Altered TFTs without symptoms | **Contact specialist team for advice.**<br>During lithium treatment, TFTs are commonly abnormal; the TSH can rise early in treatment but settle with time.<br>Note that the symptoms of hypothyroidism can be difficult to discriminate from depression and common side effects of lithium. |
| | | Subclinical hypothyroidism<br>• Raised TSH<br>• Normal T4<br>Clinical features not overtly manifest | |

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| | | Overt hypothyroidism<br>• High TSH<br>• Low T4<br>Symptomatic | **Contact specialist team for advice**, which may include input from endocrinology services.<br>Thyroid hormone replacement is usually indicated and often continued throughout the course of lithium treatment. |
| | | Hyperthyroidism | **Contact specialist team for advice**, which may include input from endocrinology services. |
| **Parameter** | **Frequency** | **Result** | **Action for Primary Care** |
| • **eGFR** | **Every 6 months.**<br>More frequent monitoring (particularly renal function) may be advised by the specialist team in some circumstances (e.g. elderly, renal impairment, altered TFTs, concurrent interacting medicines). | • eGFR <45ml/min<br>• rapidly falling eGFR<br>gradual decline in eGFR | The response to impaired or deteriorating renal function should be individualised.<br>**Contact specialist team for advice, which may include input from nephrology services.** A cardiovascular risk profile may guide specialist advice and should be provided if available. Use clinical judgement to determine the urgency of consultation.<br>Anticipate the need for increased monitoring as trends in renal function are more useful than absolute values. In the elderly or those at the extremes of muscle mass, creatinine clearance provides a better estimate of renal function than eGFR.<br>**Adjustments to dose may be advised. If renal function is significantly compromised, lithium may no longer be an appropriate treatment and specialists will advise accordingly.** |
| | | **Renal function**<br>Polyuria and polydipsia | Polyuria is common with lithium and often well tolerated. Advise the patient to maintain adequate fluid intake and advocate excellent oral hygiene.<br>**Contact specialist team for advice, which may include input from nephrology services. In some instances, dose adjustment or specific treatments may be advocated.** |
| • **U&Es**<br>• **Calcium** | **Every 6 months.**<br>More frequent monitoring (particularly renal function) may be advised by the specialist team in some circumstances (e.g. elderly, renal impairment, altered TFTs, concurrent interacting medicines). | **U&Es or calcium out of range** | Check that the most recent 12-hour plasma lithium level is in the desired range and act accordingly if not.<br>Determine whether there are symptoms and signs related to the electrolyte disturbance or lithium toxicity.<br>Consider arranging an ECG in those at risk for QT prolongation.<br>Contact specialist team for advice. Changes in calcium levels may reflect parathyroid dysfunction and input from endocrinology services may be indicated. |
| • **Height, weight, and BMI.** | **Every 6 months.**<br>More frequent monitoring (particularly renal function) | **Weight and BMI**<br>Outside healthy range | Provide appropriate support on multicomponent interventions to increase physical activity levels, improve eating behaviour and quality of diet. Remind patient of the importance of |

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| | may be advised by the specialist team in some circumstances (e.g. elderly, renal impairment, altered TFTs, concurrent interacting medicines). | | maintaining adequate fluid intake and avoiding dehydration while exercising.<br>Consider measuring waist circumference for individualised monitoring.<br>Patients should be instructed to avoid sudden changes in diet, especially avoiding low sodium diets. Lithium levels are influenced by body weight and so for patients being supported to lose weight, lithium levels may need to be checked more frequently (akin to other situations of caution). Use clinical judgement, lithium levels and the rate of weight loss when determining the frequency of blood tests.<br>**If rapid weight gain – discuss with specialist** |
| **Additional monitoring – bipolar disorder** | | | |
| **Diet, nutritional status and level of physical activity,**<br>**Cardiovascular status including pulse and BP, LFTs,**<br>**Metabolic status including fasting blood glucose, $HbA_{1c}$ and blood lipid profile.** | | Annually as part of physical health check recommended in NICE CG185 Bipolar disorder: assessment and management. | |
| **Physical health check (bi-polar disorder)** | | Any physical health problems should be treated by the appropriate primary care health professional and communicated to the specialist team within 14 days. | |