Classification: Official

Publication approval reference: PAR1621_vi

National Lithium Shared Care Protocol: *for use locally in Doncaster and Rotherham*

Lithium for patients within adult services (under RDaSH).

4 July 2022, National Version 1, approved locally on 16.06.23

Review date – January 2025

The content of this shared care protocol was correct as of January 2022. As well these protocols, please ensure that summaries of product characteristics (SPCs), British national formulary (BNF) or the Medicines and Healthcare products Regulatory Agency (MHRA) or NICE websites are reviewed for up-to-date information on any medicine.

Specialist responsibilities

- Assess the patient and provide diagnosis; ensure that this diagnosis is within scope of this shared care protocol (section 2) and communicated to primary care.
- Use a shared decision making approach; discuss the benefits and risks of the treatment with the patient and/or their carer and provide the appropriate counselling (see section 11) to enable the patient to reach an informed decision. Obtain and document patient consent. 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 advise of the necessity for long-term monitoring.
- Ensure that the patient/guardian/carer is clear what is being monitored and by whom. Extra monitoring needed for dose changes will be organised by specialist team and conveyed to patient.
- Assess for contraindications and cautions (see section 4) and interactions (see section 7).
- Conduct required baseline investigations and initial monitoring (see section 8).
- Initiate and optimise treatment as outlined in section 5. Prescribe the maintenance treatment for at least 12 weeks.

- Once treatment is optimised, complete the shared care proforma, and send to patient's GP practice detailing the diagnosis, current and ongoing dose, any relevant test results and when the next monitoring is required. Include contact information (section 13). The target lithium range for the patient must be included.
- Prescribe sufficient medication (for at least one month) to enable transfer to primary care, including where there are unforeseen delays to transfer of care.
- Conduct the required reviews and monitoring in section 8. After each review, advise primary care whether treatment should be continued, confirm the ongoing dose, and whether the ongoing monitoring outlined in section 9 remains appropriate. ***(In Rotherham Place, provide patient with blood request form to be taken to GP practice.)***
- Inform primary care if the patient misses any appointments.
- Reassume prescribing responsibilities if a woman becomes or wishes to become pregnant.
- Provide advice to primary care on the management of adverse effects if required.

Primary care responsibilities

- Respond to the request from the specialist for shared care. It is asked that this be undertaken within 14 days of the request being made, where possible.
- If accepted, prescribe ongoing treatment as detailed in the specialists request and as per section 5, taking into any account potential drug interactions in section 7.
- Adjust the dose of lithium prescribed as advised by the specialist.
- Conduct the required monitoring as outlined in section 9. ***In Rotherham Place, bloods to be taken at GP practice as per Phlebotomy LES (using supplied blood request form).***
- Ensure that the patient/guardian/carer is clear what is being monitored and by whom.
- Confirm the specialists have provided the patient/guardian/carer with appropriate information sheet(s) for monitoring and/or to alert other clinical staff to the treatment they are receiving.
- Manage adverse effects as detailed in section 10 and discuss with specialist team when required. Communicate any incidental finding of abnormal results to the specialist.
- 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
- 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.
- Refer the management back to the specialist if the patient becomes or plans to become pregnant.

- Stop treatment as advised by the specialist, or immediately if intolerable side-effects occur, provided that it is safer to do so than to continue this therapy.
- Assess for interactions with lithium when starting new medications.
- In patients with CKD stage 3a or worse to carry out annual ACR, in line with renal guidance.

Patient and/or carer responsibilities

- Take lithium as prescribed and avoid abrupt withdrawal unless advised by the primary care prescriber or specialist.
- 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. Keep contact details up to date with both prescribers. Be aware that medicines may be stopped if they do not attend.
- Report adverse effects or any concerns to their primary care prescriber. Seek immediate medical attention if they develop any symptoms as detailed in section 11.
- 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.
- Carry the Lithium Alert Card at all times.
- Share the contents of the Lithium Record Book with healthcare professionals who may be involved in the management of the clinical condition or either the prescribing or dispensing of lithium preparations.

1. Background

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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. Both the specialist and GP should sign the proforma with a record kept in the GP and specialist records. Full details will be given of the prescribing regime (brand, form, strength, and dose of medication) and follow-up plan. The patient will be asked to make arrangements with their GP for continued supply.

2. Indications

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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 CG90: Depression in adults: recognition and management
- Treatment and prophylaxis of aggressive or self-harming behaviour

- Augmentation of antidepressants‡ See NICE NG222: Depression in adults: treatment and management

The decision to give prophylactic lithium usually requires specialist advice and must be based on careful consideration of the likelihood of recurrence in the individual patient, and the benefit weighed against the risks. The full prophylactic effect of lithium may not occur for six to twelve months after the initiation of therapy.

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

3. Locally agreed off-label use

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To be agreed and completed locally (include supporting information)

Not applicable.

4. Contraindications and cautions

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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 (reduce dose)

- 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.
- Concurrent electroconvulsive treatment (may lower seizure threshold)
- Cardiac disease
- May exacerbate psoriasis
- Diuretic treatment (risk of toxicity)
- 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.
- Myasthenia gravis
- Avoid abrupt withdrawal

Long-term use of lithium has been associated with thyroid disorders and mild cognitive and memory impairment. Long-term treatment should therefore be undertaken only with careful assessment of risk and benefit, and with monitoring of thyroid function every 6 months (or more often if there is evidence of deterioration).

The need for continued therapy should be assessed regularly and patients should be maintained on lithium after 3-5 years only if benefit persists.

5. Initiation and ongoing dose regimen

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- Transfer of 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 stabilisation:

Lithium carbonate

Typically 400 mg 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 509 mg or 520 mg 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 (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.

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. It is also important to consider any change in symptoms, adverse effects, pregnancy or planned pregnancy or drug levels in the toxic range.

Dose adjustments should be done on an individual basis. The objective is to adjust the dose to maintain serum lithium concentrations as follows:

- Aim for 0.6-0.8 mmol per litre normally (may be lower in the elderly)
- Aim for 0.8-1.0 mmol per litre if patient has relapsed previously on lithium or has sub-syndromal symptoms

Levels as low as 0.4 mmol per litre can be adequate following approval by the clinician.

If an adult with bipolar disorder needs plasma lithium levels maintained above 0.8 mmol per litre, they should have their lithium levels monitored at least every 3 months.

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.

6. Pharmaceutical aspects

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Route of administration:	Oral
Formulation:	**Lithium is available as lithium carbonate (tablet formulations) and lithium citrate (liquid formulations). The patient should be prescribed and maintained on the same brand and formulation of lithium. If a switch in brand or formulation is considered, refer to the specialist team. Lithium tablets and liquids are not interchangeable.** **Lithium Carbonate:** • Priadel® 200 mg and 400 mg prolonged-release tablets • Camcolit® 400 mg controlled release tablets *(£££)*

	• Liskonum® 450 mg controlled release tablets *(£££)* • Lithium carbonate Essential Pharma: 250 mg film-coated tablets (immediate release) *(£££)* *(£££) = higher cost* **Lithium Citrate:** • Priadel® Liquid: 520 mg/5 mL strength sugar-free, pineapple flavoured syrup • Li-Liquid®: 509 mg/5 mL and 1,018 mg/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.**
Administration details:	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
Other important information:	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.

7. Significant medicine interactions

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The following list is not exhaustive. Please see BNF or SPC for comprehensive information and recommended management.

The following medicines should not be prescribed without discussion 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
- **Some SGLT2 inhibitors,** such as empagliflozin and dapagliflozin (emerging evidence)

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.

8. Baseline investigations, initial monitoring and ongoing monitoring to be undertaken by specialist

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Monitoring at baseline and during initiation is the responsibility of the specialist; only once the patient is optimised on the chosen brand of lithium with no anticipated further changes expected in the immediate future will request for prescribing to be transferred to the GP.

Ongoing monitoring is to be continued via the relevant Lithium Clinic. Annual PHC to be performed as per agreed Place arrangements.

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 (HbA_{1c}) 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 review:
Review patient "at least" every 12 months to assess their mental health, effectiveness of treatment and the ongoing need for lithium. Routinely monitor for side-effects and symptom control.

9. Ongoing monitoring requirements to be undertaken by secondary care (and primary care)

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See section 10 for further guidance on management of adverse effects/responding to monitoring results.

- **Doncaster Place**: this is done in the Lithium Clinic (with some exceptions, for example patient unable to travel to the lithium clinic).
- **Rotherham Place**: Lithium Clinic to provide patient with blood request form. ***Bloods to be taken at GP practice as per Phlebotomy LES (using supplied blood request form)*** with results going back to Lithium Clinic.

- The Lithium Clinic should inform the GP after every clinic review that actioned blood results (for info only) are visible in SystmOne practices, or via ICE for EMIS practices.
- The annual physical health checks (PHC) should be undertaken as per the relevant Place set-up. Where possible, the annual bloods should coincide with the physical health checks, to ensure the best use of appointments.

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. • Record results in the patient's record as well as patient-held purple lithium pack, or other suitable recording mechanism. • It is advisable to document the actual time interval between the last dose and the blood sample	**Weekly until stable, then at least every 12 weeks for the first year, then every 6 months.** More frequent long-term monitoring may be advised by the specialist team in some circumstances (e.g. elderly; renal impairment; people who are at risk of impaired renal or thyroid function, raised calcium levels or other complications; altered laboratory parameters, such as last plasma lithium level at 0.8mmol per litre or higher; poor symptom control or

<table>
<tr><td></td><td>adherence; concurrent interacting medicines) or if most recent 12-hour plasma lithium level is at the threshold of target range.
Consider additional monitoring whenever there is a change in the patient's circumstances, e.g. intercurrent illness, suspected toxicity.</td></tr>
<tr><td>U&Es, including eGFR
Calcium
TFTs</td><td>Every 6 months after the first year.

More frequent monitoring, e.g. every 3 months, may be advised by the specialist team in some circumstances (e.g. elderly, renal impairment, altered TFTs, concurrent interacting medicines).

The renal function in patients with CKD 3a or worse should be assessed weekly until stable, then three monthly.

Any additional monitoring required in patients with impaired renal function if advised by nephrologists to RDaSH:

Any decision to discontinue or alter Lithium doses should only be done by secondary care unless acute toxicity is suspected.

<table>
<tr><th>CKD stage</th><th>Monitoring advice</th></tr>
<tr><td>3a (eGFR 45-60)</td><td>Monitor Lithium and eGFR 3 monthly

Monitor ACR annually (early morning sample)</td></tr>
</table>
</td></tr>
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	Bone biochemistry annually
3a (and ACR>30) 3b (eGFR 30-45)	Monitor Lithium and eGFR 3 monthly Monitor ACR annually (early morning sample) Bone biochemistry annually Review risks and benefits of continuing Lithium by liaising with the mental health consultant
4-5 (eGFR <30)	Specialist to review continued prescribing of Lithium

Guidance for referral to Nephrology:

Referral to nephrology should be made by secondary care mental health services and GP practices should be kept informed of this.

• CKD stage 4-5 (or 3a/b if ACR>30) on at least 2 measurements of over a period of 3 months, to exclude acute reversible changes

• Acute kidney injury: Possible AKI (rapid rise in serum creatinine/fall in eGFR, acute illness) or hyperkalaemia: Discuss with nephrologist immediately or admit under general medicine

	• Proteinuria (ACR>30) • Deteriorating renal function eGFR reduction by >5 ml/min/1.73 m2 in one year or >10 ml/min/1.73 m2 in 5 years • If any other specialist concerns. **If abnormal TFTs:** • GP to liaise with the mental health consultant • Specialist to consider risk/benefit of lithium • Manage thyroxine in line with local guidance (seeking advice from endocrinology if necessary)
Signs of toxicity 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 – physical health checks (SMI)	**Frequency**
Height, weight, and BMI. **Diet, nutritional status and level of physical activity.** **Cardiovascular status including pulse and BP.** **Metabolic status including fasting blood glucose, HbA_{1c} and blood lipid profile.** **LFTs.** **Smoking status** **Alcohol intake**	Annually as part of physical health check recommended in NICE CG185 Bipolar disorder: assessment and management. To be performed as per agreed arrangements at Place

(If relevant) If PHC 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.

10. Adverse effects and other management

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Any serious adverse reactions should be reported to the MHRA via the Yellow Card scheme. Visit www.mhra.gov.uk/yellowcard

For information on incidence of ADRs see relevant summaries of product characteristics

Result	Specialist action
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.	
12-hour plasma lithium level. Below target range 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.
Above target range 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. **Withhold lithium if there are features of toxicity.** If ≥2.0mmol/L – consider sending patient to A&E, based on clinical presentation (e.g. features of toxicity)
Within target range but toxicity suspected	Specialist team to consider the severity of symptoms and the certainty of toxicity. Use clinical judgement to determine the urgency of referral to A&E

NB: range for each patient to be determined by the specialist team. Note that local reference ranges may vary	
Within target range but marked change since last level (and there has been no dose change) 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). More frequent monitoring may be required.
Thyroid function Altered TFTs without symptoms	During lithium treatment, TFTs are commonly abnormal; the TSH can rise early in treatment but settle with time. Note that the symptoms of hypothyroidism can be difficult to discriminate from depression and the common side effects of lithium.
Subclinical hypothyroidism • Raised TSH • Normal T4 - Clinical features not overtly manifest	Consider input from endocrinology services. The optimal management of subclinical hypothyroidism during lithium treatment remains controversial, with different thresholds for treatment advocated. Anticipate the need for additional monitoring, investigations and potentially thyroid hormone replacement based on specialist recommendations.
Overt hypothyroidism • High TSH • Low T4 • Symptomatic	Consider input from endocrinology services. Thyroid hormone replacement is usually indicated and often continued throughout the course of lithium treatment.

Hyperthyroidism	Requires input from endocrinology services.
Renal function 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. Consider input from nephrology services. In some instances, dose adjustment or specific treatments may be advocated.
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. Determine whether there are symptoms and signs related to the electrolyte disturbance or lithium toxicity. Consider arranging an ECG in those at risk for QT prolongation. Changes in calcium levels may reflect parathyroid dysfunction and input from endocrinology services may be indicated.
eGFR <45ml/min rapidly falling eGFR gradual decline in eGFR	**The response to impaired or deteriorating renal function should be individualised.** Consider 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. **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. **Adjustments to dose may be advised. If renal function is significantly compromised, lithium may no longer be an appropriate treatment. GP to liaise with MH specialists on best course of action/plan.**
Weight and BMI 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 maintaining adequate fluid intake and avoiding dehydration while exercising. Consider measuring waist circumference for individualised monitoring. 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.
Signs of toxicity Typical signs and symptoms include diarrhoea, vomiting, loss of appetite, muscle weakness, lethargy, dizziness, ataxia, lack of coordination, tinnitus, blurred vision, coarse tremor of the extremities and lower jaw, muscle hyper-irritability, choreoathetoid movements, dysarthria, and drowsiness	If lithium toxicity is suspected, do an urgent lithium level immediately.

Physical health check (SMI)	Any physical health checks should be performed as per agreement at Place.

11. Advice to patients and carers

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The specialist will counsel the patient with regard to the benefits and risks of treatment and will provide the patient with any relevant information and advice, including patient information leaflets on individual medicines.

The patient should be advised to report any of the following signs or symptoms to their specialist 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).

At the start of treatment patients should be given suitable information on lithium and means to keep a record of their plasma lithium levels, such as a purple lithium pack supplies of which can be ordered from nhsforms@mmm.com or accessible at [ARCHIVED CONTENT] Safer lithium therapy (nationalarchives.gov.uk) **.**

Additional advice for patients/carers:

- Patients must attend regularly for monitoring and review appointments to ensure their lithium dose remains safe and effective, and bring their purple lithium pack to keep a record of their lithium levels.
- Patients should notify their specialist straight away if there is any change in their health, e.g. an infection, or significant weight loss. Additional lithium monitoring may be required.
- Lithium should be taken regularly, as prescribed. If doses are missed, patients should not attempt to catch up or double dose.
- Patients should not stop taking lithium suddenly – doing so increases the chance of relapse. If lithium is to be stopped, it should be reduced over at least four weeks and preferably three months.
- 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. If NSAIDs are to be prescribed, these should be on a regular (not PRN) basis. The person should be monitored monthly until a stable lithium level is reached, and then every 3 months.
- 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/

National Patient Safety Agency purple lithium pack: Supplies of the booklets can be ordered from nhsforms@mmm.com. 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

12. Pregnancy, paternal exposure and breast feeding

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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.

Patients of child-bearing potential should be advised to use a reliable form of contraception. It is the responsibility of the specialist to provide advice on the need for contraception to patients on initiation of lithium, and at each review. Under shared care agreements, the ongoing responsibility for providing this advice rests with both the GP and the specialist.

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/ https://www.sps.nhs.uk/articles/safety-in-lactation-drugs-for-bipolar-disorder-hypomania/

Paternal exposure:

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

13. Specialist contact information

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Doncaster Place:

Name: *Laura Damms / Sue Gill*

Role and specialty: *Clinical Lead / Team Manager*

Daytime telephone number: ***03000 212 401***

Email address: *laura.damms@nhs.net* / *sue.gill1@nhs.net*

Alternative contact: *N/A*

Out of hours contact details: *N/A*

Rotherham Place:

Name: *Jo Painter / Cheryl Jenkinson*

Role and specialty: *Nurse Consultant – Adult Mental Health*

Daytime telephone number: ***03000 215 777***

Email address: *rdash.rothclozapinelithium@nhs.net*

Alternative contact: *Jane Curtis – Manager North Locality and Health and Wellbeing Team*

Out of hours contact details: *N/A – patient would need to attend A&E*

14. Additional information

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Where patient care is transferred from one specialist service or GP practice to another, a new shared care agreement must be completed.

Ensure that the specialist is informed in writing of any changes to the patient's GP or their contact details (if not automatically pulled through from GP record).

15. References

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16. Other relevant national guidance

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- Shared Care for Medicines Guidance – A Standard Approach (RMOC). Available from https://www.sps.nhs.uk/articles/rmoc-shared-care-guidance/
- NHSE guidance – Responsibility for prescribing between primary & secondary/tertiary care. Available from https://www.england.nhs.uk/publication/responsibility-for-prescribing-between-primary-and-secondary-tertiary-care/
- General Medical Council. Good practice in prescribing and managing medicines and devices. Shared care. Available from https://www.gmc-uk.org/ethical-guidance/ethical-guidance-for-doctors/good-practice-in-prescribing-and-managing-medicines-and-devices/shared-care
- NICE NG197: Shared decision making. Last updated June 2021. https://www.nice.org.uk/guidance/ng197/.

17. Local arrangements for referral

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Define the referral procedure from specialist to primary care prescriber & route of return should the patient's condition change.

- Specialist to primary care via SCP proforma.
- Route of return via discussions between GP/specialist

Shared care development (localisation of national SCP)

Faiza Ali, Razwan Saleem and Melissa Goodlad.
On behalf of NHS South Yorkshire

Dr. S. Mehta, Stephen Davies.
On behalf of RDaSH

Doncaster Place APC date: 29/06/23
Doncaster Place MOG date: 08/06/23
Rotherham Place MMC date: 22/03/23 & 28/06/23
RDaSH MMC date: 16/06/23