Shared care protocol:

Lithium for patients within adult services

6 October 2023, Version 2.0

Review date – October 2025

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.

Introduction

This document is adapted from the national shared care protocol to be used for adults being prescribed lithium within Hertfordshire Partnership University NHS Foundation Trust (HPFT).

HPFT 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 plasma lithium levels, such as the lithium treatment booklet or provide instructions for the patient to download the recommended medication management app, e.g. MindMeds app.
- 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 4 weeks** and until optimised.

Working in Partnership:
Hertfordshire Partnership University NHS Foundation Trust
Hertfordshire and West Essex Integrated Care Board

- Discuss contraceptive use with female patients of childbearing age, and document their current method of contraception. Female patients of childbearing potential should use effective contraceptive methods during treatment with lithium (see **Error! Bookmark not defined.**). Prescribe and document effective contraception if the patient is an inpatient. If patient is an outpatient, direct the patient to their GP to obtain effective contraception. Ensure that effective contraception has been initiated before prescribing lithium as outpatient.
- Reassume prescribing responsibilities if a woman becomes or wishes to become pregnant.
- Explain what a shared care arrangement means for the patient and why it might be an option in their case. The patient or their carers should have the opportunity to ask questions and explore other options if they don't feel confident that shared care will work for them.
- Obtain the patient's agreement to be involved in a shared care model. As part of the consent process, patients must be made fully aware of all monitoring requirements, in line with national guidance on consent. Document in EPR the patient's agreement.
- Discuss the importance of taking the lithium treatment booklet or medication management app, e.g. MindMeds App to all appointments and the pharmacy when prescriptions are dispensed, and document this.
- Once treatment is optimised, complete the shared care documentation and (Appendix 1) send to the 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 plasma lithium range for the patient must be included.
- Prescribe sufficient medication to enable transfer to primary care (usually 14 days unless in special circumstances which may warrant a shorter supply), 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.
- Provide advice to primary care on the management of adverse effects if required.

Primary care responsibilities

- Respond to the request from the HPFT specialist for shared care in writing. 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 HPFT specialists request and as per section 5, taking into 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. Communicate any abnormal results to the specialist.

- Update the patient's lithium treatment booklet (issued by specialist), or remind patient to update their medication management app, e.g. MindMeds App with plasma lithium levels/ monitoring results, and check these results are appropriate before issuing prescriptions for lithium.
- Update the lithium treatment booklet or remind patient to update their medication management app, e.g. MindMeds App if lithium treatment is changed (whether brand, formulation, dose, frequency, or timing), following communication with the secondary care prescriber.
- Inform the secondary care prescriber of any physical illness/ medicine that may affect the patient's treatment with lithium.
- Manage adverse effects as detailed in section 10 and discuss with specialist team when required.
- 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 not within 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.
- Assess for interactions with lithium when starting new medications.
- Telephone details (including out-of-hour contact numbers) and (if appropriate) secure email addresses of both parties (secondary care prescriber and GP) should be exchanged and recorded. This will enable the practice to access timely advice, guidance and information if problems arise and also enable secondary care clinicians to easily contact the GP if necessary.

If further information is required contact **Single Point of Access (SPA)-** Tel: *0300 777 0707* Email: *hpft.spa@nhs.net*

Patient and/or carer responsibilities

- Take lithium as prescribed and avoid abrupt withdrawal unless advised by their prescriber.
- Attend regularly for monitoring and review appointments with primary care and HPFT specialist and bring their lithium treatment booklet or medication management app, e.g.

MindMeds App to keep a record of plasma 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 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 not drink more than 14 units per week on a regular basis. 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.
- Patients must ensure they bring their lithium treatment booklet or medication management app, e.g. MindMeds App to their GP/ Specialist during all appointments.

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 Responsible Clinician at HPFT 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. The preferred brand of lithium in Hertfordshire is **Priadel®,** however some patients may for individual reasons be established on other brands. 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.

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 CG90: Depression in adults: recognition and management

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

3. Locally agreed off-label use

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No additional off-label indications have been agreed upon or will be included

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
- Hyponatraemia, including dehydrated patients, those on a low sodium diet or conditions predisposing to low sodium (e.g. severe diarrhoea and/or vomiting and concurrent infections, especially if sweating profusely)
- Untreated hypothyroidism
- Severe renal impairment (eGFR of 15-29 ml/min/1.73m^2)
- Pregnancy (especially the first trimester), unless considered essential
- Breastfeeding

Precautions:

- Mild to moderate renal impairment (eGFR of 30-89 ml/min/1.73m^2)- closely monitor plasma lithium concentration.
- Elderly patients may exhibit toxicity at plasma levels ordinarily tolerated by younger patients and lithium excretion may be reduced due to age-related decreases in renal function in this group of 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 convulsions may be increased if co-administered with drugs that lower the seizure threshold or in patients with epilepsy.
- Benign intracranial hypertension may occur – patient to be advised to report persistent headache or visual disturbance.
- Avoid in patients with congenital long QT syndrome and prescribe with caution to those with predisposing factors for QT prolongation (uncorrected hypokalaemia, bradycardia, predisposing drugs).
- 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.

5. Initiation and ongoing dose regimen

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- Transfer of monitoring and prescribing to primary care is normally after at least 12 weeks, or 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 HPFT 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:

The initial stabilisation/prescribing of lithium must be carried out by the initiating HPFT specialist.

	Priadel® tablets	**Priadel® liquid**	**Li-Liquid®**
Adults (body-weight up to 50kg)	Initially 200-400mg daily	Initially 520mg twice daily	-
Adults (body-weight 50kg and above)	Initially 0.4-1.2g daily	Initially 1.04 -3.12g daily in 2 divided doses	-
Elderly	Initially 200-400mg daily	Initially 520mg twice daily	-
Adults (average body-weight 70kg)	-	-	Initially 1018-3054mg in divided doses (in the morning and in the evening)
Elderly or adults (body-weight below 50kg)	-	-	Initially 509mg in divided doses (in the morning and in the evening)

Lithium carbonate

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 the initiating specialist team).

Lithium carbonate tablets should be prescribed unless there is a specific problem such as swallowing difficulties.

Lithium citrate

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.

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 HPFT 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.

Dosage must be individualised depending on lithium plasma levels and clinical response. The dosage necessary to maintain lithium plasma levels within the therapeutic range varies from patient to patient. The specialist will be responsible for stabilising the patient and advising on the target range for the patient.

Stopping lithium treatment

The decision to stop treatment will be the responsibility of the HPFT 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. However, in certain exceptional circumstances, if someone develops lithium toxicity, treatment may need to be withheld immediately.

6. Pharmaceutical aspects

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Route of administration:	Oral
Formulation:	**The brand Priadel® is recommended for use within HPFT and is available as 200mg and 400mg modified release tablets.** Using a single brand (Priadel®) throughout HPFT should help to minimise medicines-related errors, however there may be individual cases where other brands are continued. **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. Lithium tablets and liquids are not interchangeable.** **Lithium Carbonate:** • **Priadel® 200 mg and 400 mg prolonged-release tablets (HPFT approved)** • Camcolit® 400 mg controlled release tablets • Liskonum® 450 mg controlled release tablets • Lithium carbonate Essential Pharma: 250 mg film-coated tablets (immediate release) **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.

<table>
<tr><td></td><td><u>Always prescribe lithium by brand name.</u> 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.</td></tr>
<tr><td>Administration details:</td><td>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.</td></tr>
<tr><td>Other important information:</td><td>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.</td></tr>
<tr><td>Priadel®liquid & tablet equivalence</td><td>Care is needed with Priadel® 520mg lithium citrate / 5ml sugar-free liquid. 520mg lithium citrate is equivalent to 204mg lithium carbonate. When switching from tablet to liquid, 5ml of 520mg/5ml lithium citrate liquid should be prescribed for every 200mg lithium carbonate tablet, see table below.

<table>
<tr><th>“Priadel®” lithium carbonate prolonged release tablet dose</th><th>“Priadel®” lithium citrate 520mg/5ml equivalent dose</th></tr>
<tr><td>200mg</td><td>5ml</td></tr>
<tr><td>300mg</td><td>7.5ml</td></tr>
<tr><td>400mg</td><td>10ml</td></tr>
<tr><td>500mg</td><td>12.5ml</td></tr>
<tr><td>600mg</td><td>15ml</td></tr>
<tr><td>700mg</td><td>17.5ml</td></tr>
<tr><td>800mg</td><td>20ml</td></tr>
</table>
</td></tr>
</table>

900mg	22.5ml
1000mg	25ml

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.

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**.**

The following medicines must not be prescribed without consultation with HPFT 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.

8. Baseline investigations, initial monitoring, and ongoing monitoring to be undertaken by HPFT 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 medication with no anticipated further changes expected in immediate future will prescribing and monitoring be transferred to primary care.

Baseline investigations for all indications:	**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 • Urea and electrolytes (U+Es), including calcium and eGFR • 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 (if bipolar disorder):	• Cardiovascular status including pulse and blood pressure (BP) • Metabolic status including fasting blood glucose or HbA_{1c} and blood lipid profile. • Liver function tests (LFTs).
Initial monitoring of lithium:	• 12-hour plasma lithium levels one week after initiation and one week after any change in dose or formulation. 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 of lithium:	**Review patient at least every 12 months** to assess their mental health, effectiveness of treatment and the ongoing need for lithium.

9. Ongoing monitoring requirements to be undertaken by primary care

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

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 in the lithium treatment booklet, or the patient can update their medication management app, e.g. MindMeds App. • 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.** 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. **Consider additional monitoring whenever there is a change in the patient's circumstances, e.g. intercurrent illness.**
U&Es, including eGFR **Calcium** **TFTs** • **Height, weight, and BMI.**	**Every 6 months.** 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 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. **Cardiovascular status including pulse and BP.** **Metabolic status including fasting blood glucose or HbA_{1c} and blood lipid profile.** **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 HPFT 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	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.	
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. Contact specialist team for advice if suspected that the dose is too low.

12-hour plasma lithium level- 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.** Contact specialist team for advice in all cases. If ≥2.0mmol/L – consider sending patient to A&E, based on clinical presentation (e.g. features of toxicity) and inform specialist team.
12-hour plasma lithium level WITHIN target range but marked change since last level. 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.
12-hour plasma lithium level WITHIN target range but TOXICITY suspected **Possible signs of lithium toxicity** • 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 and seek HPFT specialist advice.** Referral to secondary care may be required depending on the severity of symptoms and the certainty of toxicity. Use clinical judgment to determine the urgency of referral.
Thyroid function	Contact specialist team for advice.

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	Contact specialist team for advice, which may include 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	Contact specialist team for advice, which may include input from endocrinology services. 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.
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. 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 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. Contact specialist team for advice. 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. 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. 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 and specialists will advise accordingly.

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.
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.

11. Advice to patients and carers

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The HPFT 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.

At the start of treatment patients should be given suitable information on lithium and means to keep a record of their plasma lithium levels, via medication management app, e.g. MindMeds App or lithium treatment booklet. Additional lithium treatment booklets can be ordered by e-mailing hpft.medsmanagement@nhs.net.

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).
- **Renal dysfunction** (including polyuria and polydipsia)
- **Benign intracranial hypertension** (persistent headache and visual disturbance).

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 lithium treatment booklet or medication management app, e.g. MindMeds App to keep a record of their lithium levels.
- 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.
- 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 by the prescriber. 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:

- HPFT Choice and Medication website: https://www.hpft.nhs.uk/information-and-resources/pharmacy-and-medicines-optimisation/medication-information/
- NHS: https://www.nhs.uk/medicines/lithium/
- MIND: https://www.mind.org.uk/information-support/drugs-and-treatments/lithium-and-other-mood-stabilisers/lithium/
- MindMeds App is available for Apple and Android, respectively, at:

  MindMeds on the App Store (apple.com)

  MindMeds - Apps on Google Play

12. Pregnancy, paternal exposure and breast feeding

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It is the responsibility of the HPFT 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/

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. HPFT Specialist contact information

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Contact Details *(please provide details of different sites where applicable)*	**Single Point of Access (SPA)** Tel: 0300 777 0707 Email: hpft.spa@nhs.net
Primary care clinicians can obtain support/advice on lithium prescribing for patients historically discharged from follow-up by HPFT	
Colne House 21 Upton Road, Watford WD18 0JL	Tel: 01923 837000
Hertsmere Civic Offices Elstree Way, Borehamwood WD6 1WA	Tel: 0208 7313000
The Marlowes Health and Wellbeing Centre 39-41 Marlowes, Hemel Hempstead HP1 1LD	Tel: 01442 275613
Waverley Road 99 Waverley Road, St Albans AL3 5TL	Tel: 01727 804700
Rosanne House Parkway, Welwyn Garden City AL8 6JE	Tel: 01707 364000
Saffron Ground Ditchmore Lane, Stevenage SG1 3LJ	Tel: 01438 792000
Holly Lodge 45 Church Lane, Cheshunt EN8 0DR	Tel: 01992 818600
Cygnet House 1 Old College Court, Ware SG12 0DE	Tel: 01920 443900
Centenary House Grammar School Walk, Hitchin SG5 1JN	Tel: 01462 482900
Oxford House London Road, Bishops Stortford CM23 3LA	Tel: 01279 464800

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.

15. References

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- Martindale: The Complete Drug Reference. Accessed via www.medicinescomplete.com on 16/02/2021.
- Summary of Product Characteristics. Priadel® 400mg prolonged release tablets. Essential Pharma. Date of revision of the text: 24/08/2020. Accessed via https://products.mhra.gov.uk/ on 17/02/2021.
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- National Patient Safety Agency. Safer Lithium Therapy. 2009. Archived resources available via: [ARCHIVED CONTENT] Safer lithium therapy (nationalarchives.gov.uk)

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/.

Version	2.0
Developed by	HPFT Pharmacy and Clinical Leads and HWE ICB PMOT
Approved by	HWE APC and HPFT DTC
Date approved/updated	November 2023 HWE APC and October 2023 HPFT DTC
Review date:	The recommendation is based upon the evidence available at the time of publication. This recommendation will be reviewed upon request in the light of new evidence becoming available.
Superseded version	1.2 approved March 2018 HMMC and December 2017 HPFT DTC Reviewed and updated using the NHS England national shared care protocol template: Lithium for patients within adult services

Appendix 1: Shared Care Request letter (HPFT Specialist to Primary Care Prescriber)

Dear : *[insert Primary Care Prescriber's name]*

Patient name:*[insert patient's name]*
Date of birth: *[insert date of birth]*
NHS Number*: [insert NHS Number]*
Diagnosis: *[insert diagnosis]*

As per the agreed *[insert APC name]*shared care protocol for *[insert medicine name]* for the treatment of *[insert indication],* this patient is now suitable for prescribing to move to primary care.

The patient fulfils criteria for shared care and I am therefore requesting your agreement to participate in shared care. Where baseline investigations are set out in the shared care protocol, I have carried these out.

I can confirm that the following has happened with regard to this treatment:

	Specialist to complete
The patient has been initiated on this therapy and has been on an optimised dose for the following period of time:	
Baseline investigation and monitoring as set out in the shared care documents have been completed and were satisfactory	*Yes / No*
The condition being treated has a predictable course of progression and the patient can be suitably maintained by primary care	*Yes / No*
The risks and benefits of treatment have been explained to the patient	*Yes / No*
The roles of the HPFT specialist team/ Primary Care Prescriber / Patient and pharmacist have been explained and agreed	*Yes / No*
The patient has agreed to this shared care arrangement, understands the need for ongoing monitoring, and has agreed to attend all necessary appointments	*Yes / No*
I have enclosed a copy of the shared care protocol which covers this treatment/the SCP can be found here (insert electronic/ web link)	*Yes / No*
I have included with the letter copies of the information the patient has received	*Yes / No*
I have provided the patient with sufficient medication to last until	
I have arranged a follow up with this patient in the following timescale	

Treatment was started on *[insert date started]* and the current dose is *[insert dose and frequency]*.

If you are in agreement, please undertake monitoring and treatment from *[insert date]* NB: date must be at least 1 month from initiation of treatment.

The next blood monitoring is due on *[insert date]* and should be continued in line with the shared care guideline.

Please respond to this request for shared care, in writing, within 14 days of the request being made where possible.

Appendix 2: Shared Care Agreement Letter (Primary Care Prescriber to HPFT Specialist)

Primary Care Prescriber Response

Dear *[insert Doctor's name]*
Patient *[insert Patient's name]*
NHS Number *[insert NHS Number]*
Identifier *[insert patient's date of birth and/oraddress]*

Thank you for your request for me to accept prescribing responsibility for this patient under a shared care agreement and to provide the following treatment

Medicine	Route	Dose & frequency

I can confirm that I am willing to take on this responsibility from *[insert date]* and will complete the monitoring as set out in the shared care protocol for this medicine/condition.

Primary Care Prescriber signature: _____Date: _____

Primary Care Prescriber address/practice stamp

Appendix 3: Shared Care Refusal Letter (Primary Care Prescriber to HPFT Specialist)

Re:

Patient *[insert Patient's name]*
NHS Number *[insert NHS Number]*
Identifier *[insert patient's date of birth and/oraddress]*

Thank you for your request for me to accept prescribing responsibility for this patient.

In the interest of patient safety NHS *[insert CCG name]*, in conjunction with local acute trusts have classified *[insert medicine name]*as a Shared Care drug, and requires a number of conditions to be met before transfer can be made to primary care.

I regret to inform you that in this instance I am unable to take on responsibility due to the following:

		Tick which apply
1.	**The prescriber does not feel clinically confident in managing this individual patient's condition, and there is a sound clinical basis for refusing to accept shared care** As the patients primary care prescriber I do not feel clinically confident to manage this patient's condition because *[insert reason]*. I have consulted with other primary care prescribers in my practice who support my decision. This is not an issue which would be resolved through adequate and appropriate training of prescribers within my practice. **I have discussed my decision with the patient and request that prescribing for this individual remain with you as the specialist, due to the sound clinical basis given above.**	

2.	**The medicine or condition does not fall within the criteria defining suitability for inclusion in a shared care arrangement** As the medicine requested to be prescribed is not included on the national list of shared care drugs as identified by RMOC or is not a locally agreed shared care medicine I am unable to accept clinical responsibility for prescribing this medication at this time. **Until this medicine is identified either nationally or locally as requiring shared care the responsibility for providing this patient with their medication remains with you**	
3.	**A minimum duration of supply by the initiating clinician** As the patient has not had the minimum supply of medication to be provided by the initiating specialist I am unable to take clinical responsibility for prescribing this medication at this time. Therefore can you please contact the patient as soon as possible in order to provide them with the medication that you have recommended. ***Until the patient has had the appropriate length of supply the responsibility for providing the patient with their medication remains with you.***	
4.	**Initiation and optimisation by the initiating specialist** As the patient has not been optimised on this medication I am unable to take clinical responsibility for prescribing this medication at this time. Therefore can you please contact the patient as soon as possible in order to provide them with the medication that you have recommended. ***Until the patient is optimised on this medication the responsibility for providing the patient with their medication remains with you.***	

5.	**Shared Care Protocol not received** As legal responsibility for clinical care lies with the clinician who signs the prescription, I need to ensure that I am in possession of sufficient clinical information for me to be confident to prescribe this treatment for my patient and it is clear where each of our responsibilities lie to ensure the patient is safely managed. For this reason I am unable to take clinical responsibility for prescribing this medication at this time, therefore would you please contact the patient as soon as possible in order to provide them with the medication that you have recommended. ***Until I receive the appropriate SCP, responsibility for providing the patient with their medication remains with you.***	
6.	**Other (Primary Care Prescriber to complete if there are other reasons why shared care cannot be accepted)**	

I would be willing to consider prescribing for this patient once the above criteria have been met for this treatment.

NHS England 'Responsibility for prescribing between Primary & Secondary/Tertiary care' guidance (2018) states that "when decisions are made to transfer clinical and prescribing responsibility for a patient between care settings, it is of the utmost importance that the GP feels clinically competent to prescribe the necessary medicines. It is therefore essential that a transfer involving medicines with which GPs would not normally be familiar should not take place without full local agreement, and the dissemination of sufficient, up-to-date information to individual GPs." In this case we would also see the term GP being interchangeable with the term Primary Care Prescriber.

Please do not hesitate to contact me if you wish to discuss any aspect of my letter in more detail and I hope to receive more information regarding this shared care agreement as soon as possible

Yours sincerely

Primary Care Prescriber signature: _____

Date: _____

Primary Care Prescriber address/practice stamp