Specialist Pharmacy Service

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National shared care protocol:

Lithium for patients within adult services

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The content of this shared care protocol was developed nationally in January 2022 and reviewed by EPUT in June 2023. As well as this protocol, 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 Essex Partnership University NHS foundation Trust (EPUT)

EPUT Specialist responsibilities

- Assess the patient, determine and provide diagnosis; ensure that this diagnosis is within scope of this shared care protocol (see section 2) and communicated to primary care with involvement of the community mental health teams.
- Use a shared decision making approach; discuss and document 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.
- Assess for contraindications and cautions (see section 4) and interactions (see section 7).
- Conduct required baseline investigations and initial monitoring (see section 8).
- Discuss contraceptive use with female patients of child-bearing age, and document their current method of contraception. Female patients of child-bearing potential should use effective contraceptive methods during treatment with lithium (see 20). 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 for the outpatient.

- 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 the patient's agreement.
- Initiate and optimise treatment as outlined in section 5. Prescribe the maintenance treatment for at least 4 weeks and until optimised.
- Discuss the importance of taking the Lithium Treatment record to all appointments and the pharmacy when prescriptions are dispensed, and document this.
- Once treatment is optimised, complete the shared care documentation and send to patient's GP practice detailing the brand of lithium prescribed, 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 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.
- 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

If further information is required contact 0300 1230808 (EPUT contact centre).

- Respond to the request from the specialist for shared care in writing. It is asked that this be undertaken within 14 days of the request being made, where possible.
- If not accepted, document in the primary care record that this patient is not in a shared care agreement for Lithium.
- If accepted, prescribe ongoing treatment as detailed in the specialist's 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. Communicate any abnormal results to the specialist. Update the patient's lithium record book with lithium levels / monitoring results, and check these results before issuing prescriptions for lithium.

- Update the lithium record book if lithium treatment is changed (whether brand, formulation, dose, frequency, or timing), and inform secondary care prescriber of the changes.
- Inform the secondary care prescriber of any physical illness / medicine that may affect the patient's treatment with lithium.
- Ask the patient about any feature of lithium toxicity, hypothyroidism, renal dysfunction (including polyuria and polydipsia) and benign intracranial hypertension (persistent headache and visual disturbance) and remind patient of the signs and symptoms that need to be looked out for, including when and how to seek medical advice, at every consultation.
- 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 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.
- 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.

Patient/Carer responsibilities

- Ensure a clear understanding of their treatment, side effects and monitoring parameters.
- Take lithium as prescribed and avoid abrupt withdrawal unless advised by their prescriber.
- Attend regularly for monitoring and review appointments with primary care and specialist.
- Ensure they bring their purple lithium record booklet 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 any changes in symptoms and any 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 GP and be aware they should discuss the use of lithium with their pharmacist before purchasing any over-the-counter medicines.
- Use an **appropriate form of contraception**, as agreed with their doctor/nurse/sexual health service.
- Maintain an adequate fluid intake and avoid major changes in diet.
- Moderate their alcohol intake and be aware of the importance of not binge drinking as this may destabilise lithium levels.
- To declare any use of illicit substances and seek appropriate support.
- Not to drive or operate heavy machinery if lithium affects their ability to do so safely.
- 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.
- Present their Lithium record book to their GP/Specialist during all appointments
- Present record book when collecting medication from any Pharmacy.

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. Intermittent or unstable treatment with lithium may worsen the outcome of the underlying diagnosis.

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, previous relapses or when sub-threshold symptoms of illness are associated with functional impairment. 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. Excluding excessive ingestion, toxicity most commonly arises due to a reduced elimination of lithium. Toxicity can also occur when levels are in the 'therapeutic range'. **The Responsible Clinician at EPUT will determine the target range for each patient and advise the primary care prescriber accordingly.**

~~Elimination of~~ Lithium is renally excreted and toxicity in itself can also induce renal impairment hence why blood tests are required every 6 months. Long term use can also impair the thyroid and parathyroid glands. Lithium brand names cannot be used interchangeably. They should be prescribed by a specific brand name and formulation because of its narrow therapeutic range and

differences in bioavailability. Any lack of clarity on exactly which preparation is to be prescribed can result in either a toxic or sub-therapeutic dose.

Lithium should always be prescribed by brand and form; tablets and liquids are not interchangeable. The preferred brand of lithium tablets in EPUT 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 years or older.

Children or adolescents are not routinely prescribed lithium and therefore any shared care agreement should be made on an individual basis.

2. Indications

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Indications:

- Treatment and prophylaxis of mania and hypomania
- 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 NG222: Depression in adults: recognition and management
- Treatment and prophylaxis of aggressive or self-harming behaviour
- Augmentation of antidepressants‡ See NICE NG222: 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 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	Cautions
• Hypersensitivity to lithium or any of the excipients • Addison's disease • Cardiac disease associated with rhythm disorder • Cardiac insufficiency • Personal or family history of Brugada syndrome • Patients with abnormal sodium levels, including those on low sodium diets • Dehydrated patients • Untreated hypothyroidism • Severe renal impairment (GFR <30 mL/min) although in exceptional cases lithium may be continued with specialist nephrology input • Pregnancy (especially the first trimester), unless considered essential • Breastfeeding	• Mild to moderate renal impairment (GFR >30mL/min to <60mL/min) • Avoid abrupt withdrawal of the medication. • Use in elderly patients • Adequate and stable sodium and fluid intake should be maintained. This may be of special importance in hot weather. • Review lithium dose if diarrhoea and/or vomiting present and in cases where the patient has an infection and/or profuse sweating. Adjustments may be required. • Risk of seizures may be increased if co-administered with drugs that lower the seizure threshold, or in patients with epilepsy. • Cardiac disease • May exacerbate psoriasis • Surgery: **Discontinue 24 hours prior to major surgery** and re-commence post-operatively once kidney function and fluid-electrolyte balance is normalised.

5. Initiation and ongoing dose regimen

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- Transfer of monitoring and prescribing to primary care can occur:
  1. After at least 12 weeks,
  2. Once the patient's dose has been optimised and with satisfactory investigation results for at least 4 weeks.

- The responsibility of the specialist is to:
  1. Specify the duration of treatment and frequency of reviews
  2. Initial starting dose and initiated maintenance dose.

3. Specify the brand prescribed
4. Dose/formulation adjustments.
5. Termination of treatment.

Initial stabilisation:

The initial stabilisation and prescribing will be carried out by the initiating specialist.

Lithium carbonate	Lithium citrate
Typically, the starting dose is 400 mg once daily (200mg in elderly), then adjusted according to patient response and 12-hour plasma levels (usually between 0.4-1.0 mmol/litre). In some scenarios, such as acute mania, a higher starting dose may be preferable. Doses may initially be divided throughout the day, but once-daily administration is preferred when plasma lithium concentration is stabilised in the target range (as specified by specialist team) due to monitoring of lithium levels and as it is associated with lower risk of renal adverse effects. Tablets should be prescribed unless there is a specific problem with swallowing difficulties.	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 of lithium citrate ARE NOT equivalent to lithium carbonate (bioavailability is significantly different).** **Extra care must be taken when prescribing lithium in liquid form, as strengths and formulations can vary under the same brand name.**

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.

Stopping lithium treatment

Abrupt discontinuation of lithium increases the risk of relapse. 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 however in some cases such as toxicity lithium may have to be stopped abruptly with close monitoring of the patient.

6. Pharmaceutical aspects

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Route of administration:	Oral
Formulation:	**The brand Priadel® is recommended within EPUT and is available as 200mg and 400mg modified release tablets.** Using a single brand (Priadel) throughout EPUT will help to reduce 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. 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)

	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. **<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.**
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 when appropriate for the dose, e.g. 300mg, 500mg 700mg, 900mg. 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; **<u>a double dose should not be taken to make up for a missed dose.</u>** 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.
<u>Liquid and tablet dose equivalence</u>	

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.

"Priadel" Lithium carbonate modified release tablet dose	"Priadel" lithium citrate 520mg/5ml equivalent dose
200mg	5ml
300mg	7.5ml
400mg	10ml
500mg	12.5ml
600mg	15ml
700mg	17.5ml
800mg	20ml
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**. Discuss with specialist team.**

The following medicines MUST NOT be prescribed without consultation with specialists:

- **Medicines that may increase plasma lithium concentrations** (by reducing renal elimination) and so risk toxicity:
  - NSAIDs (including cyclo-oxygenase 2 inhibitors). If NSAID use is unavoidable, a dose reduction of lithium may be required and levels should be monitored more frequently; discuss with specialist team. 'As required' use of NSAIDs should be avoided since it may cause fluctuations in lithium levels and makes monitoring levels challenging.
  - Diuretics, particularly thiazide diuretics
  - Angiotensin converting enzyme (ACE) inhibitors and angiotensin II receptor antagonists
  - Other drugs which alter electrolyte balance with the potential to alter lithium clearance e.g. steroids.
  - Certain antibiotics including metronidazole and tetracyclines
- **Medicines that may decrease plasma lithium concentrations** (by increasing renal elimination) and so risk loss of efficacy:
  - Theophylline
  - Products which contain sodium bicarbonate e.g. antacids
- **Medicines that may increase risk of neurotoxicity** when co-administered with lithium:

- Calcium channel blockers with cardiac effects (e.g. verapamil, diltiazem)
- Antipsychotics (e.g. haloperidol, olanzapine, clozapine, flupentixol, chlorpromazine)
- Antidepressants with a serotonergic action (e.g. SSRIs, tricyclic antidepressants, venlafaxine, duloxetine)
- Carbamazepine

- **Medicines associated with QT prolongation** (e.g. amiodarone, macrolides, tricyclic antidepressants) – potential for additive effects when co-administered with lithium.
- **Medicines that lower seizure threshold** (e.g. SSRIs, tricyclic antidepressants, antipsychotics) – increased risk of seizures

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 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, 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 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	**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, 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 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	Management 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	Ensure level was taken 12 hours after lithium dose. Assess adherence, including discussion with patient and check of GP clinical systems. Offer advice on adherence if appropriate.

NB: range for each patient to be determined by the specialist team. Note that local reference ranges may vary	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 A&E services if signs of toxicity.
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. More frequent monitoring may be required.
12-hour plasma lithium level WITHIN target range but TOXICITY suspected **Possible signs of lithium toxicity** • Severe tremor • Stomach pain along with nausea and diarrhoea • Muscle weakness and myalgia • Ataxia • Dysarthria • Blurred vision • Confusion • Drowsiness and lethargy	Contact specialist team for advice. Referral to secondary care may be required depending on the severity of symptoms and the certainty of toxicity. Use clinical judgement to determine the urgency of referral. If lithium toxicity is suspected, **do an urgent lithium level immediately and seek specialist advice.**

Thyroid function Altered TFTs without symptoms	Contact specialist team for advice. 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 and Normal T4 levels (Clinical features may not be present)	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 **Or Hyperthyroidism**	Contact specialist team for advice, which may include input from endocrinology services. For overt hypothyroidism, thyroid hormone replacement is usually indicated and often continued throughout the course of lithium treatment.
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.

Arrythmias Lithium can cause cardiac arrhythmia, mainly bradycardia, sinus node dysfunction and ECG changes such as reversible flattening or inversion of T-waves and QT prolongation or unmask Brugada syndrome.	ECG should be performed shortly after initiation of treatment by the specialist team where indicated (see section 8) . Also, at any point where the patient develops symptoms such as blackouts, fainting, dizziness, laboured breathing, palpitations, or seizures. Seek advice from initiating specialist.
U&E abnormalities (including serum phosphate? and calcium)	Check that the most recent 12-hour plasma lithium level is in the desired range or 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.
Changes to **estimated glomerular filtration rate.** - 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. 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 and 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 and BMI 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 and seek specialist advice. Referral to secondary care may be required depending on the severity of symptoms and the certainty of toxicity. Use clinical judgement to determine the urgency of referral.

Physical health check (bipolar 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 specialist will counsel the patient about 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 serum lithium levels, for example the NHS Health Monitor for Lithium app, or 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) .

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

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

Additional advice for patients/carers:	
Monitoring and review	Patients **MUST ATTEND** regularly for monitoring and review appointments to ensure their lithium dose remains safe and effective and bring their purple lithium record book to keep a record of their lithium levels.
Efficacy	For acute indications such as mania, 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.

Change in health	Patients **MUST 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
Missed doses	Lithium **MUST be taken regularly**, as prescribed. If doses are missed, patients should not attempt to catch up or double dose.
Not stopping therapy	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.
Same brand	**The same brand of lithium MUST 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 fluid intake and dietary regime	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.
Concurrent Illness	Substantial changes in plasma lithium levels can occur if patients develop diarrhoea or vomiting, or if they become acutely ill for any reason. **Patients MUST seek medical advice in such instances.**
Alcohol Consumption	**Excessive alcohol consumption MUST BE AVOIDED** as it can lead to dehydration, increasing plasma lithium levels and so risk of toxicity.
New prescriptions and concurrent medicines	Patients should be warned about common drug interactions and advised to present their 'Lithium record book' whenever they redeem a new prescription. They should **specifically be advised NOT to take over the counter (OTC) NSAIDs** as these can increase plasma lithium levels and so risk toxicity.
Driving and performing skilled tasks	**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.

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 an app is available for android users, at: 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:

Lithium should not be used during pregnancy, especially in the first trimester (risk of teratogenicity, including foetal heart malformations). 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.

If a patient becomes pregnant whilst on lithium, the specialist team should be informed immediately (but **DO NOT STOP** taking the lithium).

Women 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. Specialist contact information

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Name: *[insert name]*

Role and specialty: *[insert role and specialty]*

Daytime telephone number: *[insert daytime telephone number]*

Email address: *[insert email address]*

Alternative contact: *[insert contact information, e.g. for clinic or specialist nurse]*

Out of hours contact details: *[insert contact information, e.g. for duty doctor]*

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.

15. References

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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/.

17. Local arrangements for referral

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

To be agreed and completed locally

EPUT Medicines Management Group: July 2023 **Last updated: N/A**

Appendix 1: Shared Care Request letter (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 specialist/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 12 weeks 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 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 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 ICB 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 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