Protocol for the Safe Use of Lithium

Version number :	4
Consultation Groups	ELFT Medicines Committee
Approved by (Sponsor Group)	Medicine Committee
Ratified by:	Medicines Committee
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Executive Director lead :	Paul Gilluley
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Next Review date:	September 2023

Services	Applicable
Trustwide	x
Mental Health and LD	
Community Health Services	

Version Control Summary

Version	Date	Author	Comment
1	February 2011	Veena Shivnath, Senior Pharmacist; Shameem Mir, Chief Pharmacist	
2	February 2012	Veena Shivnath, Senior Pharmacist; Shameem Mir , Chief Pharmacist	Addition of shared care protocol as an Appendix
3	March 2016	Tabassam Beg, Clinical Pharmacist	• Section 1.1 Plasma level target changed in line with NICE guideline. Date of NICE guideline updated • Section 1.4 added • References: updated to reflect most recent NICE guideline. • Plasma level interpretation and toxicity guidelines updated
4	September 2020	Poonam Divani, Clinical Pharmacist; Tabassam Beg, Lead Pharmacist	• References: updated to reflect most recent NICE guideline • Removal of out-dated NPSA data • Adjustment to monitoring information to ensure adherence to NICE guidance • Removal of paper monitoring form • Addition of electronic Lithium monitoring completion advice • Amendment of contents page to electronic word format

Contents

1. Introduction

1.1 Lithium has a narrow therapeutic range. People who are prescribed lithium must have regular blood tests to ensure the dose they are taking leads to a plasma drug level of between 0.4 and 1.0 mmol/L (lower end of the range for maintenance therapy and elderly patients). Keeping plasma levels in this range gives the best chance of attaining the desired therapeutic outcome, whilst reducing (though not eliminating) the risk of harmful lithium toxicity occurring.

1.2 The NICE guideline (2020) for bipolar disorder recommends that patients prescribed lithium should have weight or BMI, ECG (for people with cardiovascular disease or risk factors for it), renal and thyroid function tests checked before treatment is initiated and then re-checked at least once every 6 months. The guideline also recommends that lithium plasma levels should be checked one week after starting lithium and one week after any dose change, then re-checked at least once every 3 months after levels have stabilised.

1.3 Despite the need for regular monitoring, local and national audits have identified a sub-optimal degree of lithium monitoring and of patient information provision, especially with regards adverse effects, interactions and symptoms of toxicity (refer to Appendix 1 for details about prescribing and monitoring lithium for inpatients, and Appendix 2 for the Standard Operating Procedure for lithium prescribing for outpatients).

1.4 In December 2009, the NPSA made recommendations that patients on lithium therapy should be monitored in both primary and secondary care and the results of monitoring should be communicated between both parties and the patient. A patient booklet, alert card and record book have been developed to support communication between healthcare providers and empower patients taking lithium. This informs patients of key aspects of their treatment including side effects and toxicity. These resources should be made available to all patients on lithium therapy and their use supported by healthcare professionals.

1.5 The Prescribing Observatory for Mental Health (POM-UK) conducted an audit of lithium monitoring in 2016 in sixty-three participating Trusts including ELFT. Since the baseline audit in 2008, there has been an increase in the proportion of patients who, at initiation of treatment with lithium, were informed of the potential side effects, the signs and symptoms of toxicity, and the risk factors for toxicity at ELFT. Clinical practice in relation to monitoring of patients established on lithium also showed improvement. There was a consistent increase from baseline in the proportion of patients with documented measures over the year of U&Es and creatinine, thyroid function tests, serum lithium, and body weight/obesity. The proportion of such patients with mood disorder who had a documented plasma lithium level between 0.4 and 0.8 mmol/l had increased to more than three-quarters. Nevertheless, the data collected reveal that the documentation of baseline tests and on-treatment monitoring of lithium within mental health services still falls short of the standards derived from specific recommendations in the National Institute for Health and Clinical Excellence (NICE) guidance on bipolar disorder.

2. Scope

2.1 This protocol has been developed to promote the safe use of lithium therapy in line with the previous NPSA alert, the Quality Outcome Framework (QOF) and NICE guidelines (2014) to ensure safety and avoid harm to patients. This protocol pertains to all services and directorates across the ELFT together with other primary and secondary care providers to ensure all organisations are working towards the same objective in ensuring safety and monitoring of lithium treatment. It is the responsibility of both primary and secondary care to take necessary actions to improve outcome and experiences of patients on lithium.

3. Responsibilities of the Mental Health Trust

3.1 Prescribers/Consultants

3.1.1 Ensure all baseline tests are carried out at initiation of lithium therapy (Appendix 1, 2) Inform the patient about lithium inclusion in their treatment regime, explain the rationale behind lithium monitoring, educate patient about benefits and risks of lithium, side effects and the need to inform a health care professional in case of any side effects suffered, recognise signs and symptoms of lithium toxicity, other medication to avoid which interferes with lithium, what to do in case of vomiting, diarrhoea.

3.1.2 Discuss the risks associated with lithium and pregnancy with female patients, and perhaps the need for contraception. The discussion must be fully documented in the notes.

3.1.3 Ensure patient has been provided with the information booklet, lithium alert card and record book by contacting the clinical pharmacist. All treatment details (brand, form, dose etc.) and lithium blood results must be entered in the record book together with the relevant blood tests.

3.1.4 Ensure the Psychotropic Medication Monitoring form on RiO is complete (see Appendix 5)

3.1.5 Advise the patient to have this record book with them whenever visiting a doctor or community pharmacy and inform loss of this book to the GP or CMHT staff or pharmacist.

3.1.6 Ensure documentation of the contents of discussion about lithium therapy in medical notes.

3.1.7 Ensure blood tests are done for maintenance therapy, after each dose change and every 3 months. See Appendix 1.

3.1.8 Inform GP on discharge that the patient has been started on lithium, and instruct the GP about monitoring requirements via discharge letter. Please see Appendix 3 Shared Areas of Responsibility Arrangement on Discharge.

3.1.9 Provide advice to GPs if mental state changes or in case of adverse effects.

3.1.10 Ensure lithium blood levels are done 12 hours post dose and if patients are on lithium liquid that the morning dose is withheld until the blood test is done.

3.1.11 Any changes in blood tests results or changes in therapy must be communicated to GPs.

3.2 Responsibilities of ELFT Pharmacists

3.2.1 Ensure lithium is prescribed by brand name. If it is prescribed generically, the pharmacist must endorse all prescriptions, including discharge summaries, with the brand name.

3.2.2 Ensure lithium is monitored in accordance with this protocol.

3.2.3 Provide education session on lithium therapy to patients and carers, discuss benefits adverse effects, interactions (see Appendix 4) with other medication either prescribed by doctors or bought over the counter such as herbal medicines with diuretic potential, indigestion remedies and any NSAIDs.

3.2.4 Advise ward doctors about lithium monitoring, refer to Appendix 1

3.2.5 Counsel patient at discharge about adherence/concordance to lithium therapy, to obtain further supplies from GP and report any side effects suffered after discharge either to GP or the community team and the community pharmacist. Check Shared Areas of Responsibility Arrangement on Discharge (Appendix 3).

3.2.6 Work in collaboration with ward doctors to ensure lithium monitoring is done (see Appendix 5).

3.2.7 Communicate results of blood tests to the medical team in order to optimise dosage

3.2.8 Liaise with pathology staff about all lithium results communication to the appropriate parties including GPs.

3.2.9 Ensure patient records are up to date regarding most recent lithium blood levels and any other tests relevant to lithium therapy and document details in medical notes. If lithium levels are not within therapeutic range, the prescriber must be contacted. The prescriber must also be notified if any of the tests relevant to lithium therapy are not within normal range.

3.2.10 Inform Consultant and GP if concomitant interacting drug is prescribed and give advice about dose adjustment of lithium and additional monitoring.

3.2.11 Ensure blood lithium level is checked at each dispensing and patients are informed about carrying their record book with them to all appointments and when collecting medication from community pharmacies.

3.3 Responsibilities of Nurses

3.3.1 Ensure that patients understand the reason for lithium therapy.

3.3.2 Ensure that weight is recorded at initiation of treatment with lithium followed regular intervals during admission

3.3.3 Ensure lithium blood levels are done 12 hours post dose and if patients are on lithium liquid that the morning dose is withheld until the blood test is done.

3.3.4 Report any side effects experienced by the patients whilst an inpatient to the medical team and make an entry in the medical notes to that effect.

3.3.5 Inform the medical team if patient suffers from any gastrointestinal problems i.e. diarrhoea, vomiting as this would affect the lithium blood level and can lead to toxicity.

3.3.6 Counsel patient at discharge about adherence to lithium therapy and obtaining further supplies from GP and the importance of carrying their lithium booklet.

3.3.7 Encourage patients to report any side effects suffered after discharge either to GP or the community team and community pharmacists.

4. Responsibilities of General Acute Hospital

4.1 Ensure patient is prescribed the correct dose and brand of lithium.

4.2 Update patient records with the most recent lithium blood levels and any other relevant tests.

4.3 Monitor for drug interactions with any new medication prescribed which may alter lithium levels and monitor levels as soon as possible.

4.4 Provide ongoing verbal and written information about new medication with lithium therapy.

4.5 Seek advice from consultant psychiatrist about any concerns relating to lithium therapy.

4.6 Monitor for side effects and in case of renal impairment seek advice about appropriate dose in such cases and monitor lithium levels regularly.

4.7 Ensure patients have their lithium booklet with them and if not then supply one.

4.8 Enter all lithium blood results in the record book together with the relevant blood tests.

5. Responsibilities of the Clinical Commissioning Groups

5.1 Inform all GPs and Community Pharmacies of this Protocol.

5.2 Provide GPs with support relating to responsibilities with lithium patients.

5.3 Provide feedback to Trusts via Medicines /Prescribing / Drug and Therapeutics Committees.

5.4 Liaise with the appropriate parties in case of difficult / interface issues that may arise as a result of this protocol.

6. Responsibilities of General Practitioners

6.1 Ensure that lithium monitoring is carried out in line with the protocol - refer to Appendix 1 and 2

6.2 Complete patient lithium 'purple' record book as necessary with any dose changes and recent lithium blood levels.

6.3 Discuss any concerns relating to lithium therapy with the appropriate consultant psychiatrist for the patient and refer patient back to secondary care if patient discontinues treatment and suffers a worsening mental state.

6.4 Ensure that newly prescribed medicines do not interact with lithium. If a medicine that can alter lithium levels is prescribed then additional monitoring should be put in place. Ensure patient and consultant are fully informed of any changes to medication. to avoid any harm and patient should be fully informed about this.

6.5 Inform the consultant psychiatrist of any concordance/adherence issues.

6.6 Shared Areas of Responsibility Arrangement on Discharge (Appendix 3).

6.7 Provide ongoing advice to the patient and monitor general health.

6.8 In case of signs of lithium toxicity, stop treatment, monitor blood lithium level and inform the relevant consultant psychiatrist.

6.9 If side effects are suffered, inform the relevant consultant psychiatrist.

6.10 In case of abnormal renal function and thyroid function tests, liaise with consultant to discuss relevant actions.

6.11 Inform female patients about the need for continuous contraception throughout lithium therapy and seek specialist advice in case patient become pregnant.

7. Responsibilities of Community Pharmacists

7.1 Check that blood tests are monitored in accordance with this protocol by checking lithium booklets before dispensing a repeat prescription for lithium. See Appendix 2.

7.2 If generic lithium has been prescribed, confirm the brand name.

7.3 Check for all drug interactions, including over-the-counter (OTC) medicines.

7.4 At the start of lithium therapy and throughout their treatment, ensure patients receive appropriate verbal and written information

7.5 Refer the patient back to the Mental Health team or GP if there are any concerns relating to compliance or lithium therapy in general

8. Provision of Advice to Patients

8.1 Patients must be informed about the following:

a) Blood tests should be explained; renal and thyroid functions tests
b) Report all side effects experienced; gastrointestinal disturbances (nausea- try and take lithium with food), fine tremor, polydipsia (increased fluid consumption) having to have more drinks than normal, polyuria (increase of urinary frequency), weight gain, and hypothyroidism (underactive thyroid) are amongst the most common side effects.
c) Refer to the Summary Product Characteristics for a more comprehensive list of side effects at https://www.medicines.org.uk/emc/ (for *Camcolit, Li-liquid*) and https://products.mhra.gov.uk/ (for Priadel, Liskonum and other brands).
d) To seek immediate urgent advice if they develop the following signs and symptoms due to a high level of lithium in blood:

- Confusion, coarse tremor,
- Loss of balance
- Slurred speech
- Visual disturbances
- Marked trembling
- Nausea, vomiting, stomach ache and diarrhoea
- Abnormal general weakness or drowsiness

e) Risk factors for lithium toxicity must be discussed and documented in medical notes; if they develop diarrhoea/vomiting which can lead to dehydration, the need to consume plenty of fluids.
f) Importance of maintaining an adequate fluid intake, at least drink 10-12 cups of fluid a day (water, juices) and in hot weather/during activities that can lead to sweating (sauna, hot baths, exercise) to be aware of fluid loss.
g) The need to check with the doctor/pharmacist whether other medicines bought over the counter may interfere with lithium, avoid taking non-steroidal anti-inflammatory medication such as ibuprofen or any other cold/flu remedies which may alter lithium levels.
h) Inform dentists/doctors/pharmacist about lithium treatment.
i) Women of child bearing age must be informed about the need for contraception whilst on lithium and discuss risks to the foetus if become pregnant- can cause Ebstein's anomaly, a heart defect.
j) Report an increase in thirst or an increase in frequency of urine to the medical team.
k) Not to increase or reduce dose, seek advice from consultant psychiatrist/GP if wish to discontinue lithium therapy even when well because of the risk of relapse.
l) Weight gain with lithium: monitor food intake, avoid high calorific value beverages (e.g. carbonated soft drinks) and food with high fat content (i.e cakes, pastry).
m) Ensure that a lithium record book is taken to every outpatient, GP appointment and community pharmacy visit and in case of admission to hospital.
n) Maintain same salt intake during lithium treatment as an alteration of salt intake can affect lithium levels. Keep all medication out of reach of children.

10.1 Inform GP/CMHT in case of mood changes

9. Blood Results

9.1 Each local site has a designated laboratory where blood samples are sent for analysis. State the urgency of testing on the blood request form if lithium toxicity is suspected and a telephone call should be made to reinforce the need for urgent results.

9.2 Blood results can be viewed via the intranet if clinicians have liaised with their IT departments about access to their local laboratory and blood results. These are then usually posted to the relevant clinician and wards. It is very important to complete the blood request form legibly with all requested details otherwise this will delay blood results and sometimes blood results are sent to wrong departments.

10. Dissemination and Implementation

10.1 This protocol will be circulated to Clinical Directors and Service Managers who will be required to cascade the information to team members for briefing and information to encourage safe use of lithium.

11. Audit and Review

11.1 This protocol will be reviewed in 3 years unless legislation changes and lithium use should be audited on a regular basis to ensure safety and appropriate monitoring of lithium therapy.

12. References

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Appendix 1 In-patient Prescribing & Monitoring of Lithium

Indications	• Mania and hypomania • Prophylaxis of bipolar affective disorder • Recurrent depression • Control of aggressive behaviour or intentional self-harm
Baseline tests	• **Renal function tests**- Urea & Electrolytes (U&Es), e-GFR and creatinine • **Calcium levels** • **Thyroid Function tests (TFTs):** TSH and T4 • **Full Blood Count** • **Weight or BMI** • **ECG**- for those with risk factors for or existing/family history cardiovascular disease
Prescribing Note that various lithium preparations are not interchangeable, preferable to prescribe by **brand name** i.e Priadel or Camcolit. If there is a change in brand, then need to monitor lithium level as at initiation.	• **Start at 400mg** at night (200mg-250mg in the elderly). • **Dose** is usually guided by plasma level and clinical status, increase slowly to minimise side effects: • ***Bipolar:*** 0.6 – 0.8 mmol / l (0.8 – 1.0 mmol / l if previously on lithium and relapsed / sub-syndromal symptoms) • Monitor plasma level after **1 week** of starting • A repeat lithium level should be taken **4-7 days** following a change in dose or change/ addition of an interacting medication. Following this, a plasma level should be done weekly until level is stable (typically up to 5 weeks). • Once daily dosing preferable to encourage adherence and prevent side effects related to high peak levels (tremor, urinary frequency, GI effects) • Blood should be taken **12 hours** post dose • Liquid should be prescribed twice daily and level done prior to morning dose • **Stopping lithium:** Reduce the dose gradually over at least 4 weeks, and preferably over up to 3 months (even if the patient is taking another antimanic agent). If lithium treatment is stopped or is about to be stopped abruptly, consider changing to an atypical antipsychotic or valproate (please refer to MHRA safety advice on valproate use by women and girls), and monitor closely for early signs of mania and depression.

Monitoring	• **Plasma lithium:** Monitor plasma level after **1 week** of starting and **4-7 days** after every dose change or change/ addition of an interacting medication until levels are stable and then every **3 months** for the first year**.** After the first year, measure plasma lithium **every 6 months**, or every **3 months** for people in any of the **following groups**:
	  ○ older people
	  ○ people taking drugs that interact with lithium
	  ○ people who are at risk of impaired renal or thyroid function, raised calcium levels or other complications
	  ○ people who have poor symptom control
	  ○ people with poor adherence
	  ○ people whose last plasma lithium level was 0.8 mmol per litre or higher.
	• **U&Es and TFTs** every 6 months
	• **Weight or BMI** every 6 months
	• **Calcium** every 6 months
	• **eGFR** every 6 months
	• **Physical assessment** for signs of toxicity.
	• **More frequent tests than 6 months if there is evidence of:**
	  ○ impaired renal or thyroid function
	  ○ raised calcium levels
	  ○ increase in mood symptoms that might be related to impaired thyroid function
	  ○ clinical deterioration
	  ○ abnormal results
	  ○ a change in sodium intake
	  ○ patient taking other prescribed medication which interacts with lithium e.g. ACE inhibitors, NSAIDs or diuretics.

- **Monitoring Summary table**

Test	Baseline	1 week after initiation	1 week after dose change	Weekly until levels are stable	Every 3 months for the 1st year	Every 6 months from initiation *(or more frequent – see above)*
Weight/BMI	✓					✓
ECG	✓					
TFTs	✓					✓
Calcium	✓					✓
U&Es (includes creatinine)	✓					✓
eGFR	✓					✓
FBC	✓					
Plasma Lithium level *(or more frequent if in patient in group outlined above)*		✓	✓	✓	✓	✓

Management of blood levels and signs of toxicity

- **Lithium level <1 but signs of moderate or severe toxicity:**

  stop lithium and refer to secondary care.

- **Lithium level 1.0-1.5 mmol/l:**

  Examine for signs of toxicity: if none, repeat blood test. If still above target range, reduce dose and repeat blood test after a week.

- **Lithium level > 1.5 mmol/l <u>AND/OR</u> signs of MILD toxicity:**

  Stop lithium, **immediate referral to Specialist team** who initiated lithium treatment, daily follow-up. Note: plasma levels may still be rising, monitor for signs of moderate / severe toxicity over next 7 days.

- **Lithium level > 2 mmol/l <u>AND/OR</u> signs of MODERATE/ SEVERE toxicity:**

  Stop lithium. **Immediate referral to A&E** for possible diuresis and inform responsible secondary care clinician. Investigate reason for toxicity.

Symptoms of lithium toxicity

Please note that lithium toxicity is a clinical diagnosis and <u>can occur even at therapeutic lithium plasma levels</u>.

Symptoms of lithium toxicity:

MILD	• **Nausea** • **Diarrhoea**	• **Severe fine tremor**	• **Poor concentration**
MODERATE	• **Vomiting**	**Cerebellar signs:** • **Coarse tremor** • **Cerebellar ataxia** • **Slurred speech**	• **Drowsiness** • **Disorientation**

		SEVERE	• **Incontinence**	• **Choreiform movements** • **Parkinsonism** • **Myoclonus** • **Cerebellar dysfunction** • **Spasticity** • **EEG abnormalities** • **Renal failure** • **Seizures**	• **Apathy** • **Coma**

Appendix 2 ELFT Outpatient Lithium Prescribing and Monitoring

Standard Operating Procedure

Principles

Safety in the prescription and monitoring of Lithium has been the subject of a National Patient Safety Agency alert which is due for introduction by the end of December 2010. All NHS organisations are required to have safe systems in place by that date. Pharmacists (including community pharmacists) will not dispense medication to patients who do not have current (as defined within the required monitoring frequency) blood levels, renal function and thyroid function tests. The systems being introduced are similar to those already in place for other high risk medications e.g. Methotrexate and Warfarin.

A Purple Pack has been developed, containing a Patient information book, a results record book, and a contact's information card

Procedure for The Prescriber

1. When the decision is taken to initiate lithium treatment as an outpatient and the patient has consented, the patient is given the purple lithium information booklet out of the Purple Pack. This is recorded in the patient's notes.

2. A Patient Information leaflet for lithium must be printed off from the Trust Intranet and given to the patient with attention drawn to interactions with other medicines such as antacids containing sodium, and advice on water and salt intake

3. The patient has the following tests ordered: Urea and Electrolytes, Creatinine, Thyroid Function. An ECG should be requested if there is a history of cardiac disease or the patient has cardiovascular risk factors. The height and weight of the patient must be recorded in the notes. (See Appendix 1)

4. If the blood results are within normal range then lithium treatment can be prescribed. The initial dose, and the blood results must be recorded in the purple record book and the Pack, including the contact details card, given to the patient. The contact details and patient demographics must be also completed by the prescriber

5. The patient will need to show the results record book to the pharmacist when presenting a lithium prescription for medication to be dispensed and bring it with them to every appointment with the doctor.

6. If the blood results are not within normal range then specialist advice should be sought and lithium must NOT be started.

7. After initiating treatment a lithium level must be taken after one week.

8. A dose change can be initiated after receiving the blood result. Both the first level and the new dose must be entered into the patient's results record booklet.

9. Until a stable dose and satisfactory blood level (usually 0.4 -1.0mmol/l) is achieved, the patient's lithium level must be measured one week after each dose change. Each time results and dose must entered into the results record booklet.

10. Once a stable dose and satisfactory lithium level is achieved then the lithium level must be measured every three months

11. Undertake more frequent tests if there is evidence of clinical deterioration, abnormal blood test results, a change in sodium intake, or symptoms suggesting abnormal renal or thyroid function such as unexplained fatigue, or other risk factors, for example, if the patient is starting medication such as ACE inhibitors, non-steroidal anti-inflammatory drugs, antacids or diuretics.

12. Arrange thyroid and renal function tests every 6 months, and more often if there is evidence of changed thyroid or impaired renal function.

13. Enter the dates of future tests into the clinic diary with prompts for obtaining and checking results one week later.

14. Initiate closer monitoring of lithium dose and blood serum levels if urea and creatinine levels become elevated, and assess the rate of deterioration of renal function. The decision whether to continue lithium depends on clinical efficacy, and degree of renal impairment; prescribers must consider seeking advice from a renal specialist and a clinician with expertise in the management of bipolar disorder on this.

15. Most patients will have their care handed over to a G.P. once stable. In complex shared care arrangements the important principle **that the prescriber monitors** must always be adhered to.

Appendix 3: Shared Areas of Responsibility Arrangement on Discharge

Referral Criteria

Prescribing responsibility will only be transferred when the consultant and the patient's GP consider the patient's condition to be **stable**. Shared Areas of Responsibility assumes communication between the specialist, GP and patient.

Referral of the patient to the GP will be subject to the GP's agreement. The areas below indicate the areas of responsibility to be decided by discussion between the GP and consultant.

The patient will be given a supply of lithium sufficient for 2 weeks' maintenance therapy upon discharge from secondary care.

Patients should be under regular follow-up which provides an opportunity to discuss drug therapy.

Monitoring outline below, is essential for patient safety and treatment. The clinician (e.g. GP / specialist) who prescribes the drug must, before issuing any further prescriptions for lithium, check for up to date lithium levels and other blood test results.

Shared Areas of Responsibility

GPs Responsibilities

- To prescribe monthly supplies of lithium
- To refer back to the consultant if:
  - Patient relapses
  - Patient has intolerable side effects
  - Non-compliance is suspected

- To Monitor physical health monitoring in community which is summarised in table below:

Test	Baseline	1 week after initiation	1 week after dose change	Weekly until levels are stable	GP- Every 3 months for the 1st year	GP- Every 6 months from initiation *(or more frequent – see above)*
Weight/BMI *(can be annually***)**	✓					✓
ECG	✓					
TFTs	✓					✓
Calcium	✓					✓
U&Es (includes creatinine)	✓					✓
eGFR	✓					✓
FBC	✓					
Plasma Lithium level *(or more frequent if in patient in group outlined above see appendix 1)*		✓	✓	✓	✓	✓

Taking lithium levels:

- Advise the patient that the blood level should be taken approximately 12 hours post dose. If a twice daily regime is prescribed, the patient should be advised to withhold morning dose until after the blood sample has been taken.

- Patients **must have regular blood tests** to ensure the lithium plasma drug level is within the **agreed target range** as specified by the specialist. (please see below)

Indication for Lithium	Target dose (mmol/L)
Acute treatment of Mania	0.8 – 1.0
Maintenance treatment for bipolar disorder	0.6 – 0.8
Augmentation of antidepressant in depression	0.6 – 1.0
Minimum effective level for prophylaxis	0.4

To assess for signs of toxicity

- To undertake more frequent tests if there is evidence of clinical deterioration, abnormal results, a change in sodium intake, symptoms suggesting abnormal renal or thyroid function (e.g. unexplained fatigue), or if patient is prescribed medication

Community Consultants Responsibilities

- Outpatient appointments every 1-12 months based on clinical need

Clinical Information

Indications	• Mania and hypomania • Prophylaxis of bipolar affective disorder • Recurrent depression • Control of aggressive behaviour or intentional self-harm
Baseline tests	• **Renal function tests**- Urea & Electrolytes (U&Es), e-GFR and creatinine • **Calcium levels** • **Thyroid Function tests (TFTs):** TSH and T4 • **Full Blood Count** • **Weight or BMI** • **ECG**- for those with risk factors for or existing/family history cardiovascular disease
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• Blood should be taken 12 hours post dose
• Liquid should be prescribed twice daily and level done prior to morning dose
• Stopping lithium: Reduce the dose gradually over at least 4 weeks, and preferably over up to 3 months (even if the patient is taking another antimanic agent). If lithium treatment is stopped or is about to be stopped abruptly, consider changing to an atypical antipsychotic or valproate (please refer to MHRA safety advice on valproate use by women and girls), and monitor closely for early signs of mania and depression.</td></tr>
<tr><td>Duration of treatment</td><td colspan="3">Usually long term N.B. abrupt withdrawal worsens prognosis</td></tr>
<tr><td rowspan="10">Adverse Effects</td><td>Adverse Effect</td><td>Frequency (in maintenance therapy)</td><td>Management</td></tr>
<tr><td>Weight gain</td><td>Common</td><td>Give advice on diet and exercise</td></tr>
<tr><td>Hypothyroidism</td><td>Common</td><td>Refer to consultant</td></tr>
<tr><td>Polyuria and polydipsia</td><td>*Uncommon</td><td>Give advice on reducing fluid intake</td></tr>
<tr><td>Diarrhoea</td><td>*Uncommon</td><td>May be a sign of **toxicity (see below). Give advice on fluid and salt replacement</td></tr>
<tr><td>Nausea/vomiting</td><td>*Uncommon</td><td>Give after food. Use a slow release preparation</td></tr>
<tr><td>Dermatological effects (including exacerbation of existing dermatological conditions)</td><td>Uncommon</td><td>Refer to consultant</td></tr>
<tr><td>Sexual dysfunction (decreased lipido, erectile dysfunction, priapism and decreased sperm motility)</td><td>Uncommon</td><td>Refer to consultant</td></tr>
<tr><td>Fine tremor</td><td>Uncommon</td><td>Refer to consultant</td></tr>
<tr><td>**Toxicity (see below) N.B. can be fatal</td><td></td><td>Stop lithium and refer to A&E</td></tr>
<tr><td colspan="3">**With appropriate maintenance therapy, these adverse effects are uncommon. If they persist, refer the patient back to the consultant.</td></tr>
<tr><td>Monitoring requirements</td><td colspan="3">• Plasma lithium: Monitor plasma level after 1 week of starting and 4-7 days after every dose change or change/ addition of an interacting medication until levels are stable and then every 3 months for the first year. After the first year, measure plasma lithium every 6 months, or every 3 months for people in any of the following groups:
○ older people
○ people taking drugs that interact with lithium
○ people who are at risk of impaired renal or thyroid function, raised calcium levels or other complications
○ people who have poor symptom control
○ people with poor adherence
○ people whose last plasma lithium level was 0.8 mmol per litre or higher.
• U&Es and TFTs every 6 months
• Weight or BMI every 6 months
• Calcium every 6 months
• eGFR every 6 months
• Physical assessment for signs of toxicity. Monitor the person at every appointment for symptoms of neurotoxicity, including paraesthesia, ataxia, tremor and cognitive impairment, which can occur at therapeutic levels of lithium.
• More frequent tests than 6 months if there is evidence of:
○ impaired renal or thyroid function
○ raised calcium levels
○ increase in mood symptoms that might be related to impaired thyroid function
○ clinical deterioration
○ abnormal results</td></tr>
</table>

- a change in sodium intake
- patient taking other prescribed medication which interacts with lithium e.g. ACE inhibitors, NSAIDs or diuretics.

- **Monitoring Summary table**

Test	Baseline	1 week after initiation	1 week after dose change	Weekly until levels are stable	Every 3 months for the 1st year	Every 6 months from initiation *(or more frequent – see above)*
Weight/BMI	✓					✓
ECG	✓					
TFTs	✓					✓
Calcium	✓					✓
U&Es (includes creatinine)	✓					✓
eGFR	✓					✓
FBC	✓					
Plasma Lithium level *(or more frequent if in patient in group outlined above)*		✓	✓	✓	✓	✓

Management of blood levels and signs of toxicity

- **Lithium level <1 but signs of moderate or severe toxicity:**

  stop lithium and refer to secondary care.

- **Lithium level 1.0-1.5 mmol/l:**

  Examine for signs of toxicity: if none, repeat blood test. If still above target range, reduce dose and repeat blood test after a week.

- **Lithium level > 1.5 mmol/l AND/OR signs of MILD toxicity:**

  Stop lithium, **immediate referral to Specialist team** who initiated lithium treatment, daily follow-up. Note: plasma levels may still be rising, monitor for signs of moderate / severe toxicity over next 7 days.

- **Lithium level > 2 mmol/l AND/OR signs of MODERATE/ SEVERE toxicity:**

  Stop lithium. **Immediate referral to A&E** for possible diuresis and inform responsible secondary care clinician. Investigate reason for toxicity.

Symptoms of lithium toxicity

Please note that lithium toxicity is a clinical diagnosis and can occur even at therapeutic lithium plasma levels.

Symptoms of lithium toxicity:

MILD	• **Nausea** • **Diarrhoea**	• **Severe fine tremor**	• **Poor concentration**
MODERATE	• **Vomiting**	**Cerebellar signs:** • **Coarse tremor** • **Cerebellar ataxia** • **Slurred speech**	• **Drowsiness** • **Disorientation**
SEVERE	• **Incontinence**	• **Choreiform movements** • **Parkinsonism** • **Myoclonus** • **Cerebellar dysfunction** • **Spasticity** • **EEG abnormalities** • **Renal failure** • **Seizures**	• **Apathy** • **Coma**

Appendix 4 Drug Interactions

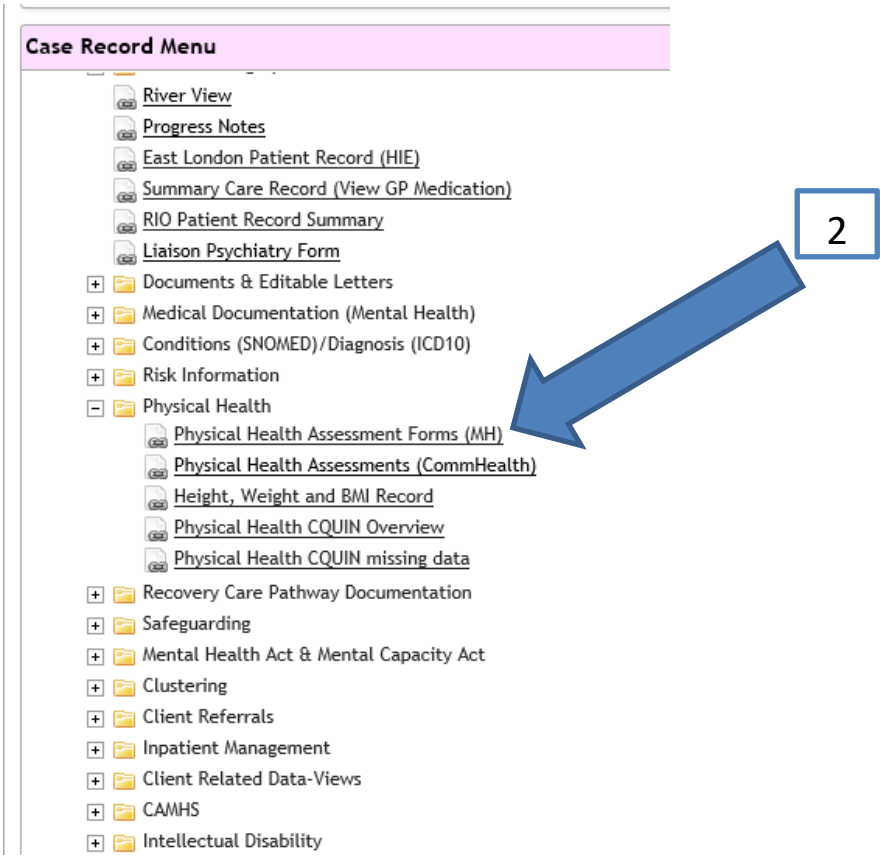
Class of Drug	Example	Interaction Effects
Alcohol		Increased tremor/shakiness with chronic alcohol use
Angiotensin-converting enzyme (ACE) inhibitors ACE-2 inhibitor	Enalapril, captopril, Lisinopril Losartan, candesartan, valsartan	Lithium toxicity due to sodium depletion, Lithium toxicity due to reduced aldosterone levels
Antibiotic	Doxycycline, tetracycline, levofloxacin, metronidazole	Can increase lithium level due to reduced lithium excretion
Anticonvulsant/Antiepileptics	Carbamazepine, phenytoin, Valproate, topiramate	Increased neurotoxicity of both drugs at therapeutic doses Valproate may aggravate tremor Neurotoxicity may occur without any increase of lithium plasma level Altered Lithium level possible
Antidepressant Cyclic, MAOIs, RIMA SSRIs	Desipramine, tranylcypromine, Moclobemide Fluoxetine, fluvoxamine, sertraline	Synergistic antidepressant effect in treatment resistant patients, may increase lithium tremor Increase lithium level, possible neurotoxicity and serotonergic effects
Antihypertensive	Amiloride, spironolactone, thiazides, triamterene, methyldopa, B-blockers: propranolol, oxprenolol	Increase lithium effects and toxicity Treatment of lithium tremors, propranolol lowers glomerular filtration rate
Antipsychotic	Haloperidol (high doses), flupentixol, fluphenazine, chlorpromazine, clozapine	Increased neurotoxicity possible at therapeutic doses in rare cases
Calcium channel blocker	Verapamil, diltiazem	Increased neurotoxicity with symptoms such as ataxia, confusion and somnolence. May increase lithium level
Caffeine		Reduce lithium level by increased lithium excretion
Diuretics	Bendroflumethiazide, furosemide	Increase lithium level

NSAIDS	Ibuprofen, diclofenac, naproxen, mefenamic acid	Increased lithium level, monitor level regularly
Sodium salt	Antacids, Gaviscon®. Sodium bicarbonate containing antacids or urinary alkalising agents.	Increased intake causes a reduced lithium level

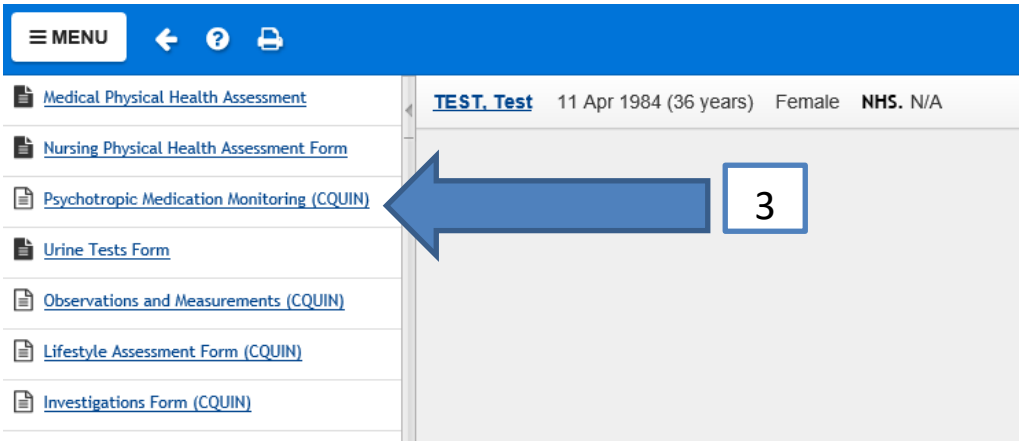
Appendix 5 **Psychotropic Medication Monitoring Form (electronic Lithium Monitoring form)**

Please see instructions below on how to access and complete this form. The completion of this form helps ensure all monitoring associated with lithium therapy is recorded and easily accessible.

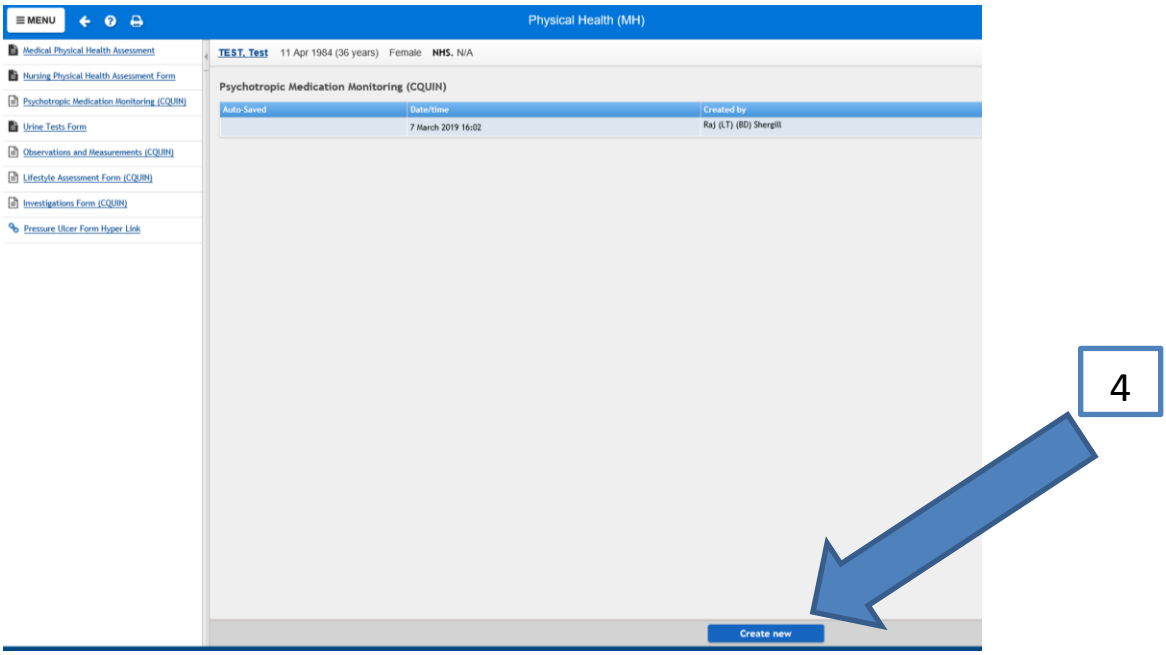
1. Access patient records on RiO
2. Open 'Physical Health' folder under 'Case Record Menu' and select 'Physical Health Assessment Forms (MH)



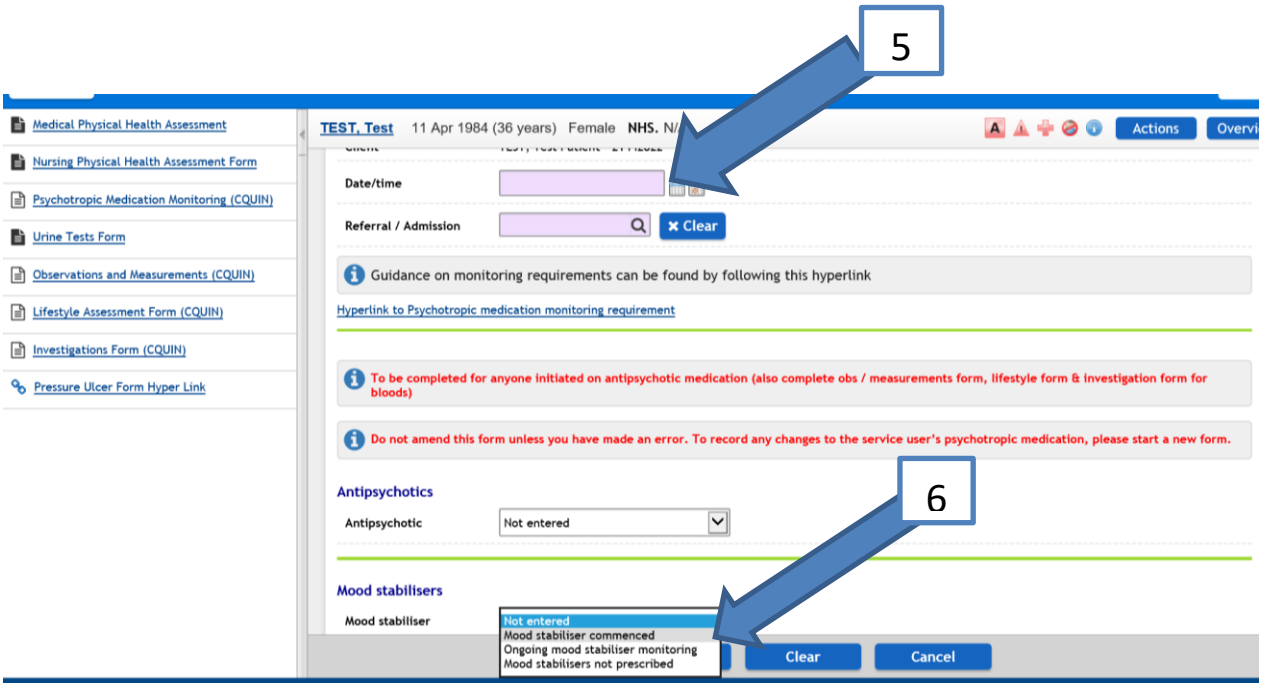
3. Select 'Pscyhotropic Medication Monitoring (CQUIN)'



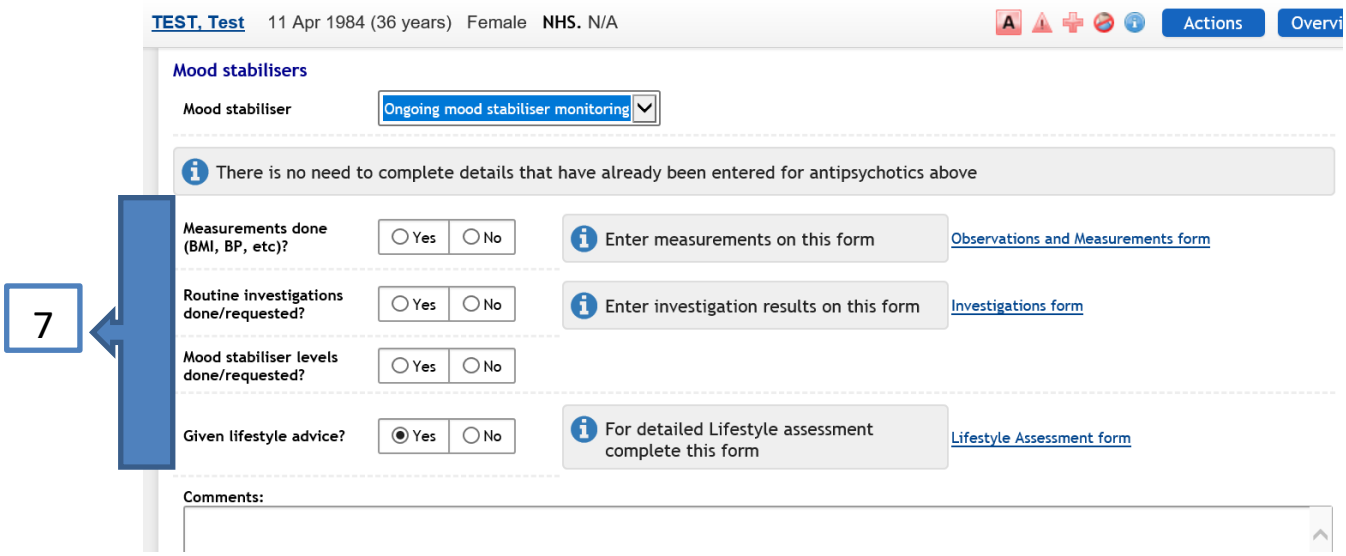
4. Select the 'Create new' tab



5. Populate the date/time
6. Select the drop down menu next to ‘mood stabilsers’ and select the relevant option



7. Check to see if measurements, routine investigations, mood stabiliser levels, lifestyle advice have been recorded by clicking on the hyperlinks to the corresponding forms. Select ‘Yes’ or ‘No’ as appropriate.



8. Once complete, click on the 'Save' tab.