East London NHS
NHS Foundation Trust

Protocol for the safe use of lithium

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Ratified by:	Medicines Committee
Date ratified:	January 2016
Name of originator/author:	Veena Shivnath, Senior Pharmacist, Newham; Shameem Mir, Chief Pharmacist
Name of responsible committee/individual:	Medicine Committee
Circulated to:	ELFT Medicines Committee
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Third Edition	March 2016
Review due:	March 2019
Target audience:	All clinicians in secondary and primary care.
Comments to:	Shameem Mir

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

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 0.6 and 1.0 mmol/L. 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. The NICE guideline (2014) for bipolar disorder recommends that patients prescribed lithium should have 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.

1.2 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).

1.3 The National Patient Safety Agency (NPSA) received 567 incident reports between October 2003 and December 2008 relating to lithium use, 2 reports were of severe harm, 34 moderate and 531 low or no harm. 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. To further ensure safety in management of patients on lithium, the NPSA has recently launched a lithium patient pack which should be provided to all patients on lithium. The lithium pack comprises of a record book and an alert card to facilitate communication of lithium monitoring between healthcare providers.

1.4 The Prescribing Observatory for Mental Health (POM-UK) conducted an audit of lithium monitoring in 2013 in fifty-seven 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 lithium monitoring form (Appendix 3) is completed.

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.

3.1.8 Inform GP within 2 weeks of starting a patient on lithium, and instruct the GP about monitoring requirements. Agree shared care arrangement on discharge. See Appendix 4.

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 5) 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 care arrangements with GPs.

3.2.6 Work in collaboration with ward doctors to ensure lithium monitoring is done.

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 patients 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 interact 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 by weekly weights.

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 Ensure that the GP liaison form at discharge is sent to GP either via the patient or by faxing and confirming the fax or directly by sending it via email.

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

3.3.8 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

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

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

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

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

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

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

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

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

5. Responsibilities of the Clinical Commissioning Groups

5.1.1 Inform all GPs and Community Pharmacies of this Protocol.

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

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

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

5.2 Responsibilities of General Practitioners

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

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

5.2.3 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.

5.2.4 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.

5.2.5 Inform the consultant psychiatrist of any concordance/adherence issues. Adhere to arrangement agreed within shared care protocol.

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

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

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

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

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

5.3 *Responsibilities of Community Pharmacists*

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

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

5.3.3 Check for all drug interactions including over-the-counter medicines.

5.3.4 At the start of lithium therapy and throughout their treatment patients receive appropriate ingoing verbal and written information.

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

6. Provision of Advice to Patients

6.1 Patients must be informed about the following:

a) Lithium therapy and the monitoring required during treatment inclusive of the pre-treatment blood tests.
   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/
   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.
p) Inform GP/CMHT in case of mood changes

7. Blood Results

7.1 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.

7.2 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.

8. Dissemination and Implementation

8.1 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.

9. Audit and Review

9.1 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.

10. References

1. BNF No 70, September 2015.
2. Summary of Product Characteristics for Priadel, https://www.medicines.org.uk/emc/ [accessed 17.11.2015]
3. National Institute for Health and Clinical Excellence. Bipolar disorder. The management of bipolar disorder in adults, children and adolescents, in primary and secondary care, Clinical Guidance 185, http://www.nice.org.uk, 2014.
4. NPSA Alert 2009.
5. Taylor D et al. Maudsley Prescribing Guidelines 2009.
6. Bazire S. et al. Psychotropic Drug Directory 2010.
7. Bezchlibnyk-Butler et al. Clinical Handbook of Psychotropic Drugs, 16th edition.
8. Prescribing Observatory for Mental Health UK (POM-UK). Monitoring of patients prescribed lithium. Prepared by the Prescribing Observatory for Mental Health-UK for East London NHS Foundation Trust. 2013 The Royal College of Psychiatrists.

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), or e-GFR, or creatinine clearance • **Thyroid Function tests (TFTs):** TSH and T4 • **Full Blood Count** • **Weight and BMI** • **ECG**- in 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 change brand, then need to monitor lithium level as at initiation.	• **Start at 400mg** at night (200mg 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 and **1 week** after every dose change until levels are stable. • 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, and monitor closely for early signs of mania and depression.
Monitoring	• **Plasma lithium:** Monitor plasma level after **1 week** of starting and **1 week** after every dose change until levels are stable and then every **3 months.** • **U&Es and TFTs** every 6 months • **Weight or BMI** annually • **Physical assessment** for signs of toxicity. • More frequent tests if there is evidence of clinical deterioration, abnormal results, a change in sodium intake, or symptoms suggesting abnormal renal or thyroid function e.g unexplained fatigue. Or other risk factors, or other prescribed medication which interacts with lithium e.g. ACE inhibitors, NSAIDs or diuretics.
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 clinician 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.

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

Symptoms of lithium toxicity:

<table>
<tr><td>MILD</td><td>• Nausea
• Diarrhoea</td><td>• Severe fine tremor</td><td>• Poor concentration</td></tr>
<tr><td>MODERATE</td><td>• Vomiting</td><td>Cerebellar signs:
• Coarse tremor
• Cerebellar ataxia
• Slurred speech</td><td>• Drowsiness
• Disorientation</td></tr>
<tr><td>SEVERE</td><td>• Incontinence</td><td>• Choreiform movements
• Parkinsonism
• Myoclonus
• Cerebellar dysfunction
• Spasticity
• EEG abnormalities
• Renal failure
• Seizures</td><td>• Apathy
• Coma</td></tr>
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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.
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 Lithium Monitoring Form

Name: **Date of Birth:**

Height:

		Baseline	CM	CM	CM	CM
	Date					
1	**U&Es**					
2	**eGFR**					
3	**Thyroid Function**					
4	**Lithium level**					
5	**ECG**					
6	**BP**					
7	**Pulse**					
8	**Weight**					
9	**BMI**					
10	**Calcium**					

Note: Essential Monitoring: Numbers 1-5

Additional Monitoring: Numbers 6-10

CM: Continuous Monitoring

Appendix 4

Lithium

Referral Criteria

Prescribing responsibility will only be transferred when the consultant and the patient's GP consider the patient's condition to be stable or predictable.
Referral of the patient to the GP will be subject to the GP's agreement. The shaded 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.

Areas Of Responsibility

GP's responsibilities	Consultant's responsibilities
To prescribe monthly supplies of lithium To refer back to the consultant if: Patient relapses Patient intolerant of side-effects Non-compliance is suspected To monitor U&Es, renal function and TFTs every 6 months To monitor lithium levels every 3 months To monitor weight or BMI annually To assess for signs of toxicity More frequent tests if there is evidence of clinical deterioration, abnormal results, a change in sodium intake, or symptoms suggesting abnormal renal or thyroid function e.g. unexplained fatigue. Or other prescribed medication which interacts with lithium e.g. ACE inhibitors, NSAIDs or diuretics	Outpatient appointments every 1-12 months based on clinical need

Communication and Support

i. Hospital contacts:	ii. Out of hours contacts and procedures:
name: telephone no: fax no: email:	**East London NHS Foundation Trust** The duty doctor, duty nurse in charge and on-call pharmacist can all be contacted via the main switchboard.
iii. Specialist support/resources available to GP including patient information	

Clinical Information

<table>
<tr><td>Indications</td><td colspan="3">Mania and hypomania
Prophylaxis of bipolar affective
Recurrent depression
Control of aggressive behaviour or intentional self harm</td></tr>
<tr><td>Place in therapy</td><td colspan="3">Lithium may be used as first line therapy in acute mania and for the prophylaxis of bipolar illness.
Lithium may also be used as an adjunct to antidepressants when there has been an insufficient response to an antidepressant alone.</td></tr>
<tr><td>Therapeutic summary</td><td colspan="3">Lithium is a mood stabiliser. It is used in acute mania and in the prophylaxis of bipolar illness. Lithium also has antidepressant properties</td></tr>
<tr><td>Prescribing
Note that various lithium preparations are not interchangeable, preferable to prescribe by brand name i.e. Priadel or Camcolit.

If change band, then need to monitor lithium level as at initiation.</td><td colspan="3">• Start at 400mg at night (200mg 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 staring and 1 week after every dose change until levels are stable.
• 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 anitmanic agent). If lithium treatment stopped or is about to be stopped abruptly, consider changing to an atypical antipsychotic or valproate, and monitor closely for early signs of mania or 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>Adverse effects</td><td>Adverse effect</td><td>Frequency (in maintenance therapy)</td><td>management</td></tr>
<tr><td></td><td>Weight gain</td><td>Common</td><td>Give advice on diet and exercise.</td></tr>
<tr><td></td><td>Hypothyroidism</td><td>Common</td><td>Refer to consultant.</td></tr>
<tr><td></td><td>Polyuria and polydipsia</td><td>*Uncommon</td><td>Give advice on reducing fluid intake.</td></tr>
<tr><td></td><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></td><td>Nausea/vomiting</td><td>*Uncommon</td><td>Give after food. Use a slow release preparation.</td></tr>
<tr><td></td><td>Dermatological effects (including exacerbation of existing dermatological conditions)</td><td>Uncommon</td><td>Refer to consultant.</td></tr>
<tr><td></td><td>Sexual dysfunction (decreased libido, erectile dysfunction, priapism and decreased sperm motility)</td><td>Uncommon</td><td>Refer to consultant.</td></tr>
<tr><td></td><td>Fine tremor</td><td>Uncommon</td><td>Refer to consultant.</td></tr>
<tr><td></td><td>**Toxicity (see below)
N.B. can be fatal</td><td>_</td><td>Stop lithium and refer to A&E.</td></tr>
<tr><td></td><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 1</td></tr>
</table>

<table>
<tr><td></td><td>week after every dose change until levels are stable and then every 3 months.
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Weight or BMI annually
Physical assessment for signs of toxicity.
More frequent tests if there is evidence of clinical deterioration, abnormal results, a change or unexplained fatigue. Or other risk factors or other prescribed medication which interacts with lithium e.g. ACE inhibitors, NSAIDs or diuretics.</td></tr>
<tr><td>Clinically relevant drug interactions</td><td>The use of lithium with ACE inhibitors, diuretics and some NSAIDs may lead to lithium toxicity, which in some cases may be fatal. Sodium and fluid restriction may lead to lithium toxicity (see below). Theophylline and excess sodium may reduce lithium levels.</td></tr>
<tr><td>Management of blood levels and signs of toxicity</td><td>• 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:
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• Lithium level > 1.5 mmol/l <u>AND/OR</u> signs of MILD toxicity:
Stop lithium, immediate referral to clinician 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.
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• Coma</td></tr>
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Appendix 5 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	Carbamazepine, phenytoin, valproate	Increased neurotoxicity of both drugs at therapeutic doses Valproate may aggravate tremor
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
Antiepileptics	Carbamazepine and phenytoin Topiramate	Neurotoxicity may occur without any increase of lithium plasma level Altered Lithium level possible
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