Guidelines on the Safe Use of Lithium in Adults

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Issue	Date Amended	Section / Page	Author/ Amended by	Summary of Change
1	November 2017			New guidance
1.1	June 2018	Page 2 - 3 Page 4 Page 5 Page 12 Page 14		• Addition of information about Lithium app • Addition of doses for both tablets and liquid Priadel • Addition of shared care arrangements • Addition of contraindications and precaution • Changes in guidance for monitoring frequency for calcium levels and renal/ thyroid function
1.2	November 2018	Page 4 Page 5 Page 7 Page 10		• Removed duplicate information for initiation of lithium • Monitoring recommendations changed to usually 12 hours post dose lithium plasma levels taken • Removed duplicate information for continuation of lithium • Dosing information moved from page 4 to page 10 • Addition of Li-liquid preparation and dosing information • Addition of monitoring recommendations

Introduction

These guidelines are to ensure the safe use of lithium in adults in Hertfordshire Partnership University NHS Foundation Trust (HPFT) services.

In 2009, NHS Improvement (formerly known as the National Patient Safety Agency (NPSA))[1] published 'Safer Lithium Therapy'. This stated that service users prescribed lithium must be monitored in both primary and secondary care, with results shared between sectors and with the service user.[1] All healthcare organisations in the NHS where lithium therapy is initiated, prescribed, dispensed and monitored should ensure that:

- Service users prescribed lithium are monitored in accordance with NICE guidance.[2]
- There are reliable systems in place to ensure blood test results are communicated between labs and prescribers.
- At the start of lithium therapy and throughout their treatment, service users receive appropriate ongoing verbal and written information and a record to track lithium plasma levels and relevant clinical tests.
- Prescribers and pharmacists check that blood tests are monitored regularly and that it is safe to issue a repeat prescription and/or dispense the prescribed lithium.
- Systems are in place to identify and deal with medicines that might adversely interact with lithium therapy.

Service users should be informed of common adverse effects, drug interactions and symptoms of lithium toxicity. There are many clinically significant interactions with over-the-counter (OTC) medicines, alternative and prescription medicines. Maintaining an adequate fluid and salt intake is important as this can affect lithium plasma levels. Lithium has the potential to interfere with kidney and thyroid function.

Purpose and Scope

To provide guidance on the safe use of lithium within Hertfordshire Partnership University NHS Foundation Trust (HPFT).

Please consult relevant national and/or local guidelines or contact Pharmacy for specific advice.

This document does not aim to provide full prescribing guidelines and other relevant sources of information (see below) and HPFT policies should be consulted for guidance on the safe and effective prescribing of lithium. This is in addition to the relevant NICE Clinical Guidelines:

- NPSA. Safer lithium therapy. Available at: http://www.nrls.npsa.nhs.uk/alerts/?entryid45=65426
- British National Formulary (BNF)
- Summary of product characteristics (SPC)
- The Maudsley Prescribing Guidelines in Psychiatry. 12th Edition
- Psychotropic Drug Directory 2016
- HPFT Physical Health Policy

The link below can be used to order Lithium Therapy booklets to provide to service users:

NPSA Lithium Pack Order Form

There is also a lithium app called NHS Physical Health Monitor (for Lithium) which can be downloaded onto smartphones. With the app, users can:

- Record lithium treatment and levels
- Set health check reminders

- Record and email health check results
- Record mood and sleep
- Store emergency contacts and information
- Access a learning section with FAQs and Dos and Don'ts
- Password protect the app and their information

Download the Apple IPhone version of the Lithium App here:
https://itunes.apple.com/gb/app/nhs-physical-health-monitor-for-lithium/id1040946243?mt=8

Download the Android version of the Lithium App here:
https://play.google.com/store/apps/details?id=com.incentivated.nhs.HealthMonitor

The App can be used alongside/instead of the Lithium Therapy booklet.

Indications[3, 4]

The licensed indications for lithium are:

- Treatment and prophylaxis of mania (acute manic and hypomanic episodes).
- Treatment and prophylaxis of bipolar disorder.
- Treatment and prophylaxis of recurrent depression where treatment with other antidepressants has been unsuccessful.
- Treatment and prophylaxis of aggressive or intentional self-harming behaviour.

Pre-initiation of lithium in community and inpatient setting

The service user and other healthcare staff involved in the service user's care must be involved in the decision to start lithium. Consideration must be given to:

- Clinical presentation.
- Other co-morbidities including alcohol and illicit substances.
- Maintaining an adequate food and fluid intake.
- Lithium can cause nephrotoxicity which can lead to a reduction in eGFR and therefore raise lithium plasma levels.
- Lithium plasma levels >0.8mmol/L are associated with a higher risk of adverse effects and lithium toxicity in particular in those aged over 65 years and male.
- Service user preference.
- Potential adverse effects and impact on service user.
- Concurrent medicines and potential interactions (including OTC medicines and alternative medicines).
- Service user understanding and acceptance of the need for regular blood tests.
- Concordance/ adherence with oral medicines, as lithium is only available in oral formulations.
- Recognition of signs and symptoms of lithium toxicity and actions that need to be taken.
- Discuss contraception with female service users of child bearing age.

Baseline monitoring must be completed before starting lithium (see Appendix 1 and Physical Health Policy). Any discussions with the service user (and/ or carer) must be documented on the Electronic Patient Record (EPR), including written and verbal information provided about lithium (see Appendix 2 and 3).

Initiation of lithium in community and inpatient setting

Individual/ staff groups	Responsibilities
All clinical staff groups	• Should familiarise themselves with this guideline. • Should familiarise themselves with the Lithium Therapy booklet and/or lithium app. • Should familiarise themselves with the signs of lithium toxicity and actions to be taken. • Provide a Lithium Therapy booklet. • Inform the service user there is an app that can be downloaded onto smartphones that provides information about lithium and also where lithium levels, kidney checks (eGFR), thyroid function and U&Es can be recorded. • Be aware of the indication, side effect profile, monitoring and common drug interactions. • Discuss with the service user changes in alcohol intake or if they use any illicit substances. • Ensure the service user maintains an adequate food and fluid intake. • Reinforce to female service users (of child bearing potential) to use suitable contraception throughout lithium therapy. It is important to seek specialist advice if the service user is planning a pregnancy, becomes pregnant or is breastfeeding.
Prescriber	• Consult with the service user providing both written and verbal information. This may be delegated to another healthcare professional such as a pharmacist or appropriately trained nurse. Clearly document discussion and information provided in the service user's EPR. See Appendix 2 and 3 for information to be discussed with the service user. • Check baseline tests/ investigations (see Appendix 1) are satisfactory and documented in the service user's EPR and recorded in the Lithium Therapy Record book and/or lithium app before initiating treatment. • Inform the service user there is an app that can be downloaded onto smartphones that provides information about lithium and also where lithium plasma levels, kidney checks (eGFR), thyroid function and U&Es can be recorded. • Lithium must be initiated by brand (due to differences in bioavailability between the products, brands cannot be readily switched). The usual brand of lithium initiated in Hertfordshire is Priadel® for tablets and Priadel® liquid or Li-liquid® for liquid preparations. • Dosage must be individualised depending on lithium plasma levels and clinical response. The dosage necessary to maintain lithium plasma levels within the therapeutic range varies between individuals. The prescriber will be responsible for stabilising the service user and advising on the target range. • An effect may be seen within 5 – 7 days of initiating lithium in manic service users, but may take longer in the depressed bipolar service user. • Lithium has a narrow therapeutic range and therefore regular blood tests are needed. Check the lithium plasma level 4 - 7 days after initiation, dose change, change in brand/formulation or prescribing/ deprescribing of an interacting medication (see Appendix 6). Levels must be checked weekly until stabilised. • Document the lithium plasma level result in the service user's EPR, in the Lithium Therapy Record book and/or lithium app. The brand must be stated in both the Lithium Therapy Record book, on the lithium alert card and/or lithium app.

	• Review and amend the dose in view of the lithium plasma level results if clinically appropriate. Dose adjustments should be made to achieve a lithium plasma level of 0.4 - 1.0mmol/L, to avoid harm due to lithium toxicity and maintain an optimum therapeutic response. • Ensure that any dose change, lithium plasma level and blood test results are communicated to the service user. • Communicate to all healthcare professionals involved in the service user's care (including the GP and care coordinator, if designated) that lithium has been initiated and the lithium plasma level target range (and ensure this is entered in the Lithium Therapy Record book and/or lithium app). During initiation, any lithium plasma levels received must be entered into the Lithium Therapy Record book and/or lithium app and documented in the service user's EPR. • Prescribing of lithium for the indications above will be initiated in HPFT for a minimum of 12 weeks or until stable whichever is longer. Shared care must be formally accepted by the GP, by completion and return of the form provided within the shared care protocol for lithium.
Pharmacist	• Provide advice to the medical and nursing team on changes in dose, formulation or brand, contraindications, precautions, drug interactions and monitoring requirements. • Consult with the service user providing both written and verbal information about lithium if this has not already been provided, or if further information is requested. • Ensure lithium plasma levels are checked within 4 - 7 days of initiation, after every dose change during initiation and monitored weekly until stable and within the recommended range. • Ensure baseline monitoring has been carried out and is recorded in the Lithium Therapy Record book and/or lithium app. • Ensure the service user's Lithium Therapy Record book and/or lithium app contains the most recent blood test/investigation results and the corresponding doses of lithium. If not and results are accessible, record this information in the Lithium Therapy Record book and/or app, and communicate the lithium plasma level with the service user if appropriate. • Supply lithium in accordance with the prescription. **Inpatients** • Screen the prescription for appropriateness, safety and legality, and endorse the chart (refer to HPFT Clinical Pharmacy Standards for pharmacists and technicians). • Endorse on the medication chart when a Lithium Therapy booklet has been supplied. • Document the date and current lithium plasma levels on the medication chart. • Document any discussions and information provided in the service users' EPR. **Community** • Ensure an appropriate dose is prescribed with clear instructions on use, NOT 'as directed'. • Community pharmacists may not have access to blood test results and therefore must contact the prescriber to check the lithium plasma levels before dispensing the prescription. • Refer the service user back to the prescriber if there are any concerns with the lithium therapy.

Nurse (inpatient setting and if designated care co-ordinator in the community)	• Observe the service user for adverse effects (see Appendix 4 – 7). • Monitor and immediately report any signs or symptoms of lithium toxicity, or if there are any increased risk factors for developing this. Nursing staff may perform the LiSERs rating scale to monitor side effects[7] (see Appendix 7). • Ensure the nursing plan reflects the service user is prescribed lithium.

If the designated care coordinator in the community is a not a registered nurse or there is no care coordinator in place, the prescribing clinician must ensure that a robust care plan is in place to ensure that any signs or symptoms of lithium toxicity are identified promptly and managed appropriately.

Continuation of lithium or on discharge to the community

Individual/ staff groups	Responsibilities

All clinical staff groups	• Should familiarise themselves with this guideline and the Lithium Therapy booklet and/or lithium app.
	• Inform the service user there is an app that can be downloaded onto smartphones that provides information about lithium and also where lithium levels, kidney checks (eGFR), thyroid function and U&Es can be recorded.
	• Provide ongoing advice/ monitoring of general health of the service user such as maintaining an adequate food and fluid intake.
	• Ensure that the service user has a Lithium Therapy booklet and/or is using the lithium app, lithium plasma level and other monitoring parameters are within range and are recorded appropriately (see Appendix 1).
	• Should check and monitor for any signs of lithium toxicity (see Appendix 4) and actions to be taken. Inform the relevant consultant psychiatrist.
	• Discuss with the service user (see Appendix 2, 3 and 7):
	  ○ potential interactions
	  ○ side effects
	  ○ the significance of blood test results
	  ○ reinforce the importance of concordance/adherence and blood test results
	• Inform female service users (of child bearing potential) if they are pregnant or planning a pregnancy to use suitable contraception throughout lithium therapy. It is important to seek specialist advice if the service user is planning a pregnancy, becomes pregnant or is breastfeeding.

Prescriber	• The usual brand of lithium prescribed within Hertfordshire is Priadel® for tablets and Priadel® liquid or Li-liquid for liquid preparations. If a service user is admitted on a different brand, consider switching to the usual brands prescribed in Hertfordshire. Refer to the BNF, SPC or consult with a pharmacist for clarification. • Ensure the service user fully understands their treatment and monitoring requirements and if not, provide a clear explanation. • Check if the service user has had blood tests/investigations carried out in accordance with the monitoring specified in Appendix 1 and these are available in the EPR, the Lithium Therapy Record book and/or lithium app. Communicate the results to the service user and GP. If there are no current blood tests/investigations available, repeat samples must be performed and requested urgently before prescribing or changing the dose, brand or formulation. • Check if the service user has any signs of lithium toxicity (see Appendix 4). If the service user is presenting with signs of lithium toxicity a lithium plasma level and renal function test must be performed and requested urgently. Lithium treatment should be withheld until the results are available. • Take appropriate action if blood tests are abnormal. Communicate these to all healthcare professionals involved in the service user's care including the GP and care coordinator (if designated) (see Appendix 5). It is important to check the previous results for trends. • Check the previous results and consider adjusting the dose or increasing the frequency of monitoring where there is an upward trend in lithium plasma level towards toxic levels. If toxicity is suspected, a lithium plasma level must be requested urgently and stop lithium immediately. • Monitor renal function (eGFR) and note if there is a decline in renal function as this can impact on lithium plasma levels. If there is a worsening of eGFR, the

	decision to continue lithium depends on clinical efficacy and degree of renal impairment. Consider seeking advice from a renal specialist. • Communicate with the GP and service user regarding further supplies of lithium (and if there are any changes), when the next monitoring is due and who is responsible for the ongoing monitoring. The responsibilities should be documented on the service user's EPR (see Safe Use of Lithium in Adults, Shared Care Protocol). • Note: Lithium must be initiated by HPFT specialist prescribers for a minimum of 12 weeks or until stable whichever is longer. GPs will need to formally accept shared care by completing the Shared Care Agreement Form. This form will need to be scanned onto the service user's EPR.
Pharmacist	• Ensure lithium plasma levels are available within the last 3 months (6 months if the lithium plasma levels are stable) and check who if responsible for the ongoing monitoring (see Appendix 1 for frequency of monitoring). • Consider the trend in lithium plasma level results and alert the prescriber if there is an upward trend towards the toxic range so that action can be taken before toxicity develops. Conversely, sub therapeutic lithium plasma levels should be discussed with the prescriber as this may indicate poor concordance/ adherence or a need to increase the lithium dose. • In case of abnormal renal function and thyroid function tests, liaise with the relevant consultant psychiatrist to discuss the action plan. • Discuss with the prescriber sub-therapeutic lithium plasma levels as this may indicate poor concordance/adherence or a need to increase the lithium dose. • Check for any interacting medicines that have been newly started or stopped, ensuring that more frequent monitoring is carried out until lithium plasma levels are stable. Discuss with the prescriber. **Hospital pharmacists** • Prior to discharge, ensure the Lithium Therapy Record book and/or app has been updated with all the relevant blood test results, including the most recent lithium plasma level. • Inform the service user to notify the community pharmacist when purchasing any over-the-counter medicines. Inform the service user to avoid purchasing Non-Steroidal Anti-Inflammatory Drugs (NSAIDs) without medical input as these significantly interact with lithium. • Ensure the discharge notification details the most recent lithium plasma level, dose, formulation and brand, when the next blood test is due and that a Lithium Therapy booklet has been provided or the service user is using the lithium app. **Community** • Ensure an appropriate dose is prescribed with clear instructions on use, NOT 'as directed'. • Check the Lithium Therapy Record book and/or lithium app has been updated with all the relevant blood test results, including the most recent lithium plasma level. Contact the prescriber if these are not available. • Refer the service user back to the mental health team/ GP if there are any concerns with lithium therapy. • Ensure that lithium monitoring is carried out in line with Appendix 1 before issuing a repeat prescription.
Care co-ordinator (if a registered nurse)	• Identify if the service user requires any support with obtaining their medication supply from a community pharmacy (either make arrangements or speak to the team pharmacist). • Monitor and document any side effects (see Appendix 7), signs/ symptoms of

	lithium toxicity (see Appendix 4) and degree of concordance/adherence with treatment. Inform the prescriber of any concerns. • Discuss with the prescriber if the service user is considering stopping treatment after a period of relatively stable mood. • In case of abnormal renal function and thyroid function tests, liaise with the relevant consultant psychiatrist to discuss the action plan.
GP	• Respond to the consultant request for shared care once dose is stabilised within two weeks of receipt of request. • If shared care is declined: clinical rationale to be provided and GP to copy service user into decline letter so they are aware of who will be providing further supplies of medication. • Ensure lithium monitoring is carried out in line with Appendix 1 and the Lithium Therapy Record book and/or lithium app is updated before issuing a repeat prescription. • Discuss any concerns relating to lithium therapy with the consultant psychiatrist for the service user (e.g., upward trends in lithium plasma levels, concordance/adherence issues, discontinuation and/or suffers a worsening in mental state). • If signs of lithium toxicity are present, stop treatment immediately, check lithium plasma level urgently and monitor the service user. Depending on the severity of symptoms, refer to A&E (see Appendix 4). Inform the consultant psychiatrist. • In case of abnormal renal and thyroid function tests, liaise with the relevant consultant psychiatrist to discuss the action plan (see Appendix 5). • Ensure that interactions are checked before commencing any new medicines (see Appendix 6, current BNF or discuss with a pharmacist). Put in place additional monitoring if an interacting medicine is commenced. Ensure the service user and consultant psychiatrist are informed of any changes to medications to avoid any harm. • Refer back to secondary care if there are any concordance/adherence issues or if the service user discontinues treatment and suffers a worsening mental state. Inform the relevant consultant psychiatrist to discuss the action plan (see Appendix 5). If the service user is no longer with a community mental health team, SPA can be contacted to seek advice should there be any particular concerns.

If the designated care coordinator in the community is a not a registered nurse or there is no care coordinator in place, the prescribing clinician must ensure that a robust care plan is in place to ensure that any signs or symptoms of lithium toxicity are identified promptly and managed appropriately.

Dose recommendations:

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

Doses should be taken at the same time each day.
Once daily dosing at night or twice daily dosing is preferred as more information on these regimes and dose adjustments are available.

Monitoring
Lithium has a half-life of 18 – 36 hours.
On initiation: Lithium plasma levels 4 - 7days after initiation, after every dose change, change in interacting medication. Lithium plasma levels must be checked weekly until stabilised. Please refer to Appendix 1 for monitoring requirements once stabilised.

Lithium plasma levels are usually taken 12 hours post-dose. Lithium plasma levels taken 24 hours post-dose can be considered. Target ranges for lithium plasma levels must be individualised.

Target lithium plasma levels:

	12 hours post-dose	24 hours post-dose
Once daily dosage	0.7 – 1.0 mmol/L	0.5 – 0.8 mmol/L
Twice daily dosage	0.5 – 0.8 mmol/L	-

Consider maintaining a lithium plasma level between 0.8 - 1.0mmol/L (12hours post-dose monitoring) for a trial period of at least 6 months for people who:

- Have had a relapse while taking lithium in the past or
- Are taking lithium and have subthreshold symptoms with functional impairment

Interactions
Consider the impact of lithium interactions with other medicines (see Appendix 6). It is also important to note that changes in fluid and salt intake can have an effect on lithium plasma levels.

Contraindications (Refer to BNF and SPC)

- Cardiac disease, including Brugada syndrome, or a family history of Brugada syndrome
- Severe renal impairment
- Untreated hypothyroidism
- Breast feeding
- Hyponatraemia, including dehydrated patients, those on a low sodium diet or conditions predisposing to low sodium (e.g. Addison's, severe diarrhoea and/or vomiting and concurrent infections, especially if sweating profusely)
- Hypersensitivity to lithium or to any of the excipients

Precautions

- In mild/moderate renal impairment, closely monitor lithium plasma levels.
- Fluid/electrolyte imbalance – advise patient of risks and action to be taken in case of nausea, vomiting, diarrhoea, excess sweating and/or other conditions leading to salt/water depletion as increased monitoring and/or a decreased dose may be required.
- Risk of convulsions when lithium is administered in combination with drugs which lower the epileptic threshold, or in epileptics.
- Benign intracranial hypertension may occur – service user to be advised to report persistent headache or visual disturbance.
- Avoid in service users with congenital long QT syndrome and prescribe with caution to those with predisposing factors for QT prolongation (uncorrected hypokalaemia, bradycardia, predisposing drugs).
- Elderly service users may exhibit toxicity at serum levels ordinarily tolerated by younger service users and lithium excretion may be reduced due to age related decreases in renal function in the group of service users.

Stopping lithium

- If stopping lithium is planned, discuss with the service user (and carers) and other healthcare staff involved in the service user's care. Reduce the dose gradually over at least 4 weeks, and preferably up to 3 months, even if the person has started taking another mood stabilising drug.
- If abrupt discontinuation is necessary, the service user should be carefully observed for the recurrence of signs of mania or depression for at least 3 months after stopping.
- Inform the service user how to recognise early signs of relapse and to report any symptoms of relapse, depression or mania.
- Inform the GP and care coordinator that lithium is being stopped and the reasons why, and advise to monitor the service user closely for signs of mania and depression.
- Continue monitoring mood and mental state during the dose reduction and for at least 2 years after medication has stopped for early signs of mania and depression.

References:

1. National Patient Safety Agency (NPSA) Alerts Summary Lithium December 2009
2. The National Institute for Health and Care Excellence. Bipolar disorder: assessment and management CG185 updated 2016 (accessed via https://www.nice.org.uk/guidance/cg185)
3. BNF online (accessed via www.medicinescomplete.com)
4. Summary of Product Characteristics. Priadel. Sanofi. (accessed via www.medicines.org.uk)
5. Goodwin et al. Evidence-based guidelines for treating bipolar disorder: Revised third edition recommendations from the British Association for Psychopharmacology. Journal of Psychopharmacology 2016 p.1-59
6. The Maudsley Prescribing Guidelines in Psychiatry. 12th Edition
7. Haddad P, Wieck A, Yarrow M, Denham P. The Lithium Side Effects Rating Scale (LISERS) development of a self-rating instrument. European Neuropsychopharmacology 9(5): 231-232

Appendices
Appendix 1: Baseline and ongoing monitoring requirements

	BASELINE	MAINTENANCE
Serious Mental Illness (psychosis/bipolar disorder)	Full Blood Count (FBC) Urea and Electrolytes (U&Es) Renal function (serum creatinine or e-GFR) Liver Function Tests (LFTs) Fasting blood glucose (if possible), HbA_{1c} Blood lipid profile (fasting if possible) Prolactin level ECG if clinically indicated BP, weight, waist circumference	Annual health check* FBC annually U&Es 6 monthly Renal function (serum creatinine or e -GFR) 6 monthly LFTs annually Fasting (if possible) blood glucose, HbA_{1c} annually Blood lipid profile (fasting if possible) annually
Lithium	Lithium plasma level (usually 12 hours post dose) 4 - 7days after initiation until therapeutic level is reached & one week after each dose change U&Es e-GFR (renal function) Thyroid function tests Serum calcium Cardiac function: ECG if clinically indicated Blood pressure Weight and height (BMI)	Annual health check* Lithium plasma level – 4 - 6 monthly once stable** e-GFR - 6 monthly*** U&Es- 6monthly Thyroid function tests – 6 monthly*** Serum calcium 6 monthly Fasting (if possible) blood glucose, HbA1c- annually Blood lipid profile (fasting if possible)- annually *Note: monitor lithium plasma levels more frequently if urea and creatinine levels become elevated or eGFR falls over 2 or more tests and assess the rate of deterioration in renal function.*

***Annual Health Check requirements see Physical Health Policy**

**NICE Guidelines for Bipolar Disorders 2014 recommends to monitor lithium plasma levels weekly until a stable therapeutic level is achieved, then every 3 months for the first year and then every 6 months thereafter if stable, unless the service user falls into one of the following groups of people, where more frequent monitoring should be considered:

- Older adults
- Those taking other medicines that interact with lithium
- Those who are at risk of renal or thyroid dysfunction, raised calcium levels or other complications
- People who have poor symptom control
- People with poor adherence
- People whose last lithium plasma level was 0.8mmol/L or higher

*** eGFR and TFTs to be monitored more often if there is evidence of impaired renal or thyroid function, raised calcium or an increase in mood symptoms that might be related to impaired thyroid function.

Appendix 2: Consultation tips for healthcare professionals when providing information to service users/ carers about lithium

Before consultation: ensure you gather some background information regarding the service user's previous medical and drug history, current mental state and care plan.

Indication:

- Treatment and prophylaxis of mania (acute manic and hypomanic episodes).
- Treatment and prophylaxis of bipolar disorder (also known as manic depression).
- Treatment and prophylaxis of recurrent depression where treatment with other antidepressants has been unsuccessful.
- Treatment and prophylaxis of aggressive or intentional self-harming behaviour.

The decision to use lithium is usually taken by secondary care.

Onset of action: an effect may be seen within 5 – 7 days of initiating lithium in a manic service user, but may take longer in the depressed bipolar service user. Please advise the service user that it may take some time to find the correct dose for them, and that they should not attempt to make any changes themselves unless specifically told to do so by a healthcare professional.

Dosing regimen: advise that tablets should be swallowed whole and not chewed as most are modified release preparations. If they cannot be swallowed whole, they are scored and can be broken in half and then swallowed. For liquid lithium preparations, an oral measure should be provided to measure the correct amount. It should be taken as directed on the medicine label at regular times. Usually the liquid preparation is taken twice daily and tablets once daily. If the instructions specify ONCE daily, then it is usually best to take it at bedtime.

Formulations: it is important to continue with the same form and brand of lithium as they are not all bioequivalent. In Hertfordshire the brand used is Priadel®. Service users should inform healthcare professionals of the brand they take when being prescribed or dispensed further lithium.

Duration of treatment: this should be discussed at initiation as people respond differently. As well as treating the illness, lithium also helps to prevent relapse. Once lithium has been started, it may need to be taken for a long time, at least 2 or 3 years, and quite possibly much longer. For it to continue working, lithium must be taken every day as directed.

Adherence: it is important to reinforce adherence even if the service user feels better. Stopping or erratic adherence is associated with a high risk of relapse. Medication must be taken regularly to prevent an episode, rather than after symptoms occur.

Drug/ food interactions: (below is not an exhaustive list – please refer to BNF and/or product SPC)

- ACE inhibitors - decreased lithium clearance may result in toxicity; monitor lithium plasma level and renal function; consider using an alternative antihypertensive. Onset may be insidious, with toxicity occurring after several weeks.
- NSAIDs - including ibuprofen (not aspirin) can decrease lithium clearance which may result in toxicity; avoid combination unless essential; monitor lithium plasma level.
- Diuretics - all diuretics can reduce lithium clearance, but the effect of thiazides is greatest; monitor lithium plasma level closely.
- Carbamazepine, some antidepressants, diltiazem, verapamil, methyldopa, antipsychotics - enhanced risk of neurotoxicity; monitor carefully.
- Maintain an adequate fluid intake (especially in hot weather) and avoid dietary changes which reduce or increase salt (sodium) intake, including dieting without consulting a doctor.
- Alcohol and illicit drugs - both can impair psychomotor skills and can cause dehydration which can precipitate lithium toxicity.

Side effects:

- Initially drowsiness, however this tends to wear off after a couple of weeks. Service user should be advised to take care if (s)he intends to drive or use tools or machines whilst taking lithium.
- Declining or worsening of renal function needs monitoring regularly.
- Common - mild gastrointestinal effects such as nausea, a general discomfort and vertigo may occur initially, but frequently disappear after the first few days of administration. Metallic taste, weight gain, fatigue, headache, tremor, acne, psoriasis, polyuria, hypothyroidism and benign T wave changes on ECG.
- Infrequent - nephrogenic diabetes insipidus with polydipsia and polyuria, memory impairment, hair loss and hyperparathyroidism.
- Rare - cardiac arrhythmias and hyperthyroidism.

Signs and symptoms of lithium toxicity

Service user must seek immediate medical attention if s(he) develops any of the following signs or symptoms:

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

Alcohol: caution as it may potentiate sleepiness and CNS depression. It can be dehydrating but excess volume can also have a dilutional effect which could affect lithium plasma levels.

Monitoring: careful monitoring needs to be carried out. Lithium plasma levels are usually taken 12 hours post-dose 4 – 7 days after initiation, after a change of dose/formulation or introduction of interacting medication. Weekly monitoring should follow until the dose is stable, and then repeat every 3 months for the first year, then 6 monthly thereafter. If there are any complicating issues, more frequent monitoring may be indicated.

General information: be alert for signs and symptoms of lithium toxicity including: blurred vision, confusion, slurred speech, drowsiness, extreme thirst, frequent urination, dizziness, nausea and vomiting, severe tremor or twitching. If these occur, stop taking the lithium and seek medical attention urgently.

Maintain a normal diet with regular salt and fluid intake. Avoid drastic changes in diet or 'crash diets'. Drink more non-alcoholic fluid (preferably water) during hot weather and bouts of diarrhoea and vomiting, to avoid toxicity.

If weight gain or weight-related problems are experienced, the doctor may be able to organise a dietician review.

Provide written information: patient information leaflets (PILs) are usually provided with medication every time it is collected from the pharmacy. 'Purple' Lithium Therapy booklets are provided to record blood test results and general information on lithium. The purple lithium therapy booklet is important to record information to pass on to other healthcare professionals. The Choice and Medication website has patient information leaflets as well, which can be accessed via http://www.choiceandmedication.org/hertfordshire/ . There is also a lithium app which service users should be made aware of which can be used as an alternative to the purple lithium therapy booklet.

Document discussion in service user's EPR: any discussion must be documented on the service user's EPR, including any information provided (both verbal and written).

Appendix 3: Lithium Counselling Checklist

Service user name: **NHS no.:**

	Counselling point	Staff name	Comments
1.	Indication for lithium		
2.	Basic mode of action and onset of action		
3.	Purpose and importance of purple Lithium Therapy booklet. Provide a booklet for new service users and for service users where current booklet cannot be obtained. There is also an app that can be downloaded onto smartphones		
4.	Monitoring • Blood monitoring requirements and frequency • Lithium plasma levels • Target lithium plasma levels • Frequency of monitoring and where to go for monitoring • Always bring purple Lithium Therapy booklet to appointments		
5.	Dosing: • Different formulations/ brands • Take tablets at same time of day, preferably at night • Importance of adherence (ways to remember taking tablets e.g., calendar, pill reminder, reminder charts etc.)		
6.	What to do if a dose is missed		
7.	What to do if an extra dose is taken		
8.	What to do in the event of an inter-current illness, especially vomiting and diarrhoea and when receiving new medicines		
9.	Side effects of lithium		
10.	Potential drug interactions and 'OTC' medicines (especially NSAIDs)		
11.	Alcohol intake: importance of moderation		
12.	Ensure reliable contraception in women of childbearing age, need to attend anti-natal clinic as soon as possible in case of pregnancy		
13.	Inform all healthcare professionals involved in the service user's care of lithium		
14.	How to obtain further supplies of lithium		
15.	Who to contact for advice/ further information		

All service users must have a purple Lithium Therapy booklet and lithium alert card. The booklet MUST be fully completed and the service user advised to keep the booklet and alert card with him/her at all times, and show it to anyone who may prescribe medication for them, or if they intend to buy medication over the counter at a pharmacy.

Appendix 4: Management of toxic lithium plasma levels or where signs and symptoms of lithium toxicity are present.

If an individual develops toxic lithium plasma levels, the onset of symptoms may be delayed for up to 24 hours, especially in lithium naïve service users.

Toxicity (>1mmol/L)	Symptoms	Management
Asymptomatic (1-1.5mmol/L)	-	➢ Check the time of the blood sample in relation to the dose. ➢ Repeat lithium plasma levels before changing dose. ➢ If correct timing, reduce dose, repeat level in one week. Consider withholding treatment.
Mild (>1.5mmol/L)	Nausea, altered taste, diarrhoea, blurred vision, polyuria, light headedness, fine resting tremor, muscular weakness and drowsiness	➢ **Withhold** lithium. Immediate referral to clinician responsible for follow up. ➢ NB: lithium plasma levels may still be rising. Monitor for moderate/severe signs of toxicity over next 7 days.
Moderate (>2mmol/L)	Increasing confusion, blackouts, increased deep tendon reflexes, myoclonic twitches and jerks, choreoathetoid movements, urinary or faecal incontinence, increasing restlessness followed by stupor and hypernatraemia	➢ **Withhold** lithium. ➢ Immediate referral to A&E for diuresis and inform responsible clinician. ➢ Investigate reason for toxicity. ➢ NB: plasma levels may still be rising. Monitor for moderate/severe signs of toxicity over next 7 days. ➢ Deaths have been reported above 4mmol/L.
Severe	Coma, convulsions, cardiac dysrhythmias including SA block, cerebellar signs, ECG changes (sinus and junctional bradycardia), first degree heart block, hypotension or rarely hypertension, peripheral neuropathy, peripheral vascular collapse and renal failure	

Note: this is a guide for likely symptoms at various toxic levels. A service user may experience severe symptoms at lower levels than stated in the table above especially in older adults.

Consult a pharmacist for 24 hour post-dose monitoring

Lithium is very toxic and clinicians managing service users who have a high lithium plasma level and displaying severe symptoms of toxicity are encouraged to discuss these cases with the Poisons Information Service (Tel: 0344 892 0111).

Appendix 5: Managing abnormal lithium plasma levels, renal function and TFTs

Blood test	Therapeutic range*	Action	
		BELOW therapeutic range	**ABOVE therapeutic range**
Lithium (12 hours post dose. Check timing of level before adjusting dose).	0.4 - 1mmol/L	Discuss with the service user/carer, assess adherence and consider whether a dose increase is clinically indicated, if so, refer to the specialist.	**SAME DAY CONTACT.** Assess for symptoms of toxicity (see Appendix 4). Check if service user is taking prescribed dose of lithium. Service users with levels above 2 mmol/L must be referred to A&E. Progressively increasing levels are usually a consequence of deteriorating renal function. Be more vigilant with elderly service users, or those experiencing side effects which could be signs of toxicity. Withhold lithium treatment.
eGFR	>90ml/min/1.73m^2	Increase the frequency of monitoring of eGFR and lithium plasma levels. May need to decrease lithium dose. If eGFR<60ml/min/1.73m^2 increase monitoring frequency of eGFR and lithium plasma levels. A downward trend in eGFR indicates deterioration in renal function and this requires close monitoring. The decision to continue lithium depends on clinical efficacy and degree of renal impairment. Prescribers should consider seeking advice from a renal specialist. Lithium is contraindicated in severe renal insufficiency.	Not applicable.
Thyroid function	TSH 0.3 – 5.5mU/L Free thyroxine (fT4) 9 - 23pmol/L	Prescriber to assess relevance and treat	If substantially raised (TSH ≥ twice the upper limit), **SAME DAY CONTACT** with service user and agree action. Service users with a sustained increase in TSH of more than twice the upper limit of the reference range, which is confirmed with repeat testing after 2 weeks should be treated with levothyroxine.

*Note: service users differ in their target lithium plasma level e.g., older adults may have a lower target range and therefore may need a dose reduction if the lithium plasma levels are above this.

Appendix 6: Managing lithium drug interactions or drug-disease interaction

Potentially hazardous interactions. Combined administration should be avoided

Drug	Interaction effects	Risk Reduction Measures
ACE inhibitors e.g., enalapril, lisinopril Angiotensin II antagonists e.g., losartan, candesartan, valsartan	• Lithium toxicity due to sodium depletion. • Concurrent use with caution and close monitoring. • With Angiotensin II antagonists case reports of increase in lithium plasma level.	• Not clinically important in every service user. Lithium plasma level can increase over several weeks. • Monitor closely for signs of lithium toxicity and consider taking lithium plasma level. • May need to reduce lithium dose. • With Angiotensin II antagonists increase monitoring especially during the first couple of months. Note: check each medication for individual effects on lithium as some agents are safer to use with lithium.
Analgesics (NSAIDs) e.g., ibuprofen, diclofenac	Excretion of lithium reduced.	• Avoid concomitant use. • Note: aspirin does not affect lithium plasma levels.
Anti-arrhythmics e.g., amiodarone	Increased risk of QT prolongation.	• Avoid concomitant use. Manufacturer contraindicates combined use.
Domperidone	• Lithium is associated with QT prolongation or torsade de pointes. • Dangerous QT prolongation may occur if it is given with domperidone.	• Contraindicated. Consider an alternative antiemetic.
Hydroxyzine/ mizolastine	• Antihistamines such as hydroxyzine and mizolastine, and lithium are associated with a small increased risk of QT prolongation. • Concurrent use may increase the risk.	• Contraindicated. Consider an alternative antihistamine.
Methyldopa	• Neurotoxicity may occur without increasing lithium plasma concentration.	• Avoid concomitant use if possible.
Thiazide Diuretics e.g., bendroflumethiazide	• Increase lithium plasma levels, therefore increased risk of lithium toxicity. • This is a well-established and potentially serious interaction.	• Avoid if possible. Other diuretics may be safer such as loop diuretics. • Consider a lithium dose reduction and monitor lithium plasma levels.

Less significant interactions- usually without serious consequences

Drug	Interaction effects	Risk Reduction Measures
Alcohol	Increased tremor/shakiness with chronic alcohol use.	
Antibiotics e.g., metronidazole, doxycycline, tetracycline, levofloxacin	Reduced lithium excretion leading to increased lithium plasma levels.	Ensure service user is aware of the symptoms of lithium toxicity and report them immediately if they occur.
Anticonvulsants e.g., valproate, carbamazepine, phenytoin	• Increased neurotoxicity of both drugs at therapeutic doses. • Valproate may aggravate tremor.	If neurotoxicity develops, stop lithium.
Antidepressants e.g., mirtazapine, SSRIs, TCAs and venlafaxine	• Synergistic antidepressant effect in treatment resistant service users may increase lithium tremor. • Increase lithium plasma level, possible neurotoxicity and serotonergic effects.	Monitor carefully for signs of neurotoxicity.
Antipsychotics	• Increased neurotoxicity possible at therapeutic doses in rare cases. • Increased risk of QT prolongation.	• Monitor for risk of QT prolongation. • Monitor for signs of neurotoxicity.
Calcium channel blockers e.g., diltiazem, verapamil	Increased risk of neurotoxicity with symptoms such as ataxia, confusion and somnolence.	Monitor for signs of neurotoxicity.
Muscle relaxants e.g., baclofen	• Lithium enhances the effect of muscle relaxants. • Hyperkinesis caused by lithium is aggravated by baclofen.	Monitor for signs of hyperkinesis.
Parasympathomimetics	Lithium antagonises the effects of neostigmine and pyridostigmine.	
Sodium bicarbonate containing antacids e.g., Gaviscon®	Excretion of lithium increased by sodium bicarbonate therefore, reduced lithium plasma levels.	Change to an alternative antacid with lower sodium content.
Theophylline/ aminophylline	Increased excretion of lithium. Reduced lithium plasma level. Depressive and/ or manic relapse may occur if the lithium dose is not adjusted.	Monitor lithium plasma levels if theophylline is stopped, started or altered.

Drug-Disease Interaction

- If renal impairment exists, avoid use of lithium (if possible) or reduce dose and closely monitor serum-lithium concentration.
- Cardiac disease and conditions with sodium imbalance (e.g., Addison's disease) will require dose reduction or discontinuation. Similarly, in severe diarrhoea and/or vomiting and in concurrent infection (especially if sweating profusely).
- Psoriasis: risk of exacerbation.
- Addison's disease or other conditions with a sodium imbalance and in severely debilitated or dehydrated service users.
- Avoid in untreated hypothyroidism.
- Use with caution in service users with myasthenia gravis because exacerbation of this disorder has been reported.
- Previous NMS with lithium as reintroduction has led to recurrences of NMS.

Appendix 7: Lithium Side Effects Rating Scale (LiSERS)[7]

Service user name: **NHS no.:**
Staff completing the form: **Date:**

		No		Yes		
				Mild	Moderate	Severe
1	Increased appetite	☐		☐	☐	☐
2	Increased thirst	☐		☐	☐	☐
3	Increased output of urine	☐		☐	☐	☐
4	Weight gain	☐		☐	☐	☐
5	Thyroid problems (check fatigue, dry skin, constipation)	☐		☐	☐	☐
6	Metallic Taste	☐		☐	☐	☐
7	Feeling restless	☐		☐	☐	☐
8	Dry Mouth	☐		☐	☐	☐
9	Nausea and feeling sick	☐		☐	☐	☐
10	Dizziness	☐		☐	☐	☐
11	Mild tremor (fine tremor)	☐		☐	☐	☐
12	Muscle pains and tension	☐		☐	☐	☐
13	Difficulties in memory	☐		☐	☐	☐
14	Difficulties with concentration	☐		☐	☐	☐
15	Feeling slowed down in my thinking and creativity	☐		☐	☐	☐
16	Sleep problems	☐		☐	☐	☐
17	Ankle oedema	☐		☐	☐	☐
18	Headaches	☐		☐	☐	☐
19	Excessive sweating	☐		☐	☐	☐
20	Psoriasis	☐		☐	☐	☐
21*	Blurred vision	☐		☐	☐	☐
22*	Palpitations or feeling my heart pounding	☐		☐	☐	☐
23*	Feeling drowsy and lethargic during the day	☐		☐	☐	☐
24*	Diarrhoea / vomiting	☐		☐	☐	☐
25*	Severe tremor (coarse tremor)	☐		☐	☐	☐
26*	Confusion	☐		☐	☐	☐
27*	Muscle weakness/ twitching	☐		☐	☐	☐
28*	Lack of Coordination/ unsteady on feet	☐		☐	☐	☐
29*	Slurred speech	☐		☐	☐	☐
30	Other _____	☐		☐	☐	☐

*indicates possibility of a toxic lithium plasma level: consider urgent lithium plasma level if any of these symptoms are reported. The prescriber must be promptly informed if any of these are present.
The form may be scanned onto the service user's EPR on completion.

Appendix 8: Pathology contact details

	Tel:
West Herts Pathology	01442 287 829
East and North Herts Pathology	01438 314 333
Princess Alexandra Pathology	01279 827 391
Royal Free Hospital Pathology	020 8375 1471