NHS FORTH VALLEY
Guideline for the Management of Patients on Lithium

Date of First Issue	24/12/2010	
Approved	December 2019	
Current issue date	25/02/2020	
Review Date	December 2022	
Version	4.0	
EQIA	Yes	16/01/2020
Author / Contact	Tracey Main	
Escalation Manager	Jean Logan	
Group / Committee – Final Approval	Area Drug & Therapeutics Committee	

This document can on request, be made available in alternative formats

NHS Forth Valley

Consultation and Change Record

Contributing Authors:	Michael Cohen, Dr Leslie Cruickshank, Dr Mark Holliday, Jean Logan, Dr Elaine McCabe. Dr Gillian McLean, Tracey Main, & Karen Storey
Consultation Process:	Lithium Short Life Working Group Mental Health Drug & Therapeutics Committee Primary Care Prescribing Group Bipolar ICP group Depression ICP group
Distribution:	Consultant Psychiatrists Mental Health services General Practices Acute services

Change Record

Date	Author	Change	Version
Nov 2012	JBL	Lithium working group members included as contributing authors. Hyperlinks to ICPs included	2
Feb 2015	JBL/TM	Priadel brand as 1st line choice for new patients Sec 7.3 added and appendix 2 Sec 3.2 ECG where cardiovascular risk factors References updated Minor wording amendments	3
14/09/2017	Quality Improvement	Added one month to the review date at the request of Jean Logan to allow time for the review process to finish	3.1

05/09/2019	Nick Higgins	Awaiting National Guideline Update – Add 6 months from today to be, reviewed again. Add Watermark as “Under Review	3.2
October 2018 – Aug 2019	TM/JL	Hyperlink to Depression and Bipolar ICP updated Inclusion of need for patient to be given NPSA Lithium therapy Booklet Dosing of Lithium changed from ‘in the evening’ to ‘at night’ As per national standards: requirement for Calcium bloods added at baseline and 6 monthly thereafter; weight removed and BMI changed to 6 monthly; FBC removed. Section 7.2 added regarding process where a GP practice opts out of the NPT LES. MH pharmacy telephone numbers updated Addition to include brand of lithium in patients record booklet Advice on prescribing in women of child bearing age updated (as per CMO letter) References updated including CMO letter for National standards	4

1. Introduction

The Lithium Short Life Working Group was convened by the Primary Care Drug & Therapeutics Committee to consider the local implementation of the recommendations contained in the National Patient Safety Agency (NPSA) Patient Safety Alert:*Safer Lithium Therapy* (NPSA 2009/PSA005). These guidelines have been, developed by the group to ensure a safe, effective and consistent approach to the prescribing and monitoring of lithium treatment across NHS Forth Valley.

2. Scope

These guidelines include advice to prescribers and other healthcare professionals on managing patients on lithium therapy across NHS Forth Valley.

3. Initiation Phase

Lithium therapy should, be initiated by a specialist in partnership with the patient's General Practitioner. Indications are, detailed within the integrated care pathways for:

- Treatment resistant depression
- Bipolar affective disorder

3.1 The nature of treatment should be, discussed with the patient, including benefits, adverse effects, causes and signs of toxicity, so, that informed verbal consent is obtained, prior to commencing treatment.
Lithium is a known teratogen. In severe mental illness, up to 80% of pregnancies are unplanned. Risks and benefits in relation to childbearing must be, discussed fully with all women of childbearing potential prior to prescription and consent appropriately recorded. This should be, revisited at least annually. Discussion should include review of contraception status and advice/signposting on effective contraception for the duration of prescribing, with preference for long-acting reversible methods.

The patient should, be given a copy of the NPSA Lithium Therapy booklet.

3.2 **Baseline tests** should be carried out prior to commencing treatment:

- ECG for people with cardiovascular disease or risk factors for it
- BMI
- Urea & Electrolytes (Include sodium, potassium, urea, creatinine & eGFR)
- Thyroid function
- Calcium

3.3 Concurrent medication including non-prescribed medicines should be checked for **interactions**, e.g. NSAIDs, ACE inhibitors, angiotensin II inhibitors, diuretics (mainly thiazides), and psychotropic medicines. Refer to Appendix 1 in the BNF for further details.

3.4 Lithium should, be **prescribed by brand name** due to the differences in bioavailability.

3.5 **Initial Dose & Therapeutic Drug Monitoring**.

Lithium has a narrow therapeutic index and should be started at low dose and titrated to achieve a therapeutic level.

The recommended therapeutic range for serum lithium is 0.4-1.0mmol/l on samples taken 12 hours after the preceding dose. Older people are more sensitive to lithium and its side effects therefore the target range for adults over 65 years is 0.4-0.8mmol/l.

The usual starting dose of lithium is 400mg for adults and 200mg for older people. Lithium level should be, checked 5-7 days after starting treatment then weekly until two similar results are, obtained at the same dose. The dose is, normally increased in 200mg increments. There is a linear response between dosing and plasma levels therefore dose increments may, be, adjusted according to the previous level.

The blood sample should be taken 12 hours post dose therefore lithium tablets are usually taken at night. If using liquid preparation in divided doses, the sample should be, taken 12 hours post the evening dose and just before the morning dose.

Different lithium branded preparations vary widely in bioavailability. **Therefore, patients prescribed lithium should always receive the same brand.** Currently there are 3 brands of lithium available – Camcolit ®, Liskonum ® and Priadel ®.

Priadel ® offers the greatest flexibility in dosing for patients and therefore in Forth Valley **Priadel® is the first choice of lithium brand** prescribed for all **new patients.** This information should, be clearly annotated in clinic letters and discharge prescriptions to GPs for any patient newly started on lithium.

4. Maintenance Phase

4.1 **The patient's mental state** should, be monitored on a regular basis via the designated healthcare professional as agreed. A review should be undertaken at least once a year according to the agreed care plan.

4.2 **A physical health check** should, be undertaken annually by the GP (Physical health guideline).

4.3 **Monitoring of serum levels and other tests** should be carried out as follows:

- ECG: annually for patients with cardiac disease
- BMI: 6 monthly
- Urea & Electrolytes: 6 monthly (3 monthly if eGFR<60* or prescribed interacting medicines see section 4.5)
- Thyroid function: 6 monthly
- Calcium 6 monthly
- Lithium level: every 3 months (AND 5-7 days after change in dose or brand)

Consider other medical co-morbidities
*See appendix 1 for managing lithium in abnormal eGFR

Adverse Effects and Toxicity

4.4 Patients should, be monitored for **adverse effects and signs of toxicity**. Adverse effects are usually, related to serum lithium concentration and are less common at levels below 1.0mmol/l. Mild gastrointestinal effects including nausea may occur initially but frequently disappear after the first few days of therapy. Fine hand tremor, polyuria and mild thirst may persist.

Signs of toxicity often occur when lithium plasma concentration is greater than 1.5mmol/l. However, symptoms may occur at levels greater than 1.0mmol/l or indeed at levels below this in older people. **If any signs of toxicity appear then lithium should be, stopped immediately,** plasma lithium level, and urea & electrolytes checked and the patient rehydrated with an increased sodium intake. A serum lithium concentration in excess of 2.0mmol/l is usually associated with severe toxicity and requires urgent treatment via hospital referral.

Toxicity indicators		
Lithium level		***Symptoms include:***
>1.0mmol/l	Mild	Nausea, diarrhoea, blurred vision, polyuria, light headedness, fine resting tremor, muscular weakness and drowsiness
>1.5mmol/l	Moderate	Increasing confusion, blackouts, fasciculation and increased deep tendon reflexes, myoclonic jerks, choreoathetoid movements, urinary or faecal incontinence, increasing restlessness followed by stupor. Hypernatraemia
>2.0mmol/l	Severe	Coma, convulsions, cerebellar signs, cardiac dysrhythmias, sinus and junctional bradycardia and first degree, heart block. Hypotension or rarely hypertension, circulatory collapase and renal failure

Risks of toxicity are increased by dehydration, renal failure, reduced or, increased sodium intake. Risk factors include diarrhoea, vomiting, diuretics, NSAIDs and other medicines, which may be associated with diarrhoea (for example antibiotics).

Drug interactions

4.5 Monitor concurrent therapies. Due to lithium's relatively narrow therapeutic index, pharmacokinetic **interactions** with other drugs can precipitate lithium toxicity. The most clinically significant interactions are with drugs that alter renal sodium handling.

Thiazide diuretics, ACE inhibitors and Angiotensin II receptor antagonists can considerably increase lithium levels and should be, avoided if possible. If co-prescribed with lithium, more frequent monitoring of e-GFR and serum lithium is essential.

Non-Steroidal Anti-inflammatory drugs (NSAIDs) and cyclo-oxygenase (Cox 2) inhibitors can increase lithium levels. If combined with lithium they should be,

prescribed regularly, not 'as required', and more, frequent lithium monitoring is required.

Co-administration of some **antipsychotics, antidepressants and carbamazepine** may increase the risk of neurotoxicity. Discontinuation of both drugs is, recommended at the first signs of neurotoxicity.

Refer to Appendix 1 in the BNF for further details.

4.6 Risks and benefits in relation to childbearing must be, discussed fully with all women of childbearing potential and this should be, revisited at least annually. Discussion should include review of contraception status and advice/signposting on effective contraception for the duration of prescribing, with preference for long-acting reversible methods.

5. Reduction/Discontinuation Phase

Lithium is often, maintained for a period of at least three years and the plan to discontinue treatment should be, discussed with the Consultant Psychiatrist. In long term, use lithium has been associated with thyroid disorders, and mild cognitive and memory impairment. The need for continued therapy should be, assessed regularly and patients should be, maintained on lithium after 3-5 years only if benefit persists.

If there is an agreed plan to discontinue lithium, it should be, reduced slowly over at least one month to reduce the risk of relapse.

Do not stop lithium abruptly unless there is an urgent indication such as overdose or toxicity.

6. Information for Patients

The NPSA Patient Safety Alert gives clear guidance that '*At the start of lithium therapy and throughout their treatment patients receive appropriate ongoing verbal and written information and a record book to track lithium blood levels and relevant clinical tests'*

It is, advised that on issuing the booklet, alert card and record book:

- *the healthcare practitioner must complete the patient's details, service providers' details and current lithium therapy*
- *the, record book should be annotated with the patient's current lithium blood level, the expected upper and lower lithium blood level range and healthcare tests results.*
- *the lithium blood level range may alter with time, and should be amended to reflect the current clinical expectation for safe and effective therapy.*
- *the brand of lithium that the patient should remain on should be annotated in the record booklet*

Refer to NPSA/2009/PSA005

Booklets can be requested from the Mental Health Clinical Pharmacy Team on 01324 566728/9 or 01324 567616 or FV-UHB.MHpharmacy@nhs.net

7. Prescribing and Monitoring Responsibilities

General practitioners should refer patients who are likely to be suffering from bipolar disorder, mania or treatment resistant depression to Specialist Mental Health Services.

7.1 Where the GP is participating in the Near Patient Testing Locally Enhanced Service (NPT LES)

7.1.1 Specialist Mental Health Services will:

- Confirm diagnosis
- Assess baseline mental state, including cognitive assessment where appropriate
- Assess need for treatment
- Arrange baseline investigations (as per 3.2)
- Issue lithium information booklet, alert card and record book
- Ensure lithium monitoring is, carried out during initiation either within the specialist service or by arrangement with the GP.
- Review and action potential drug interactions
- Follow up to assess compliance and response
- Advise on adverse effects reported by the patient or GP
- Advise on change in therapy
- Advice on reduction/continuation
- Review female patients on lithium for discussion of contraceptive need.

7.1.2 The General Practitioner if participating in NPT LES will:

- Prescribe treatment as advised by the Consultant Psychiatrist
- Consider potential drug interactions
- Undertake serum lithium monitoring as agreed with Specialist service
- Monitor, renal function, calcium, thyroid function, ECG, and BMI as described in section 4.3
- Undertake an annual physical health check as per physical health guidance.
- Liaise with the Specialist Mental Health Service if they have concerns about mental health or adverse events.
- Review female patients on lithium for discussion of contraceptive need.

7.2 In an exceptional situation where the GP Practice has opted out of the NPT LES:

The Specialist Mental Health Service must liaise with the GP Practice to determine if they are willing to undertake any elements described in 7.1.2 above. An 'exception shared care protocol' will be negotiated and agreed between both parties to ensure clarity of responsibility and continued patient safety.

7.3 Admission of patients on lithium

- All patients prescribed lithium who are, admitted to hospital should be, monitored, according to the inpatient lithium pathway (see appendix 2).

8. References

National Institute for Clinical Excellence (NICE CG 185). Bipolar Disorder: Assessment and management
Clinical Guideline 185, nice.org.uk

National Patient Safety Agency (NPSA), Patient Safety Alert NPSA/2009/PSA005, www.nrls.npsa.nhs.uk/alerts

British National Formulary current edition at www.bnf.org

The Maudsley Prescribing Guidelines 13th Edition, 2018.

CMO letter (2017) National standards for physical health for patients treated with Lithium.

Lithium and Abnormal Renal Function (eGFR) **Appendix1**

Renal function should be, monitored every 6 months for patients prescribed Lithium.
For those patients prescribed lithium where the eGFR is, reduced below 60ml/min/1.73m^2 consider referring to the Consultant Psychiatrist for review of ongoing lithium therapy.

Psychiatric factors

- At the earlier stages of chronic kidney disease, the decision to continue or stop treatment requires an individual clinical assessment of the impact on mental health, particularly if the estimated glomerular filtration rate is stable over time
- Stopping may be appropriate at an early stage if mood disorder has been stable for some years
- Monitored continuation may be appropriate if consequences of past relapse have been severe or lithium has proved to be the most effective drug

Renal factors

- Change over time is more important than a single measurement (inter-current illness can upset kidney function in chronic kidney disease)
- Graphical monitoring of the estimated glomerular filtration rate or reciprocal serum creatinine over time is a useful decision aid.
- Consider stopping lithium if clear evidence exists of persistent decline over time.
- Lithium will normally be stopped in stages 4 and 5 of chronic kidney disease.

Renal monitoring

(1) Where eGFR is moderately reduced (stage 3a; 45-59ml/min/1.73m^2) the following is recommended;

- In people with a new finding of reduced eGFR, repeat the eGFR within 2 weeks
- Check eGFR every three months
- Check for proteinuria - monitor urine protein/creatinine ratio (PCR) 6 monthly
- Complete cardiovascular risk profiling and management (consider antiplatelet drugs and statin where applicable)
- Control blood pressure to < 140mmHg systolic and 90mmHg diastolic (lower in diabetes or heavy proteinuria)

(2) Referral to nephrology should be, considered where:

- eGFR is reduced further (CKD stage 3b; 30-44ml/min/1.73m^2 , stages 4 or 5)
- Heavy proteinuria is present (urine PCR* ≥ 100mg/mmol)
- Proteinuria is present (urine PCR* ≥ 50mg/mmol) in a young patient or proteinuria is present along with haematuria
- Where eGFR has rapidly declined (a decline of > 10ml/min within one year)
- Patient has problematic polyuria or persistent electrolyte disturbance

Appendix 2

Pathway for Patients Admitted on Lithium

NHS Forth Valley

Has Medicines Reconciliation Process been completed and 2 consistent sources of Lithium dose, brand and timing identified?

NO

Decision to withhold		Process complete	
Signed		Signed	
Date		Date	
Time		Time	

YES

Do Medicines Reconciliation Lithium details match what patient states they have been taking?

NO

Decision to withhold		Process complete	
Signed		Signed	
Date		Date	
Time		Time	

YES

1) Is Patient experiencing any of these possible symptoms of Lithium toxicity? *(tick)*		**2) Has the patient been recently prescribed or taking any of the following over the counter?** *(tick)*		**3) Check the most recent U&Es and ECG. Any abnormalities?** *(tick)*	
	Nausea		NSAIDS		Yes
	Diarrhoea		ACE inhibitor		No
	Blurred Vision		Diuretics		
	Polyuria				
	Fine Resting Tremor				
	Light Headedness				
	Drowsiness				

IF YES TO ANY OF THE ABOVE FOLLOW 'YES' ARROW

YES

Decision to withhold		Blood sent for level	
Signed		Signed	
Date		Date	
Time		Time	

NO

CHECK LITHIUM LEVEL 12 hours post last dose

RESULTS - Lithium level in mmol/l

Age 18-65	Age >65		
<0.4	<0.4	Continue prescription and inform treating team	1
0.4-1	0.4-0.8	Continue	2
1-1.5	0.8-1.5	Withhold and discuss with pharmacy and treating team	3
>1.5	>1.5	Withhold and monitor for signs of toxicity. Discuss with pharmacy and treating team	4
>2	>2	Immediate physical monitoring inc U&Es and ECG. Discuss with medics/renal team	5

Decision based on Lithium level results *(tick)*

	1
	2
	3
	4
	5

Signed

Date:

Please review Lithium prescription on a daily basis including:

- Regular monitoring for signs/symptoms of toxicity
- Repeat lithium levels where clinically indicated
- Consider recommencing any withheld prescriptions dependent on blood results/ clinical pictures

Publications in Alternative Formats

NHS Forth Valley is happy to consider requests for publications in other language or formats such as large print.

To request another language for a patient, please contact 01786 434784.

For other formats contact 01324 590886,

text 07990 690605,

fax 01324 590867 or

e-mail - fv-uhb.nhsfv-alternativeformats@nhs.net