NHS FORTH VALLEY
Guideline for the Management of Patients on Lithium

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NHS Forth Valley

Consultation and Change Record

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Change Record

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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 consultation 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. The risks of lithium in pregnancy should be discussed with women of child bearing age and advice given on contraception.

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

- ECG
- Weight & BMI
- Renal Function
- Full blood count
- Thyroid function

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 psychotropics 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 is usually given in the evening. If using liquid preparation in divided doses, the sample should be taken 12 hours post the evening dose and just before the morning dose.

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.

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

- ECG: annually for patients with cardiac disease
- Weight & BMI: annually
- Renal Function: 6 monthly (3 monthly if eGFR<60*)
- Full blood count: 6 monthly
- Thyroid function: 6 monthly
- Lithium: every 3 months (5-7 days after change in dose or brand)

*See appendix 1 for managing lithium in abnormal eGFR

4.3 Patients should be routinely 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, carida dysrythmias, 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).

4.4 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.

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.*

Refer to NPSA/2009/PSA005

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.

Specialist Mental Health Services will:

- Confirm diagnosis
- Assess baseline mental state, including cognitive assessment where appropriate
- Assess need for treatment
- Undertake 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

The General Practitioner will:

- Prescribe treatment as advised by the Consultant Psychiatrist
- Consider potential drug interactions
- Undertake serum lithium monitoring as agreed with Specialist service
- Monitor full blood count, renal function, thyroid function, ECG, weight and BMI as described in section 4.3
- Undertake an annual physical health check
- Monitor the patient's mental health and advise the Specialist Mental Health Service if they have concerns regarding adverse events of ongoing therapeutic benefit.

8. References

National Institute for Clinical Excellence (NICE 2006). Bipolar Disorder: The management of bipolar disorder in adults, children and adolescents in primary and secondary care. Clinical Guideline 38, www.nice.org.uk

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

National Institute for Clinical Excellence (NICE) indicator guidance for QOF-Mental Health, July 2010, www.nice.org.uk

British National Formulary Edition 59, March 2010, www.bnf.org

The Maudsley Prescribing Guidelines 10th Edition, 2009.

Lithium and Abnormal Renal Function (eGFR)

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

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