NPSA SAFER LITHIUM THERAPY GUIDELINES FOR NHS LANARKSHIRE

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<th>Implementation Date</th>
<th>Spring 2013</th>
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NPSA Safer Lithium Therapy
Guidelines for NHS Lanarkshire

BACKGROUND

On 1st December 2009 the National Patient Safety Agency (NPSA) issued a Patient Safety Alert (NPSA/2009/PSA005) on safer lithium therapy. This alert was in response to reports of harm caused to patients, including fatalities, involving lithium therapy. The alert was developed in collaboration with the Prescribing Observatory for Mental Health (POMH-UK) of the Royal College of Psychiatrists, the National Pharmacy Association (NPA), other organisations, clinicians and patients. It was designed to help NHS organisations, including community pharmacies, in England and Wales to take steps to minimise the risks associated with lithium therapy and to ensure that potential harm to patients is minimised. The following recommendations were made:

- patients prescribed lithium are monitored in accordance with NICE guidance;
- there are reliable systems to ensure blood test results are communicated between laboratories and prescribers;
- 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*;
- 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.

* The NPSA has developed a patient information booklet, lithium alert card and record book for tracking blood tests.

Links:
http://www.rcpsych.ac.uk/quality/quality.accreditationaudit/prescribingobservatorypomh/saferlithiumtherapy.aspx
http://www.nrls.npsa.nhs.uk/alerts/?entryid45=65426

SCOTTISH IMPLEMENTATION

These recommendations were to be implemented in England and Wales by 31st December 2010 and in Scotland similar systems are expected to be actioned in 2011. It is worth noting that the Scottish Intercollegiate Guideline Network (SIGN) did not make specific recommendations for lithium monitoring in their Bipolar Affective Disorder Guideline (No. 82, ISBN 1 899893 29 6, May 2005). (http://www.sign.ac.uk/guidelines/fulltext/82/index.html)
SIGN did note that close communication and shared-care protocols between primary and secondary care were essential but did not set any standards. The National Institute of Clinical Excellence (NICE) Guideline on Bipolar Disorder (CG38, July 2006) does include guidance on initiating, monitoring, stopping, and other risks associated with lithium therapy (http://www.nice.org.uk/nicemedia/live/10990/30193/30193.pdf). These are the guidelines that the NPSA recommends following and should supersede current local hospital protocols or primary care protocols including Quality of Outcome Framework (QOF) recommendations and dovetail with the older GMS Contract (2003) SPICEpc criteria for Monitoring of Lithium Therapy (http://www.spice.scot.nhs.uk/pdf/Monitoring%20of%20Lithium%20Therapy.pdf).

WHAT THE “NICE Guidelines” SAY

Initiating lithium

- Lithium should not be initiated routinely in primary care for the treatment of bipolar disorder.
- When initiating lithium as long-term treatment, prescribers should:
  - advise patients that erratic compliance or rapid discontinuation may increase the risk of manic relapse
  - measure height and weight, renal function and thyroid function
  - arrange an ECG for patients with cardiovascular disease or risk factors for it
  - arrange a full blood count if clinically indicated
  - establish a shared-care protocol with the patient's GP for prescribing and monitoring lithium and checking for adverse effects
  - be aware that patients should take lithium for at least 6 months to establish its effectiveness as a long-term treatment.
- Serum lithium levels should be checked 1 week after starting and 1 week after every dose change and until the levels are stable. The aim should be to maintain serum lithium levels between 0.6 and 0.8 mmol per litre in people being prescribed it for the first time.
- For people who have relapsed previously while taking lithium or who still have sub-threshold symptoms with functional impairment while receiving lithium, a trial of at least 6 months with serum lithium levels between 0.8 and 1.0 mmol per litre should be considered.

Monitoring lithium

- For patients with bipolar disorder on lithium treatment, prescribers should do the following.
  - Monitor serum lithium levels normally every 3 months.
  - Monitor older adults carefully for symptoms of lithium toxicity, because they may develop high serum levels of lithium at doses in the normal range, and lithium toxicity is possible at moderate serum lithium levels.
  - Monitor weight, especially in patients with rapid weight gain.
Undertake 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 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, or diuretics.

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

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 should consider seeking advice from a renal specialist and a clinician with expertise in the management of bipolar disorder on this.

Monitor for symptoms of neurotoxicity, including paraesthesia, ataxia, tremor and cognitive impairment, which can occur at therapeutic levels.

**Stopping lithium**

- Lithium should be stopped gradually over at least 4 weeks, and preferably over a period of up to 3 months, particularly if the patient has a history of manic relapse (even if they have been started on another antimanic agent).
- When lithium treatment is stopped or is about to be stopped abruptly, prescribers should consider changing to monotherapy with an atypical antipsychotic or valproate, and then monitor closely for early signs of mania and depression.

**Risks associated with the use of lithium**

- Patients taking lithium should be warned not to take over-the-counter non-steroidal anti-inflammatory drugs. Prescribing non-steroidal anti-inflammatory drugs for such patients should be avoided if possible, and if they are prescribed the patient should be closely monitored.
- Patients taking lithium should be advised to:
  - seek medical attention if they develop diarrhoea and/or vomiting
  - ensure they maintain their fluid intake, particularly after sweating (for example, after exercise, in hot climates, or if they have a fever), if they are immobile for long periods or – in the case of older people – develop a chest infection or pneumonia
  - consider stopping lithium for up to 7 days if they become acutely and severely ill with a metabolic or respiratory disturbance from whatever cause.
# ROLES AND RESPONSIBILITIES

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<th>LITHIUM THERAPY</th>
<th>PSYCHIATRIST</th>
<th>GP</th>
<th>PATIENT or NAMED CARER</th>
<th>PHARMACIST</th>
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| **BEFORE STARTING TREATMENT** | Provide information and opportunity to discuss lithium therapy.  
Arrange BASELINE INVESTIGATIONS (at appropriate Secondary Care Psychiatric Clinic): Thyroid Function Test, height & weight, renal function test (e-GFR) and if appropriate or clinically indicated – ECG, FBC, BP, Ca2+, Glucose, Lipids, creatinine clearance and pregnancy test. Access blood results via Scottish Care Information (SCI). Liaise with GP regarding possible drug interactions (Appendix 1) should Lithium be commenced and identify any health issues that would mitigate the use of Lithium. | It is not expected that the responsibility for commencing Lithium Therapy lies with the GP. It will normally be commenced by Psychiatric Secondary Care Services. | To attend / ensure attendance at Secondary Care Psychiatric Clinic for BASELINE INVESTIGATIONS. |  |
| **INITIATING (or ADJUSTING) LITHIUM THERAPY (DOSE)** | For patients already open to Psychiatry - provide patient with patient information booklet, lithium alert card and record book for tracking blood tests. Complete all sections which require patient specific details and encourage patients to take responsibility for sharing record book with other health professionals.  
Establish protocol for lithium therapy – including blood test 7 days after dose changes until steady state reached (carried out at Secondary Care Psychiatric Clinic), review appointments, and provide a contact for any concerns or potential problems.  
Access blood results via Scottish Care Information (SCI) and liaise/inform GP regarding results and dose.  
Ensure Record Book is updated with results of most recent monitoring | It is not expected that the responsibility for initiating or adjusting Lithium Therapy dose lies with the GP. It will always be initiated or adjusted by Psychiatric Secondary Care Services. | To attend / ensure attendance for bloods tests at Secondary Care Psychiatric Clinic.  
Attendance at review appointments.  
Pick up prescription from GP to be dispensed at local pharmacy.  
To be responsible for taking record book to appointments and when visiting a pharmacy, and to request replacement record book from psychiatrist if book is lost or when all pages are complete. | Refer to patient’s Record Book prior to dispensing medication.  
Liaise with prescriber when lithium levels are out with range, or if information is incomplete or unavailable.  
Re-enforce message that patient should provide Record Book when lithium is being dispensed.  
Dispense Lithium. |
### Monitoring Maintenance Lithium Therapy

| Check patient has received (and is using) information booklet, lithium alert card and record book for tracking blood tests. |
| Liaise with GP to ensure routine monitoring continues: |
| - lithium level every 3 months |
| - TFTs every six months |
| - renal function (e-GFR) every 6 months (the above tests will be carried under the responsibility of the GP practice) |
| Take appropriate action if physical problems, side effects (Appendix 2) or abnormal blood results arise. |
| Ensure Record Book is updated with results of most recent monitoring. |
| Continue regular outpatient contact at least every 3 months (Unless otherwise agreed) |
| Respond appropriately to concerns raised by GP or patient. |

### Continuing and ensuring routine monitoring:

- lithium level every 3 months
- TFT every 6 months.
- renal function (e-GFR) every 6 months (the above tests will be carried under the responsibility of the GP practice)
- Take appropriate action if physical problems or abnormal blood results arise.
- Ensure Record Book is updated with results of most recent monitoring.
- Monitor for possible side-effects and evidence of neurotoxicity (Appendix 2).
- Have systems in place to alert prescriber should changes to other medication be likely to affect lithium therapy (Appendix 1).
- Seek review from psychiatrist if problems arise that might require review of lithium therapy.

### Attendance for bloods tests at GP Practice.

### Monitoring for possible side-effects and evidence of neurotoxicity (Appendix 2).

### Have systems in place to alert prescriber should changes to other medication be likely to affect lithium therapy.

### Dispense lithium.

### STOPPING LITHIUM THERAPY

| Discuss need to come off medication gradually over at least 4 weeks (and preferably up to 3 months). |
| Continue routine monitoring. If renal or thyroid function were the reason for stopping then establish appropriate follow-up. If alternative medication is prescribed, to ensure patient is fully informed about any new possible side-effects. |
| Establish review appointments & support for during and after this transitional period. |
| Ensure individual protocol for discontinuation is clearly communicated to patient & GP. |

### Continue routine monitoring.

### If renal or thyroid function were the reason for stopping then establish appropriate follow-up.

### As above.

### Refer to patient’s record book prior to dispensing medication.

| Liaise with prescriber when lithium levels are out with range, or if information is incomplete or unavailable. A sample letter (Appendix 3) is available. |
| Remind patient to look out for problems & issues related to lithium therapy (see Appendix 2) and that record book will be checked by pharmacist when lithium is being dispensed. |
| Have systems in place to alert prescriber should changes to other medication be likely to affect lithium therapy. |

### Dispense lithium.

### Table 1 Roles and Responsibilities
At start of Lithium Therapy and throughout their treatment patients receive appropriate ongoing verbal and written communication, in particular, the Lithium Therapy Information Pack.

### BEFORE STARTING LITHIUM THERAPY
- Consider possible drug interactions (refer to Appendix 1)

### BASELINE INVESTIGATIONS*
- TFTs
- Height & weight
- Renal Function Test (e-GFR)

### CARRY OUT IF APPROPRIATE / CLINICALLY INDICATED
- ECG
- FBC
- Ca2+
- Glucose
- Lipids
- Creatinine clearance
- Pregnancy test

### RESULTS
- Results accessed by Psychiatrist**

### INITIATION OR ADJUSTING (ie dose change) LITHIUM THERAPY
- Patient to receive (from Secondary Psychiatric Care or Nurse)
  - Information Booklet
  - Lithium Alert card
  - Record Book
  - Review Appointments
  - Blood Test 7 days after every dose change until stable*

### PATIENT TO RECEIVE
- Prior to dispensing, pharmacist should refer to patient’s record book and when concerns arise, liaise with prescriber

### MONITORING / MAINTENANCE LITHIUM THERAPY
- IF PATIENT IS NOT OPEN TO PSYCHIATRY
  - GP should consider referral of patient to Psychiatry for review and advice
  - Check patient has received and is using
  - Information Booklet, Lithium Alert Card & Record Book
- IF PATIENT IS UNWILLING OR CONTINUALLY DNAs
  - This must be recorded and reasons explored for same
  - Assess risk – in particular safety of continuing to prescribe Lithium
  - Explore alternatives i.e. continue, stop, prescribe alternative med
  - Act accordingly in best interest of patient

### CONTINUE ROUTINE MONITORING
- Lithium levels every 3 months***
- Thyroid Function Test (TFT) every 6 months***
- Renal function test every 6 months***
- Common side effects /including symptoms which may indicate potential lithium toxicity (refer to Appendix 2)

### ENSURE
- Regular psychiatric outpatient appointment at least every 3 months unless otherwise agreed

### TO ENSURE SAFE PRESCRIBING OF LITHIUM THERAPY, THE PHARMACIST SHOULD
- Refer to the patient’s record book prior to dispensing medication and
  - Liaise with the prescriber (Sample Letter - Appendix 3)
    - When lithium levels are out with usual range
    - If information is incomplete
    - If information is unavailable
  - Remind patients of the problems to look out for in relation to Lithium Therapy
  - Liaise with prescriber if adverse reactions are suspected

### LETTER MAY BE SENT FROM PHARMACIST TO DOCTOR
- Take appropriate action if problems or abnormal blood result arise
- Alert prescriber to changes in other meds
- Monitor side effects

### STopping LITHIUM THERAPY
- Come off meds gradually
  - Normally no less than 4 weeks but up to 3 months
- Continue routine monitoring
- Establish review appointments

### INDIVIDUAL PROTOCOL FOR DISCONTINUATION IS COMMUNICATED TO GP AND PATIENT

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*Outpatient – carried out by Psychiatric Secondary Care Clinic. In exceptional circumstance, if Lithium therapy has been initiated by GP, baseline investigations will be carried out under the responsibility of the GP Practice. If inpatient – it is expected that baseline investigations will be carried out in hospital.

**The Psychiatrist should access lab results electronically via Scottish Care Information (SCI).

***These blood tests will be carried out under the responsibility of the GP Practice.
LITHIUM – COMMON DRUG INTERACTIONS

The following are the most common interactions with Lithium but automated systems ought to be in place to ensure other possible interactions are brought to the attention of the prescriber or dispenser of the medication. Searches can be readily performed on sites such as www.bnf.org or www.drugs.com

**Diuretics**

Caution should be used when Lithium and diuretics are used concomitantly because diuretic-induced sodium loss may reduce the renal clearance of Lithium and increase serum Lithium levels with risk of Lithium toxicity. Patients receiving such combined therapy should have serum Lithium levels monitored closely and the Lithium dosage adjusted if necessary.

**NSAIDS**

Lithium levels should be closely monitored when patients initiate or discontinue NSAID use. In some cases, Lithium toxicity has resulted from interactions between an NSAID and Lithium. Indomethacin and piroxicam have been reported to increase significantly, steady-state plasma Lithium concentrations. There is also evidence that other nonsteroidal anti-inflammatory agents, including the selective cyclooxygenase-2 (COX-2) inhibitors, have the same effect. In a study conducted in healthy subjects, mean steady-state Lithium plasma levels increased approximately 17% in subjects receiving Lithium 450 mg b.i.d. with celecoxib 200mg b.i.d. as compared to subjects receiving Lithium alone.

**Antibiotics**

Concurrent use of metronidazole with Lithium may provoke Lithium toxicity due to reduced renal clearance. Patients receiving such combined therapy should be monitored closely.

**ACE-inhibitors**

There is evidence that angiotensin-converting enzyme inhibitors, such as ramipril and perindopril, and angiotension II receptor antagonists, such as losartan, may substantially increase steady-state plasma Lithium levels, sometimes resulting in Lithium toxicity. When such combinations are used, Lithium dosage may need to be decreased, and plasma Lithium levels should be measured more often.

**Calcium-channel blockers**

Concurrent use of calcium blocking agents with Lithium may increase the risk of neurotoxicity in the form of ataxia, tremors, nausea, vomiting, diarrhoea and/or tinnitus. Caution is recommended.

**SSRIs**

The concomitant administration of Lithium with selective serotonin reuptake inhibitors should be undertaken with caution as this combination has been reported to result in symptoms such as diarrhoea, confusion, tremor, dizziness and agitation.

**Other**

The following drugs can lower serum Lithium concentrations by increasing urinary Lithium excretion: acetazolamide, urea, xanthine preparations and alkalinizing agents such as sodium bicarbonate. The following have also been shown to interact with Lithium: methyldopa, phenytoin and carbamazepine.
COMMON SIDE EFFECTS OF LITHIUM

- Upset stomach – particularly at start of treatment;
- Fine shake – (‘tremor’) of hands;
- Metallic taste in the mouth;
- Weight gain;
- Swelling of ankles;
- Feeling more thirsty than usual and passing a lot of urine.

SYMPTOMS INDICATING POTENTIAL LITHIUM TOXICITY

- Severe hand shake (‘tremor’);
- Stomach ache along with feeling sick and having diarrhoea;
- Muscle weakness;
- Being unsteady on their feet;
- Muscle twitches;
- Slurring of words – so that it’s difficult for others to understand what they are saying;
- Blurred vision;
- Confusion;
- Feeling unusually sleepy.

THE THREE MOST COMMON CAUSES OF LITHIUM TOXICITY ARE:

- Dehydration;
- Significant changes in the level of salt in the diet;
- Drug interaction (Refer to Appendix 1). For further information please refer to www.bnf.org

The above information and further details can be found in the Lithium Therapy Important Information for Patients pack.
Dear Doctor ...............  

NPSA Safer Lithium Therapy  
Patient ........................................ CHI.................................  
Address........................................  
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In line with the Patient Safety Alert for Lithium Therapy, I want to draw your attention to the following (ticked) issue(s):

☐ The lithium level shown in the patient’s Record Book is out with the usual range.
☐ The information in the patient’s Record Book is incomplete.
☐ The patient does not have a Record Book.
☐ The patient is unwilling to share the Record Book with pharmacy staff.
☐ I have referred the patient to you because the patient reports symptoms that may be related to lithium therapy.

Additional information/comments
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Yours sincerely,