Guidelines for the Prescribing and Monitoring of Inpatient Lithium Therapy

Ratifying Committee: Drugs & Therapeutics Group
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KEY GUIDELINE ISSUES:

1. Advice on prescribing lithium
2. Advice on monitoring lithium
3. Details of key drug interactions
4. Managing patients on discharge

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Guidelines for the Prescribing and Monitoring of Inpatient Lithium Therapy

Section 1

On admission.

Doctor’s responsibilities

1. Read the clinical notes and previous prescription, check patient’s documentation (either a record book and alert card or a monitoring booklet) and identify any special instructions. Review the results of all relevant investigations (including blood test results) and identify the indication for the lithium therapy.2

2. At the earliest opportunity contact the patient’s GP for the latest medication history, if the patient is admitted without up-to-date documentation.2

3. Ensure that the patient fully understands their lithium treatment and monitoring requirements and if not, provide a clear explanation.

4. Ensure the following checks (or requests) are made before commencement of treatment:
   - ECG if history of cardiac disease, risk factors known to prolong the QT interval (e.g. uncorrected hypokalaemia, bradycardia) and/or on other psychotropics known to prolong the QT interval.
   - Weight and height
   - Urea and Electrolytes
   - Serum creatinine or eGFR
   - Serum calcium (corrected)
   - Thyroid Function Tests (TFT)
   - Full blood count if clinically indicated 1

5. Ensure the correct brand and salt of lithium is prescribed as different preparations may vary in bioavailability. Priadel® is the brand most commonly prescribed and available on the wards.

6. Key points when prescribing lithium:
   - The starting dose is normally 400mg/450mg (200mg/250mg in the elderly). Lithium plasma concentration should be checked 5-7 days (depending on renal function) after starting or changing dose and then weekly until two similar results are obtained at the same dose.1

   - The blood taken for lithium levels should be taken 10-14 (ideally 12 hours) after the last dose administered. To assist sampling, lithium is usually given as a bedtime dose so that blood can be taken the following morning.3

   - Care should be taken, including additional monitoring, when changing brands or formulations. Tablets contain lithium carbonate and the liquid contains lithium citrate. Lithium carbonate 200mg ≡ lithium citrate 509mg.3 Priadel® liquid comes as lithium citrate 520mg/mL.
Doses should be adjusted to achieve serum lithium concentration between 0.4 and 1.0mmol per litre. In people prescribed it for the first time a range of between 0.4 and 0.8mmol should be used \(^1\). The lower end of the range is usually the target for maintenance therapy and treatment of elderly patients. \(^3\)

**Inpatient drug chart should be written as follows:**

<table>
<thead>
<tr>
<th>Week 1</th>
</tr>
</thead>
<tbody>
<tr>
<td>Mo</td>
</tr>
<tr>
<td></td>
</tr>
</tbody>
</table>

**Patient Name** **************  
**Ward:** **********  
**Date**  
**Variable doses**

<table>
<thead>
<tr>
<th>DRUG</th>
<th>LITHIUM CARBONATE (PRIADEL)</th>
<th>DOSE</th>
<th>FREQUENCY</th>
<th>ROUTE</th>
<th>ADDITIONAL INSTRUCTIONS</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td></td>
<td>400MG</td>
<td>ON</td>
<td>PO</td>
<td>Li level 0.6mmol/l</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td>Before admin</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>SIGNATURE</th>
<th>DATE</th>
<th>STOPPED BY</th>
<th>STOP DATE</th>
</tr>
</thead>
<tbody>
<tr>
<td>**********</td>
<td>****</td>
<td>STOPPED BY</td>
<td>STOP DATE</td>
</tr>
</tbody>
</table>

**Section 2**

**During Admission**

When tests and measurements are undertaken, the care team must update the patient-held Lithium Treatment - Monitoring Booklet ('lithium record book') with lithium levels and other relevant results.

**Nurse’s responsibilities**

1. Nurses need to be aware of common side effects of lithium listed below and report to the ward doctor if they have concerns (see toxicity point 2.).

   - Dry mouth or metallic taste in the mouth
   - Thirst
   - Passing more urine
   - Dizziness
   - Mild diarrhoea or nausea (particularly on initiation and increases dose)
   - Mild shaking or fine tremor of the hand(s)
   - Weight gain
   - Oedema

2. Nurses need to monitor the patient and immediately report to the ward doctor if any symptoms of lithium toxicity appear such as:

   - Severe or coarse hand shaking or tremor
   - Blurred vision
- Stomach ache along with vomiting or severe diarrhoea
- Unsteadiness of their feet
- Difficulty in speaking or slurring words
- Muscle twitches
- Clumsiness
- Confusion
- Muscle weakness

**Doctor’s responsibilities**

1. Record lithium levels on the drug chart with the date of the test. (As well as entering the result in the clinical notes).

2. Be aware of any significant interacting drugs and other *risk factors* for lithium toxicity.

3. Undertake more frequent blood tests and lithium levels if there are signs of clinical deterioration, abnormal results, and symptoms suggesting abnormal renal or thyroid function such as unexplained fatigue.

4. Lithium use is associated with a range of glomerular and tubular disorders resulting in chronic kidney disease and more rarely established renal failure. Therefore with renal function it is important to monitor a trend, as results may be still in the normal range but have significantly increasing creatinine levels (especially in the elderly).

5. In CKD, the level of protein in the urine can be an indicator of nephrotoxic effects as the eGFR may not alter in the same way as patients without renal impairment. Proteinuria can also indicate other diagnoses such as infection. If proteinuria is detected then referral to a renal physician would be recommended.

6. Repeat lithium levels if initiating or discontinuing any interacting drugs. (Check at 5-7 day interval until two similar results are obtained at the same dose).

7. Repeat lithium levels if increasing or decreasing a lithium dose. (Check at 5-7 day interval until two similar results are obtained at the same dose).

8. Be aware that toxicity occurs when blood lithium concentration is greater than 1.5mmol/L. (Usual therapeutic range is between 0.4 - 0.8mmol/L for people being prescribed it for the first time.) For people who have relapsed previously while taking lithium or who have sub-threshold symptoms with functioning impairment while on lithium, the target level is normally between 0.8 – 1.0mmol/L. If levels above 1.0mmol/L are considered clinically appropriated it should be discussed with the lead consultant/medical supervisor and this discussion should be entered into the clinical notes. In addition, more frequent monitoring should be carried out, e.g. monthly, instead of 3-monthly monitoring.

9. The blood taken for lithium levels should be taken 10-14 (ideally 12 hours) after the last dose administered. To assist sampling, lithium is usually given as a bedtime dose so that blood can be taken the following morning.

10. Monitor for symptoms of neurotoxicity, including paraesthesia, ataxia, tremor and cognitive impairment, which can occur at therapeutic levels.
11. Consider stopping lithium for up to 7 days if patients become acutely and severely ill with any metabolic or respiratory disturbance.

12. **STOP lithium immediately**, if any of the symptoms of toxicity occur, (see Appendix 1). Plasma lithium levels should be urgently checked and the patient may require transfer to A&E or a medical unit for rehydration and sodium repletion. Levels of **2mmol/L** will require **urgent transfer and treatment** at an acute hospital.

13. Exclude pregnancy (and test if appropriate) in women of child bearing potential.

14. Advise women of child bearing potential starting on lithium to use suitable contraception. (If a patient becomes pregnant, refer for specialist advice).

15. Inform anyone who is involved in the patient’s care, that the patient is taking lithium.

16. Ensure that the patient has been counseled on lithium, this could be carried out by the member or the pharmacy team.

**Pharmacy team’s responsibilities**

1. Check that blood tests and lithium levels have been obtained at the appropriate times and if not inform ward staff when the blood tests are required.

2. Check that the latest lithium level (and date) is written on the drug chart. If it is not, check the clinical notes and make the appropriate drug chart entry.

3. Ask patients who have been admitted on lithium if they have a lithium monitoring booklet. Where possible, check that this is correctly completed. If left at home arrange for it to be brought in, if lost then provide a replacement.

4. Review the drug chart before any supply is made and ensure that the prescription is complete, the brand stated and that monitoring is in place. Before endorsing the chart all prescriptions must be checked for drug interactions, which must be reported back to the prescriber as necessary.

5. Ensure the importance of administering lithium in the evening is clear to the medical and nursing team.

6. **Pharmacists should avoid recommending withholding lithium therapy.** Where it is not possible to assess test results they should communicate to prescribers that lithium medication has been provided without blood test data being available. Prescribers should be asked to ensure that blood tests have been carried out at the recommended frequency and to urgently order tests if the recommended schedule has lapsed.

7. Counsel the patient on lithium if required. This should include explaining:
   - Common side effects
   - Toxic effects and if they experience any to contact A&E or GP if in hours. To also advise the patient to STOP taking their lithium until they have received medical advice.
What to do if unwell (e.g. stomach bug or food poisoning)
About avoiding dietary changes which reduce or increase sodium intake
That dehydration can cause lithium levels to rise so in extreme heat or if excessive exercise is carried out the patient must keep hydrated.
Interactions with other medication including ‘over the counter’ medicines such as ibuprofen (Nurofen®)
Signs or symptoms suggestive of hypothyroidism such as lethargy and feeling cold.
They should report any unusual signs and symptoms e.g. sore throat, bruising, mouth ulcers, nausea, vomiting, dark urine and shortness of breath.

Many of these points are covered by the Choice and Medication leaflet website leaflets or the Lithium Treatment – Monitoring Booklet. The leaflets can be found on http://www.choiceandmedication.org/sussex/

Section 3
On discharge

Doctor’s responsibilities:

1. Ensure that the primary care team is sent information concerning the clinical indication of use, intended duration of therapy, current prescription (including product brand name), and recent laboratory test results.

2. Ensure that the lithium ‘record book’ or monitoring booklet is FULLY and appropriately completed (with patient’s details, service providers’ details and current lithium therapy to track lithium blood levels and relevant clinical tests) and that it is returned to patient/carer, with the next appointment date recorded. 

3. The information component of the ‘record book’ can be provided in a larger font (available on the website) or the Communications Team can be contacted if an audio version or translation into another community language is needed.

4. Work to a shared-care protocol with the patient’s GP for prescribing and monitoring lithium and also checking adverse effects. Ensure patients receive regular measurement of serum-lithium concentration (every 3 months on stabilised regimen), and also renal function and thyroid function tests every 6 months on stabilised regimens, or more often if there is evidence of impaired renal function.

Nursing Team’s responsibilities:

1. Ensure the following are discussed with the patient (can be found in the Lithium Monitoring Booklet):
   - The dose they should be taking on discharge and the frequency.
   - The date of their next appointment for a blood test.
   - The importance of their patient-held records, i.e. alert card and Lithium Monitoring Booklet.
   - The need to take lithium at the same time each day (usually in the evening)
References


3. BNF No 66 Sept 2013.


5. Dorset Healthcare NHS Foundation Trust. Ref No CP-170-08, lithium prescribing & Monitoring Guidelines


Appendix 1 Lithium Toxicity.

<table>
<thead>
<tr>
<th>Symptoms of lithium toxicity</th>
</tr>
</thead>
<tbody>
<tr>
<td>1) Severe hand shake (tremor)</td>
</tr>
<tr>
<td>2) Blurred vision</td>
</tr>
<tr>
<td>3) Stomach ache along with feeling sick and having diarrhoea.</td>
</tr>
<tr>
<td>4) Being unsteady on their feet</td>
</tr>
<tr>
<td>5) Difficulty in speaking or slurring words</td>
</tr>
<tr>
<td>6) Muscle twitches</td>
</tr>
<tr>
<td>7) Clumsiness</td>
</tr>
<tr>
<td>8) Feeling unusually sleepy</td>
</tr>
<tr>
<td>9) Confusion</td>
</tr>
<tr>
<td>10) Muscle weakness</td>
</tr>
</tbody>
</table>

When lithium blood levels are above 2mmol/l and severe symptoms are present, the patient will require admission to a medical unit. Osmotic diuresis or forced alkaline diuresis may be required.

(Note: concurrent use of diuretics, particularly thiazides, should be avoided)³.
### Summary of Monitoring Requirements

<table>
<thead>
<tr>
<th></th>
<th>BASELINE</th>
<th>INITIATION</th>
<th>MONITORING</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Height</strong></td>
<td>✓</td>
<td></td>
<td></td>
</tr>
<tr>
<td><strong>Weight/BMI</strong></td>
<td>✓</td>
<td></td>
<td>6 monthly (more often if evidence of rapid weight gain).</td>
</tr>
<tr>
<td><strong>Urea &amp; electrolyte</strong></td>
<td>✓</td>
<td></td>
<td>If urea and creatinine levels rise see below.</td>
</tr>
<tr>
<td><strong>Serum creatinine/ renal function</strong></td>
<td>✓</td>
<td></td>
<td>6 monthly (more often if evidence of impaired renal function or if the patient starts taking drugs such as ACE inhibitors, diuretics or NSAIDs). If urea and creatinine levels rise, monitor lithium dose and blood levels more closely and assess the rate of deterioration of renal function. The decision on whether to continue the drug depends on clinical efficacy and the degree of renal impairment. Consider consulting a renal physician.</td>
</tr>
<tr>
<td><strong>Thyroid function tests</strong></td>
<td>✓</td>
<td></td>
<td>6 monthly (more often if evidence of deterioration).</td>
</tr>
<tr>
<td><strong>ECG</strong></td>
<td>✓</td>
<td></td>
<td></td>
</tr>
<tr>
<td><strong>Full blood count</strong></td>
<td>✓</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>
| **Lithium levels**   | One week after starting, and one week after every dose change and until levels are stable. (NICE)¹  
Aim for the minimum dose to achieve a therapeutic response. Usually in the range: 0.6 to 0.8 mmol/litre (NICE)¹  
A therapeutic response may be seen at a level of 0.4mmol/litre. (BNF)³  
| ✓Every 3 months.  
Normally, 0.6–0.8 mmol/litre, according to patient response, (A therapeutic response may be seen at a level of 0.4mmol/litre).  
0.8–1.0 mmol/litre if the patient has relapsed previously on lithium or has subsyndromal symptoms. (NICE)¹  
Also observe/inform patient to be aware of signs of toxicity: blurred vision, GI disturbances, muscle weakness, drowsiness, etc. These usually occur at levels >1.5mmol/litre, but can occur at lower levels.  
Monitor older adults more closely, as they are at greater risk of developing toxicity. Use lower doses. They may develop symptoms of lithium toxicity at standard therapeutic levels. |
| **Serum calcium**    | ✓        |            |            |
| **Physical health check** | ✓ | | Annually as appropriate. Raised serum calcium may indicate hyperparathyroidism. |
| **Patient’s mental state.** | ✓ | | As needed.  
Regular reviews of mental state and personal and social functioning, to ensure that symptoms (including sub-threshold symptoms) are treated if they significantly impair social functioning. |

✓: Routine essential monitoring. ⁵

An A4 version of the lithium monitoring booklet is available in the ‘Medication information leaflet’s (Trust’s own)’ section of the website for patients with impaired vision.
Information for Clinicians on Managing Lithium Drug Interactions.3,6

1. Potentially hazardous interactions. Combined administration should be avoided or only undertaken with caution and appropriate monitoring.

<table>
<thead>
<tr>
<th>DRUG</th>
<th>INTERACTION</th>
</tr>
</thead>
<tbody>
<tr>
<td>ACE inhibitors e.g. enalapril, Angiotensin-II antagonists e.g. losartan</td>
<td>Excretion reduced. Increased plasma concentration. May cause toxicity. Monitor closely for signs of lithium toxicity, and consider taking lithium levels. Be alert for the need to reduce the lithium dose (possibly by one-third to half).</td>
</tr>
<tr>
<td>Analgesics (NSAIDs) e.g. diclofenac, ibuprofen, aspirin</td>
<td>Excretion of lithium reduced. Increased risk of toxicity. Avoid concomitant use. Note - paracetamol is safer to use with lithium.</td>
</tr>
<tr>
<td>Anti-arrhythmics e.g. amiodarone</td>
<td>Risk of ventricular arrhythmias. Avoid concomitant use.</td>
</tr>
<tr>
<td>Diuretics (thiazides, potassium-sparing and loop diuretics)</td>
<td>Excretion reduced. Increased plasma concentration and risk of toxicity. Loop diuretics are safer than thiazides.</td>
</tr>
<tr>
<td>Methylldopa</td>
<td>Neurotoxicity may occur without increasing plasma concentration of lithium. Avoid concurrent use whenever possible.</td>
</tr>
<tr>
<td>Sertindole (also see antipsychotics below)</td>
<td>Increases risk of ventricular arrhythmias - avoid concomitant use.</td>
</tr>
</tbody>
</table>

2. Less significant interactions – usually without serious consequences.

<table>
<thead>
<tr>
<th>DRUG</th>
<th>INTERACTION</th>
</tr>
</thead>
<tbody>
<tr>
<td>Acetazolamide</td>
<td>Excretion of lithium is reduced.</td>
</tr>
<tr>
<td>Antacids e.g. Sodium bicarbonate</td>
<td>Excretion increased. Reduced plasma concentration.</td>
</tr>
<tr>
<td>Antiepileptics e.g. carbamazepine, phenytoin, topiramate</td>
<td>Neurotoxicity may occur without increased lithium plasma concentrations.</td>
</tr>
<tr>
<td>Antidepressants eg. SSRIs, tricyclics, venlafaxine</td>
<td>Increased serotonergic effects seen and an increased risk of CNS effects as well as risk of lithium toxicity reported. All can increase lithium toxicity without affecting lithium levels.</td>
</tr>
<tr>
<td>Antipsychotics</td>
<td>Increased risk of extrapyramidal side effects and possible neurotoxicity. Monitor for risk of QTc prolongation.</td>
</tr>
<tr>
<td>Calcium channel blockers</td>
<td>Neurotoxicity may occur with diltiazem or verapramil without increasing the plasma concentration of lithium.</td>
</tr>
<tr>
<td>Metronidazole</td>
<td>Increased risk of lithium toxicity</td>
</tr>
<tr>
<td>Muscle Relaxants</td>
<td>Lithium enhances the effect of muscle relaxants. Hyperkinesis caused by lithium is aggravated by baclofen.</td>
</tr>
<tr>
<td>Parasympathomimetics</td>
<td>Lithium antagonises the effects of neostigmine and pyridostigmine.</td>
</tr>
<tr>
<td>Theophylline</td>
<td>Increased excretion of lithium. Reduced plasma lithium concentration. Depressive and manic relapse may occur if the dosage of lithium is not raised when theophylline is given. Lithium levels should be monitored if theophylline (or aminophylline) is stopped, started or altered.</td>
</tr>
</tbody>
</table>

DRUG – DISEASE INTERACTION (Other risk factors)

- If renal impairment exists, avoid use of lithium (if possible) or reduce dose and closely monitor serum-lithium concentration.3
- Cardiac disease and conditions with sodium imbalance such as Addison’s disease will require dose reduction or discontinuation. Similarly, in severe diarrhoea and/or vomiting and in concurrent infection, (especially if sweating profusely). 3
- Psoriasis: risk of exacerbation.3

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