**Lithium**

**Mental Health Shared Care Guideline**

**Indications:** Lithium is widely used in primary and secondary care for the following:
- Prophylaxis and treatment of mania
- Prophylaxis of bipolar disorder
- Prophylaxis of recurrent depression where treatment with other antidepressants has failed
- Augmentation of antidepressant therapy (unlicensed use).

**Dosage & Administration**

Preparations vary widely in bioavailability. Lithium must be prescribed by brand and pharmaceutical formulation (not generically). Patients should be maintained on the same brand and presentation to ensure stable lithium levels. Change in brand or presentation requires the same precautions as initiation of treatment. Lithium should be prescribed by brand, stating the dose as the amount of lithium citrate to avoid dosing errors.

Lithium carbonate is currently available as:
- **Camcolit®** 250mg immediate release tablets and 400mg modified release tablets
- **Liskonum®** 450mg modified release tablets
- **Priadel®** 200mg and 400mg modified release tablets

Lithium Citrate is currently available as:
- **Priadel®** liquid 520mg/5ml
- **Li-Liquid®** 509mg/5ml (To avoid overdose, Li-Liquid 1018mg/5ml should not be prescribed)

Particular care should be given to ensuring the correct dose and frequency of administration of lithium when prescribing or administering lithium.

**Monitoring**

Regular monitoring of serum levels is mandatory due to lithium’s narrow therapeutic index. The normal therapeutic range is 0.4 – 1.0 mmol/litre (elderly 0.4 – 0.8mmol/litre).

*Blood samples must be taken 12 hours after the previous dose. The time of the sample, total daily dose and the time of the last dose must be noted on the lab request form.*

Monitor more frequently:
- after dose changes
- in elderly patients
- if there is evidence of declining renal function.

(Take samples at least 5 days after changes in dose or changes to treatment affecting lithium levels.)

**Initiation Phase**

Allow at least 5 days after initiation to achieve steady state before sampling for the first lithium level. A target serum lithium level should be set for each patient and the dose adjusted by the prescriber, if necessary, to achieve this target. The BNF recommends serum lithium levels at weekly intervals until the dose has remained unchanged for 4 weeks.

**Long Term Monitoring Requirements** (For patients with no risk factors, no serious side effects and a stable mental state)
- Every 3 months: serum lithium levels
- Every 6 months: TT4, TSH and U&E / eGFR
- Every 12 months: check weight & height (BMI)
- Assess side effects at every visit. Consider referral to specialist renal or endocrinology services if appropriate.

**Mental Health Specialist Responsibilities**

- A Register of lithium patients should be maintained and should clearly state who is responsible for routine review, monitoring and for acting on abnormal results
- Where the specialist is responsible for monitoring, they will be responsible for acting on test results and informing the patient’s GP immediately of abnormal Lithium levels together with action taken
- Confirm the diagnosis and assess risk factors
- Pre-treatment tests – U&E, eGFR, free T4, TSH, weight and height. FBC and ECG if indicated
- Educate patient and/or carer. Provide “Lithium Therapy- Important Information for Patients” pack and update patient monitoring record book with result of regular tests
- Advise GP how to initiate treatment
- If GP agrees, responsibility for monitoring may pass to GP - complete pathway referral proforma
- Communicate test results to GP (request “copy to” on lab form - state GP name and cipher code)
- Review patient at agreed regular intervals (as determined by mental health specialist)
- Advise GP on how and when to discontinue treatment.

**Primary Care Responsibilities (continued overleaf)**

- A Register of lithium patients should be maintained and should clearly state who is responsible for routine review, monitoring and for acting on abnormal results
- Provided monitoring results are satisfactory, provide the patient with repeat prescriptions - specifying strength, brand and presentation
- Monitor mental state and refer to mental health specialist for advice if treatment is ineffective
- Check for side effects, altered risk factors and signs of lithium toxicity at each appointment
Contraindications

- Dose Adjustment – where the GP is clear that this is necessary, any change must be communicated in writing to the mental health specialist – if in doubt, seek specialist’s advice
- Temporarily reduce dose or discontinue lithium in serious diarrhoea, vomiting or intercurrent infection (especially if sweating profusely) – if in doubt, seek specialist’s advice
- Review concomitant medication for possible interaction with lithium
- When responsibility for monitoring is transferred from mental health specialist, primary care will be responsible for monitoring and acting on: lithium levels, renal function, free T4, TSH, weight and height according to guidelines above and informing the specialist immediately of abnormal Lithium levels and action taken
- Inform the specialist immediately of any change in medication which could cause a potential interaction with lithium
- Communicate relevant test results (request “copy to” on lab form specifying consultant’s name and hospital) and action taken to mental health specialist including information on interacting medication
- Update patient monitoring record book with result of regular tests.

Adverse Effects, Precautions and Contraindications

The most common side effects of lithium include: GI disturbances (e.g. nausea, diarrhoea, dry mouth); fine tremor, thirst, polyuria; polydipsia; weight gain; oedema. These may be short term and can often be prevented or relieved by a moderate reduction in dose. Refer to the SPC for a full list of adverse effects.

Toxicity

It is vital to be alert for signs of lithium toxicity, which can be fatal. These include: blurred vision, muscle weakness, drowsiness, coarse tremor, slurred speech, ataxia, confusion, convulsions, nausea, vomiting and ECG changes. Toxicity can be associated with serum levels over 1.5mmol/litre but can occur without a rise in serum level. It is important to “treat the patient not the level”.

A number of factors may increase the risk of lithium toxicity including: Drug interactions (see below); renal disease; concomitant diarrhoea or vomiting (dehydration); sodium depletion.

Precautions

Abrupt cessation of lithium is strongly associated with manic relapse. For planned cessation of therapy, lithium should be withdrawn over two to four weeks. Lithium should be stopped 24 hours prior to surgery and restarted as soon as renal function and fluid balance return to normal. Ensure specialist is informed of any such changes. In order to maintain a stable electrolyte balance, diet and fluid intake should remain normal. This is especially important in hot weather or work environment. Avoid major dietary changes

Contraindications

Relative and absolute contraindications include: Pregnancy, breast-feeding, severe renal impairment, serious cardiac disease (e.g. cardiac failure, sick sinus syndrome), conditions with sodium imbalance such as Addison’s disease.

Avoiding Drug Interactions

Patients should be advised to check with their doctor or pharmacist that any new medicine (in particular those to treat pain) that is prescribed by a doctor or bought in a pharmacy or other shop, is safe to take with lithium.

<table>
<thead>
<tr>
<th>Effect of Interaction</th>
<th>Drug Group</th>
<th>Interacting drug</th>
<th>NPSA alert advises particular care</th>
</tr>
</thead>
<tbody>
<tr>
<td>Increase in Lithium Levels</td>
<td>antibiotics</td>
<td>metronidazole, tetracyclines, co-trimoxazole</td>
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<tr>
<td></td>
<td>NSAIDs</td>
<td>e.g. ibuprofen, diclofenac</td>
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<tr>
<td></td>
<td>ACE Inhibitors</td>
<td>All ACE inhibitors and angiotensin II antagonists</td>
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<td></td>
<td>diuretics</td>
<td>thiazide, loop and potassium sparing diuretics</td>
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<tr>
<td>Decrease in Lithium Levels</td>
<td>xanthines</td>
<td>aminophylline, theophylline, caffeine</td>
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<tr>
<td></td>
<td>sodium Salts</td>
<td>e.g. antacids containing sodium bicarbonate, urinary alkalinising agents</td>
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<tr>
<td></td>
<td>diuretics</td>
<td>acetazolamide</td>
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<tr>
<td>Other (No change in serum levels)</td>
<td>antiepileptics</td>
<td>carbamazepine, phenytoin</td>
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<td></td>
<td>methyldopa</td>
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<td></td>
<td>calcium channel blockers</td>
<td>diltiazem, verapamil</td>
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<td></td>
<td>antidepressants</td>
<td>SSRIs and tricyclics</td>
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<td></td>
<td>antipsychotics</td>
<td>e.g. clozapine, haloperidol, phenothiazines, sulpiride</td>
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</table>

Many of these combinations can be used safely in clinical practice but additional monitoring may be needed especially on initiation, discontinuation or dose change. GPs should liaise with the mental health specialist for further advice.

Communication

For any queries relating to this patient’s treatment with lithium, please contact the consultant named at the top of this document.

This information is not inclusive of all prescribing information and potential adverse effects. Please refer to full prescribing data in the SPC or the BNF

The Northern Ireland Lithium Pathway and Referral Proforma can be found at: http://www.hscboard.hscni.net/medicinesmanagement/Prescribing%20Guidance/Lithium/index.html

The NPSA Alert on the Safer Use of Lithium can be found at: http://www.nrls.npsa.nhs.uk/alerts/

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