Lithium

Shared care guideline

Specialist details	Patient identifier
Name: _____	
Location: _____	
Tel: _____	**Date:** _____

Introduction

Licensed Indications: Mania, bipolar disorder, recurrent depression (where treatment with other antidepressants has failed); aggressive behaviour and self-harm.

Unlicensed indications: Augmentation of antidepressant therapy; prophylaxis of cluster headache

*A lithium care pathway is available to support the shared-care arrangements for Mental Health indications. For cluster headache communication of shared-care arrangements for individual patients will be agreed and advised via usual correspondence methods.

Adult dosage and administration

Lithium must be prescribed by brand and pharmaceutical formulation as preparations vary widely in bioavailability. Patients should be maintained on the same brand and presentation to ensure stable lithium levels. A change in brand or presentation requires the same precautions as initiation of treatment.

Target serum lithium levels should be set for each patient and the dose individualised depending on serum lithium levels and clinical response. Particular care should be given to ensuring the correct dose and frequency of administration when prescribing or administering lithium.

Cluster headache: typically starting with 400mg (modified release) once a day, adjusting as necessary depending on lithium levels and response.

Lithium carbonate is currently available as:

- **Priadel®** 200mg and 400mg modified release tablets
- **Camcolit®** 400mg modified release tablets
- **Lithium Carbonate Essential Pharma®** 250 mg film-coated tablets (was Camcolit 250mg immediate release).
- **Liskonum®** 450mg 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).

If a liquid formulation is required, this should be prescribed by brand. Lithium Citrate 509mg (or 520mg) is considered similar to 200mg of lithium carbonate. Particular care should be taken if prescribing liquid preparations; lack of clarity may lead to the patient receiving a sub-therapeutic or toxic dose.

Monitoring

- Regular monitoring of serum levels is mandatory due to lithium's narrow therapeutic index.
- In people prescribed lithium for the first time, the normal therapeutic range is 0.6 – 0.8 mmol/litre
- A higher target lithium level (0.8 - 1.0 mmol/litre) should be considered for people who have previously relapsed whilst taking lithium, have sub threshold symptoms with functional impairment, acute mania, or for cluster headache patients who have not adequately responded.
- In elderly, the therapeutic range is lower (0.4 – 0.8mmol/litre)
- The specialist service will determine the target range for each patient and advise the primary care prescriber accordingly.

More frequent monitoring than recommended below may be required:

- after dose changes
- after changes in preparation
- in elderly patients
- if there is evidence of declining renal function
- after changes in other medication which may affect Lithium level

It is recommended that blood samples are taken 12 hours after the previous dose. To allow the correct interpretation of levels, it is important that the time of the sample, total daily dose and the time of the last dose is noted on the lab request form.

*****Take samples at least 5 days (and no more than 7 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 routine serum-lithium monitoring weekly after initiation and after each dose change until levels are stable on the same dose (consider an additional test after at least 5 days to confirm lithium level is stable), then every three months thereafter.

Long Term Monitoring

- Measure plasma lithium level every 3 months for the first year. After the first year, continue 3 monthly monitoring in:
    - older people
    - people taking drugs that interact with lithium
    - people who have or are at risk of impaired renal or thyroid function, raised calcium levels or other complications
    - people with poor symptom control, or poor adherence, or who are at risk of non-compliance with monitoring schedule
    - people whose last lithium level was 0.8 mmol/litre or higher.

For people who are at low risk of developing toxicity or raised lithium levels, and with good symptom control, frequency of monitoring may be reduced to every six months with the agreement of the specialist and GP.

- Measure weight or BMI (at least annually). Arrange tests for urea and electrolytes including adjusted calcium, estimated glomerular filtration rate (eGFR) and thyroid function every 6 months, and more often if there is evidence of impaired renal or thyroid function, raised calcium levels or an increase in mood symptoms that may be related to impaired thyroid function.
- Assess side effects at every visit. Consider referral to specialist renal or endocrinology services if appropriate.

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 action taken if test results are abnormal.
- Confirm the diagnosis and assess risk factors.
- Pre-treatment tests – U&E, eGFR, adjusted calcium, free T4, TSH, weight or BMI, FBC. ECG if indicated. Pregnancy test (to exclude pregnancy) if appropriate.
- Educate patient and/or carer. Provide appropriate written information (e.g. "Lithium Therapy- Important Information for Patients" pack, and/or Choice and Medication leaflet), and provide the means for patient to keep a record of their monitoring results (e.g. "Lithium Therapy Record Book")
- Advise GP how to initiate treatment, specifying and communicating target lithium level range.
- If GP agrees, responsibility for monitoring may pass to GP - communicate as per Lithium Care pathway.*
- Provide GP with advice and support in the event of abnormal monitoring results.
- Communicate all test results and side effects to GP as per Lithium Care pathway.*
- Review patient at agreed regular intervals (as determined by specialist).
- Advise GP on how and when to discontinue treatment.

Primary care 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.
- Provided monitoring results are satisfactory, provide the patient with repeat prescriptions - specifying strength, brand and presentation.
- For relevant indications 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.
- 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. For cluster headache planned dose adjustments remain the responsibility of the specialist.
- Temporarily reduce dose or discontinue lithium in serious diarrhoea, vomiting or 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 the specialist, primary care will be responsible for monitoring and acting on: lithium levels, renal function, free T4, TSH, adjusted calcium, weight or BMI according to guidelines above and informing the specialist immediately of abnormal lithium levels and action taken.
- Communicate all test results and action taken, if any, to the specialist, as per Lithium Care pathway.*
- Communicate any changes to medication which may result in a potentially hazardous interaction with lithium.
- Facilitate and support the update of the patient held monitoring record.

Adverse effects, precautions and contraindications

Adverse effects The most common side effects of lithium include: GI disturbances (eg. 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, other causes of dehydration, sodium depletion.

If toxicity is suspected:

- Stop lithium immediately
- Check lithium levels, serum creatinine, U&Es
- Refer to hospital / A&E if clinical condition warrants
- Seek advice from specialist for re-initiation of lithium.

Precautions

Abrupt cessation of lithium is strongly associated with manic relapse. For planned cessation of therapy, lithium should be withdrawn over at least four weeks (preferably up to three months).

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.

If urea and/or creatinine levels become elevated, or estimated glomerular filtration rate falls over two or more tests, discuss with specialist. More frequent monitoring may be required.

Pregnancy / contraception

Women of childbearing potential taking lithium should be advised to use effective contraception. Patients discovered or planning to become pregnant should be referred to the relevant specialist at the earliest opportunity.

Contraindications

Relative and absolute contraindications include: pregnancy, breast-feeding, severe renal impairment, cardiac disease, cardiac insufficiency, family or personal history of Brugada syndrome, untreated hypothyroidism, conditions with sodium imbalance such as dehydration, Addison's disease, low sodium diets.

Common drug interactions

Healthcare professionals should check the potential for interactions with lithium using the most up-to date sources available. 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.

Although many of these combinations can be used safely in clinical practice, the onset and degree of the interaction can vary and additional monitoring is likely to be needed especially on initiation, dose change or discontinuation, with doses adjusted accordingly. GPs should liaise with the specialist for advice.

Particular care is advised with interactions which are more likely to lead to toxicity, these are highlighted in red. If co-prescription is unavoidable, a dose adjustment of lithium may be required, levels must be monitored more frequently and patients should be assessed for signs and symptoms of lithium toxicity.

Drugs that may increase plasma lithium levels (by reducing renal elimination) and so risk toxicity:

- NSAIDs (including cyclo-oxygenase 2 inhibitors). 'As required' use of NSAIDs should be avoided where possible as it may cause fluctuations in lithium levels and makes monitoring levels challenging.
- Diuretics, particularly thiazide diuretics
- Angiotensin converting enzyme (ACE) inhibitors and angiotensin II receptor antagonists
- Other drugs which alter electrolyte balance with the potential to alter lithium clearance e.g. steroids.
- Certain antibiotics including metronidazole and tetracyclines

Drugs that may decrease plasma lithium levels (by increasing renal elimination) and so risk loss of efficacy:

- Theophylline
- Products which contain sodium bicarbonate e.g. antacids
- Acetazolamide
- Empaglifozin

Drugs that may increase risk of neurotoxicity when co-administered with lithium:

- Calcium channel blockers (e.g. verapamil, diltiazem)
- Antipsychotics (e.g. haloperidol, olanzapine, clozapine, flupentixol, chlorpromazine)
- Antidepressants with a serotonergic action (e.g. SSRIs, tricyclic antidepressants, venlafaxine, duloxetine)
- Carbamazepine
- Methyldopa
- Triptans

Drugs associated with QT prolongation (e.g. amiodarone, macrolides, tricyclic antidepressants) – potential for additive effects when co-administered with lithium.

Drugs that lower seizure threshold (e.g. SSRIs, tricyclic antidepressants, antipsychotics) – increased risk of seizures

Communication

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