

SHARED CARE GUIDELINE

DRUG NAME: Lithium

INDICATION/S COVERED:

- The management of acute manic episodes in adults.
- The management of episodes of recurrent depressive disorders where treatment with other antidepressants has been unsuccessful in adults.
- In the prophylaxis against bipolar affective disorders in adults.
- Control of aggressive behaviour or intentional self-harm in adults.

Crawley CCG and Horsham and Mid-Sussex CCG Traffic Light System Classification: Amber

NOTES to the General Practitioner (GP) or Primary Care Prescriber

Amber drugs:

For drugs which require specialist initiation and/or dose titration and specific ongoing monitoring. For initiation, dose stabilisation and prescribing (including monitoring) by a specialist until the patient is stabilised (usually for a minimum 3 months but see individual shared care guidelines) after which the GP may be asked to agree shared care through the use of shared care guidelines.

The expectation is that these guidelines should provide sufficient information to enable GPs or Primary Care Prescribers to be confident to take clinical and legal responsibility for prescribing these drugs.

The questions below will help you confirm this:

- Is the patient currently under your care? (e.g. shared care should not be agreed if the patient is currently in intermediate care following hospital discharge.)
- Do you have the relevant knowledge, skills and access to equipment to allow you to monitor treatment as indicated in this effective shared care agreement?
- Have you been provided with relevant clinical details including monitoring data?

If you can answer YES to all these questions (after reading this shared care guideline), then it is appropriate for you to accept prescribing responsibility.

If the answer is NO to any of these questions, you should not accept prescribing responsibility. You should write to the Consultant/Specialist within 28 days, outlining your reasons for NOT prescribing. If you do not have the confidence to prescribe, we suggest you discuss this with your local Trust/specialist service, who will be willing to provide training and support. If you still lack the confidence to accept clinical responsibility, you still have the right to decline. Your CCG Medicines Management Pharmacist will assist you in making decisions about shared care.

Prescribing unlicensed medicines or medicines outside the recommendations of their marketing authorisation alters (and probably increases) the prescriber's professional responsibility and potential liability. The prescriber should be able to justify and feel competent in using such medicines.

The patient's best interests are always paramount

The GP or Primary Care Prescriber has the right to refuse to agree to shared care, in such an event the total clinical responsibility will remain with the consultant.

Reason for update: Previous out of date		Prepared by: Ray Lyon, Chief Pharmacist – Strategy, Sussex Partnership Trust Updated by: Nicki Sherwood, Clinical Pharmacist, Sussex Partnership Trust
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		Ratified by Crawley CCG and Horsham and Mid Sussex CCG Clinical Policy and Medicines Approval Panel
Approved by Crawley CCG and Horsham and Mid-Sussex CCG on: 31st January 2017		

Information

This page should include general information relevant to the specific drug and indication/s. It should include information on the dose of the drug for the indication, cautions, contraindications, common side effects and interactions to look out for. This section should have input from a specialist consultant in the field.

This information sheet does not replace the Summary of Product Characteristics (SPC), which should be read in conjunction with this guidance. Prescribers should also refer to the appropriate paragraph in the current edition of the BNF.

1. Link to the relevant SPC website:

Priadel[®] 400mg prolonged release tablets www.medicines.org.uk/emc/medicine/25500

Priadel[®] 200mg prolonged release tablets www.medicines.org.uk/emc/medicine/25501

Priadel[®] 520mg/5ml liquid www.medicines.org.uk/emc/medicine/6981

Li-liquid[®] 1018mg/5ml liquid www.medicines.org.uk/emc/medicine/10680

Li-liquid[®] 509mg/5ml liquid www.medicines.org.uk/emc/medicine/10677

Liskonium[®] 450mg tablets www.medicines.org.uk/emc/medicine/6981

2. Background to use for the indication/s, including licence status:

- In the management of acute manic episodes – licensed indication.
- In the management of episodes of recurrent depressive disorders where treatment with other antidepressants has been unsuccessful – licensed indication.
- In the prophylaxis against bipolar affective disorders – licensed indication.
- Control of aggressive behaviour or intentional self-harm – licensed indication.

3. Dose & administration:

Target serum lithium concentration (mmol/l) will vary depending on the diagnosis and past response to treatment. Levels should never exceed 1.5 mmol/l and levels of 2 mmols/l would require urgent review by a doctor, particularly if presenting with signs of toxicity.

- Aim to maintain a plasma lithium level between 0.6 and 0.8mmol/l in people being prescribed lithium for the first time.
- Consider maintaining a plasma lithium level between 0.8 and 1.0mmol/l for a trial of at least 6 months for people who have had a relapse while taking lithium in the past **or** who are taking lithium and have subthreshold symptoms with functional impairment.

4. Cautions (including for pregnancy & lactation where relevant):

• General

The minimum clinically effective dose of lithium should always be used. Clear instructions regarding the symptoms of impending toxicity should be given by the doctor to patients receiving long-term lithium therapy. They should be warned of the urgency of immediate action should these symptoms appear, and also of the need to maintain a constant and adequate fluid intake. At the first sign of toxicity, the patient should consult a doctor and lithium levels should be checked. Treatment should be discontinued immediately on the first signs of toxicity.

• Monitoring recommendations

Before starting treatment with lithium, measure weight or BMI and arrange tests for urea, creatinine and electrolytes including calcium estimated glomerular filtration rate (eGFR), thyroid function and a full blood count. Arrange an ECG for people with cardiovascular disease or risk factors for it. Patients should be euthyroid before initiation of lithium therapy. Lithium therapy is contraindicated in patients with severe renal impairment, cardiac insufficiency or untreated hypothyroidism. Renal, cardiac and thyroid functions should be re-assessed regularly during treatment with lithium. For monitoring recommendations of lithium serum levels see Section 8.

• Renal Impairment

Since lithium is primarily excreted via the renal route, significant accumulation of lithium may occur in patients with renal impairment. Monitor lithium dose and plasma lithium levels more frequently if urea levels and creatinine levels become elevated, or eGFR falls over 2 or more tests and assess the rate of deterioration of renal function. If very regular and close monitoring of serum lithium levels and plasma creatinine levels is not possible, lithium should not be prescribed in this population. Lithium is contraindicated in patients with severe renal impairment. The possibility of hypothyroidism and renal dysfunction arising during prolonged treatment should be borne in mind and periodic assessments made. Patients should be warned to report if polyuria or polydipsia develop. In patients who develop polyuria and/or polydipsia, renal function should be monitored in addition to the routine serum lithium assessment.

Fluid/electrolyte balance

If episodes of nausea, vomiting, diarrhoea, excessive sweating, and/or other conditions leading to salt/water depletion (including severe dieting) occur, lithium dosage should be closely monitored and dosage adjustments made as necessary. Drugs likely to upset electrolyte balance such as diuretics should also be reported. Indeed, sodium depletion increases the lithium plasma concentration (due to competitive reabsorption at the renal level). In these cases, lithium dosage should be closely monitored and reduction of dosage may be necessary. Warn people not to take over-the-counter non-steroidal anti-inflammatory drugs and avoid prescribing these if possible. If they are prescribed, this should be on a regular (not prn) basis and the patient should be monitored monthly until a stable lithium level is reached and then every 3 months. Caution should be exercised to ensure that diet and fluid intake are normal in order to maintain a stable electrolyte balance. This may be of special importance in very hot weather or work environment. Infectious diseases including colds, influenza, chest infections, pneumonia, gastro-enteritis and urinary infections may alter fluid balance and thus affect serum lithium levels. Treatment discontinuation should be considered during any intercurrent infection.

- **Risk of convulsions**

The risk of convulsions may be increased in case of co-administration of lithium with drugs that lower the epileptic threshold, or in epileptic patients.

- **Benign intracranial hypertension**

There have been case reports of benign intracranial hypertension. Patients should be warned to report persistent headache and/or visual disturbances.

- **QT prolongation**

As a precautionary measure, lithium should be avoided in patients with congenital long QT syndrome, and caution should be exercised in patients with risk factors such as QT interval prolongation (e.g. uncorrected hypokalaemia, bradycardia), and in patients concomitantly treated with drugs that are known to prolong the QT interval. An up to date list of drugs prolonging the QTc interval, including links to relevant evidence can be found at the free to register site: <https://crediblemeds.org>

- **Brugada syndrome**

Lithium may unmask or aggravate Brugada syndrome, a hereditary disease of the cardiac sodium channel with characteristic electrocardiographic changes (right bundle branch block and ST segment elevation in right precordial leads), which may lead to cardiac arrest or sudden death. Lithium should not be administered to patients with Brugada Syndrome or a family history of Brugada Syndrome (see Section 4.3). Caution is advised in patients with a family history of cardiac arrest or sudden death. The evidence linking lithium to Brugada syndrome is based on two reported case studies⁹ the latest in 2010 (Wright & Salehian) was in a patient with lithium levels twice those usually used in practice (2.5mmol/l).

- **Elderly patients**

Elderly patients are particularly liable to lithium toxicity and may exhibit adverse reactions at serum levels ordinarily tolerated by younger patients. Caution is also advised since lithium excretion may be reduced in the elderly due to age related disease in renal function.

- **Children**

The use in children is not recommended.

5. Contraindications:

- Hypersensitivity to lithium or to any of the excipients.
- Cardiac disease.
- Cardiac insufficiency.
- Severe renal impairment.
- Untreated hypothyroidism.
- Breast-feeding.
- Patients with low body sodium levels, including for example dehydrated patients or those on low sodium diets.
- Addison's disease.
- Brugada syndrome or family history of Brugada syndrome.

6. Side effects: see also SPC for details

Adverse effects are directly related to blood levels and their frequency increase dramatically at plasma levels above 1.0mmol

- Fine tremor – (often responds to a low dose propranolol).
- Nephrotoxicity. Up to one third of patients may develop polyuria and polydipsia, which is usually reversible on withdrawal. Long-term treatment may result in permanent changes and renal impairment.
- Gastrointestinal disturbances – often at start of treatment and usually transient

- Weight gain and oedema (not to be treated by diuretics)
- Disturbances of thyroid function
- Exacerbation of psoriasis
- Raised antidiuretic hormone concentration
- Hypokalaemia, hypercalcaemia, hypermagnesemia, hyperparathyroidism
- ECG changes
- Mental dulling – reported in some patients, although others may report increase creativity due to increased organisational ability

Note: periods of gastric illness with diarrhoea or vomiting may result in salt and water depletion- this can lead to an increase in lithium levels.

Signs of toxicity (levels above 2.0mmol/l are normally considered dangerous – increased disorientation and seizures may lead to coma and death.

- Blurred vision
- Diarrhoea and vomiting
- Unsteadiness or clumsiness
- Difficulty in speaking
- Severe tremor or twitching limbs
- Greatly increase thirst and/or passing water
- Severe drowsiness and/or confusion
- Convulsions

7. Interactions:

- Diuretics (loop, thiazide, potassium sparing) => increase lithium levels
- ACE-Inhibitors & Angiotensin-II-Antagonists => increase lithium levels
- Non-Steroidal Anti-Inflammatory Drugs => increase lithium levels
- SSRIs: may increase CNS toxicity, lithium toxicity reported.
- Many other interactions are possible – refer to current edition of BNF

8. Criteria for use:

Lithium treatment should only be continued if the patient is properly monitored against the criteria set out below:

Routine monitoring

Results of routine monitoring should be recorded in a patient held lithium monitoring booklet. If the patient does not hold one, a copy should be provided for the patient and the importance of carrying the booklet for healthcare professionals to refer to should be stressed.

Routine Testing	
eGFR	Every 6 months – (3 months for elderly or where complicating factors)
Thyroid Function Tests	<ul style="list-style-type: none"> ○ Every 6 months – (every 4 to 6 weeks if TSH is raised) ○ Consider early thyroxine supplement in hypothyroid patients
Weight/BMI	Every six months
Electrolytes including calcium	Every six months

9. Any further information

- Brands of lithium are not bio-equivalent. They must be prescribed by brand name. If brands are changed the same precautions should be followed as when starting treatment. The preferred brand is Priadel[®] when initiating new patients.
- Lithium carbonate 200mg tablets contain 5.4 mmol of lithium which is approximately equivalent to 509mg/5ml lithium citrate tetrahydrate (Li-Liquid[®])
- 520mg/5ml of lithium citrate liquid (Priadel Liquid[®]) is equivalent to 204mg of lithium carbonate.
- Contra-indicated in cardiac failure, clinically significant renal impairment, Addison's disease and untreated hypothyroidism.
- Lithium levels can be affected by many other drugs please see 'Drug Interactions' for further guidance.
- Dose reduction or discontinuation may be necessary in diarrhoea, vomiting or intercurrent infection.
- Any women who is or planning **pregnancy** or to **breast feed** whilst on lithium therapy, should be referred to a specialist.
- Patients need to be made aware of what they should do if they become ill or find themselves in a situation that results in profuse sweating.

10. References:

- a. SPCs for all preparations listed in section 1 (checked on 4 February 2015)
- b. Safer Lithium Therapy, PSA 005, NPSA, 1 December 2009
- c. National Institute for Health and Clinical Excellence. Bipolar Disorder: the assessment and management of bipolar disorder in adults, children and young people in primary and secondary care. CG 185. September 2014
- d. <http://www.brugadadrugs.org/avoid/> (viewed 19 December 2016)

RESPONSIBILITIES and ROLES

Consultant/Specialist responsibilities

- 1 To discuss fully the aims, benefits, risks and side effects of treatment with the patient and/or carer and for written information to be supplied to the patient and/or carer.
- 2 To explain their role and provide written information as necessary.
- 3 Explain the treatment plan to the patient and/or carer including the dosing schedule.
- 4 Undertake baseline monitoring as required as laid out in the lithium monitoring booklet, including screening for a prolonged QTc interval and standard cardiovascular risks, including asking about Brugada syndrome and any history of it or sudden death in the family. If there concerns about Brugada syndrome or sudden death in the family, a full cardiac investigation by a cardiologist should be requested before initiating lithium to eliminate the diagnosis of Brugada syndrome in which lithium is contraindicated.
- 5 Ensure a patient information leaflet is issued and discussed, (available on the Sussex Partnership website).
- 6 To provide the patient and/or carer with printed advice including a lithium monitoring & information booklet, lithium alert card and initiation instructions.
- 7 To initiate treatment and monitor lithium levels until the dosage is stabilized by prescribing usually for a minimum of 3 months. A copy of the lithium levels should be requested for the GP.
- 8 While prescribing for this patient to monitor and evaluate response to treatment with the patient and/or carer, including adverse drug reactions, with the patient and to continue / discontinue treatment in line with the agreed treatment plan
- 9 Discuss the possibility of shared care with the patient and/or carer and ensure that they understand the plan for their subsequent treatment.
- 10 Supply GP with a summary of the patient's review (including anticipated length of treatment) and a link to the shared care guideline when requesting transfer of prescribing to GP or Primary Care Prescribers.
- 11 To provide the GP with target serum levels of lithium and to advise on actions to take when the serum level is outside the range.
- 12 To document any changes and/or results in the patient's lithium treatment - monitoring booklet.
- 13 To advise on dose alterations, abnormal results and concurrent medication.
- 14 To review the patient at least annually and when requested to by the GP to assess response, the benefits of continued treatment and which treatment is most appropriate.
- 15 Advise GP if treatment is to discontinue at any point.
- 16 Inform GP if patient does not attend planned follow-up.

GP or Primary Care Prescriber responsibilities

- 1 Continue prescribing of lithium at the dose recommended after stabilization.
- 2 Inform the Consultant/Specialist of any issues that may arise.
- 3 To monitor the prescribing rate of lithium for individual patients.
- 4 To undertake on-going monitoring as described below for GPs and act upon the results.
- 5 To document any changes and/or results in the patient's lithium treatment - monitoring booklet.
- 6 Monitor for adverse effects throughout treatment and check for drug interactions on initiating new treatments.
- 7 To report adverse drug reactions to the specialist and complete a 'yellow' card if serious.
- 8 To keep the care coordinator/mental health team informed, e.g. any change of medication prescribed for any indication.
- 9 To monitor the patient's overall health and well being.
- 10 Ensure that if care of the patient is transferred to another prescriber, that the new prescriber is made aware of the shared care guideline.
- 11 If following initiation a patient is discovered to have Brugada syndrome the lithium should be discontinued and the specialist contacted for advice. If there is concern that the patient may have Brugada syndrome following a diagnosis in a close relative, the lithium should be discontinued until the diagnosis is excluded. The specialist should be contacted for advice and informed that treatment has been discontinued until investigations have been completed.

Monitoring requirements and appropriate dose adjustment

Consultant/specialist responsibilities

To undertake baseline monitoring as required as laid out in the lithium monitoring booklet.

To undertake a baseline QTc reading and organize a full ECG if concerns about Brugada syndrome or family history of sudden death.

- 3 QTc interval as appropriate following lithium dose increase.

GP responsibilities

- 1 Lithium levels – 3 monthly (or more frequently if indicated by a dose change or illness involving fluid loss)
- 2 U&Es – 6 monthly
- 3 eGFR – 6 monthly (3 months for elderly or where complicating factors)
- 4 TSH – 6 monthly (every 4 to 6 weeks if TSH is raised)
- 5 Weight/BMI – 6 monthly
- 6 Corrected calcium – as appropriate (Raised serum calcium may indicate hyperparathyroidism)
- 7 QTc interval following the GP initiation of a new drug known to cause QTc prolongation
- 8 QTc interval following the GP increasing the dose of another drug known to cause QTc prolongation.

If lithium levels are outside the target range, the specialist should be contacted for advice. If above 1.5mmol/l then doses should be stopped and additional serum levels taken until in range. The reasons for the rise in serum level should be investigated with the patient/carer, e.g. change in lifestyle, over the counter medication, adherence problems. Advice on future dosages must also be obtained from the specialist. If serum levels are above 2mmol/l the patient should be urgently reviewed by a doctor, particularly if presenting with signs of toxicity.

GPs should order a copy of any test results for the specialist for information. Results should be provided to the patient so their lithium monitoring booklet can be updated.

Patient's/Carer's role

- 1 Ask the Consultant/Specialist or GP or Primary Care Prescriber for information, if he or she does not have a clear understanding of the treatment.
- 2 To take lithium as prescribed.
- 3 Share any concerns in relation to treatment with lithium.
- 4 Tell the Consultant/Specialist or GP or Primary Care Prescriber of any other medication being taken, including over-the-counter products.
- 5 Read the patient information leaflet included with your medication and report any side effects or concerns you have to the Consultant/Specialist or GP or Primary Care Prescriber.
- 6 Attend the follow up appointments with the consultant/specialist.
- 7 To attend appointments for monitoring blood tests.
- 8 To inform the GP if health problems arise.
- 9 To be aware of side effects, situations that could affect their lithium levels and report any relevant symptoms.
- 10 To carry their lithium monitoring record whenever consulting a healthcare professional.
- 11 To let their GP know if they ever get a diagnosis of Brugada syndrome or a close relative is ever told they have Brugada syndrome.

SHARED CARE GUIDELINE

DRUG NAME: Lithium

INDICATION:

Agreement for transfer of prescribing to General Practice or Primary Care Prescriber

Patient details:

Name:
Address:
DoB:
NHS No:
Hospital No:

Drug name and strength:

The following tests and investigations have been carried out:

Date treatment initiated:

At the last patient review the drug appeared to be effectively controlling symptoms / providing benefit:

Yes/No

The patients has now been stabilised on a dose of:

The patient has been given written information about their information:

Yes/No

The patient understands that this medication is being prescribed under a shared care agreement between their GP and specialist and they have responsibilities under the agreement to ensure they attend their GP to be regularly monitored.

Yes/No

The patient has been informed that the GP can opt-out of taking on prescribing responsibility if they do not feel clinically able to prescribe or if the patient does not attend for monitoring:

Yes/No

I will arrange to review this patient regularly. Date of next clinic appointment:

Consultant signature _____ Date _____

If the practice declines shared care, then the named consultant should be informed within 28 days of receipt of this request.

BACK-UP ADVICE AND SUPPORT

	Name / position	Telephone	Email
Specialist / Consultant:			
Alternative Specialist: (e.g. departmental contact)			
Hospital Pharmacy:	Pharmacy Office, Langley Green Hospital	01293 590429	
Out of hours: (e.g. medical team on call)			