Shared Care Guidelines for Lithium Prescribing and Monitoring

***'Offer people with bipolar disorder whose symptoms have responded effectively to treatment and remain stable the option to return to primary care for further management'*; NICE CG185**

Guidelines Objectives

To define safe and acceptable procedures for the prescribing and monitoring of lithium by primary and secondary care practitioners.

Indications for Lithium Treatment

Lithium salts are used chiefly for three indications:

1. Prophylaxis against Bipolar Affective Disorder (BAD)
2. Augmentation of antidepressant treatment in complex depression
3. Treatment of acute mania and hypomania

Lithium treatment for acute mania and complex depression should only be initiated by a specialist and will usually be started in hospital. The decision to give prophylactic treatment requires specialist advice and must be based on careful consideration of the benefits weighed against the material risks of long-term therapy.

Adults with learning disabilities should only be started on lithium in consultation with a specialist in this field

AREAS OF RESPONSIBILITY FOR THE SHARING OF CARE

This shared care guideline outlines suggested ways in which the responsibilities for managing the prescribing of lithium can be shared between the specialist and general practitioner (GP) or non-medical prescriber in primary care. **If a specialist asks the GP to prescribe a specific drug treatment, the GP should reply to this request as soon as practicable.** The doctor who prescribes the medication legally assumes clinical responsibility for the drug and the consequences of its use.

ROLES and RESPONSIBILITIES

Specialist
• To initiate lithium and establish target therapeutic levels and/or support colleagues in primary care with this, agreeing consistency of brand and formulation • To ensure that a lithium resource pack is provided to all new patients commencing treatment within secondary care services • To undertake lithium monitoring where patients continue to receive lithium treatment from secondary care • To communicate all lithium results to the GP • To ensure that the patient's mental state is reviewed in line with agreed care plan and Care Programme Approach (CPA) requirements • To provide specific advice on lithium management in complex cases

Role of Primary Care/GP Practice
• To provide maintenance lithium treatment in stabilised patients: initiation of lithium therapy may be undertaken by GPs with a special interest and competency in this clinical area • To undertake lithium monitoring and complete the lithium record book when regular medication is provided by primary care • To monitor and manage the patient's physical health where appropriate • To liaise with the mental health services regarding treatment interventions that may have a bearing on lithium treatment • To support patient adherence to treatment

Role of Patient/Carer
• To bring lithium resource pack to all clinic, GP appointments and hospital admissions • To present with up to date records to the supplying pharmacy when presenting repeat prescriptions for dispensing

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SUPPORTING INFORMATION *(*Refer to SmPC's for full guidance)

Lithium is a metal usually prescribed as lithium carbonate but is also available as the citrate salt. Lithium has a narrow therapeutic range (0.4 – 0.8mmol/L), based on a blood test taken 12 hours after the last dose of lithium, and so routine monitoring of serum lithium concentrations is an important part of treatment to ensure an effective dose and minimise adverse effects. Optimum outcome within the range of 0.4 - 0.8mmol/L does depend on clinical circumstances and patient tolerability.
Lithium is not metabolised and is almost entirely renally excreted. Renal function should, therefore, be assessed before and at regular intervals during treatment. All patients should be encouraged to maintain a good intake of fluids and to avoid sudden changes in dietary intake of salt.
Some patients may become hypothyroid on long-term lithium therapy; therefore, thyroid function must also be assessed before and during treatment.

Adverse Effects
Acute, generally self-limiting adverse effects include nausea, other gastro-intestinal disturbances and fine tremor.
Chronic adverse effects include polyuria and polydipsia, weight gain, hypothyroidism and occasional histological and functional changes in the kidney.

Signs of Lithium Toxicity
Lithium levels should be checked in any patient complaining of: severe thirst, severe diarrhoea, vomiting or anorexia, fever, loss of weight, muscle twitching, shaking of hands or legs, drowsiness, confusion, muscle weakness, slurred speech, ataxia, blurred vision or any serious intercurrent medical illness.

Management of Lithium Intoxication
Signs of lithium toxicity may be present even at a 'therapeutic' lithium level. Raised lithium levels or signs of toxicity require lithium to be reduced or stopped, at least until blood levels fall to therapeutic range and the cause of lithium toxicity has been investigated.

In all cases of suspected lithium toxicity advice should be obtained from a specialist.

As a general guide:-

Serum level 1.5mmol/l or above:

Potential symptoms: blurred vision, muscle weakness, ataxia, increasing GI disturbances (anorexia, nausea, diarrhoea), drowsiness, confusion, coarse tremor, dysarthria, poor co-ordination, muscle twitching. Fine tremor is a normal side effect, but a coarse tremor may indicate toxicity.

Action: Withhold lithium, advise patient to drink water, seek specialist advice, daily lithium levels.

Serum level 2.0mmol/l or above (severe lithium toxicity):

Potential symptoms: hyperreflexia or hyperextension of limbs, convulsions, disorientation, syncope, renal failure, circulatory failure, coma.

Action: Stop lithium immediately and seek urgent acute medical care.

Contra-indications and Precautions
Renal insufficiency (eGFR below 30ml/min or serum creatinine above 130mmol/l), heart failure, Addison's disease and untreated thyroid disorder are all contra-indications to lithium therapy. Seek specialist advice before prescribing in pregnancy and to breast-feeding mothers.

Drug Interactions with Lithium
Lithium has many potential drug interactions and staff should refer to the BNF before making adjustments to therapy. In particular, consider:

- Diuretics, especially thiazides,
- Non-steroidal anti-inflammatory drugs (NSAIDs)
- Angiotensin converting enzyme (ACE) inhibitors and Angiotensin II Receptor antagonists

These can all cause lithium toxicity as they reduce renal excretion of lithium. If they are used, lithium dosage should be reduced and levels should be checked more frequently. The patient should be assessed regularly for signs and symptoms of lithium toxicity.

NB: NSAIDs such as ibuprofen are available to purchase over the counter, without the involvement of any healthcare professional. Irregular or acute use of interacting medicines might pose a greater risk of toxicity than closely monitored regular use. Patients must be instructed to seek advice before purchasing/using other medicines.

Other interactions are listed in the BNF and SmPC.

Practical Management of Lithium Treatment
When taking blood for serum lithium level determination, use a 10ml tube for clotted blood, NOT a lithium heparin tube.

Blood should be taken 12 hours after the previous dose of lithium. A once-daily bedtime dose facilitates easier testing of blood levels. For patients prescribed lithium in divided doses, the morning dose should be deferred until after the blood test.

Initiation of Prophylaxis in Secondary Care or Primary Care Following Recommendation by a Specialist

- Monitoring as described in Table 1
- Initial dose is usually 400mg lithium carbonate at night, but should be reduced to 200-250mg in the frail or elderly. It may be higher in some instances on the advice of a specialist.
- After seven days check serum lithium level and as described in Table 2
- The target therapeutic range is usually 0.4-0.8mmol/L. For elderly patients, a slightly lower level may be effective, with higher levels sometimes used for younger and/or more manic patients.
- If necessary, adjust the dose of lithium in steps of 200-400mg (or less in the elderly) and continue monitoring weekly until the level has been stable for three consecutive weeks. There is a direct proportional relationship between lithium dose and blood levels: doubling a dose will double steady state levels. Do not exceed doses of 1600mg daily of lithium carbonate or equivalent in liquid form without first checking adherence and seeking specialist advice.

Maintenance Monitoring of Lithium
Independent of routine monitoring, patients should be seen at least once every 6 months to maintain rapport and encourage compliance, as well as monitor physical and biochemical status:

- Assess patient's mental state
- If necessary, adjust the dose as outlined above
- Monitoring as described in Table 1, but consider more frequent monitoring if there is evidence of impaired renal or thyroid function, raised calcium levels or an increase in mood symptoms that might be related to impaired thyroid function.

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Table 1. Required Monitoring

Pre-initiation:	**Every 6 months:**
Pulse and blood pressure	Pulse and blood pressure
ECG/cardiac function	Cardiac function (ECG if clinically indicated)
Weight or BMI	Weight or BMI
FBC	FBC
U&Es, inc. calcium	U&Es, inc. calcium
Creatinine	Creatinine
Thyroid function	Thyroid function
eGFR (estimated glomerular filtration rate)*	eGFR*

*Please note: for patients at extremes of weight (BMI less than 18.5kg/m^2 or greater than 30kg/m^2) it is better to use the absolute glomerular filtration weight or creatinine clearance (calculated from Cockcroft and Gault formula) when making adjustments to drug doses

Absolute GFR:

$$\text{Absolute GFR} = \text{eGFR} \left(\frac{\text{body surface area}}{1.73} \right)$$

(Cockcroft and Gault formula):

CrCl = *constant* x [(weight in kg x (140 – age in years)]

$$\text{Creatinine Clearance} = \textit{constant} \left(\frac{\text{weight in kg (140-age in years)}}{\text{creatinine in mmol/L}} \right)$$

constant: ♀ = 1.04 ♂ = 1.23

Table 2. Lithium Monitoring

Stage in Therapy	**Monitoring Interval**
Initiation	Allow minimum of 5-7 days after a dose change before testing level (longer in reduced renal function)
Dose change (inc. change in the dose of interacting medicines)	Allow minimum of 5-7 days after a dose change before testing level (longer in reduced renal function)
Early therapy – until stabilised	Check weekly until stabilised
First Year	every 3 months
After First Year	*can* reduce to 6 months
Concomitant illness	Check weekly until stabilised
Changes in diet or activity	Check weekly until stabilised

NB: Anything that alters the body's handling of salts or fluid has the potential to alter lithium handling and can lead to sub-therapeutic or toxic levels – close monitoring is essential.

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Discontinuation of Lithium

Abrupt discontinuation of lithium provokes manic relapse in 50% BAD patients within 12 weeks; therefore, therapy must not be discontinued without liaison with specialists. It is very important to reduce lithium slowly once the decision is made to come off lithium, reducing the dose slowly over at least one month. There is a very high risk of relapse for those who are non-compliant or who sporadically take lithium.

Change of Formulation/Brand of Lithium

The different preparations of lithium are not bioequivalent although a switch between brands is unlikely to require dosage adjustment; however, serum lithium levels should be checked one week after any change in brand or formulation. Particular care needs to be taken if changing from a lithium carbonate to a lithium citrate (salt used in liquid formulation) preparation to ensure that the molar dose remains the same. Priadel® is the default brand of lithium provided within WHCT

Information for Patients

A NPSA Patient resource folder must be provided to each patient on lithium. For existing patients, replacements should be provided by the service currently prescribing the lithium. For new patients the initiating service should issue the resource pack.

Resource packs should be completed by any competent practitioner together with the patient.

Copies of the resource pack can be obtained via the Pharmacy Department or via the NHS Forms and Print contract www.nrls.npsa.nhs.uk/alerts/?entryid45=65426

Further Information

Further information on lithium can be obtained from the BNF, SmPC or from the organisations and contact details in the table below:

Worcestershire Health and Care NHS Trust		**Worcestershire Acute Hospitals NHS Trust**	
Pharmacy and Medicine Management Team	Tel: 01905 733704 08:00 – 17:00 Mon - Fri	Medicines Information Worcester Royal Hospital	Tel: 01905 760111 Open Monday-Friday (except Bank Holidays) 08.30am-17:00 In emergency, on-call pharmacist available for advice outside of these hours via switchboard 01905 763333
		Consultant in Clinical Biochemistry	Tel: 01562 513085

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