


<b>SHARED CARE PROTOCOL AND INFORMATION FOR GPs</b>		
<b>Lithium</b>		
<b>Clinical Indications: Treatment and prophylaxis of mania, Bipolar disorder, Augmentation therapy in Treatment Resistant Depression</b>		
<b>Version 1</b>	<b>Date Approved: February 2009</b>	<b>Review Date: March 2011</b>

### **Introduction**

Bipolar disorder is an episodic life-long, disabling condition characterised by abnormally elevated mood or irritability alternating with depressed mood.

The use of lithium as a treatment option for prevention of relapse in bipolar disorder has been recommended by SIGN (Guideline 82) and NICE (Clinical Guideline 38).

Lithium is also widely used for the prophylaxis and treatment of mania and for augmentation of antidepressant therapy in treatment resistant depression.

### **Shared Care**

As outlined in the NHS circular 1992 (Gen 11) when a consultant considers a patient's condition is stable he/she may seek the agreement of the patient's GP to 'share' the patient's care. This protocol provides information on treatment with lithium for the shared commitment between the consultant and GP concerned. As with every situation of shared responsibility, patient welfare is paramount and there will at times be appropriate exceptions to protocol.

### **Indication for Therapy**

The aim of treatment is to control symptoms and prevent relapse in patients with conditions described in the introduction. Lithium should be initiated by or on the advice of a Consultant in Psychiatry.

### **Recommended Dosage and Administration and Monitoring**

Lithium has a low therapeutic/toxic ratio and should be started at a low dose and titrated up to achieve therapeutic levels as indicated by serum lithium monitoring.

The recommended therapeutic range is 0.5–1.0mmol/L (0.5–0.8mmol/L in elderly patients).

### **Serum Lithium monitoring**

Serum lithium should be monitored 5-7 days after initiation, then weekly until steady state is reached, then 3 monthly when stable (more frequently, typically 2 monthly in the elderly).

More frequent monitoring is required following alteration of dosage, on development of intercurrent disease, in those with or at risk of cardiac, renal or thyroid disease, signs of manic or depressive relapse, following significant change in sodium or fluid intake, if an interacting drug is being taken or if signs of lithium toxicity occur.

**Lithium serum levels should be measured 12 hours after the previous dose.**

Patients taking lithium once daily at night should have the level measured in the morning 12 hours after the previous night time dose.

Patients taking lithium twice daily should have the level measured in the morning 12 hours after the previous night time dose. The morning dose must be postponed until after the sample has been taken.

**Cardiac, renal and thyroid monitoring- minimum requirements**

Baseline ECG for those with existing cardiac disease or risk factors.

Renal function-Urea and electrolytes baseline and then every 6 months.

Calcium- baseline and then every 6 months

Thyroid function -TSH and T4 baseline and then every 6 months

More frequent monitoring may be indicated in those with or at risk of cardiac, renal or thyroid disease.

**Products available**

Two salts of lithium are available (lithium carbonate and lithium citrate) which contain different amounts of lithium (mmolLi<sup>+</sup>) and are not interchangeable.

Lithium carbonate (tablets) 200mg ≡ lithium citrate (liquids) 509mg

Preparations vary widely in bioavailability therefore any change of preparation (even those containing the same salt) requires the same precautions as initiation of treatment i.e. weekly monitoring.

**Lithium must always be prescribed by trade name**

<b>LITHIUM CARBONATE TABLETS</b>		
<b>Trade Name</b>	<b>Tablet Strength Available</b>	<b>Amount of Lithium (Li<sup>+</sup>)</b>
<b>Priadel<sup>®</sup></b>	200mg m/r (scored)	5.4mmol/200mg
	400mg m/r (scored)	10.8mmol/400mg
<b>Camcolit 250<sup>®</sup></b>	250mg (scored)	6.8mmol/250mg
<b>Camcolit 400<sup>®</sup></b>	400mg m/r (scored)	10.8mmol/400mg
<b>Liskonum<sup>®</sup></b>	450mg m/r (scored)	12.2mmol/450mg
<b>LITHIUM CITRATE LIQUID</b>		
<b>Trade Name</b>	<b>Liquid Strength Available</b>	<b>Amount of Lithium (Li<sup>+</sup>)</b>
<b>Priadel<sup>®</sup> *</b>	520mg/5ml	5.4mmol/5ml
<b>Li-liquid<sup>®</sup></b>	509mg/5ml	5.4mmol/5ml
<b>Li-liquid<sup>®</sup></b>	1018mg/5ml	10.8mmol/5ml

\*See Appendix 1- "Significant change to labelling of Priadel<sup>®</sup> liquid and information on switching between Priadel liquid and tablets."

Priadel<sup>®</sup> tablets are the most frequently prescribed lithium preparation in Fife and Priadel<sup>®</sup> liquid the most commonly prescribed liquid lithium preparation.

**Dosing frequency depends on preparation prescribed**

Liquid preparations and Liskonum tablets should be prescribed twice daily

Other lithium preparations are usually prescribed as a single dose at night.

**Interpretation of serum lithium level (Range: 0.5 – 1.0mmol/L, elderly 0.5 – 0.8mmol/L)**

<b>Level &amp; Action to Be Taken</b>	
< 0.5mmol/L & patient is well and pattern of levels has been low but within specified range for that patient.	Do not alter dose.
< 0.5mmol/L & patient unwell & pattern of levels on lower end of specified range for that patient.	Assess compliance, increase dose if appropriate, and recheck level in 5 days.
< 0.5mmol/L & is inconsistent with the trend.	Assess compliance, consider other factors e.g. drug interactions, excess fluid intake, brand change, and recheck level.
> 1.0mmol/L with no signs of toxicity.	If there is an explanation for the high level e.g. dehydration, timing of level, interacting medicines, brand change, correct where possible and recheck level.
> 1.0mmol/L with no signs of toxicity and the trend is for high end of range.	Decrease dose, encourage fluids, recheck in 5 days.
> 1.0mmol/L with no signs of toxicity and no explanation for high level.	Recheck level, investigate renal function.
If patient shows signs of toxicity Blurred vision, muscle weakness, drowsiness, coarse tremor, dysarthria, ataxia, confusion, convulsions, nausea & vomiting, ECG changes	Stop lithium immediately, measure lithium, creatinine, urea and electrolytes. <b>Refer to hospital if clinical condition warrants</b>

**Adverse effects**

Side effects may be short term and are usually dose dependent. They can often be prevented or relieved by a moderate reduction in dose.

<b>Type of adverse effect</b>	<b>Action to be taken</b>
<ul style="list-style-type: none"> <li>• <b>GI disturbances</b> e.g. nausea, diarrhoea, dry mouth</li> </ul>	Ensure patient aware of need for fluid replacement
<ul style="list-style-type: none"> <li>• <b>Weight gain</b></li> </ul>	Monitor – Advise to avoid crash diets & sugary drinks.
<ul style="list-style-type: none"> <li>• <b>Oedema</b></li> </ul>	Monitor – may respond to dose reduction.
<ul style="list-style-type: none"> <li>• <b>Fine tremor</b></li> </ul>	Consider slight reduction in dose
<ul style="list-style-type: none"> <li>• <b>Polyuria</b> (frequent urination)</li> <li>• <b>Polydipsia</b> (frequent thirst)</li> </ul>	Advise re: fluid intake. May require investigation for diabetes insipidus if persistent
<ul style="list-style-type: none"> <li>• <b>Hypothyroidism</b></li> </ul>	Consider thyroid replacement if clinically indicated
<ul style="list-style-type: none"> <li>• <b>Signs of toxicity:</b> Blurred vision, muscle weakness, drowsiness, coarse tremor, dysarthria, ataxia, confusion, convulsions, nausea &amp; vomiting, ECG changes.</li> </ul>	Stop lithium immediately, measure lithium, creatinine, urea and electrolytes. <b>Refer to hospital if clinical condition warrants</b>

### **Drug interactions**

Some medicines may result in increased lithium levels and risk of toxicity, e.g. diuretics (mainly thiazides), NSAIDs, ACE inhibitors, angiotensin II receptor antagonists, SSRIs and other psychotropic medicines, (refer to Appendix 1 in BNF).

### **Withdrawal**

Unless due to serious adverse reaction, withdrawal should be gradual and take place under the supervision of a Consultant in Psychiatry. Abrupt discontinuation increases the risk of relapse. See BNF section 4.2.3

### **Pregnancy**

Women taking lithium who are planning a pregnancy or who become pregnant must be referred to psychiatric services for advice.

### **Breastfeeding**

Lithium is excreted in breast milk with resultant risk of toxicity in the infant. Manufacturers advise to avoid.

### **Shared Care Responsibilities**

#### **Referral process**

General practitioners should refer patients who are likely to be suffering from bipolar disorder, mania or treatment resistant depression to the hospital specialist for assessment for treatment.

The hospital specialist team will advise on treatment as appropriate.

#### **Aspects of care for which the hospital specialist team are responsible:**

- Confirming diagnosis.
- Assessment of baseline mental state
- Assessing the need for treatment and the patient's fitness for medication.
- Undertake baseline investigations- urea & electrolytes, calcium, thyroid function tests.
- Arrange a baseline ECG (if there is existing cardiovascular disease or risk factors)
- Ensure that serum lithium monitoring is carried out during initial titration and after dose changes either in secondary care or by arrangement with GP.
- Consideration of potential drug interactions.
- Follow up to assess compliance and assess response.
- Evaluation of any adverse events noted by the patient/carer or GP.
- Advising on change of therapy.

#### **Aspects of care for which the General Practitioner is responsible:**

- To prescribe treatment as advised by the hospital specialist team.
- Consideration of potential drug interactions
- To carry out serum lithium level monitoring during initial titration and after dose changes if this has been agreed with the hospital specialist.
- To check serum lithium level every 3 months (or as advised by hospital specialist e.g. 2 monthly in the elderly) once stable
- To check urea & electrolytes, calcium and thyroid function tests every 6 months.
- Changing the dose of medication as advised by hospital specialist team.
- Advising the hospital specialist if they have concerns about adverse effects or ongoing therapeutic benefit.

## Appendix 1

### Significant Change to Labelling of Priadel Liquid and Information on Switching Between Priadel Liquid and Tablets

- Labels on Priadel liquid have been changed by the manufacturer and now read: “**Priadel 200mg/5ml liquid**”
- There is no change to the formulation of the product it still contains the same amount of Lithium
- Each 5ml of Priadel liquid contains 520mg of lithium **citrate** which is equivalent to 200mg of the active substance lithium **carbonate**. **N.B. The new labelling has caused confusion resulting in dosage errors, which can lead to serious toxicity.** The main cause of error is confusion between the dose expressed as the different salts.
- BNF 57 still refers to doses of Priadel liquid in milligrams of Lithium Citrate
- Priadel liquid should be given in divided doses, ideally twice daily
- All Lithium preparations must be prescribed by brand name (e.g. Priadel, Camcolit) as bioavailability varies
- Any change in formulation (e.g. tablets to liquid) or brand requires the same monitoring of lithium levels as initiation of treatment
- If there are any queries about prescribing Priadel or changing between the different preparations of Priadel please contact your local clinical pharmacist for advice or alternatively contact pharmacy services on 01383 565343

#### Equivalent doses of Priadel tablets and liquid

<b>Priadel tablets</b>	<b>Priadel 200mg/5ml liquid</b>
200mg	5ml
400mg	10ml
600mg	15ml
800mg	20ml
1g	25ml
1.2g	30ml
1.4g	35ml

The following table shows what quantity of Priadel liquid should be prescribed if switching between Priadel tablets or Priadel liquid.

<b>Priadel tablets</b>	<b>Priadel liquid</b>
200mg	2.5ml twice daily
400mg	5ml twice daily
600mg	7.5ml twice daily
800mg	10ml twice daily
1g	12.5ml twice daily
1.2g	15ml twice daily
1.4g	17.5ml twice daily

**Shared Care Lithium Treatment Plan**

<b>PATIENT SPECIFIC DETAILS</b>	<b>Consultant</b> .....
<i>To be completed at time of discharge / outpatient review and sent to patient's GP</i>	
<b>Name</b> .....	<b>DoB</b> .....
<b>Address</b> .....	
<b>CHI number</b> .....	

<b>Current indication:</b> .....
<i>(e.g. bipolar prophylaxis / augmentation)</i>
<b>Desired Therapeutic range:</b> .....
<i>(0.5 – 1.0mmol/L, elderly 0.5 – 0.8mmol/L)</i>
<b>Dosage regimen:</b> ..... <b>Brand used:</b> .....
<b>Last level:</b> ..... / ..... (date) <b>Level next due:</b> ..... (date)
<b>PHYSICAL &amp; BLOOD MONITORING TO BE CARRIED OUT BY:</b>
Psychiatrist <input type="checkbox"/> Lithium Clinic <input type="checkbox"/> Day Care Unit <input type="checkbox"/> GP <input type="checkbox"/> GP: .....
Other .....
<b>Frequency of lithium monitoring (typically 3 monthly/2 monthly in elderly)</b> .....
Completed by (sign & print name) .....
Date .....

<b>MINIMUM MONITORING REQUIREMENTS FOR ESTABLISHED LITHIUM TREATMENT</b>	
<b>NB</b> – more frequent monitoring may be required if clinical indications arise and in ‘higher risk’ patients, e.g. those on interacting drugs (see BNF), those with or at risk of renal / thyroid / cardiac disease.	
<b>BASELINE ECG DONE?</b>	Yes/No/Not required
<b>LITHIUM</b>	typically 3 monthly
NB – sample at approx. 12 hours post dose. Ensure time interval is same at each measurement, if varies, state clearly on form.	
<b>UREA &amp; ELECTROLYTES PLUS CALCIUM</b>	6 monthly
<b>T<sub>4</sub>/TSH</b>	6 monthly

<p><b>PSYCHIATRIC REVIEW</b></p> <p>GP's should consider patients for formal review by psychiatrist after 2 –5 years of lithium therapy to assess ongoing benefit.</p>
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