Hereford Hospitals NHS
NHS Trust

NHS Herefordshire

HEREFORDSHIRE SHARED CARE GUIDELINE FOR LITHIUM

Introduction

The objective of this shared care agreement is to define safe and acceptable procedures for the prescribing and monitoring of lithium by primary and secondary care practitioners. The National Patient Safety Agency (NPSA) issued an alert in December 2009[1] after deaths, severe harms and a substantial number of reports relating to lithium therapy.

For most patients, lithium is a long-term treatment. For example it is recommended that patients with bipolar disorder take lithium for at least three years[2]

Lithium has a narrow therapeutic range necessitating blood levels between (0.4 – 1.0mmol/L, based on a blood test taken 12 hours after the last dose). The lower end of this range is used for older patients and the upper end for younger patients, particularly those being treated for an episode of mania. It is possible for an elderly patient at the upper limit to experience symptoms of toxicity. NICE states when initiating long-term treatment, clinicians should aim for levels of 0.6-0.8 mmol/L, with higher levels possibly benefitting patients with predominantly manic symptoms[2].

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 should also be assessed before and during treatment.

Shared Care

In its guidelines on responsibility for prescribing between hospitals and general practitioners (circular EL(91)127), the Department of Health has advised that legal responsibility for prescribing lies with the doctor who signs the prescription.

Indication for Therapy

Lithium salts are used chiefly for three indications:

- Prophylaxis in bipolar disorder
- Augmentation of antidepressant treatment in refractory recurrent depression
- Treatment of acute mania, although this is much less common in practice

Its use for these indications is supported by the NICE guidelines for depression[3] and bipolar disorder[2].

Treatment Aim

To ensure safe and effective management of bipolar disorder and refractory recurrent depression

Dose

Dosing is by slow upwards titration to achieve a target serum level usually between 0.4 – 0.8mmol/L and occasionally up to 1mmol/l in bipolar disorder.

Preparation and Availability

Brands of lithium are **not** interchangeable due to considerable differences in product bioavailability, inter-individual variability and narrow therapeutic index and should be prescribed by brand name. Priadel® is the default brand of lithium; serum lithium levels should be checked 1 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.

For clinical practice purposes 200mg lithium carbonate m/r = 5mls Priadel liquid **5.4mmol/5ml**

****NB different strength lithium citrate solutions are available****

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Side Effects

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

Signs of Lithium Toxicity (NB may occur at therapeutic levels, particularly in older people)

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

In cases of suspected lithium toxicity, lithium should be stopped and an urgent serum Lithium level taken. In all cases of lithium toxicity advice should be obtained from a specialist.
For levels between 1.0-1.5mmol/L reduce dose and review treatment.
In mild cases of toxicity (levels between 1.5 and 2.0mmol/L), withdrawal of lithium and administration of copious fluids and sodium will often alleviate the problem. Patients with levels over 2.0mmol/L will require hospital admission for appropriate management. When toxic concentrations are reached there may be a delay of 1-2 days before maximum toxicity occurs.

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.

Clinically Relevant Drug Interactions

Diuretics especially thiazides, NSAIDs, ACE inhibitors and Angiotensin II Receptor Antagonists may 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.
See latest BNF for a detailed list of all interactions

Pregnancy/Lactation

Seek specialist advice before prescribing in pregnancy and to breastfeeding mothers

Monitoring

Pre-treatment (see Consultant request letter to GP for these results)

U&Es, Creatinine, (including calculation of GFR), Pulse and BP, TFTs, ECG (if indicated), BMI taken once only by the initiating prescriber

Parameter	Frequency of Monitoring	Result	Action
Lithium Level	3 monthly	>1mmol/L or unexpected increase in level with no dose change	Immediate referral to psychiatrist
eGFR	6 monthly	<30ml/min 30-60ml/min	Immediate referral to psychiatrist Increase monitoring frequency to 3 monthly
U&Es	6 monthly	NB lithium can cause hypercalcaemia	Report abnormal results to psychiatrist
Thyroid (usually TSH)	6 monthly	Hypothyroidism (more rarely hyperthyroidism)	Hypothyroidism managed by levothyroxine (refer for advice if necessary)
BMI	annual	>25	Weight management advice: exercise, diet etc

Practical Management

- When taking blood for serum lithium levels, use a 10ml tube for clotted blood.
- Blood should be taken 12 hours after the previous dose of lithium. A once daily bedtime dose facilitates checking blood levels and is the usual dose regimen. For patients prescribed lithium in divided doses, the morning dose should be omitted until after the blood test.
- Patients not attending for lithium levels for more than 6 months despite repeated requests should be referred back to the CMHT. Abrupt cessation of lithium is not recommended so prescription length should be gradually reduced and patients warned that prescriptions will not be issued long term unless they attend for blood tests

Recommendations to GP

- Patients should be offered a new style 'Lithium Therapy: important information for patients' booklet (purple book available from Primary Care with usual stationary order). This contains important patient information and a monitoring record book that patients complete
- Lithium values and other biochemical results must be communicated between GP and specialist services. The best way to facilitate this is at the point of requesting the test, it is made clear that a copy of the results are to be sent to the other party

Cost

Priadel 400mg tablets cost £3.35 for 100 tablets (BNF March 2010); other brands are a similar cost

Contacts – back up advice and support

Contact Details	Phone	Bleep	Fax	E-mail
Consultant	Patient's usual psychiatrist and care co-ordinator			
Medicines Information	01432 364017		01432 364055	ruth.bader@hhtr.nhs.uk
Mental Health Pharmacist	01432 347617	07966 056566	01432 347660	yvonne.coats@herefordpct.nhs.uk

References:

1. NPSA alert: http://www.nrls.npsa.nhs.uk/resources/type/alerts/?entryid45=65426 accessed online April 2009
2. NICE CG38 Bipolar Disorder 2006: http://www.nice.org.uk/cg38 accessed online April 2009
3. NICE CG90 Depression 2009: http://www.nice.org.uk/CG90 accessed online April 2009

Shared Care Responsibilities

	Consultant/Specialist Responsibilities	Tick
1	Discuss benefits and side effects of treatment with patient; provide new style lithium therapy booklet; counsel women on necessary contraception	
2	Carry out any pre-treatment assessment or tests	
3	Start lithium, arrange for serum level monitoring, titrate and stabilise dose. Inform GP and copy any test results during stabilisation period	
4	Ask GP if they are willing to participate in Shared Care – issue letter	
5	Promptly communicate any changes to GP	
6	Evaluate and advise on adverse events noted by GP or patient	
7	Review the patient's condition and monitor the response to treatment regularly	
8	Advise GP on when and how to discontinue treatment	
9	Ensure clear arrangements for GP back-up, advice and support	
10	On notification from GP of monitoring results out of range, respond to GP by fax / letter detailing action taken and any dose change	

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	GP Responsibilities	Tick
1	Reply to the request for Shared Care within 14 days of request	
2	Prescribe lithium under the guidance of the hospital Consultant, noting any restrictions to supply quantity. Check patient has 'purple book'	
3	Report unacceptable adverse reactions to the hospital Consultant	
4	Monitor and record therapy in line with practice policy and in accordance with the Shared Care; copy results to Consultant, encourage patient to complete record book	
5	Liaise with the hospital Consultant regarding any complications of treatment	
6	Respond to any discontinuation plan advised by Consultant	
7	Discontinue shared care and refer back to Consultant patient becomes pregnant	

	Community Pharmacist Responsibilities	Tick
1	For generic prescriptions provide continuity by dispensing the same brand each time and request brand prescription from prescriber	
2	Check patients have a new style lithium therapy booklet (purple book, similar to anticoagulant 'yellow book' available from Primary Care with usual stationary order)	
3	Check blood tests are being monitored regularly and that it is safe to dispense the prescribed lithium (see NPA standard operating procedure)	
4	As a principle do not refuse to dispense lithium but consider referral and telephone/fax communication with prescriber	
5	When dispensing lithium or advising on counter medicines check for interacting drugs	
6	Check if the patient is taking any OTC medicines, in particular NSAIDs and sodium-containing antacids	

	Hospital Pharmacist Responsibilities	Tick
1	For generic prescriptions, confirm and endorse brand usually supplied	
2	Check patients have the new style "purple book"	
3	Check patient is not prescribed any interacting medication. Intervene and recommend safer alternatives, or appropriate dose modification, if an interacting medication is prescribed. Where possible discontinue interacting medications	
4	Check blood tests are being monitored regularly and that is safe for patient to continue lithium	
5	Monitor for signs of toxicity such as thirst, diarrhoea, vomiting, fine tremor. Refer to clinician if toxicity is suspected	
6	Request blood levels are taken if no record of level, or after 7 days of a dosage, or formulation change	

	Patient Responsibilities	Tick
1	Read information provided in purple book and give consent for the chosen treatment	
2	Inform Consultant and GP of any other medication they may be taking or start taking during treatment, including over the counter medicines or herbal remedies	
3	Attend appointments and have recommended tests at recommended intervals	
4	Be aware of possible side-effects, especially signs of high lithium level and report promptly to GP or Consultant	
5	Keep lithium therapy record book safe, update blood test results in your book and carry lithium treatment card	
6	Maintain usual adequate diet and fluid intake	
7	Seek advice and support from GP or Consultant as soon as possible if pregnant or planning a pregnancy	
8	Store and handle the medication safely	

Signatures

Patient _____ Consultant _____GP_____

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