SHARED CARE GUIDELINE

Pennine Care NHS
NHS Foundation Trust

Title: **Lithium treatment in persons aged 12-18 years**	
Scope: Pennine Care NHS Foundation Trust To support an individualised care pathway where this has been previously agreed with the GP only	**Version: 2**
Issue date:	18 January 2013
Replaces:	Version 1
Author(s)/Originator(s)	Pennine Care NHS Foundation Trust
To be read in conjunction with the following documents:	British National Formulary (BNF) (www.bnf.org) Summary of Product Characteristics (SPC) (http://www.medicines.org.uk/emc/) NICE Clinical Guideline 38 Bipolar Disorder (www.nice.org.uk)
Authorised by:	Drugs and Therapeutics Committee Pennine Care NHS Foundation Trust
Date authorised:	12 October 2012
Review Date:	12 October 2015

1. Introduction

Lithium salts are used in the prophylaxis and treatment of mania, in the prophylaxis and treatment of bipolar disorder, as concomitant therapy with antidepressant medication in patients who have had an incomplete response to treatment for acute depression in bipolar disorder, in the prophylaxis of recurrent unipolar depression, and in the treatment of aggressive or self-mutilating behaviour.

Lithium may also be used as an adjunct in the treatment and prophylaxis of schizoaffective disorder. (This is an unlicensed indication)

Lithium salts would be considered for patients in the 12-18 age group as

- Treatment augmentation in acute mania where the response to first line antipsychotic medication has been inadequate, or
- A second line option for prophylaxis in bipolar disorder (or schizoaffective disorder – this is an unlicensed indication), or
- Treatment for acute episodes of mania in children who have responded to lithium before and whose symptoms are not severe

Lithium has a narrow therapeutic range necessitating the maintaining of serum levels at between 0.4 and 1.0 mmol/litre (BNF). NICE clinical guideline 38 (Bipolar Disorder) recommends that clinicians should aim for levels of 0.6-0.8 mmol/litre for prophylaxis.

If the concentration of lithium in the blood becomes too high, toxic symptoms may occur, which may lead to acute renal failure, convulsions, coma, and ultimately, death. In addition, lithium treatment increases the risk of clinical hypothyroidism up to five-fold. As it is excreted predominantly through the kidneys, plasma levels of lithium can be affected by fluid balance and renal function. These considerations mean that patients taking lithium must be subject to a continuous programme of regular blood monitoring.

Close monitoring is also needed because children and adolescents may be more prone to adverse effects of medication. The clinical decision to prescribe lithium in this age group should be made by the responsible consultant following documented peer review by a colleague with experience in this area or a Tier 4 CAMHS consultation/second opinion.

Informed consent should be acquired from the parents/carers as well as the young person. This should include a discussion on safe storage and handling of the medication. A care plan and/or treatment information should be shared and discussed using child-friendly and developmentally appropriate language.

Treatment with lithium will be initiated and stabilised by the Consultant, who should retain responsibility for its overall supervision and periodic review. However, general practitioners and community pharmacists process most prescriptions for lithium. It is essential that all prescribers ensure that appropriate and regular monitoring takes place, and that the results are communicated effectively between primary and secondary care.

2. Scope

Pennine Care NHS Foundation Trust
To support an individualised care pathway where this has been previously agreed with the GP only

3. Clinical condition being treated

Licensed indications:
Treatment and prophylaxis of mania, bipolar disorder, and recurrent depression; aggressive or self-mutilating behaviour.

NICE clinical guideline CG38 recommends lithium both as sole treatment for acute mania, or as an adjunct to antipsychotic treatment, if the initial response has been inadequate. It also recommends lithium be considered for long-term prophylaxis, particularly if it has previously been effective.

Lithium salts would be considered for patients in the 12-18 age group for

- Treatment augmentation in acute mania where the response to first line antipsychotic medication has been inadequate, **or**

- A second line option for prophylaxis in bipolar disorder (or schizoaffective disorder – this is an unlicensed indication), **or**
- Treatment for acute episodes of mania in children who have responded to lithium before and whose symptoms are not severe

4. Product and prescribing information

- Dosage must be individualised depending on serum lithium levels and clinical response; the minimum effective dose should be sought and maintained.
- Due to inter-brand variations in bioavailability, lithium preparations must always be prescribed by proprietary name.
    - Pennine Care NHS Foundation Trust routinely uses Priadel brand.
- To avoid confusion, doses of **lithium citrate liquid preparations** should be prescribed in millilitres (mls).
    - A 5ml dose of the lithium citrate liquid formulations **520mg/5ml or 509mg/5ml** may be considered equivalent to 200mg of lithium carbonate.
    - A 5ml dose of lithium citrate liquid **1.018g/5ml** may be considered equivalent to 400mg of lithium carbonate.
- Further prescribing details may be obtained from the BNF and SPC.

Proprietary name	Formulation	Initial dose range	
		Treatment	Prophylaxis
Lithium carbonate			
Priadel*	Modified release tablets 200mg, 400mg	400mg-1.2gram daily as a single dose, or in two divided doses	400mg- 1.2gram daily as a single dose, or in two divided doses
Camcolit	Tablets 250mg, Modified release tablets 400mg	1-1.5gram daily	300-400mg daily
Liskonum	Modified release tablets 450mg	225-675mg twice daily	225-450mg twice daily
Lithium citrate			
Priadel liquid *	Sugar free solution 520mg/5ml	Adjust to achieve serum lithium concentration of 0.4-1mmol/litre	
Li-Liquid *	Solution 509 mg/5ml Solution 1.018g/5ml	Adjust to achieve serum lithium concentration of 0.4-1mmol/litre	

* The manufacturers of Priadel tablets and liquid, and of Li-liquid state that these preparations are 'not recommended' for use in children. The prescriber must therefore take responsibility for an 'off-label' use of a licensed medicine.

5. Treatment regimen

Pre-treatment examination

Pre-treatment examination should include the following:

- Clinical evaluation of the patient's physical health
    - General health, body weight and height
    - Cardiovascular health, blood pressure, pulse; an ECG should be performed if there are risk factors for, or existing cardiovascular disease.
    - Consideration may be given to a consultation with a cardiologist.

- Laboratory investigations
    - Thyroid function test
    - Renal function
    - Full blood count (if clinically indicated)

- Exclusion of pregnancy

Treatment initiation

The required dose of lithium is prescribed either once or twice daily.

Serum lithium concentration must be measured four to seven days after dosage initiation, then weekly until the dose has been stable for one month.

Blood samples for lithium levels must be taken 12 hours after a dose. Where samples are taken earlier or later than 12 hours post-dose it is important that this is made clear on the request form so that appropriate interpretation of the result can be made.

NICE clinical guideline CG38 (Bipolar Disorder) recommends that clinicians should aim for levels of 0.6-0.8 mmol/litre for prophylaxis, up to 1.0mmol/litre in acute mania.

Monitoring

The following parameters should be monitored on a regular basis:

- The patient's mental state
- Plasma lithium levels, to be measured four to seven days after any dose change, then weekly until levels are stable (that is within the range specified for the patient). Then every three months but more often if there is clinical deterioration, or abnormal renal or thyroid function
    - Dosage should be reduced if serum levels are 1-1.5 mmol/litre
- Thyroid function test every 6 months; more often if there is evidence of deterioration
- U&Es every 3 months, eGFR every 6 months; more often if there is evidence of deterioration, or the patient starts taking drugs such as ACE inhibitors, diuretics or NSAIDs
- Body height and weight monthly for 6 months, then every 6 months; dietary advice may be given.

Treatment should be stopped for 48 hours and advice sought from a Consultant if serum levels exceed 1.5 mmol/litre and/or the patient shows signs of toxicity (see below)

Serum levels of 2.0 mmol/litre and over require urgent treatment at an Accident and Emergency department. Treatment details can be found in the BNF under 'Emergency Treatment of Poisoning.'

6. Regimen Management

Responsibilities of the Consultant

- To assess the patient, make a diagnosis, and determine whether lithium treatment is indicated.
- To ensure that the patient and carers are fully informed about the treatment, including potential side effects, drug-diet interactions, drug-drug interactions, the need for regular blood tests and that erratic compliance or rapid discontinuation may increase the risk of relapse. Also that when treatment is 'off-label' that the patient and carer understand the ramifications of this.
- To obtain informed consent to treatment.
- To write to the General Practitioner (GP) detailing the diagnosis and treatment details, requesting that shared care procedures, including prescribing, commence at a mutually agreed time.
- To provide the GP with information regarding the decision to prescribe and peer review by a colleague with experience in this area or a Tier 4 CAMHS consultation/second opinion.
- To initiate and titrate the medication to a suitable dose
- To undertake appropriate tests, both prior to and during the commencement of treatment
- To provide the patient with a Lithium Therapy Information and Record Pack, and explain its use. To co-operate with the GP in making arrangements for all test results to be entered in the Record Book.
- To provide child/adolescent friendly information leaflets
- To communicate regularly and promptly with the GP regarding any test results and any modifications in treatment.
- To be available for advice.
- To monitor and liaise with the GP regarding any adverse drug reactions (ADRs) which have occurred, including the reporting of serious ADRs to the MHRA.

Responsibilities of the GP

- To reply to the request for shared care as soon as possible.
- To continue prescribing of the medication in the community under the guidance of the Consultant/specialist team.

- On the basis of clinical and biochemical data, to make dose adjustments as necessary, or to refer to the Consultant for specialist advice.
- To provide the patient and carers with any information they require regarding lithium treatment, including potential side effects, drug-diet interactions, drug-drug interactions, and the need for regular blood tests.
- To undertake appropriate investigations during treatment if requested to do so.
- To monitor the patient's condition, including performing blood and biochemical tests at the appropriate intervals.
- To communicate promptly the results of abnormal/ out of range tests to the Consultant.
- To co-operate with the Consultant in ensuring that test data are entered in the patient's Lithium Record Book.
- To refer to the Consultant/specialist team for advice regarding treatment/side effects, and concerns about compliance and/or suspected drug misuse.
- To monitor and liaise with the Consultant regarding any ADRs which have occurred, including the reporting of serious ADRs to the MHRA.
- If unable to agree to the sharing of care and the prescribing of medication, to contact the Consultant within 14 days, stating the nature of the concern.

7. Summary of cautions, contra indications, side-effects

- Lithium is a human teratogen. Females of child-bearing potential should be advised to use a reliable form of contraception. Where pregnancy is planned, consideration may be given to discontinuation of lithium therapy. If lithium treatment is to be continued during pregnancy, the patient should be referred for specialist care

- Lithium treatment is contraindicated in:
    - severe cardiac disease
    - clinically significant renal impairment
    - breast feeding
    - untreated hypothyroidism
    - low sodium, for example in patients on low sodium diets
    - Addison's disease
    - hypersensitivity to lithium or any excipients used in manufacture

- Caution should be exercised to ensure that diet and fluid intake are normal. This may be of special importance in hot weather, or during infectious diseases, including influenza, gastro-enteritis or urinary infections, when dose reduction may be required.

- Patients should be warned to report if polyuria or polydipsia develop

- Side effects include
    - gastro-intestinal disturbances

- metallic taste in the mouth
- mental slowness
- fine tremor
- renal impairment – polyuria and polydipsia
- weight gain
- hypothyroidism

- Signs of toxicity
  - blurred vision
  - nystagmus
  - diarrhoea and vomiting
  - muscle weakness
  - coarse tremor
  - sedation, confusion, drowsiness
  - convulsions
  - slurring of words
  - ataxia
  - renal impairment

- Drug-drug interactions
  - The following drugs may not be prescribed without consultation with the specialist:
    - ACE inhibitors, amiodarone, angiotensin-II receptor antagonists, antacids, antidepressants (SSRI, tricyclic, venlafaxine), antipsychotics, non-steroidal anti-inflammatory drugs, thiazide and potassium-sparing diuretics.
  - The following drugs may be prescribed with caution:
    - carbamazepine, clonazepam, diltiazem, metronidazole, phenytoin, theophylline, verapamil

Further details may be obtained from the BNF or the SPC.

8. Special considerations

Lithium must always be prescribed by proprietary name. Prescribing must ensure that patients are always maintained on the same brand, and care should be exercised when transferring patients to or receiving from, for example, different geographical areas, or care sectors.

If a decision is made to change a dosage form, for example from tablets to liquid, serum levels should be measured weekly and doses adjusted until therapeutic equivalence is assured.

9. Back-up care available to GP from Hospital

- Written correspondence from the Consultant following appointments and follow-up visits.
- Telephone advice from the Consultant during office hours.

10. Statement of agreement

Shared care is an agreement between the GP and the Consultant. This form is a request by the Consultant to share the suggested care pathway of your patient. GPs unable to agree to the sharing of care and initiating the suggested medication, should make this known to the Consultant within 14 days, stating the nature of the concern.

11. Written information provided to the patient

The patient and/or carers must receive a Lithium Information/Record Pack from the Consultant upon initiation of the treatment. The patient must bring the Record Book to all Consultant and GP appointments where it will be updated by the health professional conducting the appointment. The patient must also produce the book to any health professional involved in other aspects of their care, for example pharmacists and dentists.

All dispensed supplies of medication will include a manufacturer's Patient Information Leaflet.

12. Supporting References

British National Formulary Edition 64, September 2012
NICE Clinical Guideline CG38 (Bipolar disorder) www.nice.org.uk accessed 14th Sept 2012
Summary of Product Characteristics, Priadel www.medicines.org/emc accessed 14th Sept 2012