East Lancashire Health Economy Medicines Management Board
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Lancashire Medicines Management Group NHS

SHARED PRESCRIBING GUIDELINE

Drug: LITHIUM

Introduction

Licensed Indications:

1. In the management of acute manic or hypomanic episodes.
2. In the management of episodes of recurrent depressive disorders where treatment with other antidepressants has been unsuccessful.
3. In the prophylaxis against bipolar affective disorders.
4. Control of aggressive behavior or intentional self-harm.

Background:

Lithium salts have a narrow therapeutic/toxicity ratio and regular monitoring is required. Prescribing is by brand name and Lancashire Care NHS Foundation Trust prescribes Priadel when initiating patients on lithium.
Information from the Priadel SPC notes the following target serum lithium concentration ranges in mmol/L

	At 12 hours	At 24 hours
Once daily dosage	0.7 - 1.0	0.5 - 0.8
Twice daily dosage	0.5 -0.8	

Nb. The dose and optimal Lithium levels may vary from patient to patient depending on the specific indication. The BNF 70 notes that the average target range for the above indications is between 0.4 mmol/L and 1 .0 mmol /L. The lower end of the range can be used for prophylaxis in Bipolar disorder. Higher levels above 0.75 mmol/L offer additional protection against manic symptoms and control of aggressive behavior and intentional self-harm.

Facilities for monitoring serum lithium concentrations must be available whenever it is prescribed. Communication of the results of tests between primary and secondary care is essential for safe and effective patient care.

Formulation

Tablets as brand Priadel, 200mg and 400mg

Dose & Administration

Treatment and prophylaxis,

Adults over 50 kg: Initially 0.4-1.2g orally daily, usually as a single dose in the evening but can be given in 2 divided doses. Liquid preparations should be prescribed as a twice daily regimen. Dose should be adjusted following Lithium levels. Lithium levels should be checked 4-7 days following Initiation, then weekly until desired therapeutic range achieved.

Elderly or patients less than 50kg: initial dose of 200-400mg. Dosage increments of 200 to 400mg every 3 to 5 days are usual thereafter with weekly monitoring of Lithium levels to guide dosage requirements until desired therapeutic range achieved.

Secondary Care Responsibilities are:

1. Lithium therapy will be instigated in secondary care for patients who meet the diagnostic criteria listed above.
2. Before commencing treatment baseline monitoring will be undertaken as listed below.
3. Provide patients and carers with any information both written and verbal to facilitate concordance.
4. Women of childbearing age should be advised of the risk of teratogenic effects and the need for effective contraception while taking Lithium.
5. The patient and carer will be advised of risk situations.
6. Patients will be advised that erratic compliance or rapid discontinuation may increase the risk of manic relapse
7. Patients will be provided with the NPSA lithium pack including lithium level record book
8. Treatment will be initiated
9. Monitoring will be continued until steady state lithium levels are obtained.
10. Older adults need to be monitored carefully for symptoms of lithium toxicity because they may develop high serum levels of lithium at doses in the normal range and lithium toxicity is possible at moderate serum levels.
11. Where urea and creatinine levels become elevated, closer monitoring of lithium levels and dose will be undertaken and an assessment made of the rate of deterioration of renal function. Prescribers will consider seeking advice from a renal specialist regarding ongoing treatment
12. Treatment will be stopped if considered no longer appropriate. Lithium should be stopped wherever possible over at least 4 weeks, but preferably over a period of three months particularly if the patient has a history of manic relapse.

Following instigation of the drug the patient will be maintained on Lithium for a minimum period of three months to establish response and tolerability.

During this period the medication will be supplied by the hospital.
After this period the patient will be reassessed in secondary care and if;

- The illness has stabilised
- The side effects of the medication are manageable
- The target serum level has been achieved
- Adherence to the regime is established

Then a shared prescribing agreement between primary and secondary care to manage the patient will be progressed as follows: -

1. A referral letter will be sent to the patient's general practitioner asking them to consider the prescribing of lithium under shared care arrangements this will state if the indication is unlicensed.
2. The shared prescribing guideline will be included with the referral letter.
3. The general practitioner will be informed of the target therapeutic serum level for each individual patient
4. Test results will be communicated to the general practitioner (complete "copy to.." section on the pathology lab form)
5. The patient will be provided with a further 28 days of medication by the hospital during this process to allow continuity of treatment.
6. The patient will be informed of the process.
7. The patient's response will be reviewed at regular intervals (to be determined by the LCFT prescriber)
8. The patient will be reviewed promptly where the GP undertaking shared care indicates that there are signs of renal impairment, unacceptable side effects or deterioration in mental state. Where a GP indicates possible signs of toxicity the patient will, dependent on the clinical picture and/or lithium level results, be reviewed the same day by secondary care services or where emergency management is indicated be sent to casualty or the medical assessment unit for immediate intervention

Once all of the above is in place and the general practitioner has agreed to participate in the shared care arrangements a record will be made in the patient's hospital notes and the patient will be informed that their next supply of medication will be obtained from their GP.

Baseline monitoring undertaken by secondary care

Baseline Monitoring
Full blood count Blood glucose Lipid profile Urea electrolytes Including calcium Liver function tests Thyroid function tests ECG if there are risk factors for or existing cardiovascular disease Weight and height
Continuation monitoring will be continued until steady state lithium levels are obtained and the patient is transferred to primary care

Primary Care Responsibilities

Primary Care Responsibilities **are**:

1. To undertake monitoring as set out below under 'monitoring in primary care' and consider using an agreed READ code in the patient records for the monitoring
2. To undertake continuation monitoring as set out and take appropriate action if these tests are abnormal.
3. To reduce the dose or discontinue treatment in serious diarrhoea, vomiting or intercurrent infection (especially if sweating profusely). Consideration should be given to stopping lithium for up to seven days if the patient becomes acutely and severely ill with a metabolic or respiratory disturbance of any cause
4. To stop lithium if signs of toxicity occur and contact the consultant psychiatrist for advice on treatment and future management.
5. To refer back to secondary care for specialist advice if the treatment is ineffective or if the patient develops unacceptable side effects. This is particularly important where patients develop signs of renal impairment.
6. To review the patient in accordance with NICE guidance and advice from LCFT.
7. To re-refer the patient if concerns about mental state, tolerability or continued appropriateness of lithium treatment arise
8. To provide the patient with repeat prescriptions. Specify the brand on the prescription. Incorrect dosing can occur if the patient changes preparations.
9. To make a clear statement in the primary care notes showing where monitoring is being carried out.

Monitoring Required in Primary Care

1. To take serum lithium levels at three monthly***** intervals and after any dose changes, change of preparation, during an acute UTI, or changes in other medication which may affect lithium levels. Samples must be taken at least 12 hours post dose, and the time of the sample, total daily dose and the time of the previous dose noted on the sample. In the event of a twice daily dosing regimen, the morning dose should be omitted until after the blood sample has been taken.
2. To check lithium levels more frequently in elderly patients or in anyone taking interacting medications.
3. To check patients for side effects and signs of lithium toxicity at each appointment. **Toxicity can occur without apparent increase in serum level, and it is important to "treat the patient not the leve**l". Signs of neurotoxicity which can occur at therapeutic levels include paraesthesia, ataxia, tremor and cognitive impairment.
4. To share results with secondary care.
5. To record results in patient's lithium monitoring booklet.

Continuation Monitoring	**Additional Information**
Serum lithium levels seven days after initiation or a dose Increase. Continue weekly until stabilised, then every three months up until the first year of treatment, then every 6 months thereafter for stable patients.* **U & E's** every six months unless clinical signs of a deterioration or prescribed drugs such as ACE inhibitors, diuretics, NSAID's. **TFT's** every six months unless clinical signs of a deterioration Blood glucose and blood pressure annually Lipid profile annually in those over 40 years **Weight** annually or more frequently if significant weight gain occurs	*****Recent NICE CG185 update notes that following the first year of treatment, Lithium level monitoring can extend to 6 monthly for stable patients. **Maintain 3 monthly monitoring for the following patient groups:** Elderly, poor adherence, interacting drugs, impaired renal or thyroid function, poor symptom control, Or lithium levels over 0.8 mmol/L Results of all tests performed should be shared by primary and secondary care.

Adverse Effects

Thirst, polyuria, GI upset, Diabetes insipidus – may inhibit ADH (must maintain fluid intake), Acne, Cardiac arrhythmias, Weight gain, oedema, Hypothyroidism, Lethargy, feeling cold, vertigo. **Please refer to the BNF or other texts for full list.**

Signs of Lithium Toxicity

Mild: Nausea, diarrhoea, blurred vision, polyuria, light headedness, fine resting tremor, muscular weakness and drowsiness.

Moderate: Increasing confusion, blackouts, fasciculation and increased deep tendon reflexes, myoclonic twitches and jerks, choreoathetoid movements, urinary or faecal incontinence, increasing restlessness followed by stupor. Hypernatremia.

Severe: Coma, convulsions, cerebellar signs, cardiac dysrhythmias including sinoatrial block, sinus and junctional bradycardia and first degree heart block. Hypotension or rarely hypertension, circulatory collapse and renal failure.

Action to be taken if level over target range

Serum levels over 1.00 mmol/ L should trigger investigation for presence side effects.
If Serum level 1.5mmol/l or above, or mild symptoms of lithium toxicity present.
Action: Withdraw treatment and seek advice

Serum level 2.0mmol/l or moderate/severe signs of lithium toxicity
Action: Withdraw treatment and seek urgent medical care

Drug Interactions

ACE inhibitors and Angiotensin II antagonists	**Increased lithium levels due to reduced excretion**	
NSAIDs and Cox 2 Inhibitors	**Increased lithium levels due to reduced excretion**	**Aspirin, sulindac are usually safe and low dose ibuprofen may be safe**
SSRI's & Triptans	**Increased risk of CNS effects and risk of serotonin syndrome**	
Methyldopa	**Neurotoxicity with no increase in plasma levels.**	
Antipsychotics	**All antipsychotics can increase the risk of EPSE and neurotoxicity but it is rarely seen in practice. May increase the risk of neuroleptic malignant syndrome**	**Rarely seen in practice. Commonly used combination**
Diuretics	**Increased lithium levels due to reduced excretion.**	**Loop diuretics appear less likely than thiazides to increase lithium levels.**
Tetracyclines	**Increased lithium levels due to reduced excretion**	
Calcium channel blockers	**Signs of neurotoxicity may occur. Lithium levels may increase**	
Theophylline, Caffeine	**Excretion increased causing decreased lithium levels**	
Carbamazepine, phenytoin	**Neurotoxicity with no increase in plasma levels**	
Metronidazole	**Increased risk of lithium toxicity**	
Steroids	**May alter levels by affecting electrolyte balance**	
Salt or sodium bicarbonate containing preparations	**Increases lithium excretion so reduces lithium levels.**	**Low salt increases lithium level.**

Caution is also advised with drugs that prolong the QTc interval or lower seizure threshold.
Please refer to the BNF or other texts for full list.

Contraindications

Hypersensitivity to lithium or it's excipients, breast feeding, severe renal impairment (may be given if closely monitored in mild to moderate renal impairment), untreated hypothyroidism, cardiac disease or insufficiency, hyponatraemia, Addison's disease, Brugada syndrome or family history of Brugada Syndrome

Lithium should not be used in pregnancy, especially the first trimester, unless considered essential

Contact Details

As per correspondence from LCFT

This guidance does not replace the SPC's, which should be read in conjunction with this guidance.