CARDIFF AND VALE (C&V) UHB CORPORATE MEDICINES MANAGEMENT GROUP SHARED CARE COMMITTEE

SHARED CARE AND NEAR PATIENT TESTING

Drug: LITHIUM **Protocol number: CV 12**

Indication: PROPHYLAXIS OF MANIA, BIPOLAR DISORDER, RECURRENT DEPRESSION

General Guidance

This protocol sets out details for the shared care of patients taking **lithium** and should be read in conjunction with the General Guidelines for Shared Care. Sharing of care requires communication between the specialist, GP and patient. The intention to share care should be explained to the patient by the doctor initiating treatment. **The doctor who prescribes the medication legally assumes responsibility for the drug and the consequences of its use.** The prescriber has a duty to keep themselves informed about the medicines they prescribe, their appropriateness, effectiveness and cost. They should also keep up to date with the relevant guidance on the use of the medicines and on the management of the patient's condition.

Background

Lithium is used in the prophylaxis and treatment of mania, bipolar disorder, recurrent depression and in aggressive and self-harming behaviour (BNF). Long-term treatment should be undertaken only with careful assessment of risk and benefit. The need for continued therapy should be assessed regularly and patient should be maintained on lithium only if benefit persists.

Responsibilities

A. Consultant responsibilities

1. When treatment is **initiated** send Shared Care (SC)/ Near Patient Testing (NPT) request form with Shared Care Protocol to GP.
2. Baseline and continued monitoring until patient is stabilised of biochemical parameters (see page 2) (If Near Patient Testing not agreed then monitoring will be continued after patient is stabilised)
3. Initiate therapy following full discussion with the patient of benefits and risks and provide patient with a patient information booklet, lithium alert card and record book. Complete the patient's details, service providers' details and current lithium therapy. Annotate the record book with the patient's current lithium blood level, the expected upper and lower lithium blood level range and healthcare tests results.
4. Titrate lithium dose adjusting dose as appropriate and undertake monitoring of clinical response and side effects.
5. When a GP positive response to SC / NPT has been received and patient has been stabilised send a letter to GP "handing over" the Shared Care / Near Patient Testing of the patient to the GP.
6. To counsel female patients to take contraceptive precautions during treatment. Record in GP referral letter that contraceptive advice has been given.
7. Ensure that patient is suitable for SC/NPT, considering whether the patient will comply with attending GP surgery for monitoring.
8. To inform patient to **stop** lithium and contact their GP immediately for a serum

lithium level if any toxic symptoms occur.

9. Respond to any request from GP to review the patient due to adverse effects of therapy.
10. Advise the GP on continuing or stopping lithium therapy following medical review of the patient and associated drug therapy
11. If NPT not agreed notify GP if patient is failing to attend for appropriate monitoring and advise GP on appropriate action.
12. If GP in agreement, discharge individual patients to Primary Care monitoring with the understanding that the GP will have urgent access to advice and/or review from the initiating Consultant Psychiatrist. This applies to individual patients who have been stable for at least two years (stable mental status and monitoring as listed above within normal parameters) in whom long-term treatment with lithium is considered appropriate.

B. General practitioner responsibilities

1. Within one week of receipt return the completed SC/NPT request form to indicate whether or not willing to undertake Shared Care/Near Patient Testing.
2. Prescribe lithium as part of the Shared Care agreement.
3. Monitor the general health of the patient.
4. Where Near Patient Testing is agreed monitor the parameters indicated (see page 2). Document results in the patient's monitoring booklet and report to and seek advice from the consultant on any aspect of patient care which is of concern.
5. Report adverse effects of therapy to the consultant and the Medicines and Health Care products Regulatory Agency (MHRA).
6. If NPT not agreed, to act on advice provided by the Consultant if the patient does not attend for appropriate monitoring.
7. Refer patient back to Secondary Care if Near Patient Testing agreed and patient persistently fails to attend for monitoring.
8. GP to refer patients to the consultant team every five years, to have specialist review of the ongoing need for continuation of Lithium treatment with the careful assessment of risk and benefit. (this refers to patients detailed in point 12, Consultant responsibilities)

C. Patient responsibilities

1. Consent to treatment with lithium.
2. Attend regular appointments with specialist centre and GP.
3. Report any side effects to the specialist or GP whilst taking lithium.
4. Provide monitoring booklet to be updated.

Dosage Regimen

For Adults the normal starting dose is 400mg – 600mg daily of lithium carbonate. In elderly patients or those weighing less than 50kg the starting dose should be reduced to 200mg – 400mg daily of lithium carbonate. The dose can then be adjusted according to serum lithium levels. It should be prescribed as a **SINGLE DOSE AT NIGHT** ideally to improve adherence, allow ease of Therapeutic Drug Monitoring and reduce the risk of renal changes longer-term.

Lithium has linear pharmacokinetics provided renal function is stable. Therefore a 25% increase in dosage should increase lithium plasma by 25%.

Plasma lithium levels

Indication	ONCE DAILY dosing
Prophylactic therapy	0.4 – 0.8mmol/L
Treatment of acute mania	0.8-1.2mmol/L
Increased risk of toxicity	>1.4mmols/L
Life threatening toxicity	>3.5mmols/L

Please refer to summary of product characteristics for twice daily dosing target levels

NICE guidance recommends maintaining serum lithium levels between 0.6 and 0.8 mmol/L in patients prescribed for the first time. It also recommends a trial of at least 6 months with serum lithium levels between 0.8 and 1.0 mmol/L for patients, who have relapsed previously while taking lithium or who have sub-threshold symptoms with functional impairment while receiving lithium.

Available Formulations:

As bioavailability varies between formulations/ brands, **remaining on the same formulation/ brand is imperative.** At C&V the lithium **preparation of choice is** Lithium Carbonate as **Priadel® Modified Release Tablets.** The **brand** of Lithium should be **documented on** all **prescriptions** and in the patients **Purple Monitoring Booklet.** Priadel® is available as 200mg scored tablets (may be halved to obtain 100mg dose) and 400mg tablets.

Lithium is also available as Lithium Citrate as a liquid formulation if needed. As a general rule lithium carbonate 200mg = lithium citrate 509mg. Please note that the Lithium citrate preparation is dosed twice daily usually.

Changes in formulation and brands should be monitored as initiating treatment. This should be undertaken by Secondary care and in liaison with the Mental Health Pharmacy Team at Hafan-Y-Coed. For information on other brands of Lithium Carbonate please refer to the Summary of Product Characteristics available at: www.medicines.org.uk. Or contact Hafan- Y-Coed Pharmacy Team 02921 824801.

Monitoring Recommendations

Before treatment -baseline monitoring by secondary care

- ECG if history of cardiac disease /cardiovascular risk factors or risk factors known to prolong the QT interval (e.g. uncorrected hypokalaemia, bradycardia) and/or on other psychotropics known to prolong the QT interval.
- Weight and BMI
- Creatinine and electrolytes and eGFR
- Serum calcium (corrected)
- Thyroid Function Tests (TFTs)
- Full blood count

During treatment

Initial monitoring by secondary

Lithium plasma levels*- seven days after initiation and then weekly after every dose change and until dosage has remained constant for four weeks and steady lithium levels are achieved

Monitoring by GP once treatment is stable

- Lithium plasma levels*- every 3 months and one week after any dose or preparation change.
- Creatinine& electrolytes, eGFR, calcium (corrected), and thyroid function tests every 6 months.
- Weight and general health checks annually. Weight should be monitored 3 to 6 monthly in patients with rapid weight gain.

***(12 hours post night time dose i.e. between 10am and 12 noon) and before morning dose if patient on twice daily dosing of lithium)*

Lithium levels

- If the Lithium level is below the target range or above the target range but the patient has no symptoms of toxicity, the GP should inform the Consultant team at the earliest opportunity. (See target ranges).
- If the Lithium level is above the target range and the patient has symptoms of toxicity, GP to refer the patient immediately to the Consultant team, or if not practicable (out of working hours), to Accident and Emergency. GP to WITHHOLD further Lithium prescription.
- If the Lithium level is above 1.5mmol/L and the patient has symptoms of toxicity or if the level is above 2mmol/L GP to refer the patient to Accident and Emergency. GP to WITHHOLD further Lithium prescription.

Increased monitoring of renal function tests, TFTs and lithium levels are recommended if there are signs of clinical deterioration, abnormal results, and symptoms suggesting abnormal renal or thyroid function such as unexplained fatigue, or if patient is on other medicines which interact with lithium and can potentially cause lithium toxicity.

Lithium use is associated with a range of glomerular and tubular disorders resulting in chronic kidney disease and more rarely established renal failure. Hence it is important to monitor a trend with renal function, as results may be still in the normal range but have significantly increasing creatinine levels (especially in the elderly).

Monitor for symptoms of neurotoxicity, including paraesthesia, ataxia, tremor and cognitive impairment, which can occur at therapeutic levels.

Thyroid Function Tests:

In patients with a sustained increase in TSH of greater than twice the upper limit of 'normal' (~10 mU/L) which is confirmed by repeat testing after 2 weeks, GP should consider treatment with levothyroxine.

A patient with a TSH which is around double the normal upper limit (~10 mU/L) or between the upper normal limit and double the normal upper limit (~5.0 mU/L - ~10mU/L) may require additional monitoring and possible treatment with levothyroxine.

Renal Function:

If creatinine and electrolyte levels become elevated, and if there is trend suggestive of deterioration of renal function, GP to refer the patient to Renal specialist as well as to seek input and advice by the consultant team. The decision to continue lithium treatment depends on clinical efficacy and degree of renal impairment. Similarly, if there is raised calcium levels, GP to seek advice from endocrine specialist and consultant psychiatrist team.

Adverse effects
Long term treatment with lithium may be associated with persistent parathyroidism and hypercalcaemia, weight gain, changes in glucose tolerance, nephrogenic diabetes insipidus, nephritic syndrome. In some patients goitre can be induced as lithium can inhibit thyroid hormone release. Hypothyroidism can be successfully managed with thyroxine. Lithium is also teratogenic. Monitor older adults 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 lithium levels.

Stop lithium and contact the relevant consultant team if any of the following occurs: Lithium toxicity usually occurs when levels are above 1.5mmol/L, but can occur within the therapeutic range. Symptoms of toxicity include: nausea and vomiting (first signs of toxicity- if present a lithium level should be done), anorexia, diarrhoea and vomiting, muscle weakness, lack of co-ordination, tinnitus, blurred vision, ataxia, coarse tremor, dysarthria, confusion and in severe toxicity, drowsiness or lethargy, stupor, coma, renal impairment, cardiac arrhythmia and death. **NB Urgent Creatinine and electrolytes and lithium levels if acute toxic effects suspected.**

Interactions

The table below summarises important interactions with lithium. Please note that this list is not exhaustive and the BNF/ Summary of Characteristics should be consulted before initiating any new medicine concurrently. As a rule, if any medication acts on or via the kidney or affects sodium homeostasis an interaction is possible.

When assessing such interactions please consider

- Monitoring the lithium level more frequently
- If the lithium dosage has already been adjusted to compensate for an interacting drug

Please liaise with Secondary care prior to commencing an interacting drug if the combination is imperative and no alternative is available. Dose alteration and re-stabilisation of treatment will need to occur.

Interacting medicine	Comments
Diuretics	Lithium excretion is especially reduced by thiazides diuretics. Loop, potassium sparing diuretics and aldosterone antagonists also reduce excretion- increased lithium plasma concentration.
Metronidazole and tetracyclines	May reduce lithium clearance, thus increasing plasma concentrations
ACE inhibitors and Angiotensin II receptor blockers	Increase lithium plasma concentrations
Medicines which prolong QTc interval	Effects may be additive and increase the risk of arrhythmia including torsades de pointes
NSAIDs (including COX-2's)	Reduces lithium excretion – avoid if possible. Warn patients not to buy Over the Counter NSAID's
Antidepressants: SSRI/ Tricyclics/ SNRI	Increased risk of CNS toxicity: be mindful of signs of toxicity at 'Normal plasma levels'
Sodium containing antacids	Concurrent use can reduce Lithium levels, and potentially precipitate toxicity when antacids stopped

Special recommendations

Patients taking lithium should be advised to seek medical attention if they develop diarrhoea and/or vomiting,

Patients should maintain an adequate fluid intake particularly after sweating, (for example after exercise, in hot climates, or if they have a fever), if they are immobile for long periods or-in the case of older people-develop a chest infection or pneumonia.

Patients should avoid dietary changes which might reduce or increase sodium intake.

Consider stopping lithium for up to 7 days if they become acutely and severely ill with a metabolic or respiratory disturbance from whatever cause.

Caution with the elderly.

Lithium is contraindicated during pregnancy and breastfeeding. Lithium dose will need to be reduced in renal disease.

Contact details

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