HERPC

Hull & East Riding Prescribing Committee

Prescribing Framework for

Lithium in Affective Disorders and Cluster Headache

Patient's Name:……..… NHS Number: ……

Patient's Address:……...……(Use addressograph sticker)

GP's Name:……..

Communication

We agree to treat this patient within this Prescribing Framework

Specialist Prescriber's Name…… Prof Reg. No. ……

Specialist Prescriber's Signature…… Date:……

Where prescriber is <u>not</u> a consultant:

Consultant's Name: …… GMC No ……..

Consultant's Signature ……..... ……. Date:…….

GP's Signature:…… Date:……..

GP's Name (if different from listed above)……..

The front page of this form should be completed by the specialist and the form sent to the patient's general practitioner.
The patient's GP should sign and **<u>send back to specialist</u>**, to confirm agreement to enter into shared care arrangement. If the General Practitioner is **<u>unwilling</u>** to accept prescribing responsibility for the above patient the specialist should be informed within two weeks of receipt of this framework and specialist's letter.

Full copy of framework can also be found at http://www.hey.nhs.uk/herpc/amber.htm

1. Background

Lithium is an alkali metal available for medical use as lithium carbonate or lithium citrate. The exact mechanism of action of lithium is not known. However, lithium modifies the production and turnover of certain neurotransmitters, particularly serotonin, and it may also block dopamine receptors. Lithium also modifies concentrations of some electrolytes, particularly calcium and magnesium, and it may reduce thyroid activity.

Initiation of lithium in patients who have not taken lithium before to treat bipolar disorder should not be carried out in primary care, except under shared care arrangements (NICE CG185). Lithium is also indicated for prophylaxis of cluster headache (BNF- unlicensed use)

Lithium has a narrow therapeutic index, requiring careful monitoring of plasma levels in order to ensure effectiveness and prevent toxicity

These guidelines aim to provide a framework for the prescribing of lithium by GPs and to set out the associated responsibilities of GPs and hospital specialists who enter into the shared care arrangements.

2. Indication

Lithium (*Camcolit*® / *Liskonum*® / *Priadel*®*, LiLiquid*®) may be used for the management and prophylaxis of
-Bipolar affective disorder (BPD)
-Acute manic / hypomanic episodes
-Treatment resistant or recurrent depressive disorders
-Aggressive behaviour or intentional self-harm
-Cluster headache (BNF- unlicensed use)

3. Dose

Initiation of lithium should be by or under the supervision of a specialist only.

Greater caution must be taken in older adults (over 65 years) or frail adults or patients with renal impairment who may require a third to a half less lithium due to reduced clearance.

When prescribing, the brand of lithium should always be specified to ensure bioequivalence.

4. Duration of treatment

The duration of treatment will vary according to the individual patient, specific information will be provided to the GP on dose alterations and on length of treatment. There is a significant risk of relapse if patient therapy is suddenly discontinued.

5. Contraindications and cautions

Hypersensitivity to lithium or to any of the excipients, cardiac disease, QT prolongation, clinically significant renal impairment, untreated hypothyroidism, breast-feeding, and patients with low body sodium levels (including dehydrated patients or those on low sodium diets, Addison's disease.

Lithium therapy should not be used during pregnancy, especially during the first trimester, unless considered essential.

6. Adverse effects

Side effects are usually related to plasma levels and are less common in patients with lithium levels less than 1.0 mmol/L. however **elderly patients may be particularly sensitive to side effects, even at levels below 1.0mmol/L**

Adverse reactions usually subside with a temporary reduction or discontinuation of lithium treatment. Mild gastrointestinal effects such as nausea, a general discomfort and vertigo, may occur initially, but frequently disappear after the first few days of lithium administration. Fine hand tremors, polyuria and mild thirst may persist.

Blood and lymphatic system disorders	Leucocytosis
Endocrine disorders	Hypercalcaemia, hypermagnesemia, hyperparathyroidism have been reportedLong-term adverse effects may include thyroid function disturbances such as euthyroid goitre and/or hypothyroidism and thyrotoxicosis. Lithium-induced hypothyroidism may be managed successfully with concurrent levothyroxine
Metabolism and nutrition disorders	Weight increase, hyperglycaemia
Psychiatric disorders	Confusion, delirium
Nervous system disorders	Tremor, especially fine hand tremors, dysarthria, myoclonus, benign intracranial hypertension. Ataxia, hyperactive deep tendon reflexes, slurred speech, dizziness, stupor, coma, myasthenia gravis, giddiness, dazed feeling, memory impairment. Vertigo, impaired consciousness, abnormal reflexes, convulsions, extrapyramidal disorders, encephalopathy, cerebellar syndrome (usually reversible), nystagmus (and associated falls) Peripheral neuropathy may occur on long-term treatment and is usually reversible at cessation of lithium
Cardiac disorders	Cardiac arrhythmia, mainly bradycardia, sinus node dysfunction, peripheral circulatory collapse, hypotension, ECG changes such as reversible flattening or inversion of T-waves and QT prolongation, AV block, cardiomyopathy
Gastrointestinal disorders	Abdominal discomfort, taste disorder, nausea, vomiting, diarrhoea, gastritis, salivary hypersecretion, dry mouth, anorexia
Skin and subcutaneous tissue disorders	Folliculitis, pruritus, papular skin disorders, acne or acneform eruptions, aggravation or occurrence of psoriasis, allergic rashes, alopecia, cutaneous ulcers
Musculoskeletal	Muscle weakness
Renal and urinary disorders	Polydipsia and/or polyuria and nephrogenic diabetes insipidus, histological renal changes with interstitial fibrosis after long term treatment have been reported. This is usually reversible on lithium withdrawal. Long-term treatment with lithium may result in permanent changes in kidney histology, formation of renal microcysts, and impairment of renal function. High serum concentrations of lithium including episodes of acute lithium toxicity may aggravate these changes. Rare cases of nephrotic syndrome have been reported.
General disorders and	Peripheral oedema.

administration site conditions	Urticaria and angioedema, attributed to some excipients such as acacia powder (or Arabic gum)
Reproductive	Sexual dysfunction
Senses	Dysgeusia, blurred vision, scotomata

Patients presenting with the following signs of toxicity should be advised to stop taking lithium immediately and urgent lithium levels undertaken. Levels over 1.5mmol/L may require urgent hospital treatment:
GI: increasing anorexia, diarrhoea, vomiting
CNS: muscle weakness, lack of co-ordination, drowsiness or lethargy progressing to giddiness with ataxia, tinnitus, blurred vision, dysarthria, coarse tremor and muscle twitching leading to seizures and coma.

7. Interactions

Reduced excretion of lithium leading to increased plasma levels of lithium	**Increased excretion leading to reduced plasma levels of lithium**	**Interactions causing neurotoxicity**
ACE Inhibitors, Angiotensin II inhibitors Loop, thiazide and associated diuretics Metronidazole NSAIDs (azapropazone, diclofenac, ibuprofen, indometacin, mefenamic acid, naproxen, parecoxib, piroxicam, rofecoxib, valdecoxib, ketorolac), Tetracyclines	Acetazolamide Xanthines (theophylline and caffeine) Products containing sodium bicarbonate	SSRI's increased risk of serotonin syndrome Antipsychotics may lead in rare cases to neurotoxicity in the form of confusion, disorientation, lethargy, tremor, extra-pyramidal symptoms and myoclonus Methyldopa Calcium channel blockers Carbamazepine

If medicines that interact with lithium must be prescribed, this should be on a regular (not p.r.n.) basis and monitoring should be undertaken monthly until a stable lithium level is reached and then every 3 months

Details of contraindications, cautions, drug interactions and adverse effects listed above are not exhaustive. For further information always check with BNF www.bnf.org.uk or SPC (www.medicines.org.uk).

Full prophylactic effect may not occur for 6-12 months after initialisation of therapy. Monitoring of the patient remains the responsibility of the specialist team until the patient is transferred to shared care prescribing. .

Baseline and Initiation Monitoring

Prior to initiating therapy tests for urea and electrolytes including calcium, estimated glomerular filtration rate (eGFR), thyroid function and a full blood count should be carried out. (Any abnormality in thyroid function should be corrected prior to initiating therapy). An ECG should be undertaken for people with cardiovascular disease or risk factors for it

Weight or BMI should be monitored prior to initiating therapy

During initiation lithium levels should be monitored weekly until dose has remained unchanged for 4 weeks. Additional monitoring should be carried out until levels become stable if any medication is prescribed, discontinued or altered which has the potential to interact to alter lithium levels

Monitoring Plasma Lithium Levels on Transfer to Shared Care

All patients should have plasma lithium levels monitored every 3 months during the first year of treatment. Subsequently levels must be measured every 6 months and every 3 months for any patients:

- Who are older people (over 65 years)
- Prescribed medication interacting with lithium
- At risk of impaired renal or thyroid function, raised calcium levels or other complications
- With poor symptom control or poor adherence
- Whose last level was 0.8 mmol per litre or more

Lithium dose and plasma lithium levels should be monitored more frequently if urea levels and creatinine levels become elevated, or eGFR falls over 2 or more tests, and an assessment of the rate of deterioration of renal function carried out.

HTFT has developed an electronic record for all patients initiated on Lithium; this system will keep a record of Lithium Levels at the appropriate intervals, a record of compliance with treatment, and other physical monitoring and requirements as described by NICE CG185. This electronic record will improve HTFT facilities to generate regular reports to highlight any discrepancies with monitoring recommendations while patients are under specialist care.

Lithium levels outside of therapeutic range should be discussed with the specialist

Monitoring Biochemical and Thyroid Function on transfer to Shared Care

On transfer to shared care, urea and electrolytes including calcium, estimated glomerular filtration rate (eGFR) and thyroid function must be checked every 6 months.

Raised calcium levels or an increase in mood symptoms might be related to impaired thyroid function.

More frequent monitoring should be carried out if there is evidence of impaired renal function (eGFR below 60ml/min)

- In people with a new finding of reduced eGFR, repeat the eGFR within 2 weeks
- Increase monitoring frequency to every three months

Abnormal results should be discussed with the specialist including any rise in TSH (even within normal limits)

Monitoring Physical Health on Transfer to Shared Care

Weight or BMI should be monitored every 6 months. Additionally for patients prescribed lithium for bipolar disorder the following checks should be carried out at least annually

- diet, nutritional status and level of physical activity
- cardiovascular status, including pulse and blood pressure
- metabolic status, including fasting blood glucose, glycosylated haemoglobin (HbA1c) and blood lipid profile
- liver function

Requirements for Sampling for Plasma Lithium Level Monitoring

Steady state lithium levels (5 to 7 days after initiation, dose change, or introduction/change in medication that affects lithium levels) should be checked 12 hours after a dose of a slow release preparation. In the case of twice daily levels should be taken before the morning dose.
Doses should be adjusted according to plasma levels, depending on the individual and condition treated. The specialist will advise on the appropriate level for each individual patient.

The following post 12 hour slow release dose levels are for guidance only, for specific patients the specialist will advise on the patients individual target level

- Acute Mania 0.8 to 1.0 mmol per litre
- Maintenance in affective disorder 0.6 to 0.8 mmol per litre
  (In elderly patients, levels of 0.4 to 0.6 mmol per litre may be appropriate)
- Cluster Headache 0.6-1.0 mmol/L (levels above 1.0 mmol/L occasionally required and will be monitored by specialist)

For patients on twice daily dosing on IMMEDIATE RELEASE lithium reference levels do not fall within these guidelines. The specialist will provide details and further information is available in the product SPC.

Further advice on the requirements for sampling, interpretation of lithium levels and very urgent results can be sought from Biochemistry on 01482 607753. Advice is also available from Humber NHS Foundation Trust Pharmacy Department on 01482 301724

9. Information to patient

All patients should be provided with a Lithium Treatment Pack including a record book, a patient information booklet “Important Information for Patients” and a lithium card at the beginning of treatment
Patients should be specifically warned not to take over-the-counter non-steroidal anti-inflammatory drugs

Patients should be informed to contact their GP immediately if any of the following signs of toxicity occur: increased anorexia, diarrhoea, vomiting or muscle weakness. Lack of coordination, drowsiness or lethargy progressing to giddiness with ataxia, tinnitus, blurred vision, dysarthria, coarse tremor and muscle twitching leading to seizures and coma.

Additionally patients should seek advice when planning for pregnancy or having an unexpected pregnancy.

10. Responsibilities of clinicians involved

Stage of Treatment	Hospital Specialist	General Practitioner
Initiation	• Selection of suitable patient • Perform baseline BMI or weight, urea and electrolytes including calcium, estimated glomerular filtration rate (eGFR), thyroid function and a full blood count and ECG when appropriate • Provide patients with the Record Book, "Important Information for Patients" and the Lithium Card at the beginning of the treatment • Monitor lithium plasma levels and adjust dose • Continue lithium prescribing until patient is on a stable dose	• Liaise with Community Psychiatric Nurses (CPNs) and the specialist • Investigation and treatment of any baseline thyroid function abnormalities • Re-introduction of lithium in patients restarting lithium, in consultation with the specialist • Take over prescribing responsibility once the patient is on a stable dose.
Maintenance	• Provide support to GP • Advise on dose alterations when necessary. • Monitor response to treatment during dose titration • Inform patient of the need to contact the GP or specialist if pregnancy is planned or confirmed • Advise patient that abrupt withdrawal of lithium is associated with significant risks of relapse • Co-ordinate planned withdrawal of lithium with the patient and GP	• Monitor lithium levels at least every 3 months during the first year of treatment • After first year - monitor lithium levels every 6 months or every 3 months for any patients: - Who are older people (over 65 years) - Prescribed medication interacting with lithium - At risk of impaired renal or thyroid function, raised calcium levels or other complications - With poor symptom control or poor adherence - Whose last level was 0.8 mmol per litre or more • Adjust dose according to result, seeking advice from specialist when necessary • Monitor lithium levels until they become stable if medication is prescribed or changed that has the potential to interact to alter lithium levels • Monitor urea and electrolytes including calcium, estimated glomerular filtration rate (eGFR) and thyroid function every 6 months • Undertake more frequent monitoring if there is evidence of impaired renal (eGFR<60ml/min) or thyroid function, raised calcium levels or an increase in mood symptoms • Monitor response to treatment and refer to specialist if deterioration in patients' mental state (or headaches) occurs. • Liaise with CPN and the specialist when required, e.g. if patient has not been monitored at required interval • Co-operate with the specialist in any planned withdrawal of lithium

Stage of Treatment	Hospital Specialist	General Practitioner
Planned or unexpected pregnancy	• Weighing the balance of risk and benefit with the patient • Produce treatment plan with patient	• Refer patient to the specialist if pregnancy is planned or confirmed • Liaise with the specialist to support the patient

Contact Details:

Humber NHS Foundation Trust: contact as advised in clinic letter

Hull University Hospitals NHS Trust

During office hours: Neurology secretaries 01482 675592

Out of hours: Contact on-call Neurologist via Switchboard: 01482 875875

Advanced Clinical Pharmacist – Neurology and Stroke – Priscilla Kanyoka e-mail Priscilla.kanyoka@nhs.net 01482 311 679

APPROVAL PROCESS

Written by:	**Jackie Stark (Principal Pharmacist, Clinical Services)**
Consultation process:	***Dr Ahmed, Consultant Neurologist, HEY*** ***Medicines Management Interface Group***
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