NHS
Pan Mersey
Area Prescribing Committee

SHARED CARE FRAMEWORK

LITHIUM in Adults

SHARED CARE

1.Background

Lithium is a well-established treatment for mood disorders. It may also be prescribed by consultant neurologists for prophylaxis of cluster headache (unlicensed indication.) Effective prophylaxis enables people to live a full life in the community; it is therefore more appropriate to have follow up appointments and monitoring, to support lithium treatment, in the community. Lithium treatment should not be stopped suddenly, as this can cause relapse.

In December 2009 the National Patient Safety Agency (NPSA) issued a patient safety alert entitled 'Safer lithium therapy' (NPSA 2009/PSA005)[(5)] in response to reports of harm and fatalities resulting from failure to monitor lithium therapy correctly. The alert was developed to help NHS organisations in England and Wales to take steps to minimise the risks to patients associated with lithium therapy. The NPSA highlighted that problems are also likely to occur if patients are not informed of the known side effects of lithium or symptoms of toxicity.

The NPSA developed several actions as well as documents to help overcome the identified safety risks. The documents included a purple information booklet; a monitoring booklet; to record blood results and an alert card to be carried by the patient. These documents are available at: http://webarchive.nationalarchives.gov.uk/20171030124420/http://www.nrls.npsa.nhs.uk/resources/?entryid45=65426&p=9

2.Licensed Indications

Acute manic or hypomanic episodes

Recurrent depressive disorders where treatment with other antidepressants has been unsuccessful

Prophylaxis against bipolar affective disorders

Aggressive behaviour or intentional self- harm

3.Locally agreed off-label use

Cluster headache on consultant neurologists' advice

4.Initiation and ongoing dose regime

Treatment with lithium is initiated and stabilised by a consultant psychiatrist / consultant neurologist or with consultant psychiatrist / neurologist oversight/supervision. The specialist will retain responsibility for its overall supervision and periodic review as per agreed care plan.

Due to its narrow therapeutic index, lithium must be prescribed by brand to avoid the risk of toxic or sub-therapeutic levels caused by the variable bio-availabilities of the different preparations.

Transfer of monitoring and prescribing to Primary care would normally be once the patient is established on a maintenance dose and is deemed to be stable.

The duration of treatment will be determined by the specialist based on clinical response and tolerability.

Priadel is the brand of lithium recommended in the Pan Mersey area. Other brands are available and must be continued in stabilised patients.

Priadel tablets contain lithium carbonate which is relatively insoluble
Priadel liquid contains lithium citrate

NB: 5ml of lithium citrate 520 mg in 5ml liquid is equivalent to approximately 204mg of lithium carbonate[2]

NB: Other brands of lithium are available e.g. Camcolit, Liskonum, Li-Liquid. For doses of other lithium preparations see current BNF.

Adults:
Dosage must be individualised depending on serum lithium levels and clinical response. The dosage necessary to maintain serum lithium levels within the therapeutic range varies from patient to patient. The minimum effective dose should be sought and maintained.

As a general rule, the following dosing schedule is recommended. Please refer also to the specific recommendations for the different indications as listed below:

In patients of average weight (70kg) an initial dose of 400-1,200mg of Priadel in tablet form may be given as a single daily dose in the morning or on retiring. Alternatively, the dose may be divided and given morning and evening. Convention is to take the dose in the evening to support therapeutic drug monitoring 12 hours later the following morning. The tablets should not be crushed or chewed.

In practice, a low dose of 200- 400mg daily (100 - 200mg in the elderly) of Priadel is commenced and increased as required until the correct serum level is reached.

Five to a maximum of seven days after starting treatment, serum lithium levels should be measured. Blood samples should be taken 12 hours after the previous dose of lithium (24 hours in exceptional circumstances, just before the next dose is due), to measure the serum lithium level at its trough. The serum level should not exceed 1.5 mmol/l. Optimal maintenance serum levels may vary from patient to patient. The specialist service will determine the target range for each patient and advise the primary care prescriber accordingly.

When changing between lithium preparations, serum lithium levels should first be checked, then the new preparation started at a daily dose as close as possible to the dose of the other form of lithium.

As bioavailability varies from product to product (particularly with regard to retard or slow-release preparations), a change of product should be regarded as initiation of new treatment.

With Priadel, the objective is to adjust the dose so as to maintain the “Target” serum lithium concentrations as specified by the specialist

Serum lithium levels should be monitored weekly until stabilisation is achieved. The serum level should not exceed 1.5 mmol/l. The dose should be adjusted to ensure the serum level does not exceed the therapeutic range as stated by the specialist. Urgent psychiatric/medical review needed if levels exceed 1.5mmol/L (1.0mmol/L in the elderly) or patient displaying toxicity. If =/> 2.0mmol/L (1.2mmol/L in the elderly) - withhold treatment and send the patient to A&E and inform specialist team.

Following stabilisation of serum lithium levels, the period between subsequent measurements can be increased gradually, but should not normally exceed three months.

Additional measurements should be made following alteration of dosage, on development of inter-current disease, signs of manic or depressive relapse, following significant change in sodium or fluid intake, or if signs of lithium toxicity occur.

If lithium is to be discontinued, particularly in cases of high doses, the dose should be reduced gradually.

Elderly patients or those below 50kg in weight
These patients often require lower lithium dosage to achieve therapeutic serum lithium levels. Starting doses of 100 – 200mg daily of Priadel tablets are recommended. Dosage increments of 100 – 200mg) every 5-7 days are usual. For prophylaxis, a serum lithium level of 0.4 to 0.8 mmol/l would be expected.

Children and adolescents:
Not recommended, and not covered by this shared care framework.

The patient will be reviewed by the specialist service at 12 monthly intervals or less.

Dose adjustments and consequent monitoring will be the responsibility of the initiating specialist unless directions have been discussed and agreed with the primary care clinician.

Termination of treatment will be the responsibility of the specialist. Clinicians, patients, and carers should be aware that abrupt discontinuation of lithium increases the risk of relapse. If lithium is to be stopped, the dose should gradually be reduced over a period of at least four weeks but preferably over a period of up to three months.

5.Baseline investigations, initial monitoring, and dose titration to be undertaken by specialist

Baseline

U&Es, eGFR, TFTs, calcium, weight/BMI, cardiac function (BP, pulse, and lipid profile), FBC
If for bipolar: Cardiovascular status including pulse and BP, Metabolic status including fasting blood glucose, HbA1c and blood lipid profile & LFTs.
If indicated:
ECG if indicated following a risk assessment and medication review carried out by the specialist to include current or future risk of cardiac arrhythmia
Pregnancy test in women of child-bearing age

Initiation

Lithium levels weekly until stabilisation achieved, after which the period between subsequent measurements can be increased gradually to a maximum of three months.
U&Es, TFTs, calcium and weight every 6 months

Compliance should be considered when interpreting each serum level result

Specialist Checklist

Specialist to ensure that they have covered all necessary information – patient counselling, purple book, baseline and initiation monitoring, dosing (same brand), what to do if missed doses/illness/side effects/toxicity, potential OTC side effects, pregnancy & breastfeeding (if appropriate), who to contact for advice etc.

6.Ongoing monitoring requirements to be undertaken by primary care

Monitoring	Frequency
Lithium level **Compliance should be considered when interpreting each serum level result**	Every 3 months, seek advice from initiating specialist should results be outside target range. Record results in purple lithium book or use NHS Health If =2.0mmol/L - send patient to A&E and inform specialist team.
U&Es,	Every 6 months (or more frequently if requested by specialist service) , seek advice from initiating specialist should results be deranged or eGFR noted to be falling over time
TSH and, if abnormal progress to T4, calcium, weight/BMI	Every 6 months, seek advice from initiating specialist should results be deranged
ECG – if the patient has been previously assessed as being at higher risk of cardiac arrhythmia, particularly QT prolongation, or is on other medications that could cause arrhythmia	Annual
Signs of toxicity Enquire about and document signs and symptoms which might indicate toxicity, e.g. paraesthesia, ataxia, tremor, cognitive impairment. Note: lithium toxicity may be seen where lithium levels do not appear high (ie in normal therapeutic range)	Every consultation

7.Pharmaceutical aspects

Route of administration

Oral

Formulations

- Priadel tablets 200mg
- Priadel tablets 400mg
- Lithium carbonate 250mg M/R tablets
- Camcolit 400mg M/R tablets
- Liskonum M/R 450mg tablets

- *Priadel liquid 520mg in 5ml
- *Li-Liquid 509mg in 5ml
- *Li-Liquid 1,018mg in 5ml

*Liquid and twice daily dosing can cause monitoring problems so should only be done in exceptional circumstances as directed by a specialist

Legal category

POM

8.Contraindications and Cautions

Please note this does not replace the Summary of Product Characteristics (SPC) and should be read in conjunction with it. SPC

- Hypersensitivity to lithium or excipients.
- Cardiac disease associated with rhythm disorder (Cardiac arrhythmia).
- Cardiac insufficiency (Heart failure).
- Severe renal impairment.
- Untreated hypothyroidism.
- Breast-feeding.
- Low body sodium levels, e.g. in dehydrated patients or those on low sodium diets.
- Addison's disease.
- Brugada syndrome or family history of Brugada syndrome

Cautions

- Mild to moderate renal impairment
- Use in elderly patients
- Adequate and stable sodium and fluid intake should be maintained. 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.
- Review lithium dose if diarrhoea and / or vomiting present and in cases where the patient has an infection and / or profuse sweating. Adjustments may be required.
- Risk of seizures may be increased if co-administered with drugs that lower the seizure threshold, or in patients with epilepsy.
- Cardiac disease
- May exacerbate psoriasis
- Surgery: discontinue 24 hours prior to major surgery and re-commence post-operatively once kidney function and fluid-electrolyte balance are normalised. Discontinuation is not required prior to minor surgery, providing fluids and electrolytes are carefully monitored.

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

9.Significant drug interactions

For a comprehensive list consult the BNF [2] BNF British National Formulary - NICE ; *Summary of Product Characteristics* [1] SPC or Stockley's Drug Interactions.[3]
Seek advice from the initiating specialist if there are any concerns about interactions.

Concomitant drugs that increase lithium levels risking toxicity

- ACE inhibitors/Angiotensin II receptor antagonists
- Diuretics especially thiazides.
- Other drugs that reduce sodium levels
- NSAIDS (including topical)
- Certain antibiotics including metronidazole and tetracyclines

Concomitant drugs that reduce lithium levels risking illness relapse

- Theophylline
- Sodium containing products (e.g. antacids or urinary alkalinising agents)

Drugs that may increase risk of neurotoxicity when co-administered with lithium:

- Calcium channel blockers (e.g. verapamil, diltiazem)
- Antipsychotics (e.g. haloperidol, olanzapine, clozapine, flupentixol, chlorpromazine)
- Antidepressants with a serotonergic action (e.g. SSRIs, tricyclic antidepressants, venlafaxine, duloxetine)
- Carbamazepine

Drugs associated with QT prolongation (e.g. amiodarone, macrolides, tricyclic antidepressants) – potential for additive effects when co-administered with lithium.

- Drugs that lower seizure threshold (e.g. SSRIs, tricyclic antidepressants, antipsychotics) – increased risk of seizures

Care should be taken on initiation, dose adjustment or discontinuation of any interacting medicines. The onset and degree of the interaction can vary and additional lithium monitoring is likely to be indicated, with doses adjusted accordingly.

10.Adverse effects and management

Adverse effect	Management
Hypothyroidism, hyperparathyroidism, serum calcium or phosphate abnormalities	Seek advice from initiating specialist
Deterioration in renal function	Seek advice from initiating specialist
Polyuria and polydipsia	Polyuria is common and often well tolerated. Advise the patient to maintain adequate fluid intake and advocate excellent oral hygiene. Contact specialist team for advice, which may include input from nephrology services.
Risk of arrhythmia. Lithium can cause cardiac arrhythmia, mainly bradycardia, sinus node dysfunction and ECG changes such as reversible flattening or inversion of T-waves and QT prolongation, or unmask Brugada syndrome. Concurrent prescribing of other drugs with a risk of prolonging the QT interval	ECG* should be performed shortly after initiation of treatment by the specialist team. Also, at any point where the patient develops symptoms such as blackouts, fainting, dizziness, laboured breathing, palpitations, or seizures. Also, if any new medication is added which may increase the risk of arrhythmia. Seek advice from initiating specialist regarding the risks and benefits of ongoing prescribing.
Possible signs of lithium toxicity • Severe hand shake (tremor) • Stomach ache along with nausea and diarrhoea • Muscle weakness • Ataxia muscle twitches • Slurring of words • Blurred vision Confusion • Feeling unusually sleepy	Seek advice from initiating specialist

* As access to ECGs and interpretation varies according to CCG area, a plan should be agreed between the specialist and GP at the start of shared care, as to how the patient will access an ECG should it become necessary.

11.Advice to patients and carers

The specialist will counsel the patient with regard to the benefits and risks of treatment and will provide the patient with any relevant information and advice. This will include patient information leaflets and a copy of the purple 'Lithium Therapy: Important Information for Patients' booklet'. The specialist will advise the patient to retain the printed information for future reference.

12.Pregnancy, paternal exposure and breast feeding

Manufacturer advises effective contraception during treatment for women of childbearing potential.

Inform the mental health consultant or neurologist if a patient is planning to become pregnant for treatment options to be considered or neurologist as patients on lithium can be referred into local Perinatal Teams for pre-conception counselling. Pregnancy should ideally be avoided – Inform initiating specialist immediately if the patient becomes pregnant whilst taking lithium (but do not stop the lithium).

Lithium is present in breastmilk risking toxicity in infant – avoid breastfeeding.

Paternal exposure: Animal studies have reported spermatogenesis abnormalities that may lead to impairment of fertility- it is unknown if this risk applies to humans.

13.Specialist contact information

See appendix 3

14.Additional information

Where patient care is transferred from one specialist service or GP practice to another, a new shared care agreement must be completed.

Prescribing responsibility will only be requested, following initiation and stabilisation with associated counselling and monitoring and when the consultant and the patient's GP agree that the patient's condition is stable.

The shared care agreement will cease to exist, and prescribing responsibility will return to secondary care, where:

- The clinical situation deteriorates such that stability is not achieved.
- The clinical situation requires a major change in therapy.
- The GP feels it to be in the best stated clinical interest of the patient for prescribing responsibility to transfer back to the Consultant.

There must be discussion between the Consultant and GP on this matter and an explanation by the GP of the reason(s) for transferring back prescribing responsibility. The Consultant will accept such a transfer within a timeframe appropriate to the clinical circumstances.

15.References

1. Lithium carbonate. Summary for Product Characteristics accessed 04/03/2022 Lithium SPC
2. British National Formulary accessed 04/03/2022 LITHIUM CARBONATE | Drug | BNF content published by NICE
3. Stockley's Drug Interactions e-version accessed 04/03/2022 https://about.medicinescomplete.com/publication/stockleys-drug-interactions/
4. NICE CG185: Bipolar disorder: the assessment and management of bipolar disorder in adults, children and young people in primary and secondary care; Published September 2014. Last updated April 2018. NICE CG 185
5. NPSA Safer Lithium Therapy. 2009 National Web Archives - Safer lithium therapy
6. Prescribing Observatory for Mental Health (2019). Topic 7f. Monitoring of patients prescribed lithium. Prescribing Observatory for Mental Health, CCQI 306 (data on file).

16.To be read in conjunction with the following documents.

- Policy for Shared Care (Appendix 1).
- Shared care agreement (Appendix 2).

Appendix 1

Policy for Shared Care

Shared care is only appropriate if it provides an optimum solution for the patient and it meets the criteria outlined in the Shared Care section of the Pan Mersey Definitions and Criteria for Categorisation of Medicines in the Pan Mersey Formulary document.

Before prescribing responsibilities are transferred to primary care:

- Prescribing responsibility will only be transferred when the consultant and the patient's GP agree that the patient's condition is stable.
- All information required by the shared care framework for the individual medicine has been provided to the patient and the patient's GP i.e.
- Patients will only be referred to the GP once the GP has agreed to the Shared Care Agreement and returned signed copies.

Inherent in any shared care agreement is the understanding that participation is at the discretion of the GP, subject to the availability of sufficient information to support clinical confidence.

Specialist Responsibilities in Shared Care

- To initiate the medicine, prescribe, monitor for toxicity and efficacy as described by the shared care framework until the patient is stabilised.
- To ensure the patient or their carer:
    - Is counselled with regard to the risks and benefits of the medicine.
    - Is provided with any necessary written information to the patient with regard to the individual medicine including patient information leaflets on individual drugs.
- Obtain and document informed consent from the patient when any medicines are prescribed for an off-label indication for any condition
- To be familiar with the shared care framework.
- To provide all information to the patient's GP as required by the shared care framework when prescribing responsibility is initially transferred and at any subsequent times as necessary for safe and effective treatment of the patient.
- To assess the patient regularly as necessary for the duration of therapy.
- To review the patient promptly if required by the GP.
- To meet any additional requirements as required by the individual medicine shared care framework.
- To communicate failure of a patient to attend a routine hospital review and advise the GP of appropriate action to be taken.

Primary Care Responsibilities in Shared Care

- To reply to a written request for Shared Care within 21 days ensuring both copies of the Shared Care Agreement are signed if appropriate.

If agreeing to shared care, the GP is asked:

- To prescribe, manage and monitor the medicine as advised by the Specialist and in line with the individual Shared Care Framework. Urgent psychiatric/medical review needed if levels exceed 1.5mmol/L (1.0mmol/L in the elderly) or patient displaying toxicity. If =/> 2.0mmol/L (1.2mmol/L in the elderly) - withhold treatment and send patient to A&E and inform specialist team.
- To review the patient as required by the Shared Care Framework
- To make appropriate and contemporaneous records of prescribing and/or monitoring and to note the existence of the Shared Care Agreement on the patient`s clinical record. A Snomed code of "268529002 Shared Care- Specialist/GP" can be used.
- To be familiar with the individual Shared Care Framework.
- To report any adverse effects of treatment to the specialist team.
- To inform the Specialist of any relevant change in the patient's circumstances.
- To seek Specialist advice as appropriate.
- To meet any additional requirements as required by the individual Shared Care Framework.
- To respond to Specialist communication relating to any change or addition to the patient's treatment covered by the Shared Care Agreement.

Where the GP wishes to withdraw prescribing, for example when the patient fails to attend for monitoring, they need to give the specialist team a minimum of 14 days' notice of their need to resume responsibility for prescribing. The specialist is required to acknowledge this request within the 14-day time period.

Appendix 2

Shared Care Agreement

Lithium

Request by Specialist Clinician for the patient's GP to enter into a shared care agreement

Part 1

To be signed by Consultant / Prescribing member of Specialist Team

Date _____

Name of patient_____

Address _____

_____

Patient NHS No _____

Patient hospital unit No _____

Diagnosed condition _____

Dear Dr_____

I request that you prescribe

Lithium

for the above patient in accordance with the enclosed shared care framework.

Prescribed dose: ……

Last Prescription Issued: ….. / ….. / ….. Next Supply Due: ….. / ….. / …..

Date of last blood test: ….. / ….. / ….. Date of next blood test: ….. / ….. / …..

Frequency of blood test: ……

I confirm that the patient has been stabilised and reviewed on the above regime in accordance with the Shared Care Framework and Policy.

I confirm that if this is a Shared Care Agreement for a drug indication which is unlicensed or off label, informed consent has been received.

Previous Investigations Completed	**Date**	**Result**	**Next date due**
Lithium level			
U&Es including calcium; creatinine			
eGFR			
TFTs			
FBC			
Weight / BMI			

Blood Pressure			
ECG, if cardiac arrhythmia and/or any changes in history as set out in section 10 above			

Further blood tests for lithium monitoring and associated physical health checks are due as per schedule in Section 6 of this shared care agreement unless stated otherwise in the attached clinic letter.

Purple lithium booklet provided ☐

Patient counselled on:

- Pregnancy issues ☐
- Interactions with OTC medicines ☐
- Driving implications ☐
- Need to carry alert card (from purple booklet) ☐
- Occasions to show purple record booklet ☐
- Need to update booklet information ☐

All reviews for overall monitoring of disease status and efficacy of treatment will continue to be done by specialist team as per the attached shared care framework.

Patient's next review date: ……. / ……. / …….

Licensed Use: YES / NO (specialist please delete as appropriate)

Details of Specialist Clinicians

Name _____Date_____

Consultant / Prescribing member of Specialist Team (circle or underline as appropriate)

Signature _____

In all cases, please also provide the name and contact details of the Consultant.

When the request for shared care is made by a prescriber who is not the consultant, it is the supervising consultant who takes medico-legal responsibility for the agreement.

Consultant: _____

Contact details:

Telephone number: _____Ext:_____

Address for return _____

of documentation

_____

_____

Please add patient addressograph here

Part 2

To be completed by Primary Care Clinician

I agree to prescribe _____for the above patient in accordance with the enclosed shared care framework.

Usual GP signature _____Date _____

GP name _____Please print

GP: Please sign and return a copy within 21 calendar days to the address above

OR

GP- If you do not agree to prescribe, please delete the section above and provide any supporting information as appropriate below:

Appendix 3 Support and Advice

Mersey Care NHS Foundation Trust excluding Mid-Mersey

Contact details for Access teams:-

- Single Point of Access Team (SPA) Liverpool - 0151 330 7207
- Single Point of Access Team (SPA) South Sefton, North/South Sefton, Southport & Formby - 01704 383075

Alternatively, contact the Mersey Care NHS Trust switchboard on 0151 473 0303 and ask to be connected to the appropriate assessment team or consultant/medical secretary, consultant on call or relevant community mental health team (CMHT) OR follow link to the Mersey Care website for further contact details
http://www.merseycare.nhs.uk/gps-and-referrers/mental-health-referrals/

Mid-Mersey Division of Mersey care NHS Foundation Trust

24 hrs a day, 7 days a week, 365 days per year

The team practitioners will screen the referral and a priority will be assigned; 24hrs emergency, urgent 72hrs and routine 10 days.

Crisis Resolution & Home Treatment

- St Helens 01744 621 688
- Knowsley 0151 290 4999
- Halton 01928 753 981
- Warrington 01925 666 647

Early Intervention Teams

- Halton & Warrington EIT 0151 422 6826
- St Helens &Knowsley EIT 01744 646 102

Recovery and Later Life Teams

- Halton Recovery Team 01928 753 968
- Halton Later Life team 01928 753 162
- Knowsley Recovery Team 0151 430 1621
- Knowsley Later Life Team 0151 676 5262
- St Helens Recovery Team 01744 736 708
- St Helens Later Life team 01744 646 321
- Warrington Recovery Team 01925 666 660
- Warrington Later Life Team 01942 664 041

Consultants Consultation

Contact the Assessment Team; the team consultant and speciality doctor have availability weekdays 12pm – 1pm to speak direct to GPs.

The assessment service does not provide stand-alone counselling, substance misuse services (including detoxification) or social care assessment.

The Walton Centre NHS Foundation Trust

Telephone the Trust switchboard to contact consultants or their secretaries:

0151 525 3611