

SHARED CARE FRAMEWORK

LITHIUM in Adults

SHARED CARE

1. Background

This shared care framework aims to provide clarity on the responsibilities of all professionals involved in commissioning and prescribing across primary, secondary and tertiary care. Good organisation of care across the interface between primary and secondary/tertiary care is crucial in ensuring that patients receive high quality care – and in making the best use of clinical time and NHS resources in all care.

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: Safer lithium therapy documents

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.

APC board date: 27 July 2022 | Last updated: July 2022

Shared Care Framework

Review date: July 2025 (or earlier if there is significant new evidence relating to this recommendation) Version: 2.0

APC administration provided by Midlands and Lancashire Commissioning Support Unit

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 carbonate²

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 weight/BMI	progress to T4, calcium,	Every 6 months, seek advice from initiating specialist should results be deranged
	ECG – if the patient had assessed as being at harrhythmia, particular on other medications arrhythmia	nigher risk of cardiac rly QT prolongation, or is	Annual
	Signs of toxicity Enquire about and do symptoms which migl paraesthesia, ataxia, t impairment.	nt indicate toxicity, e.g.	Every consultation
	Note: lithium toxicity lithium levels do not a therapeutic range)	may be seen where appear high (ie in normal	
7. Pharmaceutical aspects	Route of administration:	Oral	
	Formulation:	 Camcolit 400mg Liskonum M/R 45 *Priadel liquid 52 *Li-Liquid 509m *Li-Liquid 1,018n *Liquid and twice daily d 	DOmg te 250mg M/R tablets M/R tablets 50mg tablets 20mg in 5ml
	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 postoperatively 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	Adverse effect	Management
and 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 C agreed between the specialist and GP at the start of shared 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 and breastfeeding	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 2		
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.		
15. References	 Lithium carbonate. Summary for Product Characteristics accessed 04/03/2022 <u>Lithium SPC</u> British National Formulary accessed 04/03/2022 <u>LITHIUM CARBONATE Drug BNF content published by NICE</u> Stockley's Drug Interactions e-version accessed 04/03/2022 <u>https://about.medicinescomplete.com/publication/stockleys-drug-interactions/</u> 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. <u>NICE CG 185</u> NPSA Safer Lithium Therapy. 2009 <u>National Web Archives - Safer lithium therapy</u> Prescribing Observatory for Mental Health (2019). Topic 7f. Monitoring of patients prescribed lithium. Prescribing Observatory for Mental Health, CCQI 306 (data on file). 		
7. To be read in conjunction with the following documents	 Policy for shared care (Appendix 1) Shared care agreement (Appendix 2) RMOC Shared Care for Medicines <u>Guidance</u> NHSE/NHSCC guidance – items which should not be routinely prescribed in primary care: guidance for CCGs <u>NHSE 2019</u> NHSE policy- Responsibility for prescribing between Primary & Secondary/Tertiary Care <u>NHSE</u> 		

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.

- Prescribing responsibility will only be transferred when the specialist and the patient's GP agree that the patient's condition is stable.
- Before prescribing responsibilities are transferred to primary care, all information required by the shared care framework for the individual medicine has been provided to the patient's GP.
- 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 obtain patient informed consent for sharing of care between the specialist, primary care prescriber and patient. Consenting parties must have sufficient, accurate, timely information in an understandable form. Consent must be given voluntarily and must be documented in the patient's notes. Patients should be aware that shared care will not always be the best option for them. This is a mutual agreement between the specialist and primary care, which needs to be confirmed with the shared care agreement.
- To confirm the diagnosis.
- To confirm that the patient's care can be suitably maintained by primary care, following their medicine being optimised for approximately 3 months, with satisfactory investigation results.
- To initiate the medicine, prescribe, and monitor for toxicity and efficacy as described by the shared care framework until the patient is stabilised.
- To ensure the patient or their carer:
 - o Is counselled with regard to the risks and benefits of the medicine.
 - Is provided with any necessary written information with regard to the individual medicine including patient information leaflets on individual drugs.
 - Provides informed consent when any medicine is 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.
- Following the request to the patient's GP to initiate shared care; to ensure that the patient has an adequate supply of medication (usually 28 days) until shared care arrangements are in place. Further prescriptions will be issued if, for unforeseen reasons, arrangements for shared care are not in place at the end of 28 days. Patients should not be put in a position where they are unsure where to obtain supplies of their medication.
- To assess the patient regularly as necessary for the duration of therapy. The specialist will send a written summary within 14 days to the patient's primary care prescriber, confirm that ongoing treatment with the monitored medicine is appropriate and record test results on the patient-held monitoring booklet if applicable confirm the current dosage and clearly highlight any changes made both to the patient and in writing to the patient's primary care prescriber.
- The specialist team will:

- o provide training, advice, and guidance (as appropriate) for primary care prescribers if necessary to support the shared care agreement
- o provide contact details for both working and non-working hours
- o supply details for fast-track referral back to secondary/specialist care
- o provide the patient with details of their treatment, follow up appointments, monitoring requirements and, where appropriate, nurse specialist contact details
- 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 the failure of a patient to attend a routine hospital review and advise the GP of appropriate action to be taken.
- Following the addition of a new drug to an existing regime covered by a shared care agreement, the Specialist must initiate, prescribe, and monitor the new drug in accordance with the relevant shared care agreement including subsequent review and inform the GP of this. A new shared care agreement must then be initiated for the new drug.
- Prior to transfer of prescribing, the specialist will ensure that patients (and their caregivers, where
 appropriate) are aware of and understand their responsibilities to attend appointments and the need for
 continued monitoring arrangements.

Primary Care Responsibilities in Shared Care

- To prescribe within their own level of competence.
- 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.
- 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 "268529002
 Shared Care- Specialist/GP" can be used. Where applicable, keep the patient-held monitoring record up
 to date with the results of investigations, changes in dose and alterations in management.
- To be familiar with the individual shared care framework, have the information and knowledge to understand the therapeutic issues relating to the patient's clinical condition and undergo any additional training if necessary.
- To report any adverse effect in the treatment of the patient to the specialist team, and via the MHRA Yellow Card Scheme https://yellowcard.mhra.gov.uk/.
- 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 or monitoring covered by the shared care agreement.
- Where community nurse involvement is required in the administration of medicines under a shared care
 framework, nurses should be provided with adequate information and guidance by the prescriber or the
 specialist. Arrangements should be made in good time for any potential problems to be resolved to ensure
 that patient care is not compromised

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.

Patient Responsibilities in Shared Care

- To provide their informed consent for sharing of their care with the specialist and primary care prescriber.
 Consenting parties must have sufficient, accurate, timely information in an understandable and accessible format. Consent must be given voluntarily and must be documented in the patient's notes. Supporting information is available from NICE Making decisions about your care
- To take their medication as agreed, unless otherwise instructed by an appropriate healthcare professional.
- To meet all necessary monitoring arrangements to ensure the safe prescribing of their medication, and to alert the prescriber where these arrangements are not met.
- To attend all follow-up appointments with the primary care prescriber and specialist. If the patient is unable to attend any appointments, they should inform the relevant practitioner as soon as possible and arrange an alternative appointment.
- Inform healthcare professionals of their current medications, both prescribed and purchased elsewhere prior to receiving any new prescribed or over-the-counter medication.
- Report all suspected adverse reactions to medicines to their primary care prescriber.
- Store their medication securely away from children and according to the medication instructions.
- Read the information supplied by their primary care prescriber, specialist and pharmacist and contact the relevant practitioner if they do not understand any of the information given.

Appendix 2

Shared Care Request letter (Specialist to Primary Care Prescriber)

Request by specialist clinician for the patient's GP to enter into a shared care agreement

To be signed by consultant / prescribing member of specialist team (circle or underline as appropriate)

Dear [insert Primary Care Prescriber's name]

Patient name: [insert patient's name]

Date of birth: [insert date of birth]

NHS Number: [insert NHS Number]

Diagnosis: [insert diagnosis]

Please add patient addressograph here

As per the agreed Pan Mersey APC shared care framework for [insert medicine name and dose] for the treatment of [insert indication], this patient is now suitable for prescribing to move to primary care.

The patient fulfils criteria for shared care, and I am therefore requesting your agreement to participate in shared care. Where baseline investigations are set out in the shared care protocol, I have carried these out.

I can confirm that the following has happened with regard to this treatment:

	Specialist to complete
The risks and benefits of treatment have been explained to the patient	Yes / No
The patient has agreed to this shared care arrangement, understands the need for ongoing monitoring, and has agreed to attend all necessary appointments	Yes / No
A copy of the shared care framework which covers this treatment/the shared care framework can be found here (insert electronic/ web link)	Yes / No
I have provided the patient with sufficient medication to last until	
I have arranged a follow up with this patient in the following timescale	

If you have provided supporting information to the patient, please insert a copy here

Treatment was started on [insert date started] and the current dose is [insert dose and frequency].

If you are in agreement, please undertake monitoring and treatment from [insert date] NB: date must be at least 1 month from initiation of treatment.

The next blood monitoring is due on [insert date] and should be continued in line with the shared care guideline.

Frequency of blood test:

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.

Please could you reply to this request for shared care and initiation of the suggested medication to either accept or decline within 14 days.

Details of Specialist Clinicians

Name	Date	
Consultant / prescribing member of specialist team (circle or ur	nderline 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 specialist, it is the supervising consultant who takes medico-legal responsibility for the agreement.		
Consultant:		
Contact details		
Telephone number:	Ext:	
Address for return of documentation		
	·······	

Shared Care Agreement Letter (Primary Care Prescriber to Specialist)

Primary Care Prescriber Response

Dear [insert Doctor's name]

Patient [insert Patient's name]

NHS Number [insert NHS Number]

Identifier [insert patient's date of birth and/or address]

Thank you for your request for me to accept prescribing responsibility for this patient under a shared care agreement and to provide the following treatment

Medicine	Route	Dose & Frequency

I can confirm that I am willing to take on this responsibility from [insert date] and will complete the monitoring as set out in the shared care protocol for this medicine/condition.

Usual (GP signature:	Date
Usual (GP name:	(please print)
GP:	P: Please sign and return a copy within 21 calendar days to the address above	
GP Practice address/practice stamp		

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