Shared Care Guideline
for
Lithium Therapy

This shared care guideline (SCG) has been written to enable the continuation of care by primary care clinicians of patients initiated on Lithium Therapy by SWYT consultant psychiatrists, where this is appropriate, and in the patients' best interests. Primary care will only be requested to take over prescribing of lithium therapy within its licensed indication unless specifically detailed otherwise below.

Introduction

Indication/Licensing information
Licensed for the treatment and prophylaxis of mania, bipolar disorder, recurrent depression (augmentation), aggressive or self-mutilating behaviour.

NICE guidelines [CG185] suggest lithium as part of the acute treatment for mania and depression, and for long term prophylaxis in bipolar disorder.
NICE guidelines [CG90] suggest augmenting an antidepressant with lithium, when there has been an inadequate response to antidepressant monotherapy.

Lithium must be started by specialist mental health services (community or hospital) and should not be prescribed in primary care, except when under share care agreement.

Pharmacology
The exact mechanism of action of lithium is unknown.

Dosage and administration
Lithium is available as a modified release tablet (lithium carbonate) and as a liquid (lithium citrate).
The dose is adjusted according to serum-lithium concentration; doses may be initially divided throughout the day, but once daily administration is preferred when serum-lithium concentration stabilised.
Liquid (lithium citrate) is generally continued as a divided dose.

Several different brands and formulations of lithium are available (Priadel Tablets, Priadel Liquid, Camcolit, Liskium, Li- Liquid and Lithium carbonate Essential Pharm)

Preparations vary widely in bioavailability; preparations are **not** interchangeable.
Patients should be kept on the same brand and formulation.
Changing the preparation requires the same precautions as initiation of treatment.

Priadel (lithium carbonate) 200mg and 400mg tablets are the preferred brand locally.

Lithium must be prescribed by brand name and formulation must be specified.

Responsibilities of the specialist clinician initiating treatment

Summary

- To assess the suitability of the patient for treatment (including confirming the patient has no contra-indications to treatment and considering the relevance of any cautions, including interactions).
- Discuss the pros and cons of treatment with the patient. Ensure the patient is aware of:
  - Brand and formulation of lithium
  - Dosage
  - Monitoring requirements
  - Side effect
  - Signs and symptoms of toxicity
  - Avoid significant changes in salt/fluid intake and the importance of keeping hydrated.
  - Seek medical advice if becoming acutely unwell for any reason, particularly fever, vomiting or diarrhoea.
  - Avoid over-the-counter NSAIDs, e.g. Ibuprofen
  - Poor adherence or rapid discontinuation may increase the risk of relapse

    Female patient only:
  - Use of effective contraception in women of childbearing age
  - Seek medical advice if planning or become pregnant.
- The patients should be issued with a NPSA Lithium Therapy pack containing an information booklet, alert card and record book (purple book). Details including brand of lithium, monitoring etc should be detailed in the record book.
- To discuss the patient's responsibilities (see below) in relation to the shared care agreement.
- To initiate therapy and stabilise with lithium, arrange prescriptions and evaluate over the first 12 weeks.
- To perform baseline tests and routine monitoring until the patient is stable and at least 12 weeks of treatment (see monitoring section). Ensure all required tests are within accepted parameters. Results should be recorded in the patient's notes and patient purple record book.
- Write to the patient's GP requesting whether he or she is willing to participate in shared care. Provide the GP with a summary of information relating to the individual patient to support the GP in undertaking shared care.
  Enclose a completed Shared Care Agreement form (appendix A) with the letter when requesting GP to take over prescribing. Specialist should indicate specific diagnosis clearly and make sure the diagnosis is covered by the share care guidelines before requesting GP to take over prescribing.
- To advise the GP when the patient will next be reviewed by the specialist, but if ongoing specialist co-ordination of the patient's care is not required and can be safely discharged back to their GP, an individual care plan should be agreed on a case-by-case basis. This may include the access to advice and intervention of that specialist in a timelier manner than via a new referral and may fall outside shared care arrangement. The Proforma for patients discharged from the mental health service (Appendix B) should be completed by the mental health team and sent to the GP on discharge.
  Typically, the patient's condition and treatment should be reviewed at least once a year until the patient is discharged from the mental health service where this is possible.
- Advise the GP on when to adjust the dose, stop treatment, or consult with the specialist.
- To monitor the patient for adverse events and report to the GP and where appropriate Commission on Human Medicines/MHRA (Yellow Card scheme).
- To provide the GP with contact details in case of any queries.
- To provide patient / carer with contact details for support and help if required, both in and out of hours

Specialists should be clear in their communication (letters) to GPs if they want GPs to take over prescribing or if the letter is just a treatment progress information / feedback.

Responsibilities of the primary care clinician

Acceptance of Responsibility by the Primary Care Clinician
It is optional for the primary care clinician to participate in taking on responsibility for shared care for the patient. Primary care clinicians will take on shared care only if they are willing and able.

Summary

- To reply to the request for shared care as soon as possible.
- To prescribe Lithium by brand and formulation, and adjust the dose as recommended by the specialist.
- To ensure there are no interactions with any other medications initiated in primary care.
- To continue monitoring physical parameters such as lithium plasma levels, renal function including urea, creatine, eGFR, electrolytes (including calcium), thyroid function and weight/BMI as agreed with secondary care (refer to monitoring section below) and record results in patient's purple record book
- To inform the specialist if the patient discontinues treatment for any reason.
- To seek the advice of the specialist if any concerns with the patient's therapy. For example:
  - Patient or general practitioner is **not** comfortable to continue with the existing regime due to either change in condition or drug side effects, and a change in treatment may be required.
  - Advice in respect of concordance.
  - Lithium levels above target range but ≤1mmol/l
  - Patient condition deteriorating
  - Pregnancy/breast feeding
  - Kidney disease or progressive deterioration in renal function (see monitoring below)
- Discontinue lithium as directed by the specialist if required or immediately if an urgent need to stop treatment arises.
- To conduct an annual medication review or more frequently if required.
- To identify adverse events if the patient presents with any signs and liaise with the hospital specialist where necessary. To report adverse events to the specialist and where appropriate the Commission on Human Medicines/MHRA (Yellow Card scheme).

GPs should not routinely issue prescriptions until they are asked to take over prescribing by the specialist

Responsibilities of Patients or Carers

Summary

- To be fully involved in, and in agreement with, the decision to move to shared care.
- To attend hospital and primary care clinic appointments for reviews and routine monitoring. The patient should bring their purple book with them during appointments.
- Present rapidly to the primary care prescriber or specialist should their clinical condition significantly worsen.
- Report any suspected adverse effects to their specialist or primary care prescriber whilst taking lithium.
- To read the product information given to them, familiarise themselves with how to take lithium, common side effects and when to seek help or attend A&E if suspecting lithium toxicity.
- To take lithium as prescribed.
- Inform the specialist, primary care prescriber or community pharmacist dispensing their prescriptions of any other medication being taken – including over-the-counter medication.
- To carry lithium alert card with them and present if needed in other health care settings e.g. dentist, A&E etc.

Clinical Particulars

The details of side-effects, cautions, contraindications and interactions are not a complete list and the current BNF (https://www.medicinescomplete.com/#/) and the SPC (https://www.medicines.org.uk/emc/) remain authoritative.

BNF therapeutic class	Section 4.2.3 Drugs used for mania and hypomania
Cautions and Contraindications	Caution is advised in cardiac disease; concurrent ECT (may lower seizure threshold); diuretic treatment (risk of toxicity); elderly (reduce dose); epilepsy (may lower seizure threshold); myasthenia gravis; psoriasis (risk of exacerbation); QT interval prolongation; review dose as necessary in diarrhoea; review dose as necessary in intercurrent infection (especially if sweating profusely); review dose as necessary in vomiting; surgery. Long-term use of lithium has been associated with thyroid disorders and mild cognitive and memory impairment. Long-term treatment should therefore be undertaken only with careful assessment of risk and benefit, and with monitoring of thyroid function every 6 months (more often if there is evidence of deterioration). The need for continued therapy should be assessed regularly and patients should be maintained on lithium after 3–5 years only if benefit persists. Lithium is contraindicated in Addison's disease; cardiac disease associated with rhythm disorder; cardiac insufficiency; personal or family history of Brugada syndrome; low body sodium levels, including low sodium diets or dehydration; untreated hypothyroidism; Clinically significant renal impairment. Lithium should generally be avoid in people with history of diabetes insipidus; refusing regular bloods tests; at risk of overdose; breastfeeding (see below). Unless there is an urgent clinical need, lithium therapy should not be suddenly discontinued as it increases the probability of a relapse of mental health symptoms. When it is deemed necessary to discontinue Lithium, it should be done over a period of at least a month, but longer is preferred.
Pregnancy and breast feeding	GPs should seek urgent advice of the specialist if patient is planning to or becomes pregnant. Patient will most likely need treatment reviewed by specialist mental health service. Lithium should not be abruptly stopped unless directed by the specialist. GPs should seek urgent advice of the specialist if patient is planning or is breast feeding. **First trimester:** Avoid if possible (risk of teratogenicity, including cardiac abnormalities) **Second, third trimesters**: Dose requirements increased (but on delivery return to normal abruptly); close monitoring of serum-lithium concentration advised (risk of toxicity in neonate) **Breast Feeding:** lithium present in milk and risk of toxicity in infant—manufacturers advise to avoid
Adverse Drug Reactions	Common side effects include GI disturbances (e.g. nausea, vomiting, diarrhoea, dry mouth), sedation, fine tremor, metallic taste, polyuria, polydipsia, weight gain, oedema/swollen ankles. Significant side effects include hypothyroidism (rarely hyperthyroidism), parathyroid disease, renal impairment, hypercalcaemia, hypermagnesaemia, QT interval prolongation/arrhythmias, leucocytosis, exacerbation of skin conditions.

	Lithium toxicity If lithium toxicity is suspected, arrange an urgent lithium level immediately and seek specialist advice. <u>Lithium level 1.0-1.5 mmol/l:</u> Examine for signs of toxicity and seek urgent advice from specialist. <u>Lithium level > 1.5 mmol/l AND/OR signs of mild toxicity:</u> Stop lithium and seek urgent advice from specialist. Daily follow-up required as plasma levels may still be rising, continue to monitor for signs of moderate-severe toxicity over next 7 days. Consider the patient's overall physical health and comorbidities if need immediate referral to A&E. The risk of toxicity is greater in people with hypertension, diabetes, congestive heart failure, chronic renal disease, schizophrenia, Addison's disease, and COVID-19. Mild symptoms may develop at lower levels than full toxicity, but still need rapid assessment, particularly in elderly and emaciated patients. <u>Lithium level > 2 mmol/l AND/OR signs of moderate-severe toxicity:</u> Stop lithium. Immediate referral to A&E. Inform specialist for urgent review. Symptoms of lithium toxicity include increasing gastro-intestinal disturbances (**vomiting, diarrhoea, anorexia**), visual disturbances (**blurred vision**), polyuria, **muscle weakness**, fine tremor increasing to **coarse tremor (particularly extremities and lower jaw)**, CNS disturbances (**confusion**, **drowsiness/lethargy,** increasing to lack of coordination (falls), restlessness, dizziness, ataxia, stupor), tinnitus, dysarthria, abnormal reflexes, myoclonus **(muscle twitches),** choreoathetoid movements, dysarthria**,** incontinence, hypernatraemia. Signs of severe toxicity include cardiac arrhythmias (including sino-atrial block, bradycardia and first-degree heart block), blood pressure changes/circulatory failure, hyperreflexia and hyperextension of limbs, syncope, toxic psychosis, seizures, polyuria, dehydration, electrolyte imbalance, renal failure, coma and sudden death reported.
Monitoring	**<u>Responsibilities of the specialist clinician initiating treatment</u>** **<u>Baseline Tests</u>** Weight and BMI Renal function including urea, creatine, estimated glomerular filtration rate(eGFR), electrolytes (including calcium) Thyroid function FBC ECG for patients with established or risk of cardiovascular disease **<u>Routine monitoring</u>** Lithium plasma levels should be measured 1 week after starting, and 1 week after every dose change, and continued weekly until levels are stable (typically 4 weeks). Doses should be adjusted to achieve a serum-lithium concentration of 0.4 – 1 mmol/litre. Lithium levels should be routinely measured every 3 months for the first year. Specialists should continue monitoring until shared care is established. **<u>Responsibilities of the primary care clinician</u>** **<u>Routine monitoring</u>** Following initiation and established stable dose, lithium levels should be routinely measured every 3 months for the first year. After the first-year lithium levels should be monitored every 3-6 months. More frequent monitoring maybe indicated for some patients. Additional lithium monitoring is recommended if urea or creatine level increase or eGFR falls over 2 or more tests and assess the rate of deterioration of renal function.

Weight/BMI, renal function including urea, creatine, eGFR and electrolytes including calcium should be monitored every 6 months on stabilised regimens. More frequent monitoring maybe indicated for some patients.

People with serious mental illness (SMI) including bipolar disorder are at greater risk of poor physical health and have a higher premature mortality than the general population. Patients should have an annual physical health check including blood pressure, pulse, lipid profile, liver function test, fasting blood glucose or HbA1c from their primary care provider.

If the patient deteriorates or a change in treatment may be required, please refer to secondary care.

Lithium levels should be measured 12 hours post-dose.

Lithium monitoring summary

Parameter	Standard care	Special considerations
Lithium serum level	3 monthly for the first year. After the first year every 6 months	Every 3 months for: • Older people (over 65yrs) • People taking drugs that interact with lithium (e.g. NSAIDS, diuretics, ACE inhibitors) • People who are at risk of impaired renal or thyroid function, raised calcium levels or other complications such as significant cardiac disease • At risk of significant changes in sodium or fluid intake • People who have poor symptom control • People with poor adherence • People whose last plasma lithium level was 0.8 mmol per litre or higher
Serum creatinine and eGFR*	6 monthly	More frequently than 6 monthly if evidence of impaired renal function e.g. eGFR less than 60ml/min (do whenever a serum Lithium is done) or if urea or creatine level increase or eGFR falls over 2 or more tests and assess the rate of deterioration of renal function. If eGFR falls below 60ml/min, consider referring to specialist for review of the ongoing need for lithium eek further advice. Over 65s at least every 3-6 months
Serum calcium	6 monthly	Over 65yr or cardiac disorder; at least every 6 monthly. More frequently if found that calcium level is raised and seek further advice.
Thyroid function test	6 monthly	More frequently than 6 monthly if there is evidence of impaired thyroid function or an increase in mood symptoms that might be related to impaired thyroid function.

	Weight/BMI	6 monthly	
	ECG	Initially and if clinically indicated	
	Physical health check (blood pressure, pulse, lipid profile, liver function test, fasting blood glucose or HbA1c)	Annually	

Interactions

Interactions that increase or decrease the excretion of lithium require increased monitoring to reduce the risk of lithium toxicity and/or deterioration in the patient's mental health.

Interactions that prolong the QT interval and increase the risk of ventricular arrhythmias should be avoided unless advised otherwise. Some interaction may increase the risk of developing hypokalaemia (potentially increasing the risk of ventricular arrhythmias).

ACEI Inhibitors	Excretion of lithium reduced by ACE inhibitors (increased plasma concentration)	Unpredictable and develops over several weeks.
Amiodarone	Avoidance of lithium advised by manufacturer of amiodarone (risk of ventricular arrhythmias). If concurrent use is unavoidable consider ECG monitoring recommended	Amiodarone has a long half-life; there is a potential for drug interactions to occur for several weeks (or even months) after treatment with it has been stopped
Angiotensin-II Receptor Antagonists	Excretion of lithium reduced by angiotensin-II receptor antagonists (increased plasma concentration)	Similar precautions as ACE Inhibitor
Antipsychotics	Increased risk of neurotoxicity without raised serum lithium levels extrapyramidal side-effects, QTc interval prolongation when lithium given with antipsychotics	Concurrent use can be advantageous
Antidepressants, SSRI	Increased risk of neurotoxicity/serotonin syndrome when lithium given with SSRIs. Possible lithium toxicity reported. Citalopram may increase risk of ventricular arrhythmias/QTc prolongation	Concurrent use can be advantageous
Antidepressants, Tricyclic	Increased risk of neurotoxicity/serotonin syndrome when lithium given with SSRIs. May increase risk of ventricular arrhythmias/QTc prolongation	

	Carbamazepine/ Oxcarbazepine	Lithium given with carbamazepine/oxcarbazepine increases the risk of neurotoxicity without increasing plasma concentration of lithium	Concurrent use can be advantageous
	Calcium Channel Blockers (Diltiazem and verapamil)	Neurotoxicity may occur when lithium given with diltiazem without increasing plasma concentration of lithium	
	Diuretics, Loop	Excretion of lithium reduced by loop diuretics (increased plasma concentration and risk of toxicity)—loop diuretics safer than thiazides	
	Diuretics, Potassium-sparing and Aldosterone Antagonists	Excretion of lithium reduced by potassium-sparing diuretics and aldosterone antagonists (increased plasma concentration and risk of toxicity)	
	Diuretics, Thiazide and related	Excretion of lithium reduced by thiazides and related diuretics (increased plasma concentration and risk of toxicity)—loop diuretics safer than thiazides Avoidance is advised.	
	Metronidazole	Increased risk of lithium toxicity when given with metronidazole	Interactions do not apply to topical metronidazole preparations
	NSAIDs	Excretion of lithium reduced by NSAIDs (increased risk of toxicity)	Interactions do not generally apply to topical NSAIDs. If NSAIDs are necessary, additional monitoring required. PRN use should be avoided.
	Tetracyclines	Excretion of lithium may be reduced by tetracyclines	
	Theophylline/ Aminophylline	Excretion of lithium increased by theophylline by 20-30% Increased risk of hypokalaemia	Monitor lithium and potassium concentrations closely.
Re-Referral guidelines	Seek the advice of the specialist regarding any concerns with the patient's therapy, as highlighted above in "Responsibilities of the primary care clinician". Specialist can advise if appropriate to re-refer or if medication can be safety continued in primary care.		
Ordering information	Lithium must be prescribed by brand name and formulation must be specified.		

Communication and contact details

Specialist to primary care clinician
The specialist will inform the primary care clinician when they have initiated lithium. When the patient is near completing the satisfactory initiation period, the specialist will write to the primary care clinician to request they take over prescribing and where possible give an indication as to the expected length of treatment. The specialist will also send a shared care request form to support the primary care clinician in undertaking shared care. (Appendix A)

Primary Care Clinician to specialist
If the primary care clinician has concerns over the prescribing of lithium, they will contact the specialist as soon as possible.

Contact names and details

Contact Details	Telephone number	Email
Barnsley Single Point of Access (SPA)/ Barnsley CORE Team/ East Enhanced Team	01226 645000	SPA:BarnsleyMentalHealthSpa@swyt.nhs.uk
Dr A Meenadchisundaram (CORE)	01226 645000	ampi.meenad@swyt.nhs.uk
Dr A Karan (CORE)	01226 645000	anil.karam@swyt.nhs.uk
Dr K Fletcher (CORE)	01226 645000	kelsey.fletcher@swyt.nhs.uk
Dr K Rele (West Enhanced Team)	01226 644190	kiran.rele@swyt.nhs.uk
Dr S Chari (Early Intervention Team)	01226 644166	suresh.chari@swyt.nhs.uk
Kendray Hospital Pharmacy Team	01226 644338	KendrayPharmacyTeam@swyt.nhs.uk
Chris Lawson (Head of Medicines Management, NHS Barnsley CCG)	01226 433798	chris.lawson@nhs.net

References

- British National Formulary, BNF accessed online www.medicinescomplete.com Accessed 7.2.22
- Summary of Product Characteristics, SPC accessed online from www.medicines.org.uk Accessed 7.2.22
- NICE Clinical Guidelines [CG185]. Bipolar Disorder: assessment and management. https://www.nice.org.uk/guidance/cg185 Accessed 7.2.22
- NICE Clinical Guidelines [CG90]. Depression in adults: recognition and management. https://www.nice.org.uk/guidance/CG90 Accessed 7.2.22
- Specialist Pharmacy Service, SPS accessed online www.sps.nhs.uk Accessed 7.2.22

Development Process

This guidance has been produced by Matthew Tucker, Advanced Clinical Pharmacist following an AMBER classification status of lithium therapy by the Barnsley Area Prescribing Committee. This guideline was ratified by the Area Prescribing Committee on 13th April 2022.

Appendix A – Shared Care request form (Amber) for Lithium Therapy

- Specialist to complete when requesting primary care clinician to enter a shared care arrangement.
- Primary care clinician to return signed copy of form.
- Both parties should retain a signed copy of the form in the patient's record.

From (**Specialist**): _____ **To** (**Primary care clinician**): _____

As per the agreed Barnsley shared care guideline for Lithium therapy, this patient is now suitable for prescribing to move to primary care.

The patient fulfils the criteria for shared care and I am therefore requesting your agreement to participate in shared care. I have carried out baseline tests and initial monitoring as detailed in the shared care guideline.

Patient details

Name: _____ DOB: _____

NHS Number: _____

Address: _____

Diagnosed condition: _____

Amber Drug details

Drug/Brand name: _____ Dose and frequency: _____

Lithium level target range: _____

Date of initiation: _____ Length of treatment: _____

The patient has been provided with sufficient medication to last until: _____

The patient will be reviewed by the consultant on: _____

The patient should be reviewed by the primary care clinician by: _____

Monitoring

The following monitoring should be undertaken by the primary care clinician. Refer to the monitoring section of the shared care guideline.

Parameter	**Date next test due**	**Frequency**
Lithium serum level		
U+Es/eGFR and Creatine		
Calcium profile		
Thyroid function test (TFT): TSH/T4		
Weight/BMI		

Communication

Consultant
Telephone number: _____ Fax number:_____

Email address: _____

Specialist Nurse
Telephone number:_____ Fax number: _____

Email address: _____

Confirmation of acceptance of shared care

Specialist (Doctor/Nurse) name: _____

Specialist (Doctor/Nurse) signature: _____ Date: _____

I, _____ can confirm I :

☐ accept the request to participate in shared care for the patient named above and will complete the monitoring as set out in the shared care guideline for this medicine/condition.

☐ reject the request to participate in shared care for the patient named above. The reason for this being ……

Signature of primary care clinician: _____Date:_____

To save resources you have been sent appendix A of the shared care document. The full document *(Shared Care Guideline for Lithium Therapy*, *date approved April 2022)* can be accessed on the Barnsley BEST website at the following link:
http://best.barnsleyccg.nhs.uk/clinical-support/medicines/shared-care-guidelines/
Or via the Barnsley Area Formulary www.barnsleyformulary.nhs.uk

Appendix B – Proforma for patients discharged from mental health services prescribed lithium therapy

Only to be considered for patients stable on lithium for a minimum of 6 months.

From (**Specialist**): _____ **To** (**Primary Care Clinician**): _____

The following patient is deemed suitable for discharge and therefore no longer needs to be reviewed by the mental health team. The patient has been stable on lithium therapy for at least 6 months and there are no planned changes.

The consultant psychiatrist should also send a covering letter stating patient is suitable for discharge from mental health services.

Patient details

Name: _____ DOB: _____

NHS Number: _____

Address: _____

Lithium details

Brand name: _____ Formulation: _____

Dose and frequency: _____ Lithium level target range: _____

Monitoring

The following monitoring should be undertaken by the primary care clinician.
Monitoring should continue until directed otherwise.

Parameter	**Date next test due**	**Frequency**
Lithium serum level		
U+Es/eGFR and Creatine		
Calcium profile		
Thyroid function test (TFT): TSH/T4		
Weight/BMI		

Previous test results can be accessed from ICE.

Re-Referral guidance
If the primary care clinician has concerns regarding deteriorating mental state, please ring the contact telephone number provided.
Please seek advice if aware of:

- Any new risks that may destabilise lithium levels (change in physical health status, new drug interaction etc)
- Patient develops new significant side effects
- Lithium levels outside of target range
- Pregnancy/breastfeeding
- Kidney disease or progressive deterioration in renal function
- Patient had an acute episode of lithium toxicity
- Patient discontinues lithium therapy for any reason.

Specialist can advise if appropriate to re-refer or if medication can be safety continued in primary care.
If a decision is made by the psychiatrist that the patient needs to be seen, then this appointment will be prioritised and organised by the medical secretary or relevant mental health team

Contact telephone number: _____

Consultant: _____ **Date**: _____

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http://best.barnsleyccg.nhs.uk/clinical-support/medicines/shared-care-guidelines/
Or via the Barnsley Area Formulary www.barnsleyformulary.nhs.uk