Guidelines on Safe Lithium Prescribing and Shared Care

Table of Contents

Background	2
Key references for this guidance	2
General Statements	3
Initiation of lithium – see initiation flowchart in appendix 1	5
Pre-treatment screening	5
Patient information	5
Adding the patient to the TEWV lithium register	6
Formulations of lithium	6
Adverse effects of lithium	6
Interactions with other medicines	7
On-going monitoring	8
Action in response to lithium levels	9
Renal monitoring in established lithium treatment	10
Shared Care Arrangements	11
Responsibilities of secondary care mental health services (TEWV)	11
Responsibilities of the General Practitioner / primary care team	11
Responsibilities of the dispensing Pharmacist / GP practice	12
Triggers for contacting secondary care mental health services	12
Appendix 1 – Initiation flowchart	14
Appendix 2 – Transfer request letter	15
Appendix 3 – Secondary care review template	18

Title	Guidelines on Safe Lithium Prescribing and Shared Care		
Approved by	Drug & Therapeutics Committee Date of Approval 25 th March 2021		
Protocol Number	PHARM-0024-v8	Date of Review	1 st April 2024

Background

Lithium is used for the prophylaxis and treatment of mania, hypomania and depression in bipolar disorder, and in the prophylaxis and treatment of recurrent unipolar depression. Lithium is also used as concomitant therapy with antidepressant medication in patients who have had an incomplete response to treatment for acute bipolar depression and to augment other antidepressants in patients with treatment-resistant depression (unlicensed indication, but supported by NICE). It is also licensed for the treatment of aggressive or self-harming behaviour.

Lithium reduces both the number and severity of relapses - it is more effective in preventing manic than depressive relapse. NICE recommends that a mood stabiliser should be prescribed prophylactically after a single manic episode that was associated with significant risk and adverse consequences - NICE supports the use of lithium as a first-line mood stabiliser.

Intermittent treatment with lithium may worsen the natural course of bipolar illness, this has led to recommendations that lithium treatment should not be started unless there is a clear intention to continue for at least 3 years. There is no evidence to suggest that if lithium treatment is effective for the first ten years that effectiveness is lost in the second or third decade of treatment.

Lithium has a narrow therapeutic range; long term use is associated with renal damage and hypothyroidism. Therefore, lithium should not be prescribed unless responsibilities and arrangements for regular monitoring of lithium levels and other essential parameters have been established.

Extra care is required when prescribing lithium for:

- the elderly;
- patients with reduced renal function (eGFR < 60ml/min);
- pregnant women and women of child bearing age;
- patients who have high risk factors for physical illness e.g. hypertension, diabetes, obesity, smoking, urine outflow problems;
- patients taking NSAIDs, ACE-inhibitors, angiotensin-2 antagonists or diuretics;
- patients with learning disabilities

Patients prescribed lithium must have a medication alert activated on their electronic patient record and must be easily identifiable by search on GP clinical records (i.e. lithium added to their repeat prescription).

Key references for this guidance

- NICE CG185 Bipolar disorder: assessment and management (September 2014, last updated February 2020)
- Maudsley Prescribing Guidelines in Psychiatry, 13th edition
- British National Formulary online via <u>Medicines Complete</u>

Title	Guidelines on Safe Lithium Prescribing and Shared Care		
Approved by	Drug & Therapeutics Committee Date of Approval 25 th March 2021		
Protocol Number	PHARM-0024-v8	Date of Review	1 st April 2024

General Statements

- Treatment with lithium should be initiated in secondary mental health services
- Regular checks on lithium levels, renal function and thyroid function are essential for safe prescribing.
- Prescribing and monitoring responsibility should remain with secondary care services
 until a shared care arrangement is agreed with their GP. This includes patients
 discharged from inpatient settings who have been newly initiated on lithium –
 responsibility for such patients should initially transfer to the appropriate community
 mental health team.
- Prescribing and monitoring responsibility of patients with a target lithium level >1 mmol/L must not transfer to primary care.
- Whilst transfer of prescribing and monitoring responsibility is appropriate in other high
 risk or vulnerable patients, consideration should be given to a higher frequency of
 specialist review.
- A patient's clinical condition must be stabilised* before requesting shared care. Once
 the patient is stabilised on lithium they should be considered for shared care between
 mental health services and the GP. This will normally occur following the 3 month
 monitoring check.
 - *For the purposes of transfer of prescribing and monitoring responsibility, patients are regarded as stabilised once they have shown a response to lithium and there are no recognised problems with compliance or significant acute risks of harm to themselves or to others, or experiencing significant side effects. Their lithium dose will be stable and a 3 month check of lithium plasma levels completed.
- Prescribing and monitoring tasks for patients on lithium must stay together. A reliable system for accessing monitoring results at the time of prescribing must be in place.
 Prior to issuing a prescription, the prescriber must check that all necessary monitoring tests have been completed and that it is safe to issue a prescription. Where this is not the case, arrangements for monitoring tests should be made as soon as possible
- Whoever initiates tests for monitoring lithium therapy is responsible for acting on the results, particularly increases in lithium levels, levels outside normal/target ranges or results that indicate deteriorating renal or thyroid function
- The Trust maintains a register of lithium patients and the Lithium Registers Team will routinely check WebICE for monitoring results, alerting the TEWV team if monitoring is overdue or if lithium levels indicate that action is required.
- Prescribers must have a system for checking, identifying and dealing with medicines
 that might adversely interact with lithium therapy. Concurrent treatment with angiotensin
 converting enzyme (ACE) inhibitors, angiotensin-2 receptor antagonists ("sartans"),
 thiazide diuretics and non-steroidal anti-inflammatory drugs (NSAIDs) should be avoided
 if possible
- There must be effective communication between all healthcare practitioners involved with patients on lithium therapy about the target level / range, dosage, monitoring results and changes to concurrent medication.
- The dispensing pharmacist or GP practice must check that monitoring is up-to-date and that it is safe to dispense lithium, by checking the patient-held purple book or contacting the GP surgery or the TEWV lithium registers team

Title	Guidelines on Safe Lithium Prescribing and Shared Care		
Approved by	Drug & Therapeutics Committee Date of Approval 25 th March 2021		
Protocol Number	PHARM-0024-v8	Date of Review	1 st April 2024

- Patients prescribed lithium should <u>not</u> be discharged from secondary mental health services. In exceptional circumstances an individual agreement for discharge may be considered for a patient who expressly indicates that they do not want to be seen by secondary mental health services. However, discharge should only be considered if lithium treatment is stable, and the patient is adherent to treatment and compliant with monitoring requirements. Discharge arrangements should involve a proper discussion with the GP and the rationale for discharge must be clearly documented.
- Patients who have been discharged from secondary mental health services in the past should be referred back to secondary care unless the exceptional circumstances described above apply. Particular caution should be applied to patients whose lithium therapy becomes unstable (see "<u>Triggers for contacting secondary care mental health services</u>")
- Secondary mental health services have a responsibility to proactively and reactively provide advice to primary care on the management of patients treated with lithium
- Regardless of shared care arrangements in place, secondary mental health services have a responsibility to check monitoring results of all lithium patients when admitted or seen as outpatients with reference to the relevant lithium register
- The patient-held "purple" booklet, alert card and record book developed by the NPSA will be supplied to all patients on lithium and their use supported by healthcare professionals involved in providing care. Patients will also be invited to utilise the "NHS Health Monitor for Lithium" app developed by South West London and St. George's NHS Trust for iOS and Android devices.

Title	Guidelines on Safe Lithium Prescribing and Shared Care		
Approved by	Drug & Therapeutics Committee Date of Approval 25 th March 2021		
Protocol Number	PHARM-0024-v8	Date of Review	1 st April 2024

Initiation of lithium - see initiation flowchart in appendix 1

Pre-treatment screening

Screening for the risk of renal and cardiovascular disease is essential prior to prescribing lithium. The following baseline checks are required:

- eGFR
- Urea & electrolytes
- Creatinine
- Thyroid Function Tests (TFTs)
- Calcium
- Full Blood Count
- ECG (if cardiovascular disease or risk factors, e.g. family history, old age)
- Height
- · Weight and BMI
- BP

Concurrent medication must be checked for potential <u>interactions</u> <u>[template letter for obtaining medical history from GP]</u>

Patient information

The NPSA Lithium Therapy patient packs containing an information booklet, lithium alert card and record book is available from TEWV pharmacy for new patients and GP practices for longstanding patients who are identified as not having one. Further supplies of the patient pack can be ordered from current NHS Non-Secure Contract held by 3M. Orders should be sent to Email: nhsforms@spsl.uk.com An "NHS Health Monitor for Lithium" app is available for iOS and Android devices.

The "purple" booklet, alert card and record book developed by the NPSA should be made available to all patients initiated on lithium. Patient details, essential information on the patient's therapy and contacts must be completed when issuing the lithium therapy pack to patients – **for new patients**, **this is the responsibility of the TEWV team**.

Essential details to be completed: -

- Brand; strength and dose of lithium
- Individual target lithium level / range indicating maximum and minimum plasma levels
- Name of people managing lithium therapy
- Dates and results of lithium blood results, e-GFR, TFTs and weight/BMI
- Date of next check
- Any amendments to plasma level range or dose (details in the booklet and alert card must also be amended)

Confirmation that the patient has received written information and verbal advice and the necessary details have been transferred to the booklet, alert card and record book must be noted in the electronic patient record and communicated to GP when prescribing transfers

Results of lithium level tests and checks of thyroid function, renal function and weight / BMI monitoring should be recorded in the patient-held record so that healthcare professionals can track changes and have access to the information to make appropriate clinical decisions and maintain safe lithium therapy.

At the start of lithium therapy and throughout treatment patients must receive ongoing verbal and written information about minimising the risks of toxicity. This should cover:

 The importance of having regular blood tests, and the importance of blood samples for lithium levels being taken 12-14 hours after the last dose;

Title	Guidelines on Safe Lithium Prescribing and Shared Care		
Approved by	Drug & Therapeutics Committee Date of Approval 25 th March 2021		
Protocol Number	PHARM-0024-v8	Date of Review	1 st April 2024

- The signs and symptoms of toxicity; why they might occur and what to do if they do occur:
- The importance of maintaining an adequate fluid intake (e.g. during bouts of diarrhoea and vomiting or during hot weather) and informing their GP or TEWV team if acute infection occurs;
- Avoidance of big changes in dietary salt intake;
- Emphasising good compliance and not to double up if they miss a dose
- Interactions with over the counter medicines e.g. non-steroidal anti-inflammatory drugs, herbal diuretics and sodium bicarbonate containing antacids or urinary alkalinising agents;
- The importance of continuously taking the same brand of lithium;
- Women of child bearing age should be advised to use reliable contraception. Should there be a concern about them being pregnant they should immediately seek professional advice about continuing treatment;
- The importance of using the record book and them or their carer taking it whenever they visit their GP, clinic or hospital, when a new prescription is requested or when collecting a prescription from the dispensing pharmacy / GP surgery

Adding the patient to the TEWV lithium register

After initiation of lithium, the TEWV team should complete the <u>initiation template</u> with the patient's details and email this to the <u>Lithium Registers Team</u> so that the patient can be added to the relevant team register.

Formulations of lithium

Different brands and formulations of lithium are not bioequivalent and care must be taken to make sure that the patient receives the same preparation each time a prescription is supplied. Therefore, lithium should always be prescribed using the <u>brand</u> name. The brand and formulation of lithium taken by the patient must be recorded in the patient record book and on the alert card. **Priadel** is the preferred brand in TEWV. Lack of clarity over which preparation is intended when prescribing, can lead to the patient experiencing subtherapeutic or toxic lithium levels.

Particular care should be taken if there is need to switch from a tablet to a liquid formulation as different lithium salts are used in each type of formulation - refer to the current BNF for available formulations and dose equivalence, and/or seek advice from pharmacy on dose conversion.

Adverse effects of lithium

- Side effects tend to be directly related to plasma levels. Common side effects at therapeutic doses include:
 - Mild gastrointestinal symptoms (usually short-term following initiation)
 - Fine hand tremor
 - o Thirst
 - Polyuria (may occur more frequently with twice daily dosing)
 - Weight gain
- Toxicity toxic effects may occur at any plasma lithium level but reliably occur at levels
 > 1.5 mmol/L. Signs are:
 - o GI effects increasing anorexia, nausea and diarrhoea
 - o CNS effects muscle weakness, drowsiness, ataxia, muscle twitching, tremor
- If features of lithium toxicity occur, stop lithium immediately, check plasma lithium levels, creatinine, urea and electrolytes and discuss with a doctor from mental health services – see table below

Title	Guidelines on Safe Lithium Prescribing and Shared Care		
Approved by	Drug & Therapeutics Committee Date of Approval 25 th March 2021		
Protocol Number	PHARM-0024-v8	Date of Review	1 st April 2024

Interactions with other medicines

Because of lithium's narrow therapeutic index, interactions with other medicines can be highly clinically significant. Any drug that affects a patient's renal function will affect lithium levels.

The most potentially serious interactions are:

In each case, excretion of lithium is reduced, resulting in an increase in plasma levels. Try to avoid combinations of these drugs. If they *must* be used, lithium levels must be monitored more frequently (weekly x 1 month, then monthly until stable*)

must be monitored more frequently (weekly x 1 month, then monthly until stable)			
Medicine Group	Magnitude of effect	Timescale	Note
ACE inhibitors	Unpredictable	Develops	7-fold increased risk of
Angiotensin-2	Up to 4-fold	over	hospitalisation for lithium
receptor antagonists	increase in lithium	several	toxicity in the elderly
	levels	weeks	
Thiazide diuretics	 Unpredictable 	Usually	Loop diuretics are safer
	 Up to 4-fold 	apparent in	but caution still required.
	increase in lithium	first 10	Any effect will be
	levels	days	apparent in the first
			month
NSAIDs (Inc. OTC	 Unpredictable 	Variable;	NSAIDs are widely used
anti-inflammatories)	• From 10% to >4-	few days to	on a PRN basis – this is
	fold increase in	several	potentially more
	lithium levels	months	problematic
* At least two aspectative levels in toward years at stable days			

^{*} At least two consecutive levels in target range at stable dose

Less significant interactions:

Medicine / group	Effect of interaction
* Loop diuretics & potassium-sparing diuretics	Reduced excretion of lithium -
(safer than thiazides)	increase in levels & risk of toxicity
Tricyclic antidepressants	Risk of toxicity
Antipsychotics - clozapine, flupentixol,	Increased risk of extrapyramidal
haloperidol, phenothiazines, quetiapine,	side effects
risperidone, sulpiride, zuclopenthixol	
Antipsychotics - clozapine, flupentixol,	Possible neurotoxicity
haloperidol, phenothiazines, risperidone,	
zuclopenthixol	
Antipsychotics - amisulpride	Increased risk of adverse effects
	of amisulpride
Antipsychotics - olanzapine	Possible risk of lithium toxicity
Amiodarone	Risk of ventricular arrhythmias
	Increased risk of hypothyroidism
Antiepileptics - carbamazepine, phenytoin,	Possible neurotoxicity (without
Calcium channel blockers - diltiazem, verapamil	increased lithium levels)
Methyldopa	
Dapoxetine	Increased risk of serotonergic
	effects
SSRIs	Increased risk of CNS toxicity
* Sodium containing antacids	Lithium excretion increased –
* Theophylline	reduced lithium levels

* For these medicines, it is prudent to check lithium levels soon after starting or stopping treatment

Refer to current BNF for further information on interactions

Title	Guidelines on Safe Lithium Prescribing and Shared Care		
Approved by	Drug & Therapeutics Committee Date of Approval 25 th March 2021		
Protocol Number	PHARM-0024-v8	Date of Review	1 st April 2024

On-going monitoring

Plasma lithium levels:

- Blood should be consistently sampled 12 hours after the last dose was taken.
- The actual time interval between the last dose and blood sampling should be noted (and recorded in the electronic patient record if sampling performed by TEWV team) so that it can be taken into account when the result is received [for once daily dosing with modifiedrelease preparations the plasma level can be expected to fall by 0.2 mmol / L between 12 and 24 hours post dose]
- Monitor levels more frequently (monthly) if there are any complicating factors (e.g.
 impaired renal function, cardiovascular disease, elderly, acute infection esp. if leading to
 dehydration) or potential for drug interactions or deterioration in renal function or abnormal
 results.
- Record all results (plus any discrepancy in sampling time) in the patient-held record book.
- The target level / range and indication should be defined and recorded for each patient

5	a indication official be defined and recorded for each patient			
When?	What?			
1 week after initiation or after a dose/formulation change or after introduction of interacting medication, & weekly until levels are stable*	 mmol / L. Monitor for signs of neurotoxicity, blurred vision, muscle 			
At 3 months	 weakness, tremor, slurred speech and confusion. Urinary albumin creatinine ratio (ACR): NORMAL - no further regular ACR monitoring required (unless eGFR <60 ml/min, then re-check annually) PROTEINURIA (ACR >30 mg/mmol) - re-check annually HEAVY PROTEINURIA (ACR >70 mg/mmol) - refer to nephrology; consider stopping lithium 			
Every 3 months ** (once stable*)	Plasma lithium levels – as above Monitor for signs of neurotoxicity, blurred vision, muscle weakness, tremor, slurred speech and confusion.			
Every 6 months	Thyroid function tests (TFTs) – risk of hypothyroidism increased up to five-fold and is particularly high in women 40-59 years old. Consider thyroid replacement early. Renal function (e-GFR) – consider more frequent checks (3-monthly) in the elderly or established CKD. Monitoring trend in function is more useful than absolute value of test result. Consecutive results indicating reduction of renal function (especially if e-GFR is <60 ml/min, decreasing dose adjustment to maintain safe lithium level or increase in creatinine level) should prompt consideration of lithium review. Nephrology advice for GP's or other health care workers that refer to the JCUH renal unit – Stees.renal@nhs.net If lithium is discontinued due to concerns about lithium related decline in renal function, continue to monitor renal function for at least one year after lithium is stopped. Urea & Electrolytes (U&Es) Calcium (tick bone box on path lab form) - long-term treatment is associated with hyperparathyroidism and hypercalcaemia. Clinical consequences of raised serum calcium include renal stones, osteoporosis, dyspepsia, hypertension and renal impairment. Weight / BMI			

Title	Guidelines on Safe Lithium Prescribing and Shared Care		
Approved by	Drug & Therapeutics Committee Date of Approval 25 th March 2021		
Protocol Number	PHARM-0024-v8	Date of Review	1 st April 2024

- * At least two consecutive levels in target range at stable dose
- ** After 1 year of stable treatment, monitoring of lithium levels may be extended to 6-monthly in patients who meet all of the following criteria:
- Age < 65 years;
- No concurrent medicines which interact with lithium (see table);
- No risk of impaired renal or thyroid function, raised calcium levels or other complications;
- Good symptom control;
- Good adherence to prescribed dosage;
- Last plasma lithium level <0.8 mmol / L (therefore, by definition, all patients with a target level >0.8mmol / L must continue to be monitored every 3 months)

Action in response to lithium levels

- Whoever initiates tests for plasma lithium levels is responsible for acting on levels which
 fall outside the patient's target range. GPs should always discuss treatment options with
 mental health services. However, the TEWV team should proactively advise GPs if
 abnormal levels are observed when routinely checking the lithium register
- Local pathology labs have agreed that all lithium levels above 1 mmol/L will be notified immediately by phone as follows:
 - During normal working hours to the TEWV team or GP Practice sending the sample
 - Out of hours to the relevant Crisis Team or the relevant Emergency Care Centre (further assistance may then be sought from the local Crisis Team).
- The grid below sets out recommended actions to take in response to reported lithium levels relative to the patient's target level:

Reported lithium level								
		<0.4 mmol/L 0.4-0.6 mmol/L 0.6-0.8 mmol/L 0.8-1.0 mmol/L 1.0-1.2 mmol/L 1.2-1.5 mmol/L >1.5 mmol/L						
Target	0.4-0.6 mmol/L	Α	In target range	В	В	С	С	С
lithium	0.6-0.8 mmol/L	Α	Α	In target range	В	С	С	С
	0.8-1.0 mmol/L	Α	Α	Α	In target range	С	С	С
level	1.0-1.2 mmol/L	Α	Α	Α	Α	In target range	С	С

Actions (listed in suggested order, but adjust as necessary):

Check blood sampling time (ideal 12-14 hours after last dose)

Check adherence to prescribed dose (non-compliance or overdose)

Check recent trend in lithium levels

Α

Re-check levels (as soon as possible and/or after at least 5 days if dose adjusted or re-started)

Refer to / seek advice from mental health team

Adjust dose (if repeat levels out of range AND compliance / sampling time correct, OR deteriorating renal function)

Check blood sampling time (ideal 12-14 hours after last dose)
Check adherence to prescribed dose (non-compliance or overdose)
Check recent trend in lithium levels
Check renal function / recent trend in renal function
Re-check levels (as soon as possible and/or after at least 5 days if dose adjusted or re-started)
Refer to / seek advice from mental health team
Adjust dose (if repeat levels out of range AND compliance / sampling time correct, OR deteriorating renal function)

Check for symptoms / signs of toxicity

Advise patient to attend A&E (if signs / symptoms of toxicity present)

Advise patient to stop taking lithium

Check blood sampling time (ideal 12-14 hours after last dose)

Check adherence to prescribed dose (non-compliance or overdose)

Check renal function / recent trend in renal function

Refer to / seek advice from mental health team (out-of-hours consultant - 01642 838050)

Adjust dose (if repeat levels out of range AND compliance / sampling time correct, OR deteriorating renal function)

Re-check levels (as soon as possible and/or after at least 5 days if dose adjusted or re-started)

 All episodes of toxicity must be recorded in the patient record, together with details of any remedial action taken.

Title	Guidelines on Safe Lithium Prescribing and Shared Care				
Approved by	Drug & Therapeutics Committee Date of Approval 25 th March 2021				
Protocol Number	PHARM-0024-v8	Date of Review	1 st April 2024		

Renal monitoring in established lithium treatment

Normal kidney > 60	3 months after	Normal: no regular albumin creatinine ratio
function Stage 1 Stage 2	starting lithium check urinary albumin creatinine ratio (ACR)	monitoring required • Proteinuria (ACR ≥30 mg/mmol): monitor albumin creatinine ratio annually • Heavy proteinuria (ACR ≥70 mg/mmol): refer to nephrology
Stage 3A 59 - 30 -	<u> </u>	 Check eGFR every 3 months (plot graph of eGFR or reciprocal creatinine in records) Monitor ACR annually Complete cardiovascular risk profile, consider antiplatelet drugs & cholesterol lowering therapy Control BP (<140 mm systolic & 90 mm diastolic; lower in diabetes or ACR ≥30 mg/mmol) Stage 3B: measure haemoglobin annually Refer to nephrology and discuss discontinuation if: At stage 3B ACR ≥70 mg/mmol ACR ≥30 mg/mmol + haematuria Decline in GFR of ≥5ml/min over 1 year or ≥10ml/min in 5 years
Stage 4 15 – Stage 5 < 15	29 As for stages 3A & 3B	Refer to nephrology . Lithium normally contraindicated

Ref: Lithium and chronic kidney disease: Mukesh Kripalani, James Shawcross, Joe Reilly, John Main, BMJ 2009;339:b2452

Nephrology advice for GP's or other health care workers that refer to the JCUH renal unit – <u>Stees.renal@nhs.net</u>

Management of impaired urinary concentration and diabetes insipidus

Patients on lithium

- Patients on lithium presenting with the symptoms of polyuria, polydipsia and dryness of mouth
- Exclude other causes for the above symptoms and assess the functional impact of the symptoms

Patients presenting with significant functional impact

- Investigate further 24 hour urine volume, urine osmolarity
- •Referral to nephrologists if symptoms are severe or other aetiology is suspected

• Lithium - reduce the dose / consider single day dosing / discontinue

Risk-benefit analysis

• If symptoms continue (if lithium is continued or after discontinuation of lithium) - consider treating with thiazide / amiloride / indometacin

Ref: Management of the renal adverse effects of lithium: Sumeet Gupta, Mukesh Kripalani, Udayan Khastgir and Joe Reilly; APT 2013, 19:457-466

Title	Guidelines on Safe Lithium Prescribing and Shared Care				
Approved by	Drug & Therapeutics Committee Date of Approval 25 th March 2021				
Protocol Number	PHARM-0024-v8	Date of Review	1 st April 2024		

Shared Care Arrangements

Responsibilities of secondary care mental health services (TEWV)

- Initial comprehensive assessment and liaison with relevant health professionals
- Pre-treatment screening <u>as above</u> [template letter for obtaining information from GP]
- Provision of patient information <u>as above</u> including issue and completion of entries in the patient information booklet, record book and alert card
- Inform GP that lithium has been initiated (prior to formal shared care request) [template letter]
- Prescription of lithium during dose titration until the patient is stabilised, has had a 3
 month monitoring check and shared care has been formally accepted by the patient's
 GP / primary care team
- Transfer of prescribing and monitoring via a formal request to the GP and primary care
 team on an individual patient basis via a <u>standard letter</u> (appendix 2) the letter should
 specify the indication, brand name, form, current dose, personal target level / range* and
 details of planned reviews
 (* if target range above 1 mmol/L lithium prescribing and monitoring cannot be
 - (* if target range above 1 mmol/L lithium prescribing and monitoring cannot be transferred to the GP)
- Maintain oversight of patient monitoring via the weekly update of the Trust lithium register [template letter to GP re. overdue monitoring] [template letter to patient re. overdue monitoring]
- Provide a point of contact during working hours for any queries related to the prescribing and monitoring of lithium
- Review patient at least annually at each review, monitor clinical condition, review
 monitoring tests and consider appropriateness of lithium therapy. Record the review on
 the electronic patient record and provide a comprehensive report of the review to the GP
 using the standard <u>pro-forma</u> (appendix 3).
- Notify the GP and primary care team if the patient does not present for specialist reviews [template letter]
- Accept return of prescribing and monitoring responsibility if lithium therapy or clinical condition becomes unstable
- Notify the GP and primary care team if lithium therapy is discontinued [template letter]

Responsibilities of the General Practitioner / primary care team

- Acknowledge and respond to the request for shared care within 4 weeks of receipt
- Add lithium to the patient's repeat prescription (even if not yet prescribing) so that interactions will be highlighted by the clinical system
- Avoid prescribing of interacting drugs whenever possible; if unavoidable, seek advice from secondary care on adjustments to lithium dose
- Set up a code and recall system to identify patients prescribed lithium
- Provide regular, repeat prescriptions for lithium at dosage recommended by the secondary care team
- Perform blood sampling and other monitoring tests according to this <u>guideline</u>. Notify the TEWV team if sample was taken outside the 12-14 hour post-dose window

Title	Guidelines on Safe Lithium Prescribing ar	nd Shared Care		
Approved by	Drug & Therapeutics Committee	Date of Approval	25 th March 2021	
Protocol Number	PHARM-0024-v8	Date of Review	1 st April 2024	

- Review the results of monitoring tests and check that it is safe to issue repeat prescriptions.
- Seek advice from the secondary care team regarding lithium levels outside the personal target range and other tests outside normal range
- Complete entries in the patient-held record book and alert card as per guidelines
- Be aware of potential side effects and inform / seek advice of the secondary care team of suspected side effects
- Be aware of the signs of lithium toxicity and inform / seek advice of the secondary care team if the patient develops any signs of toxicity – advise patient to withhold lithium if cannot be discussed with secondary care team on same day.
- Stop issuing prescriptions if notified by the secondary care team
- Refer the patient back to specialist services for review if they become clinically unstable.

Responsibilities of the dispensing Pharmacist / GP practice

- Check that blood results are being monitored regularly and that it is safe to dispense lithium (following relevant SOPs where applicable)
- Where it is not possible to access monitoring results, lithium therapy should not be withheld. The staff responsible for dispensing a prescription should communicate to the prescriber that lithium medication has been provided without monitoring results being seen.

Triggers for contacting secondary care mental health services

Patients within shared care arrangements:

- Signs and symptoms of toxicity
- Lithium level outside the patient's personal target range
- Trend in decreasing lithium dose to keep lithium level within target range (indication of impaired renal function)
- Deterioration of renal function:
 - Downward trend in function is more indicative than absolute value of test result
 - Consecutive results indicating reduction of renal function (increase in creatinine level or decreased eGFR – less than 60ml/minute should prompt referral for consideration of lithium review)
- Patient becomes mentally unwell
- Non-compliance or suspected non-compliance with treatment or monitoring
- Pregnancy actual or planned
- Breast feeding
- Initiation of interacting medication where this is unavoidable
- Acute infection or other medical condition which may impact on lithium levels or renal function

Title	Guidelines on Safe Lithium Prescribing and Shared Care				
Approved by	Drug & Therapeutics Committee Date of Approval 25 th March 2021				
Protocol Number	PHARM-0024-v8	Date of Review	1 st April 2024		

Patients previously discharged with no planned review in secondary care

Re-referral of patients to Adult Mental Health Services will be via the single point of access; re-referral of patients to Older Peoples Services will be via the usual route. GPs are requested to clearly state reason for required review:

- Previously discharged out with the circumstances described above
- Lack of or concern over efficacy
- Intermittent or poor adherence with treatment
- Deterioration of mental state
- Tolerability or side effect problems
- Patient request to discontinue treatment or review treatment
- New medical conditions (especially management of cardiovascular risk factors or rheumatoid disease as these may be treated with medicines that affect lithium levels)
- Deterioration of medical conditions (as above)
- Deterioration of renal function (including multiple dose reduction to maintain lithium levels within target range)
- Patients without a diagnosis of bipolar disorder or refractory depression

Title	Guidelines on Safe Lithium Prescribing and Shared Care				
Approved by	Drug & Therapeutics Committee Date of Approval 25 th March 2021				
Protocol Number	PHARM-0024-v8	Date of Review	1 st April 2024		

Appendix 1 – Initiation flowchart

Initiating LITHIUM flow-chart

Please use this flow chart in conjunction with "Guidelines on Safe Lithium Prescribing & Shared Care" (includes "templates").

NOTE: IF THE SERVICE USER TRANSFERS TEAM <u>DURING</u> THIS PROCESS, PLEASE LET THE RECEIVING TEAM KNOW WHICH POINT IN THE PROCESS THEY HAVE REACHED

1.Pre-Treatment screening A. U&Es, eGFR, Creatinine, TFTs, Calcium, FBC, ECG (if risk factors), Height, Weight, BMI,BP (Can be done via a Physical Health Clinic where available) B. List of current meds from GP to check for potential drug interactions. See "template" in guidelines. C. 1:1 with service user regarding monitoring, side effects etc. including teratogenic risk (if appropriate) Give "purple" LITHIUM booklet (can be done at PHC - request on referral) 2. Prescriber to review results 3. Prescribe LITHIUM 4. Inform GP that LITHIUM has been initiated and is being prescribed and monitored by CMHT. See template in guidelines 5. Inform Pharmacy: Pharmacy to add service user to LITHIUM register for appropriate CMHT 6. LITHIUM level: 5-7 days post starting / adjusting dose *Level to be taken 12 hours post dose* 7. LITHIUM level in range? Refer to "Guidelines on Safe Lithium Prescribing" Refer back to PHC if No Yes available / appropriate 7a. Prescribe LITHIUM until 7b. Level not in range / Level transfer to Primary Care low - Prescribe adjusted dose 8. Refer to PHC (if available) for 3 monthly checks Monitoring at 3 months: LITHIUM level and Urinary Albumin Creatinine Ratio (ACR) Prescriber to review results 9b. Patient/results NOT stable: refer 9a. Patient/results stable to Guidelines on Safe Lithium 10. Transfer LITHIUM monitoring & prescribing to Primary Care

Title	Guidelines on Safe Lithium Prescribing and Shared Care				
Approved by	Drug & Therapeutics Committee Date of Approval 25 th March 2021				
Protocol Number	PHARM-0024-v8	Date of Review	1 st April 2024		

See template in guidelines

Appendix 2 – Transfer request letter



REQUEST TO TRANSFER LITHIUM PRESCRIBING & MONITORING

	INSERT CLINIC ADDRESS
Electronic Patient Record ID: NHS NO: Date of Clinic: Date Typed:	
The contents of this letter are confid	dential and may not be disclosed without the consent of the writer
GP ADDRESS	
Dear Dr	
RE	(name, DOB) (address)

The above patient has been attending our clinic and has been initiated on lithium therapy which is now stabilised. All aspects of treatment with lithium have been explained to the patient and a patient-held lithium therapy pack (purple booklet) has been completed and issued.

We feel it is now appropriate to transfer prescribing and monitoring responsibility to you in line with the agreed shared care arrangements.

Details of the patient's lithium treatment are attached, together with a summary of the shared care prescribing and monitoring requirements.

I would be grateful if you could sign, scan & email this sheet as confirmation of your acceptance of shared care for this patient

We will conduct a thorough review of this patient at least annually and provide you with a report of each review. In the meantime, please do not hesitate to contact us if you need any advice or support.

Yours sincerely

Name TEWV Prescriber

CC - Patient

Title	Guidelines on Safe Lithium Prescribing and Shared Care				
Approved by	Drug & Therapeutics Committee Date of Approval 25 th March 2021				
Protocol Number	PHARM-0024-v8	Date of Review	1 st April 2024		



TRANSFER OF PRESCRIBING & MONITORING FOR LITHIUM THERAPY

PRIVATE & CONFIDENTIAL

For advice on managing patients on lithium contact: TEWV.medicinesinformation@nhs.net

Patient name:	[Date of requ	iest:			
_		GP Name:				
NHS number:		Practice:				
Care co-ordinator:		TEWV pre	TEWV prescriber:			
Contact no.:		Contact n	Contact no.:			
Indication for lithium:		Date of ne	Date of next review:			
Brand:		Form: lie	Form: liquid / tablets (Delete as appropriate)			
Dose:		Plasma le	vel target range	ə:	mmol / L	
Required monitoring frequency (lithium le	vels):	weekly / n	nonthly / 3-mo	nthly (Delet	te as appropriate)	
Monitoring results (most recent)	Date		Result	Da	ate next due	
Plasma lithium level						
Weight / BMI						
U&Es						
e-GFR						
TFTs						
Calcium						
ECG if applicable						
FBC if applicable						
Patient given 28 day prescription on:						
Next prescription due on:						
Please contact us on the telephone number above or, if out of hours, the Crisis Team on						
(insert tel. number) if you re			,			
Signs and symptoms of toxicity						
Lithium level outside the patient's personal to						
Trend in decreasing lithium dose to keep lith	ium level	within target r	ange (indication o	f impaired r	enal function)	
 Deterioration of renal function Downward trend in function is more indi 	ioativa the	an abaaluta va	due of toot regult			
				level or dec	reased e-GFR –	
 Consecutive results indicating reduction of renal function (increase in creatinine level or decreased e-GFR – less than 60ml/minute) should prompt referral for consideration of lithium review 						
Patient becomes mentally unwell						
Non-compliance or suspected non-compliance with treatment or monitoring						
Pregnancy – actual or planned						
Breast feeding						
 Initiation of interacting medication where this is unavoidable Acute infection or other medical condition which may impact on lithium levels or renal function 						
Please scan &email confirmation of acceptance to : [insert email address]						
Signed: Name	e:			Date:		
GP / On behalf of GP						

If the patient is not concordant with monitoring requirements, please inform the Care Co-ordinator as above, who will instigate an emergency medical review. Do not continue to prescribe lithium in such circumstances.

Title	Guidelines on Safe Lithium Prescribing and Shared Care		
Approved by	Drug & Therapeutics Committee	Date of Approval	25 th March 2021
Protocol Number	PHARM-0024-v8	Date of Review	1 st April 2024



TRANSFER OF PRESCRIBING & MONITORING FOR LITHIUM THERAPY

Prescription / Monitoring Guidelines

Prescribing:

- Prescribe lithium by brand name (as advised by TEWV team)
- Do not prescribe more than 28 days' supply on each prescription
- Ensure that monitoring requirements are up-to-date and within range before issuing each prescription. Please do not re-authorise repeat prescriptions for more than 3-4 months.

Monitoring - plasma lithium levels.

- Blood should be consistently sampled 12 hours after the last dose was taken.
- The actual time interval between the last dose and blood sampling should be noted so that it can be taken into account when the result is received [for once daily dosing with modified-release preparations the plasma level can be expected to fall by 0.2 mmol / L between 12 and 24 hours post dose]
- Monitor levels more frequently (monthly) if there are any complicating factors (e.g.
 impaired renal function, cardiovascular disease, elderly, acute infection esp. if leading to
 dehydration) or potential for drug interactions or deterioration in renal function or abnormal
 results.
- Record all results (plus any discrepancy in sampling time) in the patient-held record book.
- The target level / range and indication should be defined and recorded for each patient

9	•
Every 3 months (unless advised otherwise by secondary care team)	Plasma lithium levels – as above Monitor for signs of neurotoxicity, blurred vision, muscle weakness, tremor, slurred speech and confusion.
Every 6 months (unless advised otherwise by secondary care team)	Thyroid function tests (TFTs) – risk of hypothyroidism increased up to five-fold and is particularly high in women 40-59 years old. Consider thyroid replacement early. Renal function (e-GFR) – consider more frequent checks in the elderly or established CKD. Monitoring trend in function is more useful than absolute value of test result. Consecutive results indicating reduction of renal function (especially if e-GFR is <60 ml/min, decreasing dose adjustment to maintain safe lithium level or increase in creatinine level) should prompt consideration of lithium review. Nephrology advice for GP's or other health care workers that refer to the JCUH renal unit – stees.renal@nhs.net If lithium is discontinued due to concerns about lithium related decline in renal function, continue to monitor renal function for at least one year after lithium is stopped.
	Urea & Electrolytes (U&Es) Calcium (tick bone box on path lab form) - long-term treatment is associated with hyperparathyroidism and hypercalcaemia. Clinical consequences of raised serum calcium include renal stones, osteoporosis, dyspepsia, hypertension and renal impairment. Weight / BMI

Title	Guidelines on Safe Lithium Prescribing and Shared Care			
Approved by	Drug & Therapeutics Committee	Date of Approval	25 th March 2021	
Protocol Number	PHARM-0024-v8	Date of Review	1 st April 2024	

Appendix 3 – Secondary care review template

LITHIUM REVIEW

Patient name:	DoB:			
Date of review:	Specify if (please tick):			
	3 month review □			
	6 month review □			
	Annual review □			
Current responses to treatment:				
Current blood results				
Previous blood result				
All current medication and dose				
7 iii daneni medication and dose				
Side effect profile (consider any drug				
interactions)				
Physical health checks –				
BMI:				
Weight: BP:	Lying: Standing:			
Pulse:				
ECG (if required).				
Patient & Carer perceptions				
Have they brought the Booklet? or	Yes □ No □			
Are they using the smartphone app?	Yes □ No □			
Is Booklet / app up to date?	Yes □ No □			
	140			
Plan/Outcome				

Title	Guidelines on Safe Lithium Prescribing and Shared Care		
Approved by	Drug & Therapeutics Committee	Date of Approval	25 th March 2021
Protocol Number	PHARM-0024-v8	Date of Review	1 st April 2024