NHS
Kent and Medway

Document history for Principles of Shared Care Agreements

Version	Created by	Date	Main Changes/Comments
1-6	JKM/CC/PS	July 2020	Reviewed shared care from K&M CCG areas and amended several times. Comments received from East Kent Prescribing Group.
7	JKM	05/08/2020	Reviewed comments from JPC
8	JKM	08/09/2020	Comments from MP after August JPC incorporated into document. **Under principles:** **2e.** For medicines which are prescribed under a share care arrangement, primary care prescribers **should have sufficient knowledge and experience to monitor, stop, or alter the dosage of the medicine in appropriate circumstances and have access to specialist advice to support them** *This also links with 3b and is a must and links in with my comment about other PCN member practices possibly taking on the role and/or persuading colleagues to do the right thing* **2h.** Primary care prescribers must seek further support from the referring specialist or CCG rather than decline shared care on the basis of lack of competence as default *Agree but we need to remember that GPs are not contractually obliged to agree. No change in wording needed.* **4d.** The person delivering that aspect of the shared care agreement should ensure that the resources to do this are in place in the clinical setting in which they are delivered *This relates to my comment about workload and funding which I agree is outside the scope for JPC but is important from a GP perspective and will also help with take up and sharing work within PCNs as well as minimising refusals.* **5b.** The JPC can recommend the approval of all shared care - *This should be a **must** and not a can* *Appendix 1-AREAS OF RESPONSIBILITY FOR SHARED CARE* First paragraph - If the GP is not confident to undertake these roles, then he or she is under no obligation to do so. *Ideally this needs to link to 2h* Third Bullet point – *For consistency should this say GP rather than primary care clinician* **5.** First Bullet point – *Consider adding the word stable i.e. "patient is stable on a regular dose"* **9.** *This should consider interactions with any and all repeat medication the patient is taking at the time of initiation.* Appendix 2 & 3 – comment from MP: *would prefer appendix 2 as the agreement as it is clear. Indication can be changed to diagnosis and an additional field for next blood monitoring review date (from Appendix 3). The reasons for refusal can be linked with the refusal letter reasons (September JPC to confirm)* **Comment from EI:** Can the specialist be asked to specify the length of treatment supplied to the patient in order to indicate to the GP when new supply will be required for forward planning (Completed – see point 5 Appendix 1)
V9	JKM	23/09/2020	Appendix confirmed at September JPC. Document recommended for Clinical Cabinet approval.
V10	KB/KO/PS/ JB	Aug 21-July 22	Document has been simplified. Lithium is already listed on all formularies as specialist initiation only. This guidance is aimed to support the prescribing in primary care and set out parameters for referral back to secondary care.
V11	JB/KO	08/12/2022	SGLT2 SmPC interaction update added and recommended to IMOC for approval.

Lithium Treatment Care Pathway

Lithium for patients with mania or hypomania, bipolar disorder, or recurrent depression

AREAS OF RESPONSIBILITY

This treatment care pathway outlines suggested ways in which the responsibilities for managing the prescribing of **medication** can be shared between the specialist and general practitioner (GP), including:

- Transfer of monitoring and prescribing to Primary care – normally after the patient is on regular dose and with satisfactory investigation results for at least 4 weeks.
- The specialist determining the duration of treatment based on clinical response and tolerability.
- All dose or formulation adjustments being a shared responsibility – with the GP able to refer back to KMPT or request advice as appropriate.
- Termination of treatment being the responsibility of the specialist. If there is an urgent medical need to terminate treatment this can be done by the GP and the patient fast-tracked back to KMPT by contacting the Duty Team in the CMHT. (See page 13 for contact details).

PRESCRIBING INFORMATION

1. Background

Lithium is an effective medication in management of the following indications:

- Prophylaxis and treatment of mania or hypomania
- Prophylaxis of bipolar disorder
- Treatment of recurrent depression

Lithium can have significant side-effects and interactions which need monitoring. The therapeutic range for lithium is narrow and all patients prescribed this medicine should be subject to routine monitoring. Both these factors necessitate a good understanding and communication between the different clinicians involved in the care of the client. This care pathway protocol outlines the ways in which the responsibilities for managing the prescribing of lithium can be shared between the secondary and primary care clinician. It sets out responsibilities for each party, to ensure that lithium is initiated, prescribed, dispensed, and monitored appropriately and according to the National Patient Safety Alert (NPSA) and NICE guideline [CG185]

This guideline was prepared using the most current evidence available at the time of preparation, but users should always refer to the manufacturer's current edition of the Summary of Product Characteristics (SPC) and current edition of the British National Formulary (BNF) for more details.

2. Indications (*Please state whether licensed or unlicensed)*

- Prophylaxis and treatment of mania or hypomania (licensed)
- Prophylaxis of bipolar disorder (licensed)
- Treatment of recurrent depression (licensed)

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3. Pharmaceutical aspects

Route of administration: Oral

Formulation: Tablets

Administration details: The usual starting dose is lithium carbonate 400mg at night (200mg in the elderly). Once daily dosing at night is preferred due to monitoring of lithium levels. Alternatively, the dose may be divided and given morning and evening if there is patient intolerance or patient prefers a twice daily dose. The dose of lithium is adjusted to achieve a lithium concentration that is usually between 0.4 – 1.0 mmol/litre.

Other important information: Lithium should be prescribed by brand name because of its narrow therapeutic range and difference in product bioavailability between brands. Brands are not interchangeable. The Priadel® brand is recommended within KMPT and is available as 200mg and 400mg tablets. Priadel® tablets contain lithium carbonate and are scored tablets which can and should be halved when appropriate for the dose, e.g. 300mg, 500mg 700mg, 900mg.

Liquid and tablet dose equivalence

Particular care is needed with Priadel® 520mg lithium citrate / 5ml sugar free liquid. 520mg lithium citrate is equivalent to 204mg lithium carbonate. When switching from tablet to liquid, 5ml of 520mg/5ml lithium citrate liquid should be prescribed for every 200mg lithium carbonate tablet, see table below. Liquid doses should be given in divided doses, ideally twice a day.

Liquid is usually only prescribed if the patient has difficulty swallowing or a preference for liquid medication.

Priadel® Lithium carbonate modified release tablet dose (Total DAILY dose)	Priadel® lithium citrate 520mg/5ml equivalent dose (Total DAILY dose)
200mg	5ml
300mg	7.5ml
400mg	10ml
500mg	12.5ml
600mg	15ml
700mg	17.5ml
800mg	20ml
900mg	22.5ml
1000mg	25ml

4. Exclusions or contraindications

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

- Hypersensitivity to lithium or to any of the excipients
- Cardiac disease including atrial fibrillation
- Cardiac insufficiency
- Severe renal impairment
- Untreated hypothyroidism
- Breast-feeding
- Patients with low body sodium levels, including for example dehydrated patients or those on low sodium diets
- Addison's disease
- Brugada syndrome or family history of Brugada syndrome.

N.B. Lithium should not be used during pregnancy, especially during the first trimester, unless considered essential. Please refer to the specialist.

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5. Initiation and ongoing dose regime (by specialist)

Note -

- *Transfer of monitoring and prescribing to primary care is normally **after the patient is stable on a regular dose** and with satisfactory investigation results for period of time as agreed by the specialist.*
- *The duration of treatment will be determined by the specialist based on clinical response and tolerability.*
- *Specialist to specify the length of treatment supplied to the patient in order to indicate to primary care when new supply will be required for forward planning.*
- *All dose or formulation adjustments 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.*

6. Specialist responsibilities for monitoring (including frequency)

At initiation:

- To formulate diagnosis of mania, bipolar disorder or recurrent depression following full assessment.
- Provide verbal and written patient information leaflet together with the Trust lithium therapy record book and discuss with the patient.
- To undertake baseline monitoring of U&Es, eGFR, BP and pulse, FBC, corrected calcium level, thyroid function tests, fasting blood glucose, glycosylated haemoglobin (HbA1c), fasting blood lipid profile and weight or BMI (see table below). These blood tests should be documented in the patient's electronic RiO record.
- To undertake baseline ECG for patients with cardiovascular disease or risk factors for it or where a patient is also prescribed citalopram/escitalopram, tricyclic antidepressant, venlafaxine, duloxetine or an antipsychotic.
- Discuss the anticipated benefits and side effects/ risks of lithium with patient, including checking for clinically significant drug interaction and document this on patient's electronic RiO record.
- Discuss contraceptive use with female patient of childbearing age, and document their current method of contraception. Female patients of childbearing potential should use effective contraceptive methods during treatment with lithium.
- Discuss ongoing monitoring requirements with patient, and the importance of taking the lithium therapy record book and /or a printout of blood test results to all appointments and the pharmacy when prescriptions are dispensed, and document this.
- Discuss the importance of attending appointments in order to maintain their supply of lithium.
- To explain the importance of always taking the same brand to the patient.
- To inform the GP that lithium has been initiated and that the intention is to share the care once the patient is on a stable dose.
- To prescribe lithium and monitor lithium levels until dosage stabilised.
- To document any changes and /or results in the patient's lithium therapy record book.
- The intention to share care should be explained to the patient. It is important that patients are consulted about treatment and are in agreement with it.
- Complete appendix 1 "Specialist to GP information" stating the patient details, the brand, formulation, dose, frequency, timing of lithium prescribed, and recent blood test results. This should be communicated to the GP.

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Monitoring:

Parameter	Frequency	Notes
Initial assessment of suitability for lithium treatment	**Baseline**	Communicate to the GP about outcome of the assessment and initiation of the Lithium therapy
Baseline monitoring once decision made to commence lithium treatment	**Baseline** U&Es, eGFR, BP and pulse, FBC, corrected calcium level, thyroid function tests, fasting blood glucose, glycosylated haemoglobin (HbA1c), blood lipid profile and weight or BMI	Copy to GP for information
ECG	**Baseline**	Patients with cardiovascular disease or risk factors for it Copy to GP for information
Lithium level	**Weekly until dose is stabilised**	Copy to GP for information

The above information must be shared with the GP prior to transfer of prescribing.

At review:

- Support the GP with advice on dose changes, abnormal results, and concurrent medication.
- To advise and support patient and /or carer.
- To review the patient annually or when requested to by the GP, to assess response and the benefits of continued treatment.
- To notify the GP of the patient's failure to attend appointments. If the patient fails to attend the community appointments the GP should arrange a referral to the psychiatric services. Urgent referrals can be made back to mental health services by contacting the Duty Worker in the community mental health team (See page 13 for contact details)

7. GP responsibility

Monitoring (including frequency):

Parameter	Frequency	Notes
Lithium plasma level	**3 monthly**	At one year NICE recommends that lithium monitoring frequency can be decreased – see section 8 for more details.
Weight / BMI	**6 monthly**	Monitor weight more regularly in patients with rapid weight gain. Manage weight gain in usual way with patient. If the decision is taken to stop lithium refer back to KMPT.
Urea & Electrolytes	**6 monthly**	Low Na may increase lithium levels. Low K increases the risk of QTc prolongation.
Renal function (eGFR)	**6 monthly**	Lithium can affect renal function. As renal function declines lithium levels may rise. Should this be the case refer back to KMPT for review.
Corrected calcium level	**6 monthly**	Lithium can increase calcium. Low calcium increases the risk of QTc prolongation
Thyroid Function Tests	**6 monthly**	Lithium can cause disturbances of thyroid function including (euthyroid) goitre, hypothyroidism and

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		hyperthyroidism, hyperparathyroidism, parathyroid adenoma. If these cannot be treated, then referral back to KMPT will be required to discuss termination and alternative treatments.
ECG	**Annually**	Only for those patients with cardiovascular disease or risk factors for it. Lithium can cause QTc prolongation, particularly at high levels.
Pulse	**Annually**	NICE CG185 for people with bipolar disorder.
Blood Pressure	**Annually**	NICE CG185 for people with bipolar disorder.
Lipid	**Annually**	NICE CG185 for people with bipolar disorder.
Fasting glucose and glycosylated haemoglobin (HbA1c),	**Annually**	NICE CG185 for people with bipolar disorder.
Liver function	**Annually**	NICE CG185 for people with bipolar disorder.

Review/follow up:

- Ensure the brand, formulation, dose, frequency, timing of lithium prescribed is the same as that communicated by the specialist.
- To undertake routine monitoring in accordance with NICE guideline [CG185] and take appropriate action (see table above).
- Update the patient's lithium record book with lithium levels/ monitoring results or provide the patient with a printout of the results and check these results before issuing prescriptions for lithium.
- To monitor the patient's general health and wellbeing as per NICE CG185 Bipolar guidance.
- To provide repeat prescriptions after stabilisation and to monitor for drug interactions.
- Adjust the dose of lithium with support of the specialist prescriber if the patient has lithium levels outside the therapeutic range or develops signs of lithium toxicity. See section 8 for further information.
- To report adverse drug reactions to specialist and complete Yellow Card where necessary.
- To check potential interactions with prescribed medications and take appropriate actions. Refer back to a specialist for advice if necessary. See section 9 for further information.
- To take appropriate action if there are changes to the patient's physical health. This includes those with the following underlying medical conditions: hypertension, diabetes, congestive heart failure, renal impairment, and COPD. See section 4 for further information.
- To follow up patients who fail to attend for regular blood tests.
- Refer patient to the specialist if patient is planning pregnancy or is pregnant.

8. Dose Management and lithium level monitoring (by primary care)

Therapeutic range: The objective is to adjust the dose to maintain the serum lithium plasma levels within the range 0.4 to 1.0mmol/L (0.4mmol/L in the elderly). The NICE guidance [CG185] states that when initiating long-term treatment in younger adults, clinicians should aim for levels of 0.6-0.8mmol/L normally and 0.8-1.0mmol/L in patients who have relapsed previously on lithium or have sub-threshold symptoms with functional impairment.

Normally lithium is prescribed as a nighttime dose and levels should be carried out 12 hours post-dose. Where dosing is twice a day, the morning dose should be withheld until after the sample for levels is taken.

Serum lithium level should be checked 1 week after initiation and 1 week after each dose change, then weekly until levels are stable and then every 3 months for the first year.

After the first year, plasma lithium levels can be checked every 6 months, except in the following patients, where 3-monthly monitoring is recommended:

- Elderly people (65 years or over)
- People taking drugs that interact with lithium
- People who are at risk of impaired renal or thyroid function, raised calcium levels, or other complications
- People who have poor symptom control
- People with poor adherence
- People whose last plasma lithium level was 0.8mmol/L or higher

Level and Action to be Taken - patient's specialist team should advise the lithium target levels on initiation of lithium

Results	Management
Levels < 0.4 mmol/L – level in keeping with that agreed with specialist team and patient is well	Do not alter dose
Levels < 0.4 mmol/L and lower than the range specified by the consultant OR if the patient unwell	If lower than level specified by specialist team review compliance, consider other factors e.g. drug interactions, excess fluid intake and recheck level/consult specialist team
Greater than 1.0 mmol/L with no signs of toxicity	If there is an explanation for the high level e.g. dehydration, timing of level i.e. not 12hrs post dose, interacting medicines, correct where possible and recheck level
Greater than 1.0 mmol/L with signs of toxicity (Blurred vision, muscle weakness, drowsiness, coarse tremor, dysarthria, ataxia, confusion, convulsions, nausea & vomiting,)	Stop lithium immediately, measure lithium level, urea and electrolytes, creatinine and eGFR. Refer to hospital if clinical condition warrants and consult specialist immediately for advice.

Elderly patients are particularly liable to lithium toxicity even at levels within the normal range and may exhibit adverse reactions at levels ordinarily tolerated by younger patients. Caution is also advised since lithium excretion may be reduced in the elderly due to age-related decrease in renal function. Elderly patients or those below 50kg in weight often require lower lithium dosage to achieve therapeutic lithium levels, and lithium levels may need to be lower in the elderly population and particularly in the very old and frail elderly. Reduced lithium clearance is expected in patients with hypertension, congestive heart failure or renal dysfunction.

9. Significant medicine interactions – *prescriber must consider interactions with any and all repeat medication the patient is taking at the time of initiation*

See appendix 2 and Summary of Product Characteristics and/ or BNF for full details

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Serious interactions

Drug group	Magnitude of effect	Timescale of effect	Additional information
Ace inhibitors/ Angiotensin II receptor antagonists may be associated with similar risk.	Unpredictable. Up to 4-fold increases in lithium level.	Develops over several weeks.	7-fold increased risk of hospitalisation for lithium toxicity in the elderly.
Thiazide diuretics	Unpredictable. Up to 4-fold increases in lithium level.	Usually apparent in 10 days.	Loop diuretics, e.g. furosemide, are safer. Any effect will be apparent in the first month.
NSAIDs	Unpredictable. From 10% to 4-fold increases in lithium level.	Variable; from a few days to several months.	NSAIDs are widely used on a PRN basis. Can be bought over the counter. COX-2 inhibitors are likely to carry the same risk.
Steroids	May alter lithium excretion and should therefore be avoided.		
Carbamazepine	May lead to dizziness, somnolence, confusion, and cerebellar symptoms such as ataxia.		
Selective serotonin reuptake inhibitors (SSRIs) i.e. fluoxetine	Although commonly prescribed together, consider serotonin syndrome if increased agitation/ autonomic changes, rigidity occur and consider reducing/stopping SSRI dose		
Sodium-glucose co-transporter 2 (SGLT2) inhibitors (e.g. dapagliflozin, empagliflozin)	These drugs may increase renal lithium excretion and the blood lithium levels may be decreased. Serum concentration of lithium should be monitored more frequently after initiation and dose changes. Please refer the patient back to a specialist to monitor serum concentration of lithium.		

10. Adverse effect management

Specialist to detail action to be taken upon occurrence of a particular adverse event as appropriate. Most serious toxicity is seen with long-term use and may therefore present first to GPs.

For a full list of side effects including symptoms of toxicity, please refer to the manufacturer's summary of product characteristics.
Adverse effects are directly related to blood levels and their frequency increase dramatically at plasma levels above 1.0mmol

- Mild gastrointestinal upset
- Fine tremor
- Weight gain
- Ankle oedema
- Metallic taste
- Nephrogenic diabetes insipidus, resulting in polydipsia and polyuria
- Renal toxicity – reduction in glomerular filtration rate
- Hypothyroidism
- Exacerbation of skin conditions, including psoriasis and acne

Signs of toxicity (levels above 1.5mmol/l are normally considered dangerous – increased disorientation and seizures may lead to coma and death.

- Blurred vision
- Severe diarrhoea and vomiting
- Unsteadiness or clumsiness
- Difficultly in speaking
- Severe tremor or twitching limbs
- Greatly increase thirst and/or passing water
- Severe drowsiness and/or confusion
- Convulsions

If any of these signs are experienced by the patient, then lithium therapy should be stopped immediately, and lithium levels checked urgently. Consider urgent medical referral and psychiatric advice and refer back to the specialist.

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

- Ensure that they have a clear understanding of their treatment.
- To take lithium as prescribed.
- To attend appointments for prescribing and monitoring.
- To be aware of side effects, situations which could affect their lithium levels and report any relevant symptoms.
- Ensure that their monitoring booklet is kept up to date (or that they keep a copy of their test results with the booklet) and take to all appointments with healthcare professionals and when picking up medication from the pharmacy.
- Report any changes in disease symptoms to GP.
- Alert GP of any changes of circumstance which could affect management of disease e.g. plans for pregnancy.

12. Pregnancy and breast feeding

It is the responsibility of the specialist to provide advice on the need for contraception to female patients on initiation and at each review but the ongoing responsibility for providing this advice rests with both the GP and the specialist.

If the patient becomes pregnant, the situation should be discussed urgently with the specialist

13. Specialist contact information

See details on the "Specialist to GP Information" form (Appendix 1)

14. Additional information

Discontinuation - Consult the specialist for advice if stopping lithium. For urgent discontinuation due to adverse events contact secondary mental health services for a care plan for monitoring lithium levels, relapse monitoring and general physical health monitoring.

Highest risk of relapse is within the first three months after discontinuation and so the patient should be monitored within this period. Increased risk continues throughout the first year after discontinuation, so it is important to ensure that the patient is aware of the continued risk.

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15. References

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- National Institute for Health and Care Excellence. Depression in adults: recognition and management, Clinical Guideline 90, 2016. www.nice.org.uk
- National Institute for Health and Care Excellence. Bipolar disorder: assessment and management, Clinical Guideline 185, 2016. www.nice.org.uk
- Goodwin GM. Recurrence of mania after lithium withdrawal. Implications for the use of lithium in the bipolar affective disorder. BJPsych 1994;164:149-52.
- National Patient Safety Agency. Safer Lithium therapy Patient Safety Alert NPSA 2009/PSA005. December 2009. www.nrls.npsa.nhs.uk/
- Sanofi. Priadel 200mg prolonged release tablets Summary of Product Characteristics. Last Updated on eMC 09-March-2022
- Sanofi. Priadel Liquid Summary of Product Characteristics. Last Updated on eMC 09-March-2022.

Appendix 1: Specialist to GP information
For completion by specialist with request to GP to continue to prescribe:

Lithium for patients with mania or hypomania, bipolar disorder, or recurrent depression

The expectation is that this information provides sufficient information to enable GP* to be confident to take on clinical and legal responsibility for prescribing and monitoring.
**This may be any primary care prescribing clinician*

For completion by specialist			
Patient name			
DOB			
NHS Number			
Patient weight (kg)			
Drug (s) Dose, frequency, and route at handover **Must include brand of lithium**			
Diagnosis (please indicate if unlicensed or "off-label"			
Date of first prescription by specialist			
Date next blood monitoring review is due			
Estimated date for prescribing responsibility to be with GP* (at least 28 days after first prescribing)			
Special prescribing advice for this patient, to include any other medication patient is taking for same condition			
Patient is now stabilised on a dose of		Repeat of above	
KEY PRIMARY CARE INFORMATION (refer to full Lithium Treatment Care Pathway document for full details)			
GP* Responsibilities			
MONITORING (as per Lithium Treatment Care Pathway document unless stated below)			
Frequency of GP* monitoring			
Frequency of specialist review			
TEST	NORMAL RANGE	Pre-Treatment Baseline Result (specialist responsibility)	Initiation of treatment Result (specialist responsibility)
Only complete if not as defined in the care pathway document			
ACTION TO BE TAKEN IF ABNORMAL RESULT			
TEST	RESULT	ACTION	
Only complete if not as defined in the care pathway document			

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Target lithium levels between……..mmol/L and …….mmol/L

Recent lithium levels

Dates	Lithium blood level (mmol/L)

Date next lithium level due:

Recent monitoring

Test	Result	Date next due
Weight /BMI		
Renal function (eGFR)		
Thyroid Function Tests (TFT's)		
U&E's		
BP and pulse		
FBC		
Corrected calcium level		
Fasting blood glucose		
Glycosylated haemoglobin (HbA1c)		
Blood lipid profile		
ECG (if appropriate)		

Referral back to secondary care

The patient should be referred to the secondary care specialist if the patient experiences any of the following:

- Lithium level is above 1.0mmol/L
- Patient becomes mentally unwell (shows signs and symptoms of mania or depression)
- Non-compliance or suspected non-compliance with treatment.
- Patient is planning pregnancy or is pregnant.
- Patient plans to breastfeed or is breastfeeding.
- Patient develops renal impairment, or renal impairment worsens.
- Introduction of a potentially interacting medicine.
- Overdose/suspected overdose of lithium or any other psychotropic medication.
- Patient has unmanageable side effects from lithium.

Stop lithium if signs of lithium toxicity become apparent and contact secondary care prescriber, or refer patient to A&E.

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Contact details for advice and support (hours and response time as per local arrangements). Emails are monitored throughout the working day

Please delete those that are not applicable

Community Mental Health Team name	CMHT Contact details * Contact your local Medicines Optimisation Team for copy with full contact details *	Time psychiatrist can be contacted on mobile
Ashford	*	12 – 2pm
Canterbury & Coastal	*	12 – 2pm
Dartford Gravesham & Swanley	*	12 – 2pm
Dover & Deal	*	1 – 2pm
Maidstone	*	1 – 2pm
Medway	*	Part of the Consultant Connect network, so GPs have a contact number for the 'on-call' consultant
Shepway	*	1 – 2pm
South West Kent	*	12 – 2pm
Swale	*	12 – 2pm
Thanet	*	Phone line and email manned by admin Mon - Fri 9-5; message taken, and the psychiatrist will call the GP back that day.

I (specialist) confirm the following:

- At last review the patient's symptoms were well controlled and the drug is providing benefit.
- The patient has been given written information about their medication.
- The patient understands that this medication is being prescribed with an agreement between their GP and specialist and that they also have responsibilities under the agreement.
- The patient has been informed that their GP can opt-out of taking on prescribing responsibility if the patient does not attend for treatment monitoring

Specialist Name:	
Specialist Signature:	
Direct telephone number:	
Email	
Date	

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Appendix 2: Managing lithium drug interactions or drug-disease interaction

Drug	Interaction effects	Risk Reduction measures
ACE inhibitors e.g., enalapril, lisinopril Angiotensin II antagonists e.g., losartan, candesartan, valsartan	• Lithium toxicity due to sodium depletion. • Concurrent use with caution and close monitoring. • With Angiotensin II antagonists case reports of increase in lithium plasma level.	• Lithium plasma level can increase over several weeks. • Monitor closely for signs of lithium toxicity and consider taking lithium plasma level more regularly i.e. 1-monthly rather than 3-monthly • May need to reduce lithium dose. • With Angiotensin II antagonists increase monitoring especially during the first couple of months.
Analgesics (NSAIDs) e.g., ibuprofen, diclofenac	• Excretion of lithium reduced.	• Avoid concomitant use. • Note: low dose aspirin 75mg does not affect lithium plasma levels significantly.
Anti-arrhythmics e.g., amiodarone	• Increased risk of QT prolongation.	• Avoid concomitant use. • Manufacturer contraindicates combined use.
Domperidone	• Lithium is associated with QT prolongation or torsade de pointes. • Dangerous QT prolongation may occur if it is given with domperidone.	• Contraindicated. Consider an alternative antiemetic.
Hydroxyzine/ mizolastine	• Antihistamines such as hydroxyzine and mizolastine, and lithium are associated with a small increased risk of QT prolongation. • Concurrent use may increase the risk.	• Consider an alternative antihistamine.
Methyldopa	• Neurotoxicity may occur without increasing lithium plasma concentration.	• Avoid concomitant use if possible.
Thiazide diuretics e.g., bendroflumethiazide	• Increase lithium plasma levels, therefore increased risk of lithium toxicity. • This is a well-established and potentially serious interaction.	• Avoid if possible. Other diuretics may be safer such as loop diuretics. • Consider a lithium dose reduction and monitor lithium plasma levels more regularly.
Alcohol	• Increased tremor/shakiness with chronic alcohol use.	• Alcohol should be avoided in the first month or two after starting lithium. After this alcohol can be drunk in moderation e.g. 1 to 2 units three time a week but ideally advise patient to reduce intake of alcohol as much as possible. This is because lithium and alcohol combination may increase risk of drowsiness.
Antibiotics e.g., metronidazole, tetracycline,	• Reduced lithium excretion leading to increased lithium plasma levels.	• Ensure service user is aware of the symptoms of lithium toxicity and report them immediately if they occur.
Anticonvulsants e.g., valproate, phenytoin, carbamazepine,	• Increased neurotoxicity of both drugs at therapeutic doses. • Valproate may aggravate tremor.	• If neurotoxicity develops, stop lithium.
Antidepressants e.g., mirtazapine, SSRIs, TCAs and venlafaxine	• Synergistic antidepressant effect in treatment resistant service users may increase lithium tremor. • Increase lithium plasma level, possible neurotoxicity and serotonergic effects.	• Monitor carefully for signs of neurotoxicity.
Antipsychotics	• Increased neurotoxicity possible at therapeutic doses in rare cases.	• Monitor for risk of QT prolongation. • Monitor for signs of neurotoxicity.

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	• Increased risk of QT prolongation.	
Calcium channel blockers e.g., diltiazem, verapamil	• Increased risk of neurotoxicity with symptoms such as ataxia, confusion, and somnolence.	• Monitor for signs of neurotoxicity.
Sodium bicarbonate containing antacids e.g., Gaviscon®	• Excretion of lithium increased by sodium bicarbonate therefore, reduced lithium plasma levels.	• Change to an alternative antacid with lower sodium content.
Theophylline/ aminophylline	• Increased excretion of lithium. Reduced lithium plasma level. Depressive and/ or manic relapse may occur if the lithium dose is not adjusted.	• Monitor lithium plasma levels if theophylline is stopped, started, or altered.
Sodium-glucose co-transporter 2 (SGLT2) inhibitors (e.g. dapagliflozin, empagliflozin)	• Increased renal lithium excretion. Reduced blood lithium level.	• Monitor serum concentration of lithium more frequently after initiation and dose changes. Refer patient back to specialist to monitor lithium serum concentration.

Drug-Disease Interaction

- If renal impairment exists, avoid use of lithium (if possible) or reduce dose and closely monitor serum-lithium concentration.
- Cardiac disease and conditions with sodium imbalance (e.g., Addison's disease) will require dose reduction or discontinuation. Similarly, in severe diarrhoea and/or vomiting and in concurrent infection (especially if sweating profusely).
- Psoriasis: risk of exacerbation.
- Addison's disease or other conditions with a sodium imbalance and in severely debilitated or dehydrated service users and in severely debilitated or dehydrated service users.
- Avoid in untreated hypothyroidism.
- Use with caution in service users with myasthenia gravis because exacerbation of this disorder has been reported.
- Previous Neuroleptic Malignant Syndrome (NMS) with lithium as reintroduction has led to recurrences of NMS.