BOB ICB & Frimley ICB Shared Care Protocol: Lithium for Patients Within Adult and Older Adult Services

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Lithium for patients within adult and older adult services

Shared Care Protocol

The content of this shared care protocol (SCP) is based on the NHSE/RMOC Lithium SCP. As well this protocol, please ensure that summaries of product characteristics (SPCs), British national formulary (BNF) or the Medicines and Healthcare products Regulatory Agency (MHRA) or NICE websites are reviewed for up-to-date information on any medicine.

Responsibilities	Shared care assumes communication between the specialist, GP and patient. The intention to share care should be explained to the patient and accepted by them. Patients are under regular follow-up and this provides an opportunity to discuss drug therapy. **Specialist responsibilities** • Diagnose the patient; ensure that this diagnosis is included in section 2 and communicated to primary care. • Discuss the benefits and risks of the treatment with the patient and provide the appropriate counselling (see section 11) to enable the patient to reach an informed decision. Obtain and document patient consent. • Provide verbal and written patient information including an appropriate patient information leaflet and a completed lithium booklet which includes the record book and alert card. • Inform patients of the signs of toxicity • Inform patients of child-bearing potential, of the risks from using lithium in pregnancy - see section 12 • Provide advice on the additional risks of lithium in pregnancy and advise the patient on the need for contraception, where required. As appropriate, advise the patient to obtain contraception from their GP or alternative contraception services. This discussion should happen on initiation of lithium and at each review. Give advice to primary care on continuing treatment if a woman becomes or wishes to become pregnant. • Assess for contraindications and cautions (see section 4) and consider potential drug interactions jointly with Primary Care (see section 7). • Conduct required baseline investigations and initial monitoring (see section 8). • Initiate and optimise treatment as outlined in section 5. • Prescribe the maintenance treatment for at least 4 weeks and until optimised. • Determine the target plasma lithium range for each patient and advise the primary care prescriber accordingly. • Once treatment is optimised, specialist should contact the patient's GP in writing to request shared care, providing details of the diagnosis, current and ongoing dose, target plasma level, any relevant test results and when the next monitoring is required (see appendix 1 for template letter). Include contact information (section 13). Request that lithium is prescribed by brand

and that blood test results are recorded in the lithium record book before issuing a repeat prescription.

- Ask GPs to carry out maintenance monitoring as in section 9.
- Prescribe sufficient medication to enable transfer to primary care.
- Conduct the required monitoring in section 8. After each review, advise primary care whether treatment should be continued, confirm the ongoing target plasma level and dose, and whether the ongoing monitoring outlined in section 9 remains appropriate.
- Provide advice to primary care on any switches between brands or formulations of lithium
- Provide advice to primary care on the management of adverse effects if required.
- Review patient at least every 12 months to assess their mental health, effectiveness of treatment and the ongoing need for lithium
- Provide a clear plan for lithium treatment to primary care, including anticipated duration of treatment and advise if treatment should be discontinued.
- Document all communication with primary care in the patient's electronic health record.
- When a patient is considered to have been stable mentally and functionally for a suitable period of time, liaise with the GP about the possibility of fully transferring the patient's ongoing care back to the care of the GP and no longer having specialist reviews. If the patient is fully transferred to the GP and no follow up is being undertaken in secondary care, the patient will no longer be under shared care, however the clinical information in this protocol will need to be followed by the GP. Should the GP need to contact the secondary care specialist at any point, they can access them via the referral contact information in section 13. This can be an urgent or routine referral. Alternatively, or in combination, local teams can be contacted directly via email and/or telephone number provided in discharge letters sent to the GP. The specialist will be available for queries; and may be directed to a CMHT (Community Mental Health Team) pharmacist if appropriate.

Primary care responsibilities

- Respond to the request from the specialist for shared care via email within 14 days. If acceptance/decline of shared care has not been received after 14 days, acceptance will be assumed. If accepted, prescribe ongoing treatment as detailed in the specialist's request and as per section 5 taking into any account potential drug interactions in section 7.
- Always prescribe lithium by brand and form. Discuss any changes in the brand or formulation with the specialist.
- Adjust the dose of lithium prescribed, according to the target plasma level as advised by the specialist. See section 10 for further details/advice.
- Conduct the required monitoring as outlined in section 9. Communicate any abnormal results to the specialist.
- Assess for possible interactions with lithium when starting new medicines (see section 7).
- Manage any adverse effects as detailed in section 10 or concerns about lack of ongoing therapeutic benefit. and discuss with specialist team when required.
- Be familiar with the symptoms of lithium toxicity and the common causes.

- If toxicity is suspected, withhold lithium and discuss urgently with the specialist. Plasma lithium levels should be acquired immediately to aid interpretation and facilitate specialist advice.
- If plasma lithium levels are above the specified range, check the dose, adherence, and timing of sample (repeating if necessary). Determine whether toxicity is present and discuss with the specialist with an urgency determined by clinical judgement.
- Discuss other adverse effects with the specialist team as clinically appropriate (see section 10).
- Contact the specialist perinatal team immediately if the patient becomes or plans to become pregnant.
- Be aware that abrupt discontinuation of lithium increases the risk of relapse and discontinuation should be gradual over a period of several weeks under specialist advice
- Stop treatment as advised by the specialist.
- Where a patient's ongoing care, who will be on lithium lifelong, is fully transferred back to the care of the GP and the patient is no longer having specialist reviews, prescribe, monitor and review lithium as per consultant advice (see also NICE and NPSA guidelines).
- Review patient at least every 12 months to assess their mental health and use of lithium. If there is a question about whether to continue lithium, this can be referred to the specialist.
- If there are any concerns after the patient's care has fully transferred to their GP's care and the patient is no longer having specialist reviews (i.e. the patient is no longer under shared care), seek advice from a secondary care specialist and refer the patient back for assessment as appropriate.

Patient and/or carer responsibilities

- Agree to treatment and monitoring after making an informed decision
- Agree to being under the shared care of the GP and specialist
- Take lithium as prescribed and not stop taking it without speaking to their primary care prescriber or specialist.
- Be familiar with their brand of lithium and check that they have received the correct one.
- Take doses of lithium at the same time each day and if a dose is missed, take the next scheduled dose as usual
- Attend regularly for monitoring and review appointments with primary care and specialist. Request that results are recorded in lithium booklet and bring this to each appointment.
- Be familiar with symptoms of toxicity and the common causes.
- Maintain adequate fluid intake and their usual daily salt intake, particularly in hot weather or during periods of increased activity.
- Report adverse effects to their primary care prescriber. Seek immediate medical attention if they develop any symptoms as detailed in section 11.
- Inform healthcare professionals that lithium is being taken when seeking medical or pharmacy advice
- Report the use of any over the counter medications to their primary care prescriber and be aware they should discuss the use of lithium with their pharmacist before purchasing any OTC medicines.
- Moderate their alcohol intake to no more than 14 units per week. Avoid recreational drugs.

	• Do not drive or operate heavy machinery if lithium affects their ability to do so safely. • Lithium should be stopped 24 hours before major surgery. It can be continued for minor surgery when professional advice has been sought. • Women of child-bearing potential should use reliable contraception and inform the specialist or primary care prescriber immediately if they become pregnant or wish to become pregnant.
1. Background	Lithium is licensed for the treatment and prevention of mania, bipolar depression, recurrent depression (unipolar) and aggressive/self-mutilating behaviour. It is also recommended for augmentation of antidepressants in major depressive disorder. Lithium can be very effective for acute episodes of mental illness, following which it is often continued. Likewise in prophylaxis, but longer periods of treatment may be required to establish its benefits. Not all patients respond to lithium, so the benefits and risks of continuation should be regularly and individually assessed. Lithium treatment should not be stopped suddenly, as this can cause relapse. The benefits and many of the adverse effects of lithium relate to its plasma concentration. Lithium has a narrow therapeutic window of between 0.4 and 0.8 mmol/L for most indications, although a narrower range may be specified for individual patients. Higher target plasma levels (0.8–1 mmol/litre) are occasionally recommended for acute episodes of mania or for patients who have previously relapsed or when subthreshold symptoms of illness are associated with functional impairment. **The specialist service will determine the target range for each patient and advise the primary care prescriber accordingly.** The plasma concentration of lithium is a function of absorption, distribution, and elimination. In salt form, lithium is readily absorbed from the gastrointestinal tract, but the rate and extent of absorption may differ between formulations. Levels fluctuate during distribution, so measurements are made 12 hours post-dose for monitoring purposes. Lithium is almost exclusively eliminated by the kidneys. Lithium has numerous mild side effects but can be toxic if the dose is too high. It can cause side effects within the therapeutic range and toxicity outside of that therapeutic range. Toxicity usually occurs with levels above 1.5 mmol/L but can emerge at lower levels in susceptible patients such as the elderly or those with renal impairment. Excluding excessive ingestion, toxicity most commonly arises due to a reduced elimination of lithium. Elimination is sensitive to sodium handling, so low-salt diets, dehydration, certain drug interactions and medical conditions such as Addison's disease are risk factors. Lithium toxicity can itself impair renal function, so rapid escalations in plasma levels may occur. Patients, carers, and clinicians should be familiar with the features of lithium toxicity, the common causes, and how to seek appropriate help. With long-term use, lithium can have adverse effects on the kidneys, the thyroid, and the parathyroid glands. Routine monitoring of function is therefore required. **Lithium should always be prescribed by brand and form**; tablets and liquids are not interchangeable. Extra care must be taken when prescribing liquid forms, with clarity over the name and strength of the preparation. Patients should be involved in treatment decisions and understand the importance of lithium monitoring.
2. Indications	Licensed indications: • Treatment and prophylaxis of mania • Treatment and prophylaxis of bipolar disorder

(Please state whether licensed or unlicensed)	• Treatment and prophylaxis of recurrent depression NB: lithium should not be used as a sole agent to prevent recurrent major depressive disorder, see NICE NG222 Depression in adults: Treatment and management • Treatment and prophylaxis of aggressive or self-harming behaviour • Augmentation of antidepressants in patients with treatment resistant depression‡ See NICE NG222 Depression in adults: Treatment and management ‡ Off-label indications. (Please note licensed indications vary by manufacturer).
3. Locally agreed off-label use	To be agreed and completed locally (include supporting information)
4. Contraindications and cautions Please note this does not replace the Summary of Product Characteristics (SPC) and should be read in conjunction with it.	**Contraindications:** • Hypersensitivity to lithium or any of the excipients. Excipients vary according to the preparation being used. Tablets might include glycerol monostearate, glycerol distearate, mannitol, acacia, sodium lauryl sulfate, magnesium stearate, maize starch, sodium starch glycolate, gelatin and lactose. Liquid preparations contain ethanol. • Addison's disease • Cardiac disease associated with rhythm disorder • Cardiac insufficiency • Family or personal history of Brugada syndrome • Patients with abnormal sodium levels, including dehydrated patients or those on low sodium diets • Untreated hypothyroidism • Severe renal impairment • Breastfeeding **Cautions:** • Mild to moderate renal impairment • Use in elderly patients • Adequate and stable sodium and fluid intake should be maintained. This may be of special importance in hot weather, or during infectious diseases, including influenza, gastro-enteritis or urinary infections, when dose reduction may be required. • Review lithium dose if diarrhoea and / or vomiting present and in cases where the patient has an infection and / or profuse sweating. Adjustments may be required. • Risk of seizures may be increased if co-administered with drugs that lower the seizure threshold, or in patients with epilepsy. • Cardiac disease • May exacerbate psoriasis • Surgery: discontinue 24 hours prior to major surgery and re-commence post-operatively once kidney function and fluid-electrolyte balance is normalised. Discontinuation is not required prior to minor surgery, providing fluids and electrolytes are carefully monitored. • Pregnancy Please see SPC for comprehensive information.

<table>
<tr><td>5. Initiation and ongoing dose regime

Note -
•Transfer of monitoring and prescribing to primary care is normally after the patient's dose has been optimised and with satisfactory investigation results for at least 4 weeks
•The duration of treatment & frequency of review will be determined by the specialist, based on clinical response and tolerability.
•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.</td><td colspan="2"><u>Initial stabilisation:</u>
Usual starting dose for doses for all preparations are adjusted according to patient response and serum lithium concentration.

Most patients are prescribed lithium in tablet form (lithium carbonate). Doses may initially be divided throughout the day but once-daily administration is preferred when serum-lithium concentration is stabilised to target range (specified by specialist team).
In practice, the typical starting dose is 400 mg once daily, adjusted according to patient response and 12-hour plasma levels. Lower starting doses (such as 200 mg once daily) are preferable in the elderly and/or cases in which caution is required.

In some scenarios, such as acute mania, a higher starting dose (loading) may be preferable. The BNF outlines the typical starting doses by indication and brand.

Lithium citrate is absorbed at a different rate and to a different extent (bioavailability) compared to tablet forms. Extra care must be taken when prescribing lithium in liquid form, as some offer different strengths (mg/ml) under the same brand name (Li-liquid®) and some brand names (Priadel®) are used for the liquid and tablet forms. <u>Switches between tablet and liquid formulations should be overseen by specialist services</u> as dose conversions require the calculation of milligram equivalence between lithium carbonate and lithium citrate. There is no clinically significant difference between the pharmacokinetics of Priadel® and Camcolit® modified-release tablets; however, other preparations may not be bioequivalent.

The loading period must be prescribed by the initiating specialist.

<u>Maintenance dose (following initial stabilisation):</u>
Individualised, to achieve plasma levels in the range specified for the patient.
The initial maintenance dose must be prescribed by the initiating specialist.

<u>Conditions requiring dose adjustment:</u>
Lower doses may be required in older or physically frail/ low body weight patients, in mild to moderate renal impairment and electrolyte imbalance. Dose adjustments may also be required in patients prescribed interacting medicines.

<u>Stopping lithium treatment</u>
The decision to stop treatment will be the responsibility of the specialist. Clinicians, patients, and carers should be aware that abrupt discontinuation of lithium increases the risk of relapse. If lithium is to be stopped, the dose should gradually be reduced over a period of at least four weeks but preferably over a period of up to three months.</td></tr>
<tr><td rowspan="2">6. Pharmaceutical aspects</td><td>Route of administration:</td><td>Oral</td></tr>
<tr><td>Formulation:</td><td>Lithium is available as lithium carbonate (tablet formulations) and lithium citrate (liquid formulations). The patient should be maintained on the same brand and formulation of lithium. There is no clinically significant difference between the pharmacokinetics of Priadel® and Camcolit® modified-release tablets; however, other preparations may not be bioequivalent. If a switch in brand or formulation is considered, refer to the specialist team.</td></tr>
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		Lithium tablets and liquids are not interchangeable without monitoring lithium plasma levels. **Lithium Carbonate:** • Priadel® 200 mg and 400 mg prolonged-release tablets • Camcolit® 400 mg controlled release tablets • Liskonum® 450 mg controlled release tablets • Lithium carbonate Essential Pharma: 250 mg film-coated tablets (immediate release) **Lithium Citrate:** • Li-Liquid®: 509 mg/5 mL strength cherry flavoured syrup. Please note Li-Liquid® is the preferred liquid brand of Oxford Health. • Priadel® Liquid: 520 mg/5 mL strength sugar-free, pineapple flavoured syrup. Please note Priadel® is the preferred liquid brand of Berkshire Healthcare Foundation Trust. Please note a higher strength liquid (Li-Liquid® 1,018 mg/5 mL strength cherry flavoured syrup) is available but this should not be prescribed and is not included in this shared care protocol due to safety concerns. Extra care must be taken when prescribing lithium in liquid form, as some offer different strengths (mg/ml) under the same brand name (Li-liquid®) and some brand names (Priadel®) are used for the liquid and tablet forms. **<u>Always prescribe lithium by brand name.</u> Switching preparation (either between brands of the same form or changing between tablets and liquid) requires additional monitoring to ensure that the 12-hour plasma lithium level remains in the desired range.** **Particular care should be taken if prescribing liquid preparations; lack of clarity may lead to the patient receiving a sub-therapeutic or toxic dose.**
	Administration details:	Consistency is paramount in lithium treatment and monitoring. Doses should be taken regularly, at the same time every day. Lithium carbonate tablets should not be crushed or chewed. Priadel® 200mg and 400mg tablets have score lines and can be divided accurately to provide dosage requirements as small as 100mg within product license. Liskonum® 450mg tablets are licensed to be halved for the purposes of dose adjustment. Other brands may be scored to facilitate breaking for ease of swallowing, and not to divide into equal doses. Breaking these tablets is not expected to alter their release properties but the accuracy of the division is not established

	Other important information:	If a dose is missed, then the next scheduled dose should be taken as usual; a double dose should not be taken to make up for a missed dose. For a given total daily dose, 12-hour plasma lithium levels will differ for once versus twice daily dosing schedules. The schedule should be determined by the specialist and not altered without their advice.
7. Significant medicine interactions For a comprehensive list consult the BNF or Summary of Product Characteristics. SPC	**The following list is not exhaustive; please see SPC for comprehensive information and recommended management.** **The following drugs must not be prescribed without considering the following consequences below and monitoring lithium plasma levels accordingly:** • Drugs that may increase plasma lithium concentrations (by reducing renal elimination) and so risk toxicity: ○ NSAIDs (including cyclo-oxygenase 2 inhibitors). If NSAID use is unavoidable, a dose reduction of lithium may be required and levels should be monitored more frequently. 'As required' use of NSAIDs should be avoided where possible since it may cause fluctuations in lithium levels and makes monitoring levels challenging. ○ Diuretics, particularly thiazide diuretics ○ Angiotensin converting enzyme (ACE) inhibitors and angiotensin II receptor antagonists. These should be avoided where possible. ○ Other drugs which alter electrolyte balance with the potential to alter lithium clearance e.g. steroids. ○ Certain antibiotics including metronidazole and tetracyclines • Drugs that may decrease plasma lithium concentrations (by increasing renal elimination) and so risk loss of efficacy: ○ Theophylline ○ Products which contain sodium bicarbonate e.g. antacids • Drugs that may increase risk of neurotoxicity when co-administered with lithium: ○ Calcium channel blockers (e.g. verapamil, diltiazem) ○ Antipsychotics (e.g. haloperidol, olanzapine, clozapine, flupentixol, chlorpromazine) ○ Antidepressants with a serotonergic action (e.g. SSRIs, tricyclic antidepressants, venlafaxine, duloxetine) ○ Carbamazepine • Drugs associated with QT prolongation (e.g. amiodarone, macrolides, tricyclic antidepressants) – potential for additive effects when co-administered with lithium. • Drugs that lower seizure threshold (e.g. SSRIs, tricyclic antidepressants, antipsychotics) – increased risk of seizures **Care should be taken on initiation, dose adjustment or discontinuation of any interacting medicines. The onset and degree of the interaction can vary and additional lithium monitoring is likely to be indicated, with doses adjusted accordingly. An ECG should be performed wherever there are interacting medicines or changes in treatment. If concerned about a possible interaction, discuss with specialist team.**
8. Baseline investigations, initial monitoring and ongoing monitoring to be undertaken by specialist	**Monitoring at baseline and during initiation is the responsibility of the specialist.** Only once lithium therapy is optimised on the chosen formulation with no anticipated further changes expected in immediate future will prescribing and monitoring be transferred to primary care.

<table>
<tr><td></td><td colspan="2">Recent and relevant investigation results must be documented in the corresponding letter from specialist. In the event that baseline monitoring cannot be completed, for example due to patient refusal, this will also be documented in the letter from the specialist.

Baseline (all indications):
• Creatinine and electrolytes (C+Es), including calcium and eGFR
• Thyroid function tests (TFTs)
• Electrocardiogram (ECG) recommended for patients with existing cardiovascular disease (CVD) or risk factors
• Full blood count (FBC)
• Height, weight and body mass index (BMI)
• Exclude pregnancy

Additional baseline investigations (bipolar disorder):
• Measure pulse and blood pressure. If there are risk factors for, or existing cardiovascular disease, a baseline ECG is recommended.
• Metabolic status including fasting blood glucose, HbA_{1c} and blood lipid profile.
• Liver function tests (LFTs).

Initial monitoring:
• 12-hour plasma lithium levels one week after initiation and one week after any change in dose or formulation. Typically this means levels will be monitored weekly until the desired level and clinical effect is achieved.
• Lithium levels take 4-7 days to reach steady state concentrations. Normally lithium is prescribed as a night time dose and levels should be carried out between 12 - 14 hours post-dose. Where dosing is twice a day, the morning dose should be withheld until after the sample for levels is taken. Consider ECG if clinical signs of CVD or increased risk.

Ongoing monitoring:
• Review patient at least every 12 months to assess their mental health, effectiveness of treatment and the ongoing need for lithium. Please note if the care of the patient has been fully transferred back to the GP, this review will not take place by the specialist.</td></tr>
<tr><td rowspan="3">9. Ongoing monitoring requirements to be undertaken by primary care.

See section 10 for further guidance on management of adverse effects/ responding to monitoring results.</td><td>Monitoring – all indications</td><td>Frequency</td></tr>
<tr><td colspan="2">The GP will be able to access a referral back to a secondary care specialist if needed at any point. The specialist will be available for queries; these could be directed to a CMHT pharmacist if appropriate and available.</td></tr>
<tr><td>Aim to take plasma lithium level 12 hours post-dose. In the event of twice daily dosing, delay the morning dose until after the blood test has been taken.
• Record results in patient's NPSA purple lithium pack, NHS Health Monitor for Lithium app, or other suitable recording mechanism.</td><td>Measure the person's plasma lithium level every 3 months for the first year.

After the first year, measure plasma lithium levels every 6 months, or every 3 months for people in any of the following groups:
• Older people
• People taking drugs that interact with lithium</td></tr>
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	• It is advisable to document the actual time interval between the last dose and the blood sample	• 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 per litre or higher. • People whose eGFR has declined over 2 or more tests Consider additional monitoring whenever there is a change in the patient's circumstances, e.g. intercurrent illness.
	C+Es (including calcium and eGFR), TFTs **Height, weight, and BMI.**	**Every 6 months.** More frequent monitoring (particularly renal function) may be advised by the specialist team in some circumstances (e.g. elderly, renal impairment, altered TFTs, concurrent interacting medicines).
	Signs of toxicity Enquire about and document signs and symptoms which might indicate toxicity, e.g. paraesthesia, ataxia, tremor, cognitive impairment, stomach-ache along with feeling sick or having diarrhoea, muscle weakness, being unsteady on your feet, muscle twitches, slurring of words, blurred vision, confusion, feeling unusually sleepy	**At every consultation** – consider carrying out ECG if signs of toxicity are suspected/seen.
	Additional monitoring – bipolar disorder	**Frequency**
	Diet, nutritional status and level of physical activity. **Cardiovascular status including pulse and BP.** **Metabolic status including fasting blood glucose, HbA_{1c} and blood lipid profile.** **LFTs.**	Annually as part of physical health check recommended by NICE (CG185 Bipolar disorder: assessment and management). GPs may decide to refer for Specialist review e.g. if patient is considering stopping treatment or if the effectiveness of treatment is in question/ early warning signs of relapse, like sleep disturbance Scenario: Routine bipolar disorder review | Management | Bipolar disorder | CKS | NICE

10. Adverse effects and managements **Any serious adverse reactions should be reported to the MHRA via the Yellow Card scheme** www.mhra.gov.uk/yellowcard	Result	Action for GP
	As well as responding to absolute values in laboratory tests, a rapid change or a consistent trend in any value should prompt caution and extra vigilance.	
	12-hour plasma lithium level. NB: range for each patient to be determined by the specialist team.	
	Below range	Assess adherence, including discussion with patient and check of GP clinical systems. Offer advice on adherence if appropriate (e.g. daily routines, reminders). Ensure level was taken 12 hours after lithium dose. Consider other factors e.g. drug interactions, excess fluid intake. Check mental health if lithium level is below range. Recheck level / contact specialist team for advice if suspected that the dose is too low.
	Within range **(signs of toxicity)**	Contact specialist team for advice. Referral to secondary care may be required depending on the severity of symptoms and the certainty of toxicity. Use clinical judgement to determine the urgency of referral.
	Within range **(but marked change since last level and no dose change)**	Repeat level. Assess adherence, including discussion with patient and check of GP clinical systems. Offer advice on adherence if appropriate (e.g. daily routines, reminders). Ensure level was taken 12 hours after lithium dose. More frequent monitoring may be required.
	Above range **(no signs of toxicity)**	Ensure level was taken 12 hours after lithium dose and that the correct dose has been prescribed and taken. Check for interactions, hydration, patient's physical and mental status, and features of toxicity. Repeat level if necessary. **Withhold lithium** and contact specialist team for advice. If there is a possible explanation for high lithium level, correct where possible and recheck level. If there is no explanation for the high level, recheck level, investigate renal function and if repeat level is higher than original target, refer back to specialist for advice. If the trend is for the high end of the range but is not consistent with the range

		specified by the specialist team, decrease the dose, encourage fluids and recheck in one week. The specialist can be contacted for advice if needed. If ≥2mmol/l – send patient to A&E and inform specialist team
	<u>Signs of toxicity</u> Typical signs and symptoms include diarrhoea, vomiting, loss of appetite, muscle weakness, lethargy, dizziness, ataxia, lack of coordination, tinnitus, blurred vision, coarse tremor of the extremities and lower jaw, muscle hyper-irritability, choreoathetoid movements, dysarthria, and drowsiness	If lithium toxicity is suspected, do an urgent lithium level immediately and seek specialist advice. Referral to secondary care may be required depending on the severity of symptoms and the certainty of toxicity. Use clinical judgement to determine the urgency of referral.
	Thyroid function	
	Altered TFTs without symptoms	Contact specialist team for advice. During lithium treatment, TFTs are commonly abnormal; the TSH can rise early in treatment but settle with time. Note that the symptoms of hypothyroidism can be difficult to discriminate from depression and the common side effects of lithium.
	Subclinical hypothyroidism • Raised TSH • Normal T4 Clinical features not overtly manifest	Contact specialist team for advice, which may include input from endocrinology services. The optimal management of subclinical hypothyroidism during lithium treatment remains controversial, with different thresholds for treatment advocated. Anticipate the need for additional monitoring, investigations and potentially thyroid hormone replacement based on specialist recommendations.
	Overt hypothyroidism • High TSH • Low T4 • Symptomatic	Contact specialist team for advice, which may include input from endocrinology services. Thyroid hormone replacement is usually indicated and often continued throughout the course of lithium treatment.
	Hyperthyroidism	Contact specialist team for advice, which may include input from endocrinology services.

	Renal function	
	Polyuria and polydipsia	Polyuria is common with lithium and often well tolerated. Advise the patient to maintain adequate fluid intake and advocate excellent oral hygiene. Contact specialist team for advice, which may include input from nephrology services. In some instances, dose adjustment or specific treatments may be advocated.
	C&Es (including calcium) out of range	Check that the most recent 12-hour plasma lithium level is in the desired range and act accordingly if not. Determine whether there are symptoms and signs related to the electrolyte disturbance or lithium toxicity. Consider arranging an ECG in those at risk for QT prolongation. Contact specialist team for advice. Changes in calcium levels may reflect parathyroid dysfunction and input from endocrinology services may be indicated.
	eGFR <45ml/min rapidly falling eGFR gradual decline in eGFR	The response to impaired or deteriorating renal function should be individualised. Contact specialist team for advice, which may include input from nephrology services. A cardiovascular risk profile may guide specialist advice and should be provided if available. Use clinical judgement to determine the urgency of consultation. Anticipate the need for increased monitoring as trends in renal function are more useful than absolute values. In the elderly or those at the extremes of muscle mass, creatinine clearance provides a better estimate of renal function that eGFR. Adjustments to dose may be advised. If renal function is significantly compromised, lithium may no longer be an appropriate treatment and specialists will advise accordingly.
	Weight and BMI Outside healthy range	Provide appropriate support on multicomponent interventions to increase physical activity levels, improve eating behaviour and quality of diet. Remind patient of the importance of maintaining adequate fluid intake and avoiding dehydration while exercising.

		Consider measuring waist circumference for individualised monitoring. Patients should be instructed to avoid sudden changes in diet, especially avoiding low sodium diets. Lithium levels are influenced by body weight and so for patients being supported to lose weight, lithium levels may need to be checked more frequently (akin to other situations of caution). Use clinical judgement, lithium levels and the rate of weight loss when determining the frequency of blood tests.
	Physical health check (bi-polar disorder)	Any physical health problems should be treated by the appropriate primary care health professional and communicated to the specialist team within 14 days.

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, including patient information leaflets on individual medicines.

The patient should be advised to report any of the following signs or symptoms to their GP without delay:

- Lithium toxicity (diarrhoea, vomiting, loss of appetite, muscle weakness, lethargy, dizziness, ataxia, lack of coordination, tinnitus, blurred vision, coarse tremor of the extremities and lower jaw, muscle hyper-irritability, choreoathetoid movements, dysarthria, and drowsiness)
- Signs of hypothyroidism (e.g. fatigue, cold intolerance, weight gain, constipation and depression), renal dysfunction (including polyuria and polydipsia), and benign intracranial hypertension (persistent headache and visual disturbance).

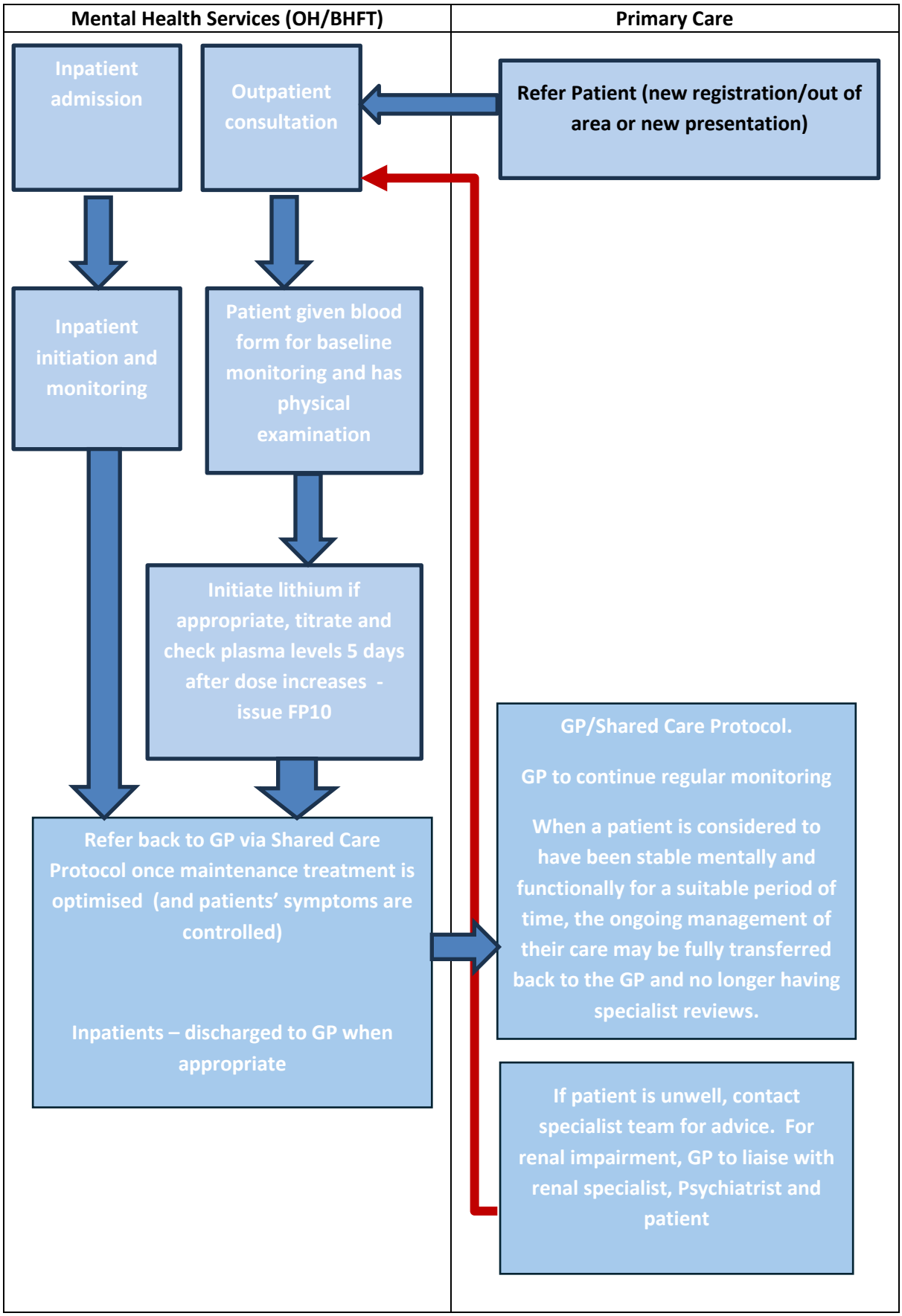
Additional advice for patients/ carers:

- Patients must attend regularly for monitoring (including blood tests) and review appointments to ensure their lithium dose remains safe and effective, and bring their purple lithium pack to keep a record of their lithium levels.
- Patients should notify their primary care prescriber straight away if there is any change in their health, e.g. an infection, or significant weight loss. Additional lithium monitoring may be required.
- Lithium should be taken regularly, as prescribed. If doses are missed, patients should not attempt to catch up or double dose
- Patients should not stop taking lithium suddenly – doing so increases the chance of relapse. If lithium is to be stopped, it should be reduced over at least four weeks and preferably three months.
- The same brand of lithium should always be taken unless otherwise instructed. Patients should become familiar with their brand and check they have received the correct one before taking.
- Changes in hydration and sodium balance can affect plasma lithium levels. Patients should maintain adequate fluid intake, particularly in hot weather or when activity levels change (such as increases in exercise or immobility). Large changes in dietary sodium should be avoided – changing dietary regime may inadvertently alter sodium intake.
- Substantial changes in plasma lithium levels can occur if patients develop diarrhoea or vomiting, or if they become acutely ill for any reason. Patients should seek medical advice in such instances.

	• Excessive alcohol consumption should be avoided as it can lead to dehydration, increasing plasma lithium levels and so risk of toxicity. • Patients should be warned about common drug interactions and advised to present their 'Lithium alert card' whenever they redeem a new prescription. They should specifically be advised not to take OTC NSAIDs as these can increase plasma lithium levels and so risk toxicity. • Lithium may impair performance of skilled tasks (e.g. driving, operating machinery). Patients with a diagnosis of bipolar disorder must notify the Driver and Vehicle Licensing Agency (DVLA). • Women of childbearing potential should be advised that lithium carries additional risks in pregnancy and of the need to use reliable contraception during treatment with lithium. They should tell their doctor straight away if they are planning a pregnancy or become pregnant while taking lithium. Lithium should not be taken if breastfeeding. • All specialist community perinatal mental health teams offer preconception appointments for women thinking of starting a family who have a severe and complex history of mental illness or are on complex medication regimes (including lithium) for their mental health. Referrals for those with a diagnosis of bipolar or schizoaffective disorder are particularly welcome as they are at higher risk of perinatal mental illness. Women should be in optimum mental health and stable for these appointments, in order to be able to discuss their history and engage in a conversation about benefits and risks of treatment options. • For acute indications such as mania or augmentation, patients may respond within days to weeks of starting lithium. Depending on episode frequency, it may take months or even years to determine whether lithium has proven effective for release prevention. **At the start of treatment patients should be given suitable information on lithium and means to keep a record of their serum lithium levels, for example the NHS Health Monitor for Lithium app, or a purple lithium pack.** **Patient information on this medicine can be found at the following links:** • NHS: https://www.nhs.uk/medicines/lithium/ • MIND: https://www.mind.org.uk/information-support/drugs-and-treatments/lithium-and-other-mood-stabilisers/lithium/ • National Patient Safety Agency purple lithium pack
12. Pregnancy, paternal exposure and breast feeding It is the responsibility of the specialist to provide advice on the need for contraception to male and female patients on initiation and at each review but the ongoing responsibility for providing this advice rests with both the GP and the specialist.	**All patients should be informed of the risks and benefits of taking this medicine during pregnancy and breastfeeding.** **Pregnancy:** Lithium should not be used during pregnancy, especially in the first trimester (increased risk of cardiac abnormalities). In certain cases where a higher risk to the patient could exist if treatment were stopped, lithium has been continued during pregnancy; under these circumstances prescribing is the responsibility of the specialist team. If a patient becomes pregnant whilst on lithium, the specialist team should be informed immediately (but do not stop the lithium). **Women of child-bearing potential should be advised to use a reliable form of contraception.** It is the responsibility of the specialist to provide advice on the need for contraception to patients on initiation of lithium, and at each review. Under shared care agreements, the ongoing responsibility for providing this advice rests with both the GP and the specialist.

	Breastfeeding: Lithium is secreted in breast milk and there have been case reports of neonates showing signs of lithium toxicity. Lithium should be avoided during breastfeeding. **Paternal exposure:** Animal studies have reported spermatogenesis abnormalities that may lead to impairment of fertility- it is unknown if this risk applies to humans.
13. Specialist contact information	**Oxford Health:** For all telephone enquiries call 01865 901000 and ask to be put through to the relevant AMHT. Alternatively, clinicians should refer using standard mental health referral pathways. **Oxfordshire referral:** Emergency response: 4 hours Urgent/Priority: 7 days Routine referral: 28 days **Bucks referral:** Emergency response: 24 hours Medication queries only: 3 days Urgent/Priority: 7 days Routine referral: 28 days **BHFT:** Please send an urgent referral (24hour) or routine (2 weeks) to CPE/gateway. This can be done via email using the standard form (usually integrated into EMIS) to gateway@berkshire.nhs.uk or via telephone 0300 365 2000. For Crisis referrals requiring 4 hour response, referrals must be called through and discussed with Duty clinician at CPE. If the patient is already open to a treatment service, such as MHICS or CMHT primary care clinician can directly speak to (MHICS/CMHT) Duty service to request an urgent response. Alternatively, or in combination, local teams can be contacted directly via email and/or telephone number provided on all the letters sent to the GP.
14. Additional information	Where patient care is transferred from one specialist service or GP practice to another, a new shared care agreement must be completed.
15. References	• eBNF accessed via www.medicinescomplete.com on 22.01.2025 • Martindale: The Complete Drug Reference. Accessed via www.medicinescomplete.com on 16/02/2021. • Summary of Product Characteristics. Priadel® 400mg prolonged release tablets. Essential Pharma. Date of revision of the text: 24/08/2020. Accessed via https://products.mhra.gov.uk/ on 17/02/2021. • Summary of Product Characteristics. Priadel® 520mg/5mL liquid. Essential Pharma. Date of revision of the text: 24/08/2020. Accessed via https://products.mhra.gov.uk/ on 17/02/2021. • Patient Information Leaflet. Priadel® 520mg/5mL liquid. Essential Pharma. Date of revision of the text: June 2020. Accessed via https://products.mhra.gov.uk/ on 23/02/2021. • Summary of Product Characteristics. Camcolit 400 mg, controlled release Lithium Carbonate. Essential Pharma. Date of revision of the text: 28/09/2020. Accessed via https://www.medicines.org.uk/emc/ on 17/02/2021. • Summary of Product Characteristics. Lithium Carbonate 250mg film coated tablets. Essential Pharma. Date of revision of the text: 28/09/2020. Accessed via https://www.medicines.org.uk/emc/ on 17/02/2021.

	• Summary of Product Characteristics. Liskonum® 450mg tablets. Teofarma S.r.l. Date of revision of the text: 14/05/2020. Accessed via https://products.mhra.gov.uk/ on 23/02/2021. • Summary of Product Characteristics. Li-Liquid 509 mg/5mL oral syrup. Rosemont. Date of revision of the text: 27/12/2019. Accessed via https://www.medicines.org.uk/emc/ on 23/02/2021. • NICE NG222: Depression in adults: treatment and management. June 2022. Accessed via https://www.nice.org.uk/guidance/ng222 • NICE CG185: Bipolar disorder: assessment and management. September 2014 (last updated February 2020). Accessed via https://www.nice.org.uk/guidance/cg185 on 17/02/2021. • Specialist Pharmacy Service. September 2020. Suggestions for Therapeutic Drug Monitoring in Adults in Primary Care. Accessed via https://www.sps.nhs.uk/articles/suggestions-for-therapeutic-drug-monitoring-in-adults-in-primary-care-2/ on 17/02/2021. • Taylor D, Barnes T, Young A. The Maudsley Prescribing Guidelines in Psychiatry. 13th ed. London: Wiley-Blackwell; 2018, pp. 205-213. • NICE Clinical Knowledge Summary. Bipolar disorder: Lithium. Last revised November 2020. Accessed via https://cks.nice.org.uk/topics/bipolar-disorder/prescribing-information/lithium/ on 17/02/2021. • NHS UK leaflet: Lithium. Accessed via https://www.nhs.uk/medicines/lithium/on 17/02/2021. • National Patient Safety Agency. Safer Lithium Therapy. 2009. Archived resources available via: https://www.sps.nhs.uk/articles/npsa-alert-safer-lithium-therapy-2009/.
16. To be read in conjunction with the following documents	• Shared Care for Medicines Guidance – A Standard Approach (RMOC). Available from https://www.sps.nhs.uk/articles/rmoc-shared-care-guidance/ • NHSE guidance – Responsibility for prescribing between primary & secondary/tertiary care. Available from https://www.england.nhs.uk/publication/responsibility-for-prescribing-between-primary-and-secondary-tertiary-care/ • General Medical Council. Good practice in prescribing and managing medicines and devices. Shared care. Available from https://www.gmc-uk.org/ethical-guidance/ethical-guidance-for-doctors/good-practice-in-prescribing-and-managing-medicines-and-devices/shared-care • NICE NG197: Shared decision making. Last updated June 2021. https://www.nice.org.uk/guidance/ng197/.
17. Local arrangements for referral Define the referral procedure from hospital to primary care prescriber & route of return should the patient's condition change.	Each mental health specialist will contact the patient's GP in writing and within this communication, will advise the GP about how to refer / escalate patients back into CMHT. Additionally, referral details can be found in box 13 above.


Mental Health Services (OH/BHFT)
Primary Care
Inpatient admission
Outpatient consultation
Refer Patient (new registration/out of area or new presentation)
Inpatient initiation and monitoring
Patient given blood form for baseline monitoring and has physical examination
Initiate lithium if appropriate, titrate and check plasma levels 5 days after dose increases - issue FP10
Refer back to GP via Shared Care Protocol once maintenance treatment is optimised (and patients' symptoms are controlled)
Inpatients – discharged to GP when appropriate
GP/Shared Care Protocol.
GP to continue regular monitoring
When a patient is considered to have been stable mentally and functionally for a suitable period of time, the ongoing management of their care may be fully transferred back to the GP and no longer having specialist reviews.
If patient is unwell, contact specialist team for advice. For renal impairment, GP to liaise with renal specialist, Psychiatrist and patient

Appendix 1: Shared Care Request letter (Specialist to Primary Care Prescriber)

Dear *[insert Primary Care Prescriber's name]*

Patient name: *[insert patient's name]*
Date of birth: *[insert date of birth]*
NHS Number*:* *[insert NHS Number]*
Diagnosis: *[insert diagnosis]*

As per the agreed **Frimley ICB shared care protocol** for *[insert medicine name]* for the treatment of *[insert indication],* this patient is now suitable for prescribing to move to primary care.

The patient fulfils criteria for shared care, and I am therefore requesting your agreement to participate in shared care. Where baseline investigations are set out in the shared care protocol, I have carried these out. I can confirm that the following has happened with regard to this treatment:

	Specialist to complete
The patient has been initiated on this therapy and has been on an optimised dose for the following period of time:	
Baseline investigation and monitoring as set out in the shared care documents have been completed and were satisfactory	*Yes / No*
The condition being treated has a predictable course of progression and the patient can be suitably maintained by primary care	*Yes / No*
The risks and benefits of treatment have been explained to the patient	*Yes / No*
The roles of the specialist/specialist team/ Primary Care Prescriber / Patient and pharmacist have been explained and agreed	*Yes / No*
The patient has agreed to this shared care arrangement, understands the need for ongoing monitoring, and has agreed to attend all necessary appointments	*Yes / No*
I have enclosed a copy of the shared care protocol which covers this treatment	*Yes / No*
I have included with the letter, copies of the information the patient has received	*Yes / No*
I have provided the patient with sufficient medication to last until	
I have arranged a follow up with this patient in the following timescale	

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

If you are in agreement, please undertake monitoring and treatment from *[insert date]* *NB: date must be at least 1 month from initiation of treatment.* The next blood monitoring is due on *[insert date]* and should be continued in line with the shared care guideline.

Please respond to this request for shared care, in writing, within 14 days of the request being made where possible.

Specialist* signature: _____

Specialist name (PRINT): _____

Specialist qualification(s): _____
Date: _____

** A healthcare professional with training and expertise in managing lithium. This may include a consultant, doctor, nurse or pharmacist.*

Appendix 2: Shared Care Agreement Letter (Primary Care Prescriber to Specialist)

Primary Care Prescriber Response

Dear *[insert Doctor's name]*
Patient *[insert Patient's name]*
NHS Number *[insert NHS Number]*
Identifier *[insert patient's date of birth and/oraddress]*

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

Medicine	Route	Dose & frequency

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

Primary Care Prescriber signature: _____

Primary Care Prescriber name (PRINT): _____

Date: _____

Primary Care Prescriber address/practice stamp

Appendix 3: Shared Care Refusal Letter (Primary Care Prescriber to Specialist)

Re:

Patient	*[insert Patient's name]*
NHS Number	*[insert NHS Number]*
Identifier	*[insert patient's date of birth and/oraddress]*

Thank you for your request for me to accept prescribing responsibility for this patient.

In the interest of patient safety, NHS Frimley ICB, in conjunction with local acute trusts have classified *[insert medicine name]*as a Shared Care medication, and requires a number of conditions to be met before transfer can be made to primary care.

Shared care is a term used within the NHS to describe the situation where a specialist doctor wishes to pass some of the patient's care, such as prescription of medication, over to their general practitioner (GP). This is something that can be requested but the guidance is that this may only be done if the GP agrees. The GP will need to consider a number of factors to decide if this is safe.

If care is transferred, from this point the primary care prescriber will be responsible for the prescriptions they sign. The GMC states that when taking on prescribing, all clinicians must keep informed about the medications they prescribe. They need to be able to recognise serious and adverse side effects and ensure that appropriate clinical monitoring arrangements are in place. They must also ensure adequate monitoring. This is a significant responsibility and decisions must be made carefully bearing this in mind.

GPs need to be mindful of focussing on undertaking essential services to put patients first and foremost before agreeing to take on extra work; not working beyond their competences or over safety limits.

If a GP feels that it is not appropriate for any reason for them to take over this extra work, then appropriate arrangements for the continuing care of the patient would be as a default that the prescribing should remain with the specialist service.

I regret to inform you that in this instance I am unable to take on responsibility due to the following:

Please do not hesitate to contact me if you wish to discuss any aspect of my letter in more detail.

Yours sincerely

Primary Care Prescriber signature: _____

Primary Care Prescriber name (PRINT): _____

Date: _____

Primary Care Prescriber address/practice stamp