Berkshire West Integrated Care System
Representing
Berkshire West Clinical Commisioning Group
Royal Berkshire NHS Foundation Trust
Berkshire Healthcare NHS Foundation Trust
Berkshire West Primary Care Alliance

Prescribing Guidelines

*Prescribing arrangement for the management of patients transferring from **Secondary Care to Primary Care***

Lithium Prescribing Arrangements

[APC PG 010a]

For the latest information on interactions and adverse effects, always consult the latest version of the Summary of Product Characteristics (SPC), which can be found at: http://www.medicines.org.uk/

Approval and Authorisation

Approved by	Job Title	Date
Drug and Therapeutics Committee, BHFT	DTC Chair	March 2018
BW Area Prescribing Committee	G Braham, Chair	January 2019
GP MOC	GP MOC Chair	January 2019

Change History

Version	Date	Author	Reason
v.2.0	August 2015	O Tahir	Update of September 2010 lithium shared care guidelines
v.2.1	July 2016	O Tahir	Review following updated NICE Guidance CG185.
v.3.0	February 2018	O Tahir	Review and update

This prescribing guideline remains open to review considering any new evidence.

This guideline should only be viewed online and will no longer be valid if printed off or saved locally

Prescribing Arrangements for the use of Lithium in Berkshire

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Reviewed By	Ozma Tahir	Lead Medicines Information and Clinical Economy Pharmacist, BHFT
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SHARED CARE CAN ONLY BE INITIATED ONCE THE GP HAS RECEIVED A WRITTEN COPY OF THE SHARED CARE PRO-FORMA FROM THE PSYCHIATRIST – The specialist should also indicate if advice for a particular patient differs to the standard shared care arrangements

Useful information for patients (including easy read leaflets), carers and clinicians about lithium, bipolar disorder and other mental health conditions can be found at the BHFT "choice and medication" website:

www.choiceandmedication.org.uk/berkshirehealthcare

Useful Contacts – Medicines Information, Pharmacy Department, Prospect Park Hospital, RG30 4EJ. Telephone number: 0118 9605075

1.1 Introduction

Lithium is indicated for long term treatment of bipolar disorder[1] used as either monotherapy or in combination with other mood stabilisers, where patients experience frequent relapse or remain functionally impaired. As lithium is considered an 'amber' medicine in the Berkshire West joint Formulary, treatment should be initiated under the supervision of a specialist in psychiatry and care may be transferred to primary care by way of a shared care agreement.

Licensed indications include:

- Treatment of hypomania and mania
- Prevention of recurrent affective episodes in bipolar illness and unipolar recurrent depression
- Augmentation of antidepressants for unipolar or bipolar depression
- Treatment of aggression or self-harm, particularly in learning disability

Lithium is also used as an adjunct in the treatment of schizoaffective disorder (although this is an unlicensed indication).

Effective prophylaxis helps patients function as well as possible at home. This can be better supported when their GP prescribes lithium in the community. This shared care guideline details how monitoring and management arrangements should be implemented to support the safe and effective use of lithium. Patients may require periodic review with their specialist mental health practitioner so it is essential to maintain good communication between primary and secondary care prescribers.

1.2 Template form for Specialist to complete and send to GP – See Appendix 2.

1. GP Responsibilities

For patients referred <u>from</u> primary care (new patients registering with GP practice or first presentation):

- GP to send Psychiatrist a summary with the referral letter, which includes; allergy status, list of current repeat medications, co-morbidities (in particular cardiac disease), recent investigations
- Relevant medical history including details of events leading up to referral

2. Secondary care specialist responsibilities

2.1 Initial Consultation:

- Confirm diagnosis
- Check medical history
- Check co-morbidities for contraindications
- Check medications for interactions and/or cautions
- Do ECG if considered clinically appropriate
- Specialist to arrange for extra scans/monitoring including; EEG, MRI or CT scan if organic aetiology suspected or drug screen and chest X-Ray where indicated

- Provide patient with a blood request form to check; FBC, blood glucose, lipid profile, renal, liver and thyroid function. Advise patient to make appointment with GP or go to local acute hospital for required blood tests as soon as possible.
- Female patients of child bearing age must be advised about speaking to their GP about using reliable contraception and if appropriate, exclude pregnancy.
- Provide patient with NPSA lithium information pack (which includes; information booklet, alert card and record book) with additional verbal advice and/or written information leaflets – as considered appropriate to patient's preference. Patient must also be advised that erratic concordance or rapid discontinuation may increase the risk of manic relapse.
- Discuss and agree with the patient if they would like to receive copies of their blood test results.

2.2 Second and subsequent consultations:

- Arrange for a blood test for plasma levels of lithium (if required), 5-7 days after starting and after *every* dose change. The patient should be informed that the blood sample is required 12 hours after the last dose of lithium taken, to ensure plasma levels reflect true 'trough' values (for once daily dosing). For patients who are prescribed lithium twice daily, they should be advised to take their morning dose AFTER the blood test.
- Patients should be told about common side effects/symptoms of toxicity. Also to contact their GP, urgently (same/next day) if they develop;
  - diarrhoea and/or vomiting (for any reason)
  - polydipsia and/or polyuria
- Patients should be told about; the importance of maintaining adequate fluid intake, avoiding low sodium diets, NOT to use *oral or topical* Non-Steroidal Anti-Inflammatory Drugs (NSAIDs) which are available over the counter from pharmacies without first consulting the GP.
- If an NPSA lithium information pack has not been issued at initial consultation, then ensure it is given at this second visit and that the patient is counselled accordingly. Details of discussion and issue of pack to be documented in the patient's RiO notes.
- Discuss shared care with the patient and agree handover to GP.

When the Specialist considers the patient clinically stable, they can send a request for shared care to the patients GP (1.2 Template letter – see above).

3. GP responsibilities

3.1 For patients where shared care proposal has been accepted, from Consultant Psychiatrist:

- To continue to monitor the patient in accordance with this document, BHFT prescribing guidelines and NICE including an annual check-up (with blood tests detailed below).
- According to the manufacturers of Priadel® (see link below), the SPC states;
  '**Monitoring recommendations**
  Before starting treatment with lithium, renal function, cardiac function and thyroid function should be evaluated. Patients should be euthyroid before initiation of lithium therapy. Lithium therapy is contraindicated in patients with severe renal insufficiency or cardiac insufficiency.
  Renal, cardiac and thyroid functions should be re-assessed regularly during treatment with lithium.'

- To check blood test results on the local pathology laboratories database when requested to issue a repeat prescription.
- If these are normal, to issue repeat prescriptions for lithium (always using brand name and form) after dose is stabilised and document this in the patient's case notes.
- To monitor symptom control, adverse effects and check the patient understands the drug information previously given.
- To be aware of interactions with other medicines if prescribed and to adjust lithium dose and monitor levels appropriately. There is a linear relationship between dose and level.
- To take a lithium blood level if; patient starts new interacting medication, urgently if physically unwell/sick, or showing signs/symptoms of toxicity.
- If a patient contacts GP regarding physical illness (vomiting/diarrhoea), they should be advised to omit or reduce their dose until a blood test result can be obtained. Dose reduction or omission should be at the clinical discretion of the GP.
- Please encourage/remind patients to bring the NPSA Lithium record book to all medical appointments, so that the blood test results may be entered and the record kept up to date
- Conduct an annual health check (as set out in 4.3 below, for patients with a diagnosis of bipolar illness) and send results to the patients nominated care coordinator and Psychiatrist, for addition to secondary care records[4]

3.2 *For patients where GPs have agreed to initiate lithium at the request of the Consultant Psychiatrist*:*

- There are some instances where for the convenience of the patient, the GP agrees to carry out the initiation of lithium under the instruction of the Outpatient Clinician. GPs may be asked to issue prescriptions and monitor in accordance with section 4; 'Prescribing Information' below.

4. Prescribing information

4.1 Initiating lithium

Priadel® tablets, lithium carbonate: Treatment and prophylaxis
ADULT over 18 years, initially 0.4–1.2 g daily as a single dose or in 2 divided doses, ELDERLY or patients less than 50 kg, initially 200–400 mg daily.

Priadel® Liquid, sugar-free, lithium citrate tetrahydrate 520 mg/5 mL (approx. Li+ 5.5 mmol/5 mL)
Treatment and prophylaxis, ADULT over 18 years, initially 1.04–3.12 g daily (10-30ml) in 2 divided doses; ELDERLY or patients less than 50 kg, 520 mg twice daily;

If patient requires a liquid preparation, then the equivalent lithium carbonate dose would be 200mg *twice daily* (or 100mg *twice daily* for older/renally impaired patients).

Note
Lithium citrate tetrahydrate 520 mg is equivalent to lithium carbonate 204 mg

*4.2 Procedure for GP Initiation (where agreed)

1. When the decision is taken to initiate lithium treatment as an outpatient and the patient has consented, *it is the responsibility of the Outpatient Psychiatrist to give the patient their purple lithium information booklet out of the Purple Pack and record this in the patient's notes.* A Patient Information leaflet for lithium must be printed off from the Trust Intranet and given to the patient with attention drawn to interactions with other medicines such as antacids containing sodium, and advice on water and salt intake.

2. The Outpatient Psychiatrist should consult with the patients GP and obtain their agreement to initiate and continue lithium prescribing.

3. The GP is then requested to order the following tests: Urea and Electrolytes, Creatinine, Thyroid Function. An ECG should be advised if there is a history of cardiac disease or the patient has cardiovascular risk factors. The height and weight of the patient must be recorded in the notes.

4. If the blood results are within normal range then lithium treatment can be prescribed. The initial dose and the blood results must be recorded in the purple record book and the Pack, including the contact details card, given to the patient. The contact details and patient demographics must be also completed by the prescriber.

5. The patient will need to show the results record book to the community pharmacist when presenting a lithium prescription for medication to be dispensed and bring it with them to every appointment with the GP. Lithium should be prescribed by brand, as it is well established that switching brands can result in adverse effects due to differences in bioavailability. Within BHFT, the Priadel® brand is routinely used for consistency.

6. If the blood results are not within normal range then specialist advice should be sought and lithium must NOT be started.

7. After initiating treatment a lithium level must be taken after one week.

8. A dose change can be initiated after receiving the blood result. Both the first level and the new dose must be entered into the patient's results record booklet.

9. Until a stable dose and satisfactory blood level (usually 0.4 -0.8mmol/l) is achieved, the patient's lithium level must be measured one week after each dose change. Each time results and dose must be entered into the results record booklet.

10. For the first year of therapy, lithium levels should be measured every 3 months, then after a year, every 6 months unless the patient is higher risk, i.e. people who:
- are older
- prescribed medicines which interact with lithium
- at risk of impaired renal or thyroid function, raised calcium levels or other complications
- have poor symptom control
- poorly concordant
- have had previous elevated plasma levels (last level > 0.8mmol/L)

11. Undertake more frequent tests if there is evidence of clinical deterioration, abnormal blood test results, a change in sodium intake, or symptoms suggesting abnormal renal or thyroid function such as unexplained fatigue, or other risk factors, for example, if the patient is starting medication such as ACE inhibitors, non-steroidal anti-inflammatory drugs, antacids or diuretics.

12. Arrange thyroid and renal function tests every 6 months, and more often if there is evidence of changed thyroid or impaired renal function.

13. Enter the dates of future tests into the clinic diary with prompts for obtaining and checking results one week later.

14. Initiate closer monitoring of lithium dose and blood serum levels if urea and creatinine levels become elevated, and assess the rate of deterioration of renal function. The decision whether to continue lithium depends on clinical efficacy, and degree of renal impairment; prescribers must consider seeking advice from a renal specialist and a clinician with expertise in the management of bipolar disorder on this.

15. ***In complex shared care arrangements the important principle that the prescriber monitors must always be adhered to.***

4.3 Particular management considerations with lithium

Consideration	Risks with lithium	Management Strategy
Elderly patients	Adverse reactions at serum levels ordinarily tolerated by younger patients. Also levels higher for given dose if poor renal function.	Aim for lower lithium levels (see below) paying particular attention to side effects.
Hot weather, exercise or work environment	Electrolyte imbalance and lithium toxicity.	Advise patients to maintain fluid intake, and avoid dehydration
Infections, diarrhoea, vomiting	Reduced lithium excretion, risk of dehydration leading to increased lithium levels.	Warn patients to maintain fluid intake. Stop lithium if symptoms of toxicity occur (see below) and check lithium level
Women of childbearing age	May lower fertility. Can be teratogenic and toxic to the foetus though maternal blood levels remain within therapeutic range.	Consult with the Medicines Information Service at Prospect Park Hospital for advice on 0118 9605075
Discontinuation	Rebound mania likely especially if lithium is taken for less than 2 years	Ensure patient is thoroughly informed of risks before treatment commences and do not initiate if compliance is likely to be erratic. If possible, discontinuation should be over at least 4 weeks.
Major surgery	Lithium prolongs actions of muscle relaxants	Lithium should be discontinued 24hours before surgery and restarted when electrolytes back to normal.
Renal Impairment	Risk of toxicity	GFR ≤ 20ml/min; Avoid if possible. Reduce dose to 50-75% and continue to monitor levels closely. GFR < 10ml/min; Avoid if possible. Reduce dose BY 50-75% and continue to monitor levels closely.

4.4 Target Plasma levels

	Plasma Level 12 hours post dose once a day dosing	Plasma Level 12hours post dose twice daily dosing
Initial target	0.6 to 0.8 mmol/L	0.4 to 0.6 mmol/L

Increased if response suboptimal to:-	0.8 to 1.0 mmol/L	0.6 to 0.8 mmol/L
Elderly	0.4-0.6 mmol/L Symptoms of toxicity may develop at standard therapeutic blood levels	
Children and adolescents	May need higher plasma levels	

On average, plasma levels fall by about 0.2mmol/L between 12 and 24 hours post dose.

Levels between 0.4mmol/L and 0.6mmol/L may be effective for prophylaxis in some people.

The serum level should not exceed 1.5 mmol/L.

4.5 Monitoring Requirements

(Based on NICE Clinical Guideline CG185; monitoring requirements for all patients with diagnosis of Bipolar Affective Disorder. These monitoring requirements also apply to patients who are prescribed lithium for other indications**)**
Ensure every patient is given the NPSA lithium information booklet, alert card and record book at initiation.

Test or measure	**Frequency**	**Comments**
Serum lithium level	7 days after every dose/ formulation change until stable or when starting or stopping an interacting medicine. 3 monthly for first year 6 monthly thereafter **(unless high risk – see section 4.2.10)**	See above
Thyroid function	Every 6 months*****	Can cause hypo/hyperthyroidism. May need to supplement with thyroxine
Lipid profile	Annual if over 40yrs	
Smoking/ alcohol status	Annually	
Renal function (U+Es, creatinine and eGFR)	Every 6 months******	20% have a small reduction in GFR usually benign but some may develop interstitial nephritis. Nephrogenic diabetes insipidus also possible. Initially reversible but may be irreversible after 15 yrs
Plasma glucose	Annually	This can rise with treatment and with diabetes insipidus

Blood pressure	Annually* (at least)	
Weight	Annually - unless increasing rapidly then more frequently	Weight increases mostly in first 2 years. 2nd most common reason for non-compliance. May be due to increased thirst. Lithium increases insulin secretion
Serum calcium, magnesium	Annually (after long term treatment)	Lithium may cause hyperparaththyroidism

* More frequently if deterioration or problems detected
** More frequently if patient starts taking any interacting drug, eg NSAIDs, ACE-inhibitors or diuretics

4.6 Side Effects and Toxicity

General principles

- The minimum clinically effective dose of lithium should always be used.
- Side effects are usually related to serum lithium concentration and are less common in patients with plasma lithium concentrations below 1.0mmol/l.
- Even a modest acute overdose in a patient on chronic lithium therapy may lead to serious toxicity as the extra vascular tissues are already saturated with lithium.
- Toxic effects reliably occur at >1.5mmol/L usually consisting of GI effects (anorexia, nausea vomiting and diarrhoea) and CNS effects (muscle weakness, drowsiness, ataxia, tremor and muscle twitching). Serum levels >2mmol/L can result in disorientation, seizure, coma and death[9].
- Mild gastrointestinal symptoms when therapy is initiated are usually transient.
- Elderly patients are more susceptible to side effects.
- Many side effects require little action other than more intensive monitoring of blood levels and reduction in dose.
- High serum concentrations of lithium including episodes of acute lithium toxicity may aggravate cardiovascular, CNS, dermatological, endocrine, gastro-intestinal, haematological, and renal changes
- In patients who develop polyuria and/or polydipsia, renal function should be monitored more intensively, with measurement of blood urea, serum creatinine and urinary protein levels in addition to the routine serum lithium assessment.
- The onset of symptoms may be delayed for 24 hours if a sustained release preparation is used.
- The risk of toxicity is greater in patients with hypertension, diabetes, congestive, heart failure, chronic renal failure, schizophrenia, or Addison's disease.
- Monitor the patient at every appointment for symptoms of neurotoxicity, including paraesthesia, ataxia, tremor and cognitive impairment, which can occur at therapeutic levels of lithium.
- In chronic kidney disease, the level of protein in the urine can be an indicator of nephrotoxic effects as the eGFR may not alter in the same way as patients without renal impairment. Proteinuria can also indicate other diagnoses such as infection. If proteinuria is detected then referral to a renal physician would be recommended[8].

Contact the Medicines Information Service at Prospect Park Hospital for further advice on 0118 960 5075.

Refer to Summary of Product Characteristics for information about cautions, adverse effects, monitoring, toxicity etc.:

http://www.medicines.org.uk/emc/medicine/25501/SPC/Priadel+200mg+prolonged+release+tablets./

4.7 Preparations available

Brand	Form	Strengths available
Priadel®	tablet	200mg and 400mg
Priadel®	liquid	520mg in 5ml approx. 5.4mmol/5ml
Camcolit®	tablets	250mg and 400mg
Liskonium®	tablet	450mg
Li-Liquid®	liquid	509mg/5ml(5.4mmol/5ml)& 1.018g/5ml(10.8mmol/5ml)

NB:

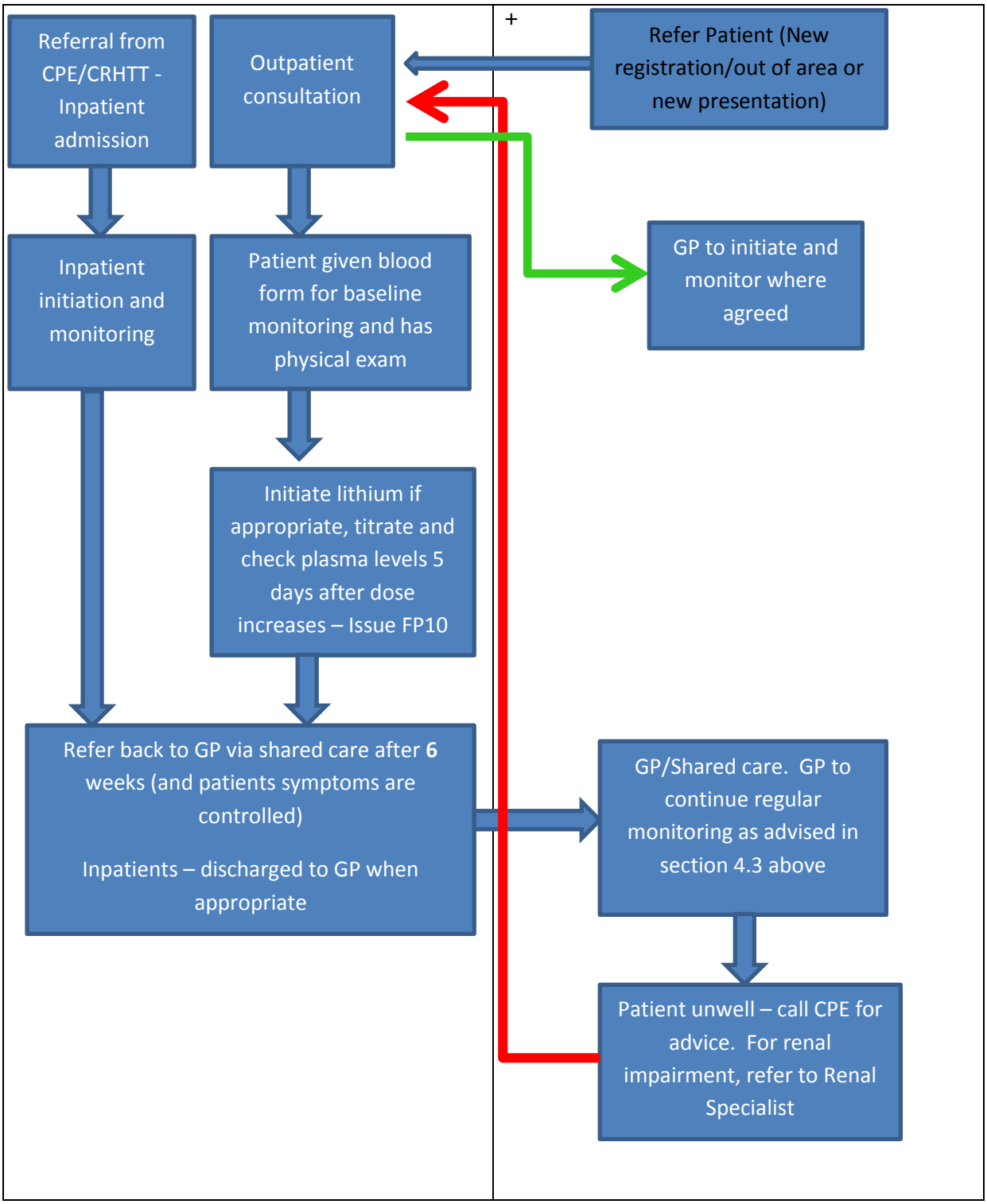
- Prescriptions should **always** state the prescribed brand name.
- Lithium brands are not interchangeable. Preparations vary widely in bioavailability
- Liskonium® and all liquid preparations should be taken TWICE DAILY as they are not sustained release.
- BHFT currently uses Priadel® brand of lithium.
- Inpatients admitted to BHFT will be considered for switching to Priadel®.
- 200mg Lithium Carbonate is equivalent to 509mg Citrate or 5.4 mmol Lithium.
- When prescribing liquids it is important to specify strength not just volume.

References

1. Martin J. BNF accessed online March 2015
2. Taylor D. et al The South London and Maudsley NHS Foundation Trust and Oxleas NHS Foundation Trust Prescribing Guidelines. 11th Ed. Informa Healthcare 2011 London.
3. National Institute for Health and Clinical Excellence Guideline 185 Bipolar disorder: The assessment and management of bipolar disorder in adults, children and adolescents, in primary and secondary care. Issued September 2014, updated Feb 2016 www.nice.org.uk
4. Summary of Product Characteristics for Priadel (Sanofi-aventis) Last updated 01/02/2018 via www.emc.medicines.org.uk
5. Bazire S. Psychotropic Drug Directory 2016 Healthcomm UK. Aberdeen
6. The Renal Drug Database. Accessed online January 2018
7. Guidelines for the Prescribing and Monitoring of Inpatient Lithium Therapy. Sussex partnership foundation trust. Updated: March 2017

Appendix 1: **'How to initiate lithium' algorithm**

BHFT	Primary Care


Referral from CPE/CRHTT - 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 exam
GP to initiate and monitor where agreed
Initiate lithium if appropriate, titrate and check plasma levels 5 days after dose increases – Issue FP10
Refer back to GP via shared care after 6 weeks (and patients symptoms are controlled)
Inpatients – discharged to GP when appropriate
GP/Shared care. GP to continue regular monitoring as advised in section 4.3 above
Patient unwell – call CPE for advice. For renal impairment, refer to Renal Specialist

Appendix 2: **Template form for Specialist to complete and send to GP**

This form is a request for the General Practitioner to take over the prescribing of lithium under the 'BHFT Lithium Shared Care Guidelines'			
GP			
Patient's Name			
NHS number		**Date of Birth**	
Patient weight (kg)		**Estimated duration for prescribing to be continued by GP**	
Diagnosis			
Lithium dose and preparation			
Date lithium initiated		**Last lithium plasma level (mmol/L)**	
Indication			
Date of last lithium level		**Target lithium plasma range (mmol/L)**	
Additional comments/advice from Consultant Psychiatrist			

Investigations done at initiation		**Continued monitoring by GP (increase frequency where needed)**		**Comments**
Lithium plasma level	See above	**Every 3 months**		
U&Es	Yes/No/NAD	**Every 6 months**	**Every 3 months for elderly and renally impaired**	
eGFR	Yes/No/NAD	**Every 6 months**		
Thyroid Function Tests	Yes/No/NAD	**Every 6 months**		
ECG needed?	Yes/No/NAD	**According to risk**		
FBC	Yes/No/NAD			
Serum calcium/magnesium	Yes/no/NAD			

We accept shared care responsibilities		
	Name/Contact number/email	**Signature and date**
Patient		
Consultant Psychiatrist		
GP		

This form should be signed by the GP then returned to the Consultant Psychiatrist and a copy be filed in patients notes.