SHARED CARE ARRANGEMENT AND PRESCRIBING INFORMATION FOR LITHIUM TREATMENT

N.B. This document should be read in conjunction with the current Summary of Product Characteristics (SmPC).

Patient safety is paramount. The prescriber who prescribes the medicine legally assumes clinical responsibility for the drug and the consequences of its use.

GENERIC AND BRAND NAME (formulations and strength)

Name: Lithium (Priadel®)

Formulation: Tablet (lithium carbonate) or liquid (lithium citrate). There are bioavailability differences between the different brands and different formulations so lithium **must** be prescribed by brand name. **Note:** Lithium citrate (Priadel®) 520mg is equivalent to lithium carbonate (Priadel®) 204mg.

Strength: 200mg or 400mg tablets, Liquid 104mg/1mL

STATUS OF MEDICINE

Licence status: Licensed

Formulary status: Formulary

Black triangle medicine: Yes ☐ No ☒

Risk minimisation materials (RMM): Yes ☐ No ☒

CONDITION(S) TO BE TREATED

- Management of acute manic or hypomanic episodes.
- Management of episodes of recurrent depressive disorders where treatment with other antidepressants has been unsuccessful.
- Prophylaxis against bipolar affective disorders.
- Management of aggressive or self-harming behaviour.

TYPICAL DOSAGE REGIME

Licensed dose	**NOTE**: Dose must be adjusted to achieve serum-lithium concentration of 0.4 to 1mmol/L. The minimum effective dose should be sought and maintained.
Route of administration	Oral
Recommended starting dose	

Body Weight	Priadel® Tablets	Priadel® Liquid
Adults (body-weight up to 50kg)	Initially 200-400mg daily	Initially 520mg twice daily
Adults (body-weight 50kg and above)	Initially 0.4-1.2g daily	Initially 1.04 -3.12g daily in 2 divided doses
Elderly	Initially 200-400mg daily	Initially 520mg twice daily

Titration dose/increment	Dosage must be individualised depending on serum lithium levels and clinical response. The dosage necessary to maintain serum lithium levels within the therapeutic range of 0.4 to 1mmol/L varies from patient to patient.
Maximum dose	Dependant on individual patient.
Situations requiring dose adjustment	See Appendix 1
Duration of treatment	Individual to each patient.

NOTE: The psychiatric and general practice records of each patient should allow identification of all patients on lithium therapy. The GP is responsible for ensuring that the general practice records clearly indicate that a patient is on lithium therapy. All therapeutic indications for lithium treatment would also be reasons for including the patient on the practice Mental Health Register. Responsibility for monitoring and follow-up arrangements of the individual patient must be agreed between the specialist and general practitioner. This should be documented in both psychiatric and general practice patient records.

When writing laboratory request forms always include details of the patient's medication

RESPONSIBILITY OF ACUTE CARE/SPECIALIST SERVICE

- Exclude any co-morbidity or concomitant medication which would contraindicate the prescribing of lithium. For patients being initiated at an out-patient clinic liaise with GP to arrange baseline monitoring and to exclude any comorbidities which would contraindicate the prescribing of lithium.
- Any potential drug interactions should also be identified.
- Ensure patient receives appropriate counselling on lithium therapy prior to initiation of treatment and record in the case notes. Patients should be provided with an appropriate patient information leaflet. The NHS Inform website is recommended.
- For women of childbearing potential the risks and benefits in relation to childbearing must be discussed fully prior to prescription and consent appropriately recorded. Discussion should include review of contraception status and advice/signposting on effective contraception for the duration of prescribing, with preference for long-acting reversible methods. The 'BUMPS' website should be used to reinforce verbal information. This should be revisited annually.
- Ensure baseline monitoring is performed and satisfactory. This should include the patient's weight or BMI, tests for urea and electrolytes including calcium, estimated glomerular filtration rate (eGFR), thyroid function and an electrocardiogram (ECG) for people with cardiovascular disease or risk factors for it.

Liaison with GP

For all patients liaise with GP to ensure responsibility for monitoring and follow-up arrangements are agreed and documented in both psychiatric and GP patient records.

Prescribing and Monitoring of Lithium

- Lithium should always be prescribed by brand name (due to variance in bioavailability).
- Dose should be adjusted to achieve serum-lithium concentration of 0.4 to 1mmol/L.

- Sample taken 10 to 14 hours post dose after 5 - 7days of treatment. Additional levels should be taken 5 - 7 days after any dose change until therapeutic levels are obtained and every 3 months thereafter.

Prescribers must check that blood tests are monitored regularly and that it is safe to issue a lithium prescription.

Supply GP with information regarding:
- Therapeutic indication for this patient and target serum lithium.
- Brand of lithium/dosage/frequency of administration.

Referral letter to GP should reference:
- The NHSG Shared Care Agreement and Prescribing Information for Lithium, which can be downloaded from the intranet.
- Whether this prescription is part of a care plan under the Mental Health (Care and Treatment) (Scotland) Act 2003 and a copy of the relevant paperwork if so.

RESPONSIBILITY OF PRIMARY CARE GENERAL PRACTITIONER

A Practice agreeing to prescribe lithium should:

Ensure the practice records clearly indicate that a patient is on lithium therapy and the patient is included in the practice Mental Health Register.

Ensure no medication is prescribed which is contraindicated with lithium treatment.

Prescribing and Monitoring of Lithium

Prior to prescribing lithium check that blood tests have been monitored regularly and that it is safe to issue a repeat prescription.
- Lithium should always be prescribed by brand name (due to variance in bioavailability).
- Serum lithium level should ideally be checked 10 to 14 hours after the most recent dose. It is important to record the time interval between the sample being taken and the last dose.
- Serum lithium levels should be maintained between 0.4 and 1.0mmol/L when taken **10 to 14 hours** after the most recent dose **unless** another range is deemed appropriate for an individual patient. It is recognised that some patients remain well on lower or higher serum levels.
- **Once a patient is stabilised on lithium therapy** the General Practitioner has primary responsibility for monitoring therapy according to Appendix 1. Further guidance can be found at NICE Clinical Guideline 185: Bipolar disorder: assessment and management and NHS Scotland Lithium Monitoring March 2019.

At every clinical contact:
- Side-effects (check if recent diarrhoea and vomiting or dehydration/over-hydration due to other causes).
- Signs and symptoms of toxicity (all episodes of toxicity must be clearly noted in the patient's clinical records and discussed with patients).
- Interacting drugs.

Where serum lithium levels are within reference range the following should be checked (as a minimum)

Every 3 months:

- Serum-lithium level.

Every 6 months:
- Electrolytes including calcium.
- EGFR.
- Thyroid function tests.
- Weight/BMI.

Annually:
- Yearly health check.
- Women of reproductive age – discussion of childbearing intentions and contraceptive status.

NOTE: More frequent monitoring may be required in the elderly.

More frequent monitoring should be undertaken in the following situations:
- Change of lithium dose or formulation.
- On development of intercurrent illness/disease.
- Signs of manic or depressive relapse.
- Following significant change in sodium or fluid intake.
- Signs of lithium toxicity.
- Evidence of deterioration of renal function or thyroid function.
- Raised calcium levels.
- Co-prescription of drugs that interact with lithium therapy.

Key points regarding monitoring:
- Relevant monitoring requirements should be undertaken at the correct frequency.
- Test results should be checked for any abnormality as soon as they are available and prior to prescribing lithium.
- Abnormal results should be acted upon without delay.
- Be alert for any of the known adverse reactions.
- Only continue to prescribe lithium if it is being satisfactorily monitored.
- Contact the specialist in the event of an adverse drug reaction, monitoring abnormality or any other issues causing concern.
- Patients should be encouraged to ensure that they attend for blood tests at the correct intervals.

RESPONSIBILITY OF THE PATIENT

- Take lithium regularly as directed by the prescriber.
- Attend for blood test as requested by specialist/phlebotomist/GP practice.
- Report any adverse effects/illness to the prescriber.
- **Missed dose:** If a dose is omitted or forgotten **do not** take a double dose. The next dose should be taken at the normal time.

PRESCRIBING INFORMATION

For specific product information consult the current summary of product characteristics (http://emc.medicines.org.uk/), the BNF/BNF for Children (https://www.medicinescomplete.com/mc/index.htm)

Other information

- Bioavailability varies between brands of lithium. To ensure that there is continuity in the product taken patients should be prescribed lithium by brand name and not by generic name.
- Lithium carbonate 250mg tablets and lithium citrate oral solution/liquid are not modified-release preparations and should be given twice a day.

CONTRAINDICATIONS

- Hypersensitivity to the lithium or to any of the excipients.
- Cardiac disease.
- 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.

PREGNANCY

Avoid if possible. Evidence of harm to foetus. Discuss with specialist.

BREAST-FEEDING

Manufacturer advises avoid. Lithium is present/excreted in breast milk. Risk of toxicity in the infant.

COMMON SIDE EFFECTS AND THEIR MANAGEMENT

Side effects of lithium	Signs of lithium toxicity
Gastro-intestinal upset particularly at the start of treatment; fine hand tremor; metallic taste in mouth; weight gain; oedema; polydipsia and polyuria; hypothyroidism; impaired renal function.	Course tremor; nausea and diarrhoea; muscle weakness; ataxic gait; myoclonic jerks; dysarthria; blurred vision; confusion; excess sedation.

COMMON DRUG INTERACTIONS (for a full list see SmPC)

There are a number of drug interactions that must be considered when a new drug is prescribed. Interacting drugs include:

- ACE inhibitors and angiotensin-II receptor antagonists increase serum-lithium concentration.
- Diuretics - increase serum-lithium concentration and risk of toxicity.
- NSAIDs including COX-2s - increase risk of toxicity.
- Certain Over the Counter products also interact with lithium. Advise patient to check with community pharmacist.

This list is not exhaustive please see the SmPC and Stockley's Drug Interactions for more information.

ADVERSE DRUG REPORTING

If an adverse reaction should occur inform relevant medical practitioner as soon as possible.

Report to the MHRA using the Yellow Card System https://yellowcard.mhra.gov.uk/

REFERENCES

- MHRA Products | Home
- BNF British National Formulary - NICE
- NICE Clinical Guideline 185: Bipolar disorder: assessment and management
- NHS Scotland Lithium Monitoring March 2019

ACUTE CARE/SPECIALIST SERVICE CONTACT INFORMATION

In the event of a concern being raised, the primary care practitioner should contact the referring specialist via the hospital switchboard, via their secretary, by e-mail or letter, whichever is more appropriate. If the concern is urgent, and out of hours advice is required, the on call specialist may be contacted via switchboard.

<table>
<tr><td>Publish:
public</td><td>Applies to:
NHS Grampian</td><td>Version: 4</td></tr>
<tr><td>Prepared by:
Angela MacManus</td><td rowspan="2">Authorised for issue by:
NHSG Medicine Guidelines and Policies Group</td><td>Document no:
NHSG/SCA/Lith/MGPG1164</td></tr>
<tr><td>Job title:
MHLDS Principal Pharmacist</td><td>Effective date: June 2021

Review Date: June 2024</td></tr>
<tr><td>Signature:
Angela MacManus
Date: June 2021</td><td>Signature:
Lesley Coyle
Date: June 2021</td><td>Supersedes:
NHSG/SCA/Lith/MGPG923</td></tr>
<tr><td colspan="3">Review/Consultation Group: This document has been reviewed and approved by the MHOMMG.</td></tr>
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Appendix 1 – Monitoring of Lithium Action to be Taken

Parameter/ test	Frequency	Action/suggested action if outside reference range
Lithium levels	**3 monthly** Trough samples for routine monitoring should be taken 10 to 14 hours after the last dose. Additional levels should be taken 5 – 7 days after the initial dose, after any dose or formulation change or introduction/discontinuation of interacting medication or if there is a suspicion of toxicity.	Confirm the timing of the blood test and compliance with lithium. Review treatment and adjust dose if clinically indicated. Lithium toxicity is defined as any lithium level >1.2mmol/L. However it should be noted that some patients may exhibit toxicity at lower doses e.g. >65year olds. **Clinical signs of toxicity** include gastrointestinal effects (increasing anorexia, nausea and diarrhoea), course tremor, ataxia, dysarthria, nystagmus, renal impairment, confusion and convulsions. **If serum level exceeds 1.2mmol/L** Check for signs of toxicity. If present a lithium level should be taken urgently and lithium withheld until it is considered clinically safe to continue with treatment. Admission to the general hospital should be considered as lithium toxicity is a medical emergency. If there are no signs of toxicity recheck the level and STOP lithium in the interim. Inform the consultant and seek an urgent review of the patient (further actions as below). **If serum level is HIGH (>l.0mmol/L <1.2mmol/L) and NO SIGNS OF TOXICITY** If there is an explanation for the high level (e.g. dehydration; dose taken within 10 hours of blood test), recheck serum lithium level. If level is part of a pattern of high levels that have bordered on being too high, decrease the dose and recheck serum lithium level after 5-7 days. If no clear explanation for high level, recheck serum lithium level in tandem with renal function, a deterioration of which may account for the high serum level. Lithium dose would then need to be reduced or stopped. **Please discuss with specialist.** Check also for changes in salt intake or the use of prescribed or over-the-counter medication which may interact with lithium.

Parameter/ test	Frequency	Action/suggested action if outside reference range
		If serum level is LOW (<0.4mmol/L) If sample taken outside 10 to 14 hour window, recheck the serum lithium level within the correct window. If patient has remained well at low levels and maintaining the patient at low serum levels is part of an overt management plan recorded in the case notes – do nothing. If non-compliance is suspected as the cause (e.g. with several normal levels and then a 'one-off' drop, or with widely varying levels) then contact the patient to discuss and then recheck serum lithium level. **If the level is part of a pattern of levels that have bordered on being too low, please discuss with specialist as dose may need to be increased.**
Urea and Electrolytes	**Baseline** Include sodium, potassium, urea, creatinine and eGFR. Patients must have adequate renal function (eGFR>60mL/min) before commencing lithium. Note in some populations the eGFR may overestimate renal function and therefore calculation of creatinine clearance would be more appropriate). **6 monthly** Monitor more frequently if evidence of deterioration, or if the patient is prescribed or takes medicines known to affect renal function e.g. ACE inhibitors, NSAIDs or diuretics.	If eGFR falls rapidly to <45mL/min review lithium treatment and refer to renal medicine. Investigate and correct for hyponatraemia/hypernatraemia.
Thyroid function	**Baseline and 6 monthly** Monitor more frequently if evidence of impaired thyroid function or an increase in mood symptoms that might be related to impaired thyroid function.	Treat as necessary.

Parameter/ test	Frequency	Action/suggested action if outside reference range
ECG	**Baseline only if appropriate** If no cardiac disease or no risk factors then baseline ECG is not necessary. Arrange an ECG for people with cardiovascular disease or risk factors for it.	Highlight and review lithium treatment with the specialist and consider cardiology advice.
Calcium	**Baseline and 6 monthly**	Treat as necessary.
Body mass Index	**Baseline and 6 monthly**	Offer lifestyle advice.
Side-effects	**At every clinical contact** Check if recent diarrhoea and vomiting or dehydration/over-hydration due to other causes.	Review lithium treatment if problematic.
Signs and symptoms of toxicity	**At every clinical contact** Reinforce education on signs and symptoms of toxicity and avoiding dehydration. Lithium toxicity is defined as any lithium level >1.2mmol/L. However it should be noted that some patients may exhibit toxicity at lower levels e.g. >65 year olds.	Check an urgent lithium level and suspend lithium treatment. Lithium treatment can only be re-introduced once toxicity has resolved and if restoration of treatment is then deemed clinically appropriate. All episodes of toxicity must be clearly noted in the patient's clinical records and discussed with patients.
Interacting drugs	Be aware that 'over the counter' medications such as ibuprofen can interact with lithium.	Review all drugs known to affect renal function.
Women of reproductive age	**Baseline and yearly** Lithium is potentially teratogenic. In severe mental illness up to 80% of pregnancies are unplanned. Risks and benefits in relation to childbearing must be discussed fully with all women of childbearing potential prior to prescription and consent appropriately recorded. This should be revisited at	For women of childbearing potential: Discussion of childbearing intentions and contraception status. Advice on risks and benefits in relation to childbearing. Advice/signposting on contraception (incl. LARC). Informed consent provided in writing. The 'BUMPS' website should be used to reinforce verbal information For women who become pregnant on lithium: Do not stop abruptly. Review risks and benefits of continuing treatment or discontinuation. Seek specialist advice regarding ongoing prescribing.

Parameter/ test	Frequency	Action/suggested action if outside reference range
	least annually. Discussion should include review of contraception status and advice/signposting on effective contraception for the duration of prescribing, with preference for long-acting reversible methods.	
Patient and care education	**Baseline and ongoing as necessary**	Provide patients with the education necessary to support informed choice and suited to their individual needs. The NHS Inform and 'BUMPS' websites are recommended.