

SHARED CARE PROTOCOL FOR THE PRESCRIBING AND MONITORING OF LITHIUM

1.0 INTRODUCTION

This protocol sets out guidelines for the assessment and treatment of patients who are prescribed Lithium and the delineated responsibilities when care for the patient is to be shared between Primary Care and Specialist Care.

Shared Care Protocols are intended to provide clear guidance to General Practitioners (GPs) and hospital prescribers regarding the procedures to be adopted when clinical (and therefore prescribing and financial) responsibility for a patient's treatment with a shared-care disease is transferred from secondary to primary care.

GPs, as independent contractors, have the right to decline to take clinical and prescribing responsibilities for a patient on their medical list who is being treated elsewhere. However the reason for this action must be documented, it would be considered exceptional for a GP to refuse to take clinical and prescribing responsibilities for an individual drug, where shared care guidelines for that drug have been adopted by NHS Rotherham CCG

If a specialist asks a GP to prescribe these drugs in relation to this disease, the GP should reply to this request as soon as practicable. The doctor who prescribes the medication legally assumes clinical responsibility for the drug and the consequence of its use.

2.0 BACKGROUND INFORMATION

2.1 INDICATIONS FOR USE

Lithium salts are used for the following indications:

- the prophylaxis and treatment of acute mania
- the prophylaxis of bipolar disorder (manic-depressive disorder)
- concomitant therapy with antidepressant medication in patients who have had an incomplete response to treatment for acute depression in bipolar disorder
- the prophylaxis of recurrent depression (unipolar illness or unipolar depression)
- the control of aggressive behaviour or intentional self-harm

In acute mania, lithium should only be used in patients who have responded to lithium before and whose symptoms are not severe.

The decision to give prophylactic lithium usually requires specialist advice, and must be based on careful consideration of the likelihood of recurrence in the individual patient, and the benefit weighed against the risks. The full prophylactic effect of lithium may not occur for six to twelve months after the initiation of therapy.

2.3 NATIONAL INSTITUTE FOR HEALTH AND CLINICAL EXCELLENCE (NICE)

NICE Clinical guideline CG 38 contains evidence-based guidance on the diagnosis and management of bipolar disorder in adults, children and adolescents, in primary and secondary care. It also gives recommendations for referral to specialist services.

Lithium is included in the following recommendations when drugs are being used to treat bipolar

disorder:

- Lithium, olanzapine or valproate should be considered for long-term treatment of bipolar disorder.

The choice should depend on:

- response to previous treatments
- the relative risk, and known precipitants, of manic versus depressive relapse
- physical risk factors, particularly renal disease, obesity and diabetes
- the patient's preference and history of adherence
- gender (valproate should not be prescribed for women of child-bearing potential)
- a brief assessment of cognitive state (such as the Mini-Mental State Examination) if appropriate, for example, for older people.
- If the patient has frequent relapses, or symptoms continue to cause functional impairment, switching to an alternative monotherapy or adding a second prophylactic agent (lithium, olanzapine, valproate) should be considered. Clinical state, side effects and, where relevant, blood levels should be monitored closely. Possible combinations are lithium with valproate, lithium with olanzapine, and valproate with olanzapine. The reasons for the choice and the discussion with the patient of the potential benefits and risks should be documented.

2.4 PRESCRIBING AND DOSAGE

The BNF recommends that prescribing for lithium is done by **brand name** as preparations vary widely in bioavailability.

Changing the preparation requires the same precautions as initiation of treatment.

In patients of average weight (70kg) a dose of 400-1200mg may be given as a single daily dose in the morning or on retiring. Alternatively, the dose may be divided and given morning and evening. However, dosage must be adjusted on an individual basis.

The objective is to adjust the Lithium dose to maintain serum lithium concentrations as below:

Aim for:

0.6-0.8* mmol per litre normally (may be lower in the elderly)

0.8-1.0 mmol per litre if patient has relapsed previously on lithium or has sub-syndromal symptoms

Levels as low as *0.4mmol per litre can be adequate following approval by the clinician

Blood samples for measurement of serum lithium concentration should be taken 12 hours from the previous dose. The dosage and times of last dose and sample taken should be noted on the Pathology request form.

2.5 ADVERSE EVENTS

Side effects are usually related to serum lithium concentration (serum level's should not exceed 1.5 mmol/l) and are less common in patients with plasma lithium concentrations below 1.0 mmol/l.

These include;

Initial therapy

Fine tremor of the hands, polyuria and thirst may occur

Body as a whole

Muscle weakness, peripheral oedema

Cardiovascular

Cardiac arrhythmia, bradycardia, oedema, sinus node dysfunction, hypotension

Central Nervous System

Ataxia, extrapyramidal symptoms, slurred speech, vertigo

Dermatology

Alopecia, acne, allergic rashes

Endocrine

Hypothyroidism, hyperthyroidism, thyrotoxicosis.

NB. Lithium treatment increases the risk of clinical hypothyroidism up to five- fold, the risk being particularly high in women who are 40-59 years old

Before beginning treatment patient should have their thyroid function evaluated and should be euthyroid before initiation of lithium therapy. Thyroid functions should be re-assessed at baseline, 6 monthly and more often if there is evidence of deterioration.

Gastrointestinal

Nausea, vomiting, diarrhoea, excessive salivation, dry mouth

Haematological

Leucocytosis

Metabolic and nutritional

Weight gain, hyperglycaemia

Renal

Polydipsia and/or polyuria, symptoms of nephrogenic diabetes insipidus Before beginning lithium treatment it is important to ensure that renal function is normal and should be re-assessed periodically.

Reproductive

Sexual dysfunction

Senses

Dysgeusia, (distortion of the sense of taste), blurred vision, scotomata (an area of lost or depressed vision within the visual field, surrounded by an area of less depressed or of normal vision)

Toxicity

Symptoms include nausea, diarrhoea, blurred vision, light headedness, drowsiness, blackouts, increasing confusion, myoclonic twitches and jerks and urinary or faecal incontinence.

Lithium salts have a narrow therapeutic/toxic ration and should therefore not be prescribed unless facilities for monitoring serum-lithium concentrations are available.

Patients receiving long term lithium therapy should be warned by the initiating physician and be given clear instructions regarding the symptoms of impending toxicity.

3.0 DRUG TREATMENT AND MONITORING

3.1 DRUG TREATMENT

1. Antimanic Drugs	Adverse effects	Therapeutic Monitoring Consultant GP	Clinical relevant drug interactions (NB. This is not a full list – refer to the BNF & SPC)
<p>Priadel</p> <p>Lithium Carbonate tablets mr 200mg & 400mg</p> <p>Treatment and prophylaxis: Initially 0.4 – 1.2g daily as a single dose or in two divided doses Elderly or patients less than 50kg: 400mg daily Children: Not recommended</p> <p>Lithium Citrate S/F liquid 520mg/5ml</p> <p>Treatment and prophylaxis: Initially 1.04 – 3.12g daily in 2 divided doses Elderly: or patients less than 50kg: 520mg twice daily</p> <p>Camcolit</p> <p>(Lithium Carbonate 250mg & 400mg tablets)</p> <p>Treatment for adult and child over 12 years: Initially 1 – 1.5g daily Prophylaxis for adult and child over 12 years: Initially 300 – 400mg daily</p> <p>Liskonum</p> <p>(Lithium carbonate mr 450mg tablets)</p> <p>Treatment for adult and child over 12 years: Initially 450 - 675mg twice daily</p> <p>Treatment for elderly: Initially 225mg twice daily Prophylaxis for adult and child over</p>	<ul style="list-style-type: none"> • GI Disturbances • Fine Tremor • Renal impairment • Weight gain • Oedema • Muscle weakness • Overdosage • CNS disturbances 	<p>Baseline assessment before initiation:</p> <ul style="list-style-type: none"> • Weight/Height/BMI • U & E's • Calcium • TFT's • ECG for those with existing cardiac disease or risk factors • Smoking • Alcohol <p>Weekly until stable then 3 monthly</p> <ul style="list-style-type: none"> • Lithium Levels • Renal function in patients with CKD 3a or worse <p>6 monthly:</p> <ul style="list-style-type: none"> • U & E's • TFT'S • Annual • Bone profile <p>After the first year: Lithium levels every 6 months, or every 3 months for people in any of the following groups:</p> <ul style="list-style-type: none"> • older people • people taking drugs that interact with lithium • people who are at risk of impaired renal or thyroid function, raised calcium levels or other complications • people who have poor symptom control • people with poor adherence • people whose last plasma lithium level was 0.8 mmol per litre or higher <p>Annually:</p> <ul style="list-style-type: none"> • Weight/Height/BMI • Blood Pressure • Smoking status • Alcohol use • ACR early morning sample in patients with CKD 3a or worse, or more frequent monitoring as per renal guidelines 	<p>Drugs which would increase lithium concentrations, e.g. Metronidazole, NSAID's, ACE inhibitors, diuretics (particularly thiazides) , drugs affecting electrolyte balance, tetracyclines</p> <p>Drugs which would decrease lithium concentrations, e.g. theophylline, caffeine, sodium bicarbonate containing products, diuretics, urea</p> <ul style="list-style-type: none"> • Neuroleptics • Methyldopa • Calcium channel blockers • Carbamazepine • Indometacin • Phenytoin

<p>12 years: Initially 450mg twice daily Prophylaxis for elderly: Initially 225mg twice daily</p> <p>Li-Liquid</p> <p>(Lithium Citrate oral solution 509mg/5ml)</p> <p>Treatment and prophylaxis for adult and child over 12 years: Initially 1.018-3.054g daily in 2 divided doses Treatment and prophylaxis for elderly or patients less than 50kg: Initially 509mg twice daily</p>		<p>As required if toxicity is suspected:</p> <ul style="list-style-type: none"> • Lithium levels <p>Routinely:</p> <ul style="list-style-type: none"> • Side effects • Symptom control <p>Patients with CKD 3b or worse:</p> <ul style="list-style-type: none"> • liaison with the mental health consultant regarding risk benefit of lithium Re • follow local renal pathway - referral to Nephrology where appropriate <p>Abnormal TFT:</p> <ul style="list-style-type: none"> • liaison with the mental health consultant regarding risk benefit of lithium • manage thyroxine in line with local guidance 	
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3.1 ADDITIONAL MONITORING IN PEOPLE WITH IMPAIRED RENAL FUNCTION

Any decision to discontinue or alter Lithium doses should only be done by secondary care, unless acute toxicity is suspected.

CKD stage	Monitoring advice
3a (eGFR 45-60)	Monitor Lithium and eGFR 3 monthly Monitor ACR annually (early morning sample) Bone biochemistry annually
3a (and ACR>30) 3b (eGFR 30-45)	Monitor Lithium and eGFR 3 monthly Monitor ACR annually (early morning sample) Bone biochemistry annually Review risks and benefits of continuing Lithium
4-5 (eGFR <30)	Refer back to RDASH Mental Health Services for review

3.2 GUIDANCE FOR REFERRAL TO NEPHROLOGY

3.2.1 Unless acutely ill refer to mental health services to plan ongoing management if;

- CKD stage 4-5 (or 3a/b if ACR>30) on at least 2 measurements of over a period of 3 months, to exclude acute reversible changes
- Proteinuria (ACR>30)
- Deteriorating renal function eGFR reduction by >5 ml/min/1.73 m² in one year or >10 ml/min/1.73 m² in 5 years

3.2.2 Acute kidney injury

- Possible AKI (rapid rise in serum creatinine/fall in eGFR, acute illness) or hyperkalaemia: Discuss with nephrologist immediately or admit under general medicine

4.1 SHARED CARE ARRANGEMENTS

Once a stable medication regime has been established (usually 3 months), physical monitoring and prescribing of amber category drugs can be transferred to primary care with agreement.

4.2 ASPECTS OF CARE FOR WHICH SECONDARY CARE TEAM IS RESPONSIBLE

- Diagnosis and assessment
- Initiation and stabilisation of drug therapy, usually but not exceptionally, a period of 3 months.
- Patient/guardian/carer education
- Ensure patient/guardian/carer is adequately informed of potential benefits and side effects of treatment
- Ensure patient/guardian/carer is adequately informed of potential harmful/toxic effects of lithium and the necessity for long term monitoring
- Ensure patient's parents/guardian/carer is fully informed of the treatment (If patient is under 16 years old)
- Provide a comprehensive treatment package in addition to medications including appropriate information/monitoring sheet(s)
- Ensure that shared care arrangements are in place before transfer of treatment
- Ensure that any changes in dose are communicated promptly to the patients GP.
- That the patient/guardian/carer is clear what is being monitored and by whom
- That the patient knows what significant adverse effects/events to report urgently and to whom they should report (specialist or GP)
- Ensure the brand of Lithium to be prescribed by the GP is noted on the shared care paperwork
- **Write to the GP after every clinic visit detailing whether the medication regime should remain the same or be changed. Specify any products /dose or frequency changes.**
- **Inform GP of latest blood results after every clinic visit detailing serum creatinine, TSH and lithium levels**
- Provide & Maintain patient with the following 3 resources:
 - Booklet "Lithium therapy important information for patients.
 - Lithium Alert Card
 - Lithium Record book containing the following details
 - Patients details
 - Service providers details
 - Current lithium therapy
 - Expected upper and lower lithium blood level range
 - Ongoing test results
 - Monitoring lithium levels at a minimum of 3 monthly intervals

Advise GP if renal function deteriorates to make referral to Nephrology

Inform GP of patient misses appointments

Extra monitoring needed for dose changes will be organised by specialist team and conveyed to patient.

Monitor side effects of medication.

Monitor patient's response to treatment

Report adverse events via the Yellow Card reporting system in the BNF or at www.Yellowcard.gov.uk.

4.3 ASPECTS OF CARE FOR WHICH PRIMARY CARE TEAM IS RESPONSIBLE

- Ensure that shared care arrangements are in place before transfer of treatment
- That the patient/guardian/carer is clear what is being monitored and by whom
- That the patient knows what significant adverse effects/events and signs of toxicity to report urgently and to whom they should report (specialist or GP)
- When the specialist initiates treatment, **reply to the request for shared care as soon as practicable**
- Confirm that proposed therapy is not contra-indicated because of concurrent therapy for other

conditions the patient may be suffering from e.g. check drug-contraindications and drug-interactions. Contact specialist team if possible interactions found

- In patients with CKD stage 3a or worse to carry out annual ACR, in line with renal guidance
- Check that the specialists have provided the patient/guardian/carer with appropriate information sheet(s) for monitoring. If appropriate information has not been provided by the specialist, the GP must contact the specialist service to ensure the information is provided
- Ensure patient's parents/guardian/carer is fully informed of the treatment (If patient is under 16 years old)
- Monitor treatment as stated in the shared care protocol

Annually:

- Weight/Height/BMI
- Blood Pressure
- Smoking status
- Alcohol use
- ACR in patients with CKD 3a or worse, or more frequently as per renal guidelines *(if 3b or worse: liaise with Mental Health consultant re risk/benefit)*

As required if toxicity is suspected:

- Lithium Levels

Routinely:

- Side effects
- Symptom control

- Complete monitoring requirements as and when requested by secondary care or if signs of toxicity are noted and provide copies of all relevant test results to secondary care
- Ensure that appropriate monitoring has taken place and the patient is engaged with the specialist service prior to issuing a repeat prescription
- Amend prescription as per requests from secondary care for dose changes in patients on established treatment
- Confirm with specialist which changes in these or other parameters should trigger urgent referral back to the specialist
- Seek specialist advice promptly as advised in the shared care protocol or if signs/symptoms of changes occur
- During the initial period prior to prescriptions being issued by the GP, ensure that the GP clinical system is adequately set up so that any contraindications to prescribing or drug interactions are highlighted to the GP
- Report adverse events via the Yellow Card reporting system in the BNF or at www.Yellowcard.gov.uk
- Contact specialist service immediately if a member of the Primary Care team becomes aware that the patient is either pregnant, or planning a pregnancy
- Report adverse events to the consultant sharing the care of the patient
- Stop treatment on advice of specialist, or immediately if intolerable side effects occur provided that it is safer to do so than to continue this therapy

4.4 PATIENT (OR GUARDIAN/CARER'S) RESPONSIBILITIES

- Discuss potential benefits and side effects of treatment with the specialist and GP. Identify whether they have a clear picture of these from the specialist and to raise any outstanding queries
- Check that where possible the specialists have provided a patient-held record or information sheet for monitoring and/or to alert other clinical staff to the treatment they are receiving
- Share any concerns they have in relation to treatment with the medicine

- Report any adverse effects to their specialist or GP whilst taking the medicine
- Report to the specialist or GP if they do not have a clear understanding of their treatment
- Participate in the monitoring of therapy and the assessment of outcomes, to assist health professionals to provide safe, appropriate treatment
- Report to the specialist or GP if they become pregnant or are planning a pregnancy
- Carry the Lithium Alert Card at all times
- Share the contents of the Lithium Record book with healthcare professionals who may be involved in the management of the clinical condition or either the prescribing or dispensing of lithium preparations

5.0 PROCEDURE FOR ADOPTING SHARED CARE

5.1 GENERAL PROCEDURE:

Shared Care (Amber) classification

The specialist will send to the GP a diagnostic assessment report and a shared care referral specifying who is responsible for monitoring. Both the specialist and GP should sign the proforma with a record kept in the GP and specialist records. Full details will be given of the prescribing regime (brand, form, strength and dose of medication) and follow-up plan.

The patient will be asked to make arrangements with their GP for continued supply.

6.0 REFERENCES

- NICE Clinical Guideline CG38: Bipolar Disorder – The management of bipolar disorder in adults, children and adolescents, in primary and secondary care November 2006
- Priadel 200mg & 400mg prolonged release tablets Summary of Product Characteristics. Last updated 23/02/2009
- Priadel Liquid Summary of Product Characteristics Last updated 27/05/2009
- Camcolit 250mg & 400mg tablets Summary of Product Characteristics. Last updated January 2009
- Liskonum 450mg tablets Summary of Product Characteristics. Last updated January 2010
- Li-Liquid Oral Syrup Summary of Product Characteristics. Last updated July 2009

This Document will be reviewed in the light of new or emerging evidence or by Sept 2018

Doncaster & Bassetlaw Area Prescribing Committee DRAFT d0. 2 Sept 2013

- British National Formulary 59: March 2010
- National Patient Safety Agency: Patient Safety Alert – Safer lithium therapy December 2009
- Doncaster & Bassetlaw Hospitals NHS Foundation Trust Pathology Handbook April 2008

7.0 SHARED CARE DEVELOPMENT WRITTEN BY:

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Updated January 2015

Raz Saleem Prescribing Advisor NHS RCCG. Incorporating NICE Clinical Guideline CG38: Bipolar Disorder – The management of bipolar disorder in adults, children and adolescents, in primary and secondary care September 2014