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CLINICAL GUIDELINE

Management of patients prescribed Lithium

A guideline is intended to assist healthcare professionals in the choice of disease-specific treatments.

Clinical judgment should be exercised on the applicability of any guideline, influenced by individual patient characteristics. Clinicians should be mindful of the potential for harmful polypharmacy and increased susceptibility to adverse drug reactions in patients with multiple morbidities or frailty.

If, after discussion with the patient or carer, there are good reasons for not following a guideline, it is good practice to record these and communicate them to others involved in the care of the patient.

Important Note:

The Intranet version of this document is the only version that is maintained.
Any printed copies should therefore be viewed as 'Uncontrolled' and as such, may not necessarily contain the latest updates and amendments.

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Management of Patients Prescribed Lithium

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Guideline Scope

These guidelines include advice to prescribers and other healthcare professionals on managing patients on lithium, e.g. monitoring requirements, managing lithium levels and also counselling points for patients.

This guidance does not cover treatment for under 18s, as this is a sub specialist area requiring tertiary referral and monitoring.

Introduction

These guidelines have been developed by a multidisciplinary team to ensure a safe, effective and consistent approach to the management of patients receiving lithium.

Lithium is mood stabilizing drug used in the treatment for bipolar disorder and as an adjunct in the treatment of depression. It has a narrow therapeutic index and requires careful monitoring to support patient safety. Lithium is teratogenic and special consideration is needed with women of child bearing potential. In addition, it can be associated with several long term health issues.

The Chief Medical Officer published advice in 2017 to ensure that the physical health of patients prescribed lithium is appropriate and effectively monitored to minimize the risk of adverse effects.

Lithium Treatment Practice Points:

To improve safety and management of patients on lithium the following practice points identify essential elements for patient care:

Practice Point 1: When lithium started in secondary care

The **Secondary Care Clinician** should notify the GP in the agreed standard letter format (see Appendix 1). Where this is done via the CMHT (i.e. not as an inpatient), please inform the Mental Health Pharmacy Team to arrange baseline & ongoing monitoring for 12 months.
Necessary information:

Treatment
• Current indication
• Dose regimen
• Brand prescribed

Monitoring
• Proposed therapeutic range
• Last recorded level
• Frequency of lithium level monitoring (three monthly for at least the first year and can be six monthly after being stable for a year (CMO letter).

• When next level due
• Other monitoring requirements – TFTs, Calcium, Urea and Electrolytes, BMI

Counseling Checklist
• Provision of Purple Lithium Handbook
• Dosage/missed dose and appropriate action
• Need for regular monitoring requirements
• Risk of hypothyroidism
• Salt/fluid intake
• Lithium side effects/toxicity risks and appropriate actions
• Drug interactions
• Pregnancy or planning to start a family**
**(Seek advice before stopping contraception or if pregnancy is suspected)

If the Purple Lithium Handbook is unavailable, there are patient information leaflets available on the NHS Choice & Medication website here: https://www.choiceandmedication.org/nhs24/printable-leaflets/

Practice Point 2: Monitoring once stable:

*After stabilization of new patients, blood lithium levels should be monitored typically **3 monthly***:

- Sample should be taken at 12 hours post dose (10-14 hours post dose)
- The time interval should be the same at each measurement
- Record on EMIS , **State sample time clearly on the form**
    - **If ACE Inhibitor, diuretic or NSAID is started or there is evidence of deterioration in renal function then eGFR should be checked more frequently**

Every 6 months – (see letter to GP – Appendix 1)

- U&Es and eGFR
- T4 /TSH
- Calcium
- Weight /BMI

Every 12 months

- ECG (if indicated, if risk factors), BP, pulse, urine dipstick

Ask about compliance, side effects, toxicity, new medicines and pregnancy planning at each interaction.

Practice Point 3: Interpreting Lithium Levels

This is a general guide to interpretation of levels, to be used in conjunction with the patient specific advice provided by the mental health team and clinical judgement. Lithium toxicity is a clinical not biochemical diagnosis. It is NOT determined by any one level (though risk increases with increasing levels). If there are no clinical signs of toxicity, but the level is 1.0 or above, please consult mental health team before dose reduction.

If the level is low (typically < 0.6 mmol/l)

- If the patient is well and the levels are consistently low but within the documented specified range for that patient (this would be unusual but might be the specialist recommendation), *do not alter dose*
- If the patient is unwell and pattern of levels have been bordering on the lower end of the range:
    - *Assess compliance*

- *Increase the dose if appropriate*
- *Recheck the level in 5 days*

- If the low level is inconsistent with the trend, i.e. a one off:
  - *Assess compliance*
  - *Consider other factors, e.g. drug interactions, excess intake of fluid, brand change*
  - *Recheck the level*

If the level is within therapeutic range (typically 0.6-1.0 mmol/l)

- If the patient is well and tolerating lithium, *do nothing!*
- If the patient is well but complaining of side effects, e.g. polyuria, polydipsia, reduce the dose and check:
  - *If change in diet e.g. dietary salt restriction or crash diets can cause blood lithium to rise*
  - *Initiation of interacting medicines by doctor or use of over the counter pharmaceuticalproducts/herbal or dietary supplement products.*
- If the patient is clinically unwell, liaise further with CPN / psychiatrist

If the level is high (typically > 1.0 mmol/l), but with no signs of toxicity

- If there is an explanation for the high level e.g. dehydration, timing of level, interacting medicines, brand change, correct where possible and recheck level
- If the level is part of a pattern of levels which have bordered on being high:
  - *Discuss with Community Mental Health Team*

  (If patient's mental health requires this dose of Lithium and there are no signs of clinical toxicity, there may be no need to reduce the dose.)

- If there is an unexplained/sudden high level:
  - *Investigate renal function*
  - *Recheck the level at next available opportunity*

Practice Point 4: Patients who require additional monitoring

Certain patients may require more frequent or additional monitoring.

- If clinical indications arise
- "high risk" patients:
  - older people (age >65)
  - 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 1.0 mmol per litre or higher.

If further concerns re eGFR, contact renal physicians.

Consider stopping lithium for up to 7 days in acute severe illness with a metabolic or respiratory disturbance from whatever cause.

Practice Point 5: Urine Dipstick Information

If urine dipstick shows more than trace of blood or protein, the dipstick should be repeated on an early morning sample. In the absence of a urinary infection, if there is a positive dipstick (for blood or protein), consider further investigation and possible referral to renal.

Practice Point 6: Side effects

It is important to enquire about side effects and to consider how these might be best managed. Some side effects can be expected but it is vital to be alert for symptoms suggestive of lithium toxicity (*see below*).

Common side effects of lithium include

- GI disturbances (e.g. nausea, diarrhoea, dry mouth)
- Weight gain
- Oedema
- Fine tremor
- Polyuria and polydipsia (avoid fluid restriction)
- Hypothyroidism
- Hypercalcaemia

Side effects may be short term and are usually dose dependent.

They can often be prevented or relieved by a moderate reduction in dose.

Practice Point 7: Patient Advice on Common Side Effects

NB. Patient information leaflets are available from the NHS Choice and Medication website: https://www.choiceandmedication.org/nhs24/printable-leaflets/

Side Effect	What happens/What you may notice	What to do about it
Tremor	Fine shaking of your hands	This is not dangerous but it can be irritating. If it annoys you, your doctor may be able to give you something for it. If it gets worse and spreads to the legs or jaw, see a doctor within 24 hours.
Stomach upset	This includes feeling and being sick and diarrhoea	If it is mild, see your Pharmacist(. If it lasts for more than a day, see your doctor* Sick day rules are to be followed and patients may purchase oral rehydration salts from community pharmacist. *GP to ensure that the patient is not dehydrated, do observsations, review other meds and for signs of toxicity, seek secondary care advice if concerned*.
Polyuria	Passing a lot of urine	Don't drink too much alcohol. Tell your doctor about it* – some blood (urea and electrolytes) and urine tests may be needed *GP may seek endocrine advice.*
Metallic taste	Your mouth tastes as if it has had metal or something bitter in it.	This should wear off after a few weeks - if not, mention this to your doctor next time you meet.* A change in dose may help
Polydipsia	Feeling very thirsty	Your mouth is dry and there may be a metallic taste. Try drinking water or low calorie drinks in moderation. Try sucking sugar free boiled sweets *GP may seek endocrine advice*.

*** The GP should: ensure that the patient is not dehydrated, do observations, review other meds and for signs of toxicity, seek secondary care advice if concerned.**

Less common side effects

Side Effect	What happens/What you may notice	What to do about it
Weight gain	Eating and drinking more. Putting on weight	Try drinking water or low calorie drinks in moderation. Exercise and a healthy diet are important - ask your Practice Nurse for general lifestyle advice.
Hypothyroidism	Low thyroid activity. You feel tired	Tell your doctor as it may be necessary for him/her to prescribe some thyroid replacement tablets.* Doctor to treat as idiopathic hypothyroidism.

Rare: ***For any of these rare adverse effects GP to take a lithium level and urea and electrolytes to assess for toxicity.***

Side Effect	What happens/What you may notice	What to do about it
Skin changes	For example:- rash, acne, psoriasis	**If you get one or more of these problems at anytime talk to your doctor or other healthcare professional straight away. If this is not possible phone NHS 24.** **You may need to stop lithium urgently and get a blood test to check the lithium level.**
Blurred vision	Your lithium level may be too high. Things look fuzzy and you can't focus properly.	
Drowsiness	Your lithium level may be too high. You feel sleepy and sluggish in the daytime	
Confusion	Your lithium level may be too high. Your mind is all mixed up	
Palpitations	Your lithium level may be too high Your heartbeat feels fast.	

* The doctor who issues your prescription or NHS 24 at evenings and weekends.

Practice Point 8: Lithium Toxicity

Signs of lithium toxicity include:

- Increasing gastro-intestinal disturbances (vomiting, diarrhoea)
- visual disturbances,
- polyuria
- muscle weakness, fine tremor increasing to coarse tremor,
- CNS disturbances (confusion and drowsiness increasing to lack of coordination, restlessness, stupor);
- abnormal reflexes, myoclonus,
- incontinence, hypernatraemia.
- Gait changes (unstable/ataxic)

With severe overdosage (serum-lithium concentration above 2 mmol/litre)

- seizures,
- cardiac arrhythmias (including sino-atrial block, bradycardia and first-degree heart block),
- blood pressure changes,

circulatory failure, renal failure, coma and sudden death reported

If patient exhibits signs of lithium toxicity:

STOP LITHIUM IMMEDIATELY

- Check lithium levels, eGFR, U&Es, Calcium
- Refer to hospital if clinical condition warrants
- Contact psychiatry team (either community team or liaison in BGH) to alert them of admission.
- Seek advice from psychiatrist for re-initiation of lithium

Practice Point 9: Brands and formulations of lithium

Different preparations of lithium may vary widely in bioavailability i.e. the amount absorbed into the blood.

- New patients in NHS Borders will be initiated on a specific lithium brand, generally Priadel
- Check that patient continues on same brand of lithium.
- All prescriptions for lithium should be written in proprietary form, i.e. brand name.
- If changing between brands or between tablets and liquid, more frequent monitoring may be required initially as the change may result in alterations in lithium levels.
- Take particular care when changing from tablets to liquid or vice versa. e.g.

Lithium *carbonate* tablet 200mg (Li +5.4 *mmol*)

is approx. equal to

Lithium *citrate* liquid 509mg/5ml (Li +5.4 *mmol*)

Practice Point 10: Drug Interactions and contra-indications to treatment

Some medicines may result in increased lithium levels and increase risk of toxicity. These include:

- Diuretics (mainly thiazides)
- NSAIDs (e.g. ibuprofen)

- ACE inhibitors
- Rarely, other psychotropic medicines like Tricyclics, Carbamazepine and SSRIs.
- Theophylline

Other interactions to be aware of
- Drugs that may prolong QT interval
- Drugs that may reduce seizure threshold

Refer to Appendix 1 in the current BNF for further details and a full list of interacting medication.

Contra- indications of lithium: Lithium therapy to be reviewed if the patient develops any of these conditions:

- Hypersensitivity to 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.

Practice Point 11: Psychiatric Review and Referral

For patients managed only in primary care, general practitioners may wish to consider referring patients for formal psychiatric review after 2-5 years of treatment, to consider appropriateness of continuing lithium therapy.

Other reasons for referral (at any stage) may include:
• Patient relapse
• Problematic side effects
• Deterioration of renal/thyroid function
• Requests to stop lithium
• Pregnancy or planning for pregnancy - see Appendix 6

Practice Point 12: Counseling Points for Patients on Lithium

Note
Patient information leaflets are available from the NHS Choice and Medication website: https://www.choiceandmedication.org/nhs24/printable-leaflets/

People taking lithium need to know the following:

1. Name of drug

Reinforce importance of continuing on same brand of lithium and if possible,attend same pharmacist.

2. What the drug is used for

Used mainly as a mood stabiliser to help normalise or even out mood swings. It also prevents mood swings in the future.
It can also be used for other reasons, e.g. to increase the effect of antidepressants when they are not working enough on their own.

3. Dosage/missed dose

Reinforce importance of taking:

- ***As directed***
- ***At same time(s) each day***
- ***With glass of water***

Important not to crush tablets as this will affect the sustained release preparations.
If dose is missed, take as soon as possible as long as it is no longer than 3 hours after the usual time. Advise that they **should not** take double the dose the following day.

4. Blood tests

Advise patient that:

- It is essential to have regular blood tests to check lithium levels and that initially they will be checked weekly. Once levels of lithium in the blood are steady,they will be checked regularly (typically 3 monthly) at 12 hours post dose.
- They will have blood tests at least every 6 months to check on kidney, thyroid and parathyroid function.

5. Other medicines

Advise patient that:

- Some medicines whether prescribed or bought from a pharmacy may result inincreased lithium levels and increase the risk of toxicity/side effects, e.g: watertablets (mainly thiazides), anti-inflammatories (e.g. ibuprofen), sodium bicarbonate(baking powder) and theophylline.
- They should always check with their doctor or pharmacist before starting any new medication.

6. Salt/fluid intake

Advise patient that:

- The amount of salt in the diet can change the level of lithium in the blood and to avoid changing from a high to low sodium diet and vice versa. It is important to maintain a good fluid intake, particularly in situations where there is a risk of

dehydration, e.g. after exercise, long distance air travel, sickness, fever, diarrhoea and hot weather.
- They should avoid crash diets.
- Seek Medical attention if they become acutely unwell or develop diarrhoea.

7. Alcohol intake

Advise patients that:
- It is best to avoid alcohol completely in lithium use and especially when first starting the medication. If you are to consume alcohol then this should be in moderation. Alcohol can both worsen psychiatric symptoms and also increase risk of dehydration when used with lithium.

8. Women of child bearing age/pregnancy

Advise patients that they should:
- Seek medical advice before stopping contraception if they are planning to become pregnant.
- Seek medical advice as soon as possible if they are taking lithium and are pregnant.

9. Compliance

Advise patient that:
- Lithium is not addictive
- It should not be stopped suddenly as original symptoms may return
- It may take several weeks or months to work
- Lithium will normally have to be taken long term, ie for at least 2-3 years
- They should carry a Lithium Treatment Card at all times – available from Pharmacies

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Appendix 1 : Letter to GP for patients on lithium (Priadel)

Letter to GP for Patients on lithium (normally Priadel)

The proprietary brand is _____ (please specify)

Dear Dr

Your patient has been recommended to commence on lithium. This proprietary brand should not be changed without considering the different bioavailability.

Please use every opportunity to encourage your patient to take the medication, (unless problems have emerged). **Research shows many patients take it only when they are due a blood test!**

Patient Specific Details	CHI No/Casenotes No: ……
Name: ……..	Consultant Psychiatrist:: ……...
Date of Birth ……	

Treatment

- Current indication …… (eg, bipolar prophylaxis, augmentation)
- Dosage regimen ……
- Brand prescribed ……
- Proposed therapeutic range (if different from 0.6-1mmol/l) ……
- Last in-patient lithium level (where relevant) ……
- Frequency of lithium monitoring (typically 3 monthly) ……..
- Next level due ……..

Other Minimum Monitoring Requirements (in primary care for all out-patients)

- Urea, electrolytes and eGFR – 6 monthly
- T4/TSH – 6 monthly
- Calcium – 6 monthly
- ECG (if indicated)/Weight/BP/pulse/urine dipstick – 12 monthly

NB: More frequent monitoring may be required if clinical indications arise and in higher risk patients, eg over 65s, those on interacting drugs, those with or at risk of renal/thyroid/cardiac disease, those at risk of non compliance

Counseling Checklist

- Compliance essential
- Dosage/missed dose and appropriate action
- Need for regular monitoring requirements
- Risk of hypothyroidism
- Salt/fluid intake
- Lithium side effects/toxicity risks and appropriate actions
- Drug interactions
- All women of child- bearing age should be counseled about the need to discuss pregnancy or planning a pregnancy with their GP.

Both the standard patient letter and patient leaflet are enclosed for your information.

Full information on lithium monitoring and your role in primary care is provided.

Key points for new patients

- Check blood level **weekly** and adjust dose accordingly as per Guidelines
- On occasions the Consultant may specify a higher level as optimal, eg in treatment refractory situations

- The guideline also confirms that any adjustment of the dose is the responsibility of the GP who will bear in mind that there is a straight-line relationship between dose and serum level, for example 400mg and level of 0.4mmols would predict 600mg, will result in level of 0.6 mmols etc. The half life is 18 to 36 hours in a person with normal renal function.
- **For interpretation of result note time post-dose of the sample; it should be 12 hours.**

- If consecutive levels are stable and in agreed therapeutic range double the interval up to a maximum of 3 months.

- Toxic levels can occur above 1.0mmol/l and patients should be assessed for need for possible urgent hospital treatment; if level is above 2mmol/l this will definitely be required.
- Compliance should always be closely monitored in this patient population.

The Community Mental Health Team will follow up your patient in the future unless advised otherwise.

Yours sincerely

Appendix 2: Letter to Patient on lithium or provide purple lithium booklet.

Letter to Patient on lithium (normally Priadel)

Dear

As I have discussed with you, I write to confirm the recommendation that you

commence on lithium (Priadel) as treatment for your bipolar illness/depression.

I enclose an information leaflet for you.

I would like to emphasise the importance of: -

- Taking your medication regularly at the same time of day, preferably in a single dose at bed time.
- Attending your Health Centre for regular monitoring of the level of lithium (normally Priadel) in a blood sample. This will normally be three monthly once your level is stable.
- You will also require your thyroid, kidney and calcium function and level checked every 6 months and your BMI, urine and pulse checked yearly
- Adjusting the dose if the GP recommends this after any of the blood test results.
- Alerting anyone treating you, for example, when on holiday or if admitted to hospital, that you are taking lithium.
- Always check with your Pharmacist before buying any medicines.
- Your medication will be adjusted to achieve a level between 0.6 and 1 on your blood test unless otherwise recommended by your psychiatrist.
- It is important that you continue the lithium for the duration recommended by your psychiatrist, usually 2 years in the first instance.
- Please bring any problems or side effects to the attention of your GP, psychiatrist or CPN so that these can be discussed with you and an appropriate plan agreed with you.