

## Lithium treatment – How to manage patients on lithium during the COVID-19 pandemic.

Please note all questions within each section are linked to each other and should be read in conjunction. Below each question is the weblink to the source of evidence to support the guidance recommendation.

Please read the following advice in combination with [national UK advice on protection/self-isolation](#).

Clinical question	Guidance
<b>Starting lithium</b>	
Can I start my patient on lithium? <a href="#">[link1]</a>	<p>Yes, but this will depend on careful consideration, balancing clinical need and the resources available to maintain the expected standards for lithium monitoring as outlined by NICE (<a href="#">QS95 – Quality statement 5</a>).</p> <p>Clinicians will need to follow the <b>usual schedule for starting lithium</b> (see footnote 1 for further <a href="#">details</a>). As this requires frequent blood level in the initial phase this will need to be carefully weighed against possible alternatives (see question 2).</p> <p>If patients are self-isolating or symptomatic with COVID-19 then initiation should be deferred – see further advice detailed in the answers to the questions below.</p> <p><b>In general, for all psychotropic medication</b></p> <ul style="list-style-type: none"> <li>Careful consideration should be given to <b>whether now is the best the time to withdraw or change</b> patients from antidepressant, anxiolytic or antipsychotic medication. In some circumstances this may be unavoidable due to clinical need, but the <b>clinical rationale should be carefully documented and arrangements for monitoring put in place</b>.</li> <li>For many patients it is <b>likely that advice will be given to continue on regular medication</b> until this can be reviewed in a face-to-face setting and the patient can be involved in shared decision making with their usual doctor or healthcare provider. This should <b>take account of the fact that anxiety and depressive and psychotic symptoms are all likely to worsen during extreme stress and social disruption</b>. Patients will be at increased risk of relapse or recurrence of affective and psychotic illness.</li> <li>Advise patients <b>to continue their current dosage</b> until the changes in health care provision necessary during the COVID-19 pandemic have been reversed, and only then consider whether dosage reductions or withdrawal might be appropriate, in discussion with their usual doctors.</li> </ul>
If I can't start my patient on lithium what options are there?	<p>The decision to use lithium or another intervention should be based on the mental health diagnosis and the available treatment alternatives, taking into account the possible restrictions in blood testing and face to face monitoring during the COVID-19 pandemic.</p> <p>Please refer to <b>local and national guidance for further advice</b>.</p> <p><b>Examples of national guidance include:</b></p>

[NICE clinical guideline 185 on bipolar disorder: assessment and management.](#)  
[BAP guidelines on bipolar disorder.](#)  
[BAP guidelines on antidepressants.](#)

Other **relevant sources of information** include:

[Lithium in the prevention of suicide in mood disorders: updated systematic review and meta-analysis.](#)

[Lithium and suicide in mood disorders: Updated meta-review of the scientific literature.](#)

[Comparative efficacy, acceptability, and tolerability of augmentation agents in treatment-resistant depression: systematic review and network meta-analysis.](#)

### Measuring lithium levels and assessing their significance in the presence of possible COVID-19

How should I advise my patients who are already established on a stable dose of lithium?

[\[link2\]](#)

[\[link3\]](#)

[\[link4\]](#)

[\[link10\]](#)

**In general, remind all patients:**

- **Not to stop lithium abruptly unless advised to do so.**
- To ensure that **they do not run out** before seeking further supplies as **there may be delays in filling prescriptions.**
- To seek medical attention if they develop **diarrhoea or vomiting or feel acutely unwell** for any reason.
- To ensure they **maintain their fluid intake**, particularly if they have a fever, if they are immobile for long periods or if they develop a chest infection or pneumonia.
- **To inform their care team of any changes to their drug treatment.**
- Not to take over-the-counter non-steroidal anti-inflammatory drugs (e.g. ibuprofen). **Patients can use paracetamol** with lithium, if required for aches/pain or flu-like symptoms.

Clinicians should follow national and local procedure for guidance in initiating and maintaining lithium treatment, assuming that the patient does not meet criteria for one of the more vulnerable groups (see question on vulnerable groups below). Footnote 1 contains guidance on these.

**Where possible, routine lithium monitoring at the suggested intervals should continue**, however, it may be possible to **extend the monitoring frequency for patients who are low risk, have been stable on lithium for over a year and are physically well.**

Patients must keep in good physical health and maintain good fluid intake and should resume normal monitoring intervals as soon as possible and safe to do so.

Advice for prioritisation of routine monitoring (including psychotropic medication) in general practice is contained [here](#).

A **helpful algorithm to balance mental health, physical and social care needs** in clinical-decision making is available [here](#).

Who are the most vulnerable groups who need more frequent monitoring of lithium levels?

[\[link2\]](#)

[\[link4\]](#)

**Higher risk patients, where 3 monthly monitoring is recommended, include:**

- the elderly (> 65 years old)
- patients that have received less than 12 months treatment
- those initiating or stopping drugs that interact with lithium (e.g. NSAIDs, ACE inhibitors, Angiotensin receptor blockers, diuretics)
- renal impairment (eGFR < 60ml/min)
- evidence of impaired thyroid function

[\[link5\]](#)  
[\[link13\]](#)

- raised calcium level
- poor symptom control
- poor adherence
- has a lithium serum level > 0.8mmol/L

What should I do if a patient on lithium is self-isolating without symptoms of infection or COVID-19?

[\[link2\]](#)  
[\[link4\]](#)

- **Continue the treatment with lithium.**
- Patients who are self-isolating might not be able attend the clinic or GP surgery for routine lithium monitoring tests.
- Consider whether the appointment can be booked for a later date. **Decisions to extend monitoring should be managed on a case by case basis but may be considered for patients who have been stable for more than one year with no other risk factors.**
- If a patient falls into one or more of the high-risk categories described above, **every effort should be made to carry out routine blood monitoring.**
- **In rare cases where it is considered unsafe to continue lithium, due to high risk and inability to carry out routine monitoring over extended periods of time, clinicians must:**
  - **Consider and discuss alternative treatments** which may be initiated in place of lithium.
  - Endeavour to **withdraw the lithium slowly** – over at least one month.

What should I do if a patient maintained on lithium describes symptoms suggestive of infection in general or of COVID-19?

[\[link1\]](#)  
[\[link2\]](#)  
[\[link3\]](#)  
[\[link4\]](#)  
[\[link10\]](#)  
[\[link11\]](#)

Be aware that:

- **Ongoing treatment, and the dose used, should be governed by lithium plasma levels.**
- **Febrile patients may become dehydrated and lithium levels may rise**, putting patients at greater risk of developing toxicity. **Look for signs of potential toxicity** such as coarse tremor, muscle weakness or twitching, gastric illness (diarrhoea, stomach ache, vomiting), unsteadiness, speech disturbance, blurred vision, confusion.

If Mild symptoms of COVID-19 infection occur:

- **Continue lithium treatment.**
- **Continue with usual monitoring where possible, although some guidelines suggest you should consider taking a lithium level at this point** – refer to local procedures for physical health monitoring in COVID positive / suspected patients.
- Advise patient to **maintain adequate fluid intake, not to take over-the-counter NSAIDs (e.g. ibuprofen) for fever, but to take paracetamol instead.**
- Advise patient to **report any worsening of COVID-19 symptoms.**
- Be aware that **any intercurrent illness**, especially one associated with fever or reduced oral intake may result in **lithium toxicity despite no change in dosage.**
- Ask about **lithium side effects or symptoms indicative of toxicity** and advise the patient to report the development of any new side effects immediately.

If Moderate to Severe symptoms of COVID-19 develop or if the infected patient is in the “higher risk” group (see above):

- Arrange an **urgent serum lithium level and renal function test** – this may be via primary care or secondary care services depending on local arrangements.
- Advise the patient to **maintain adequate fluid intake, not to take over-the-counter NSAIDs (e.g. ibuprofen) for fever, but to take paracetamol instead.**
- Advise the patient to **report any worsening of COVID 19 symptoms.**
- Ask about **lithium side effects or symptoms indicative of lithium toxicity.**

- The decision to **withhold lithium temporarily or advise a reduced dose** may be taken depending on individual patient circumstances, and with the knowledge that **sudden discontinuation of lithium is associated with a high risk of relapse**.
- Be aware that **any intercurrent illness**, especially one associated with fever or reduced oral intake may result in **lithium toxicity despite no change in dosage**.
- Depending on blood test results, clinicians may need to amend the dose and/or increase the frequency of subsequent lithium monitoring. **If the lithium levels are elevated or the kidney function is compromised, seek urgent specialist advice.**

In patients presenting with **significant flu-like/COVID-19 symptoms where there is a high risk of dehydration and/or renal impairment, or where it is not possible to reliably monitor for symptoms of lithium toxicity:**

- Withhold lithium.
- Take urgent lithium serum level and U&Es.

Can patients take ibuprofen to help with their symptoms?

[\[link1\]](#)

[\[link4\]](#)

[\[link9\]](#)

While there is currently **no strong evidence** that ibuprofen can make COVID-19 worse, **patients should be advised to take paracetamol to treat their symptoms, unless they have been advised paracetamol is not suitable for them.**

It is especially important that **patients on lithium do not initiate NSAIDs without medical advice** as the concomitant use of NSAIDs with lithium may increase the risk of lithium toxicity.

Current guidance says **not to stop regular NSAIDs that are prescribed for other medical conditions**. NSAIDs may be prescribed regularly with lithium – **provided that lithium levels are adjusted and monitored frequently** (3 monthly) (for further details, please consult local and national guidance).

Can lithium levels be affected by COVID-19 infection?

[\[link2\]](#)

[\[link3\]](#)

[\[link4\]](#)

#### Possible effects on kidney function

[Recent reports from Wuhan](#), China suggested that “kidney disease on admission and acute kidney injury (AKI) during hospitalization were associated with an increased risk of in-hospital death” in patients with COVID-19 disease. Therefore, **the possible effect of lithium on kidney function must be borne in mind when treating patients who develop the disease.**

#### Possible drug Interactions

- NSAIDs and drugs acting on the angiotensin-converting enzyme (e.g. ACE inhibitors) may be withdrawn if essential during COVID-19 infection, although this has not been recommended in any guidance. **Stopping regular NSAIDs or ACE may cause a fall in lithium levels.**
- It is worth reminding that a number of **interactions between lithium and novel agents being used to treat COVID-19 exist**. Please consult a range of available resources to check for relevant drug interactions.

#### Dehydration, fluid intake and diet

- **Dehydration or reduced fluid intake is another important cause of lithium toxicity**. Patients with COVID-19 may present with a **fever and therefore may be at risk of dehydration**. Vomiting, diarrhoea and infection (especially if sweating profusely) may require **dose reduction or discontinuation (see above)**.
- Remind all patients to **maintain their fluid intake**, particularly if they have a fever, if they are immobile for long periods or if they **develop a chest infection or pneumonia**.
- Patients who are isolated at home with limited supplies **may significantly change their diet** and therefore sodium intake which could also impact on lithium levels.

Are lithium treated patients at greater risk of COVID-19?

[\[link2\]](#)

There is **no evidence** that lithium increases the risk of developing infections such as respiratory tract infections or complications such as pneumonia.

#### How do I manage difficulties in keeping to the recommended frequency of blood testing?

Can I change the frequency of blood level monitoring (i.e. omit or delay scheduled blood tests)?

[\[link3\]](#)

[\[link4\]](#)

Standard blood tests for lithium monitoring are outlined in [NICE Guideline 185](#), updated February 2020. See footnote 1 for a summary.

Decisions to extend monitoring should be managed **on a case by case basis** but may be considered for patients who have been stable for more than one year with no other risk factors.

The majority of patients who are on lithium will be monitored in primary care and this **should be continued wherever possible**. In the event that a patient is unable to attend their usual site for a blood test, consideration should be given to **rearranging the blood test at an alternative location or using secondary care resources depending on local arrangements**.

At risk/vulnerable patients (see above) must continue to have their regular lithium monitoring every 3 months.

Do I need to consider any changes to staff training?

[\[link6\]](#)

**Consider refresher training and upskilling staff on key aspects of physical healthcare** to ensure a sufficient pool of staff is available to undertake mandatory blood testing: e.g. for patients on clozapine, lithium, or ADHD medication, this may include pharmacy staff undertaking phlebotomy training and refreshing knowledge, skills and practice in infection control (please refer to local and [national advice](#)).

#### Different formulations of lithium

Can I change to a different brand of lithium if my usual brand is in short supply or difficult to access?

[\[link7\]](#)

[\[link8\]](#)

Caution should be taken when switching between lithium products as preparations vary significantly in bioavailability. **Changing the preparation requires the same monitoring as initiation of treatment.**

If a **change in preparation** is required, follow local guidance, but in general:

- **Confirm the target plasma level.**
- Stop the original preparation and initiate the new preparation with a **standard titration plan**.
- **Check plasma level at steady state** (usually 5-7 days after initiation).
- **Adjust dose and recheck plasma levels** until target plasma level is achieved and stable.

(Please see Footnote 2 for recent UK MHRA advice on Priadel MR supplies).

#### General advice for patients/carers on managing medications and prescriptions during COVID-19

[\[link12\]](#)

In the UK, PHE advises patients as follows:

- Keep taking your medication.
- You might be able to order repeat prescriptions by phone, or online using an app or website if your doctor's surgery offers this.
- Ask your pharmacy about getting your medication delivered or think about who you could ask to collect it for you if you are self-isolating or shielding. The NHS website has more information about [getting prescriptions for someone else](#) and [checking if you have to pay for prescriptions](#).

- Continue to order your repeat prescriptions in your usual timeframe. There is no need to order for a longer duration or larger quantities.
- Your GP practice (or clinical team) may move your prescriptions to repeat dispensing arrangements, so you only have to contact your pharmacy to get a repeat of your medicine rather than your practice.
- Be careful about buying medication online. You should only buy from registered pharmacies. You can check if a pharmacy is registered on the [General Pharmaceutical Council website](#).
- You can contact [NHS 111](#) in England if you're worried about accessing medication.

**Footnote 1:** National guidance on initiating and maintaining lithium in non-vulnerable groups available [here](#).

#### **Baseline (prior to initiation)**

- U&E's including eGFR and calcium, and TFT. An ECG is recommended in patients with a history of cardiac disease or risk factors.

#### **Initiation**

- Follow standard licensed recommendations for initiation of lithium (this varies depending on the product used), adjusting dose according to plasma level and clinical effect.
- Take a trough lithium level (12 hours post dose) one week after initiation and one week after each dose change,
- then monitor levels weekly until stable,
- then every 3 months for the first year.

#### **Maintenance**

- After the first year, measure plasma lithium levels every 6 months, except in the following higher risk patients, where 3 monthly monitoring is recommended:
  - the elderly
  - those initiating or stopping drugs that interact with lithium (e.g. NSAIDs, ACE inhibitors, Angiotensin receptor blockers, diuretics)
  - established chronic kidney disease
  - evidence of impaired thyroid function
  - raised calcium level
  - poor symptom control
  - poor adherence
  - has a lithium serum level > 0.8mmol/L

**Footnote 2:** In the UK, in August 2020, the MHRA (The Medicines and Healthcare products Regulatory Agency, <https://www.gov.uk/government/organisations/medicines-and-healthcare-products-regulatory-agency>) issued a Supply Discontinuation Alert (SDA) for Priadel® 200mg and 400mg MR tablets, stating that these products, were going to be discontinued in the UK. This raised many concerns for patients across the UK as the vast majority of those taking lithium, used the Priadel brand.

In October 2020, the Competition and Markets authority (CMA) opened an investigation into Essential Pharma, the manufacturers of Priadel, on the grounds that they were suspected of abusing their dominant position in the UK. Essential Pharma responded by outlining a commitment to continue to provide Priadel for the next 5 years at an increased price. This commitment is currently under review by the CMA. More information is available [here](#).

As it stands, the Priadel brand of lithium is still available in the UK and currently do not anticipate that it will be withdrawn in April 2021. For further information refer to the [SDA](#), or to the RCPsych or local mental health trust policies.