



LITHIUM

Top tips for MURs

- Ensure that lithium is prescribed by proprietary name as plasma levels can vary between products
- Ensure that lithium tablets are swallowed whole at night
- Counsel patients on signs of lithium toxicity that need referral (see below) and common side effects (see below)
- Counsel patients on importance on maintaining adequate fluid intake
- Counsel patients on avoiding any dietary changes which reduce or increase sodium levels (do not go on a low salt diet or take sodium based antacids / urinary alkalinising agents)
- Check patient has had lithium blood tests every three months to check that levels are correct (between 0.4 and 1.0mmol/L)
- Check that the patient has had kidney and thyroid tests every six months
- Check that patient has had calcium blood tests every six months to check that levels are correct
- Check patient has a lithium booklet and alert card
- Advise patient on OTC interactions with lithium (i.e. avoid NSAIDs as can increase lithium levels)
- Advise patient that full prophylactic effect from lithium may not occur for six to twelve months after initiation
- Advise patient that continued treatment over an extended period is associated with improved outcome
- Signpost patients to local support groups or charities supporting patients with mental illness e.g. Mind, Hafal
- Report any relevant adverse drug reactions to the Yellow Card Scheme

What is lithium used for?

Lithium is licensed for use in the treatment and prophylaxis of mania, bipolar disorder and recurrent depressive disorders, as well as the control of aggressive behaviour or intentional harm.

When used for the treatment of bipolar affective disorder, ongoing, continuous treatment is important, as frequent treatment breaks worsen the prognosis of the disorder. Lithium discontinuation (even when managed gradually over a period of weeks) is associated with a high risk of relapse. Patients should be made aware of the importance of ongoing treatment, usually for at least three years.

Lifestyle issues

- Counsel patient on reducing alcohol intake to within safe limits (up to 14 units a week, spread evenly over 3 more days, with several alcohol free days)
- Counsel patients on healthy eating, exercise & weight loss (if BMI > 25kg/m²) - reduce saturated fat, increase oily fish intake, complete 30 minutes of aerobic exercise three to five times a week, reduce caffeine intake to no more than 5 cups a day and recommend 5 portions of fruit and vegetables a day
- Advise patients who smoke of the benefits of stopping smoking and how to access enhanced smoking cessation services in community pharmacy and GP practices

Red flags that need referral

- Any signs of lithium toxicity require urgent referral to A+E (nausea/vomiting, blurred vision, severe hand shake (coarse tremor), drowsiness, muscular weakness, being unsteady on your feet, confusion, seizures)
- Any sickness and diarrhoea for more than two days as dehydration may lead to toxicity
- Any symptoms of renal failure (tiredness, oedema, shortness of breath, itchy skin, nausea)
- Pregnancy, as risk of teratogenicity in first trimester and dose adjustments needed in later stages of pregnancy
- Breastfeeding as present in milk and a risk of toxicity in the infant

How does lithium work?

Lithium may alter intracellular second messenger signalling systems as well as modulating dopaminergic and serotonergic neurotransmitter pathways. However, the exact way that it works is unknown.





What are the common side effects to look out for?

Most side effects of lithium are dose related. Long term treatment may result in a reduction in glomerular filtration rate and hypothyroidism. Due to the reduction in suicide risk associated with lithium treatment (approximately 80% in patients with bipolar illness), current evidence suggests that the benefits of treatment outweigh the risk of adverse renal events in most cases¹. However, careful monitoring is essential. Lithium treatment is also associated with changes in thyroid and parathyroid function. Hyperparathyroidism is a recognised adverse effect, and calcium levels should be checked prior to and during treatment².

Common side effects	Recommendation
Tremor	A fine hand tremor is a common side effect of lithium and is not dangerous but can affect daily tasks. A worsening tremor affecting other parts of the body is a sign of toxicity and requires urgent referral.
Nausea/gastrointestinal disturbance	Mild gastro-intestinal upset can occur. If it persists for more than one day, refer to prescriber.
Polydipsia	Drink water or low calorie drinks in moderation. Suck sugar free boiled sweets.
Polyuria	Avoid excess alcohol, discuss with prescriber if problem persists.
Metallic taste	This should wear off after a few weeks. If it persists discuss with prescriber.
Weight gain	Give lifestyle advice and refer to prescriber if not tolerated. Weight monitoring is important.
Hypothyroidism	Discuss with prescriber.
Fluid retention/ankle oedema	Discuss with prescriber if troublesome.

Potential drug interactions?

Lithium has a narrow therapeutic range (usually 0.4-1.0mmol/L), therefore drug interactions resulting in increased plasma levels may lead to potentially serious toxicity and require vigilance.

Lithium levels are affected by changes in sodium concentration and by drugs which alter renal blood flow and sodium balance. The plasma concentration of lithium is increased by a number of drugs including:

- ACE inhibitors and angiotensin 2 receptor antagonists
- Diuretics especially thiazides
- Non steroidal anti-inflammatory drugs
- Carbamazepine and antidepressants can cause hyponatraemia leading to increased lithium levels.

Amiodarone should not be used in conjunction with lithium.

Neurotoxicity may occur in patients taking methyl dopa and lithium without increasing plasma concentration of lithium.

See BNF Appendix 1 for a full list of interactions and for further details.

Where can you find more information?

- NPSA has issued a safety alert for safer lithium therapy and can be found on the NPSA website (<http://www.nrls.npsa.nhs.uk/alerts/?entryid45=65426>)
- The National Centre for Mental Health (NCMH) website has downloadable patient information leaflets written by specialist mental health pharmacists and other information (<http://ncmh.info>)
- Lithium – BNF sub-section 4.2.3 Antimanic drugs
- Mental Health distance learning pack that can be found on WCPPE website (<http://www.wcppe.org.uk>)
- NICE guidance on management of bipolar disorders, self harm and depression that can be found on NICE website (<http://www.nice.org.uk>)
- British Association for Psychopharmacology bipolar guidelines can be found at their website (http://www.bap.org.uk/pdfs/Bipolar_guidelines.pdf)

References:

1. Werneke U et al. 2012, A decision analysis of long-term lithium treatment and the risk of renal failure. Acta Psychiatrica Scand. 126(3):186-197
2. McKnight RF et al 2012. Lithium toxicity profile: a systematic review and meta analysis. Lancet 379:721-728

