#### **MONOGRAPH**

# **LITHIUM**

Scope (Staff):	Medical, Pharmacy, Nursing
Scope (Area):	All Clinical Areas

# **Child Safe Organisation Statement of Commitment**

CAHS commits to being a child safe organisation by applying the National Principles for Child Safe Organisations. This is a commitment to a strong culture supported by robust policies and procedures to reduce the likelihood of harm to children and young people.

This document should be read in conjunction with this <u>DISCLAIMER</u>



QUICKLINKS				
<u>Dosage/Dosage</u> <u>Adjustments</u>	Administration	<u>Monitoring</u>	Adverse Effects	

# **DRUG CLASS**

Psychotropic drug.<sup>1</sup>

Lithium is a High Risk Medicine.

#### **INDICATIONS AND RESTRICTIONS**

Lithium is used at PCH for the following indications:<sup>1</sup>

- Prevention of manic or depressive episodes in bipolar disorder
- Treatment of acute mania
- Schizoaffective disorder and chronic schizophrenia (rarely used)
- Augmentation for treatment-resistant depression (accepted)

Lithium must be prescribed under the direction of a Child and Adolescent Psychiatrist.

#### CONTRAINDICATIONS

- Hypersensitivity to lithium or any component of the formulation<sup>2</sup>
- Significant cardiovascular or renal disease<sup>2</sup>
- Severe debilitation, dehydration, sodium depletion, concurrent use with diuretics<sup>2</sup>
- Untreated hypothyroidism<sup>2</sup>

Brugada Syndrome<sup>3</sup>

#### PRECAUTIONS<sup>1</sup>

- Hyponatraemia: increased risk of lithium toxicity. Avoid lithium or use it cautiously where sodium levels may decrease (e.g. vomiting, diarrhoea, Addison's disease).
- Thyroid disease: treat before starting lithium (often causes thyroid dysfunction, usually hypothyroidism).
- Psoriasis: may be exacerbated or precipitated.
- Although there is a low risk, lithium is possibly teratogenic in the first trimester in pregnancy.
- Treatment with medications that may contribute to serotonin toxicity.
- Avoid lithium or use it carefully in situations where its renal clearance may be decreased, e.g. with NSAIDs.
- Surgery: consider interrupting therapy as changes in fluid intake or dynamics may alter serum lithium concentrations.

#### **FORMULATIONS**

Listed below are products available at PCH, other formulations may be available, check with pharmacy if required.

- Lithium Carbonate 250 mg Tablet Lithicarb®
- Lithium Carbonate 450 mg Modified Release Tablet Quilonum SR®

Imprest location: Formulary One

# **DOSAGE & DOSAGE ADJUSTMENTS**

Therapy with lithium should always begin with conventional tablets (lithium carbonate 250 mg) to stabilise the dose.<sup>4</sup>

# Children 12-18 years:

- Lithium Carbonate 250 mg Tablet (Lithicarb®)
  - Oral, initially 250 mg 2 or 3 times daily.<sup>4</sup>
  - Adjust daily dose by 250 mg every 4–7 days according to response, tolerability and serum lithium concentration.<sup>4</sup>
- Conversion to Lithium Carbonate 450 mg Modified Release Tablet (Quilonum SR®)
  - Use the total daily dose established with conventional tablets and give <u>half of that total</u> <u>daily dose</u> every 12 hours as the slow-release form.<sup>4</sup>
  - Maintenance dose may be given once daily.

Lithium onset of action may be delayed for 6–10 days, adding a benzodiazepine or antipsychotic is usually needed in severe mania.<sup>1</sup>

Lithium must not be ceased abruptly unless discontinuation is due to significant side effects. Gradual dosage reduction over a period of at least 4 weeks (preferably over a period of up to 3 months) is advised. Patients and their carers should be warned of the risk of relapse if lithium is discontinued absuptly.<sup>5</sup>

# Renal impairment 1, 6

Clinicians should consider stopping lithium and using other suitable mood stabilisers if two
consecutive readings suggest decreasing renal function, or if the estimated glomerular
filtration rate (eGFR) is < 45 mL/min/1.73 m<sup>2</sup> using serum creatinine levels: eGFR calculator

# Hepatic impairment <sup>2</sup>

There are no dosage adjustments provided in the manufacturer's labelling.

# Pregnancy 1

- If possible, avoid use particularly during the first trimester.
- Lithium clearance increases in the second half of pregnancy so dose adjustments may be needed; use the lowest dose possible.
- During pregnancy, check lithium concentration more frequently.
- Consider reducing the lithium dose in the last days of pregnancy or stopping it for 1–2 days before planned delivery or onset of labour to avoid maternal and neonatal toxicity. Restart after delivery. Give the preconception dose as clearance returns to normal immediately afterwards.
- Greater attention to hydration is also necessary. Babies showing signs of lithium intoxication may require fluid therapy.

# ADMINISTRATION 1, 2

- Lithium should be taken with food.
- Quilonum SR<sup>®</sup> is not technically a slow-release formulation, it is a harder compressed tablet that allows release of the larger dose more slowly.<sup>7</sup> The tablet is scored and may be halved for dosing purposes.
- Do not crush or chew Quilonum SR® and avoid taking with hot drinks.
- Maintain a normal diet with regular salt and fluid intake.

#### PRESCRIBING & DISPENSING

All CAHS patients prescribed lithium must be monitored in accordance with this protocol.

CAHS <u>Lithium Initiation Checklist</u> is to be used at initiation of lithium therapy. <u>CAHS Lithium Health Facts</u> and <u>CAHS Lithium Therapy Record Booklet</u> must be provided to all patients.

All health professionals must ensure that the following are met.

#### **Prescribers:**

- a. Check that blood tests are performed and monitored regularly and that it is safe to issue a repeat prescription. Use Clinical Manager to access blood test results for Serum Lithium Level, Renal Function Test, Thyroid Function Test (TFT), Urea and Electrolytes (U&Es) and Full Blood Picture (FBP) including calcium and serum creatinine levels.
- b. Ensure that appropriate ongoing verbal and written information are provided to the patient at the start and throughout the patient's lithium therapy.
- c. Provide the patient with the <u>CAHS Lithium Therapy Record Booklet</u> to track lithium blood levels, other relevant clinical tests, prescriber details and dosing information.
- d. Ensure that a list of interactions that are likely to adversely interact with lithium therapy are identified for the patient and provided at start of therapy and on review.

#### Pharmacists:

- a. Check that blood tests are performed and monitored regularly, and it is safe to dispense the prescribed lithium.
- b. Ensure that the <u>CAHS Lithium Therapy Record Booklet</u> is provided to track lithium blood levels, other relevant clinical tests, prescriber details and dosing information. Pharmacist may record results on the patient's <u>CAHS Lithium Therapy Record Booklet</u>.
- c. Ensure that a list of interactions that are likely to adversely interact with lithium therapy are identified and provided to the patient at start of therapy and on review.
- d. Provide the patient with appropriate ongoing verbal and written information at the start and throughout the patient's lithium therapy. Document the resources and counselling provided on the Medication Management Plan (MMP) and CAHS Lithium Initiation Checklist.
- e. Counsel to ensure the patient understands the signs and symptoms of lithium toxicity. This should be recorded on the MMP.

#### MONITORING

# Baseline Tests<sup>1</sup>

- Full Blood Picture
- Urea and Electrolytes
- Renal function
- Calcium levels
- Thyroid Function Test (TFT): TSH and T4
- Parathyroid hormone concentrations
- Weight or body mass index (BMI)
- ECG in those with risk factors for or existing/family history of cardiovascular disease.

After commencing lithium, check weight, serum calcium (including ionised calcium) and parathyroid hormone concentrations, and renal and thyroid function every 3–6 months (at least annually), or as clinically indicated.

# **Serum Lithium Levels**

# Therapeutic level for treatment:

- Acute mania 0.6–1 mmol/L<sup>1,2</sup>
- Depression: 0.4–0.6 mmol/L<sup>5</sup>

#### Therapeutic level for prophylaxis:

0.4–0.8 mmol/L<sup>1,5</sup>

Serum lithium concentrations tend to fluctuate for 6–10 hours after dosing, so the 12-hour post-dose serum concentration is used for monitoring purposes.<sup>1, 5</sup>

Check serum lithium levels 5–7 days after starting treatment and after each dose change until stabilised. Steady state may not be reached for 4–7 days (longer in those with renal impairment).<sup>1</sup>

Once stable, serum lithium concentrations should be monitored once every three months.1

#### **Lithium Toxicity**

Lithium is classified as a narrow therapeutic index drug, requiring close monitoring to ensure patients' serum levels are maintained within the therapeutic range. Supratherapeutic levels, even slight elevations, may lead to increased adverse reactions and toxicity. Notably, toxicity can occur at any level.<sup>2</sup>

In acute lithium intoxication, the increase in plasma concentrations (>1.5 mmol/L)¹ can be potentially lethal. Once renal excretion reaches its maximum, lithium accumulates rapidly, and symptoms worsen. However, high plasma concentrations may cause relatively mild symptoms, and in these instances, individuals often recover without permanent neurological damage. This occurs because lithium can take up to 24 hours to cross the blood brain barrier, and brain concentrations usually peak 8 hours after oral administration.<sup>8</sup>

Symptoms such as lethargy, drowsiness, muscle weakness and hand tremor are indicative of neural toxicity and can manifest even at therapeutic concentrations of lithium.<sup>8</sup>

Symptomatically, levels for acute toxicity may be higher than for chronic toxicity.

# Early warning signs of lithium toxicity include:

- i) General flu-like illness, vomiting, increasing diarrhoea
- ii) Renal polyuria, polydipsia
- iii) Cardiac syncope, dizziness, arrhythmias, bradycardia
- iv) Neurological drowsiness, fatigue, lethargy, confusion, lack of coordination including ataxia, blurred vision, and apathy

<u>Severe toxicity</u> can result in increased muscle tone, dysarthria, coarse tremor (larger movements, especially of hands), hyperreflexia and myoclonic jerks, psychosis, seizures and coma.<sup>1</sup>

- Lithium should be withheld, and the prescriber contacted if any signs or symptoms of toxicity are present.
- Patients and their carer should be educated on these signs and symptoms and encouraged to monitor their symptoms regularly.

#### **ADVERSE EFFECTS<sup>1</sup>**

**Common:** Fine tremor, metallic taste, increased thirst, increased frequency of urination, mild nausea, diarrhoea, weight gain, fatigue, headache, vertigo, acne, psoriasis, leucocytosis, nephrotoxicity, hypothyroidism (usually asymptomatic), hypercalcaemia, hyperparathyroidism, benign T wave changes on ECG<sup>1-3</sup>

Infrequent: dry mouth, memory impairment, hair loss

Rare: arrhythmias, hyperthyroidism, nystagmus

#### **Central Nervous System:**

 May cause CNS depression, which may impair physical or mental abilities. Chronic use may cause neurotoxicity.

# **Nephrotoxicity:**

- Nephrogenic diabetes insipidus with polydipsia and polyuria is frequent (may be reversible on stopping lithium).
- Lithium treatment is associated with reduced glomerular filtration rate. Long-term treatment and episodes of acute lithium toxicity are thought to increase the risk of nephrotoxicity.<sup>1,2</sup>
- Nephrotic syndrome rarely occurs and can resolve after stopping lithium.<sup>4</sup>
- Long-term lithium treatment (>10 years) increases the risk of renal tumours e.g. cancers and oncocytomas.

#### Hypothyroidism:

 Reduces the availability of thyroxine resulting in hypothyroidism (risk six-fold higher in patients on lithium).<sup>2</sup> This may also increase the possibility of patients on lithium developing clinical depression.

#### **STORAGE**

Store below 25°C.4

# **INTERACTIONS** 3

Lithium may interact with other medications; please consult PCH approved references (e.g. <u>Clinical Pharmacology</u>), a clinical pharmacist or PCH Medicines Information Service on extension 63546 for more information

Lithium is eliminated from the body by the kidneys, hence any drugs or dietary factors that reduce kidney function may increase lithium blood levels and should be used with great caution. Such drugs include:

- Nonsteroidal anti-inflammatory drugs (NSAIDs)
- Diuretics (e.g. thiazides, potassium sparing, loop, aldosterone antagonists)
- Angiotensin converting enzyme (ACE) inhibitors
- Antipsychotics
- Acetazolamide

# Related CAHS internal policies, procedures and guidelines

**CAHS High Risk Medicines Policy** 

CAHS Lithium Therapy Record Booklet

CAHS Lithium Health Facts

<sup>\*\*</sup>Please note: The information contained in this guideline is to assist with the preparation and administration of **Lithium**. Any variations to the doses recommended should be clarified with the prescriber prior to administration\*\*

#### References

- 1. Australian Medicines Handbook. Lithium [Internet]. Adelaide (SA): Australian Medicines Handbook Pty Ltd.; 2024. [cited 2024 Feb 02]. Available from: AMH
- 2. Lexicomp Editorial Advisory Panel. Lithium Pediatric Drug Information [Internet]. Wolters Kluwer: UpToDate; 2024 [cited 2025 Apr 06]. Available from: <u>UpToDate</u>
- 3. Lithium Monograph [Internet]. Philadelphia (PA): Elsevier Inc.; 2024 [cited 2024 Jan 15]. Available from: Clinical Pharmacology powered by ClinicalKey.
- Australian Medicines Handbook: Children's Dosing Companion. Lithium [Internet]. Adelaide (SA): Australian Medicines Handbook Pty Ltd.; 2024 [cited 2024 Jan 02]. Available from: <u>AMH</u> CDC
- 5. Lithium. Royal Pharmaceutical Society of Great Britain, Royal College of Paediatrics and Child Health, British Medical Association, Neonatal and Paediatric Pharmacists Group. BNF for children 2017 [cited 20 May 2020]. Available from: BNF
- 6. Roxanas M, Grace BS and George CRP. Renal replacement therapy associated with lithium nephrotoxicity in Australia. Med J Aust 2014; 200 (4): 226-228 [cited 2024 May 14].
- 7. Quilonum SR [full product information] [Internet] 2025 [cited 2025 Apr 06]. Available from: AusDI
- 8. National Institute for Health and Clinical Excellence. Bipolar disorder: Assessment and Management (Clinical guideline 185) 2014, Updated February 2016. Bipolar disorder: assessment and management (CG185). <a href="https://www.nice.org.uk/guidance/cg185">https://www.nice.org.uk/guidance/cg185</a> [cited 2024 Sep 19].

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CHILD AND ADOLESCENT HEALTH SERVICE – CHILD AND ADOLESCENT MENTAL HEALTH SERVICE

# LITHIUM INITIATION CHECKLIST

Surname:	
Given name:	
UMRN:	
Gender:	D.O.B:
Address:	

# This checklist must be completed for all patients initiated on lithium.

- Ensure all the following information on the checklist is discussed with the patient and/or carer (as appropriate).
- The checklist should initially be completed by the prescriber, then reinforced by the
  pharmacist and nursing staff to ensure the information is understood (or where the patient
  lacks capacity ensure that adequate support systems are in place to ensure concordance).
- Where possible, written information should be provided as well as a verbal explanation.
- Staff should reinforce information at the time of discharge if the patient has been admitted.

Lithium Initiation Checklist	Information given by whom Initial and date when completed.		
Action	Doctor	Nurse	Pharmacist
Why has lithium been prescribed?			
What are the common side effects?			
What blood tests are necessary and how often are they due?			
Importance of not missing the blood test.			
What are the signs of lithium toxicity?			
Dose to be taken.			
Importance of telling other health professionals about being on lithium			
Importance of adequate fluid intake and maintaining a consistent salt intake (dehydration can affect lithium levels).			
What should you do if you miss a dose?			
Length of treatment and the person who is responsible for stopping the medication.			
Importance of not stopping suddenly.			
Who to contact in an emergency?			
CAHS Lithium Health Facts and CAHS Lithium Therapy Record Booklet provided.			
List of possible drug interactions provided.			