Specialised Medication – Lithium Guideline

1. Purpose

This document provides guidance for the prescription and administration of lithium in adult consumers and should be used in conjunction with appropriate references, including:

- Medication Prescribing and Administration Policy
- WACHS High Risk Medications Procedure
- Australian Medicines Handbook
- Therapeutic Guidelines
- Statewide Medication Formulary
- MIMS Product Information

For paediatric consumers, refer to the Perth Children's Hospital (PCH) Medication Management Manual - Lithium Monograph.

2. Guideline

2.1 Presentation[1,2,3]

- 250 mg lithium **carbonate** immediate release tablet (Lithicarb®)
- 450 mg lithium **carbonate** slow release (SR) tablet (Quilonum SR®)
- 127 mg lithium **citrate** BP per 1mL oral solution (Auspman®)
  - **127 mg** lithium **citrate** is equivalent to **50 mg** lithium **carbonate**
  - Product may not be available in all regions – consult with local hospital pharmacy department.

This document refers to dosing in terms of lithium carbonate

2.2 Indication(s)[1,2,3]

- Prevention of manic or depressive episodes in bipolar disorder.
- Treatment and prophylaxis of acute mania.
- Schizoaffective disorder and chronic schizophrenia.
- Accepted – augmentation for treatment-resistant depression.

2.3 Contraindications[1,2,3]

- Hypersensitivity to lithium or any component of the formulation.
- Severe or significant cardiovascular disease as lithium may cause electrocardiogram (ECG) changes and/or arrhythmias, such as sick sinus syndrome.
- Severe or significant renal disease.
- Severe sodium depletion and conditions associated with hyponatraemia e.g. Addison's disease, dehydration, severely debilitated consumers and consumers on low sodium diets.
- Concomitant prescription of diuretics without appropriate dose adjustment.
- Frank hypothyroidism.

2.4 Precautions[1,2,3,4]

Pregnancy
Australian Category D. Lithium use during the first trimester has been associated with a slight increase in cardiac malformation (Ebstein's anomaly). Lithium treatment during pregnancy requires specialist input and foetal monitoring. Further information available from the King Edward Memorial Hospital Drug Information Centre (Ph: 08 9340 2723) or the Pregnancy and Breastfeeding Medicines Guide, The Royal Women's Hospital Victoria available via region specific subscription (contact hospital pharmacy department).

Lactation
Lithium is excreted in breast milk with the potential to cause lithium toxicity and adverse effects in the neonate/child. Breastfeeding is not usually recommended for people taking lithium. Further information available from the King Edward Memorial Hospital Drug Information Centre (Ph: 08 9340 2723) or Pregnancy and Breastfeeding Medicines Guide, The Royal Women's Hospital Victoria available via region specific subscription (contact hospital pharmacy department).

Older Adults
Use with care in older adults as excretion may be reduced and they may be more sensitive to adverse reactions. Older adult consumers often require lower dosages and more frequent monitoring to avoid toxicity.

Surgery
Interruption of therapy perioperatively (approximately 24 hrs pre-surgery) and postoperatively is recommended as fasting and fluid/physiological changes can affect serum lithium levels.

Renal
Lithium should be used with caution in consumers with renal impairment as it is primarily excreted by the kidneys. Where possible, the use of lithium is to be avoided in consumers with severe renal impairment. Doses should be reduced, and lithium levels aimed at the lower end of the therapeutic range and more frequently monitored in renal impairment and unstable kidney function.

Hyponatraemia
Depleted sodium levels increase serum lithium levels and therefore increase toxicity.

Hypothyroidism
Lithium can cause thyroid dysfunction therefore use with caution in consumers with existing thyroid disease.

Electroconvulsive Therapy
Combined treatment with electroconvulsive therapy may increase risk of neurological events. Consider withholding doses, or at minimum a dose reduction and close monitoring if concomitant therapy is indicated.

Environmental and Lifestyle Considerations
When prescribing lithium, consideration should be given to:
- the consumer's geographical distance from healthcare facilities and ability to fulfil lithium monitoring requirements

- the risk of exposure to extremes of heat and the risk of dehydration
- ability to adhere to treatment as intermittent treatment with lithium may worsen the course of bipolar illness.

2.5 Medicines Interactions[1,2,3,4]

The following drug interactions are limited to those that occur most commonly in practice. Drug interactions with lithium are extensive and relevant references should be consulted prior to prescribing. Specialist and/or clinical pharmacist advice should also be considered.

Adjust the dose of lithium where necessary and conduct more frequent monitoring of lithium levels, renal function and clinical effects when use with medicines that interact with lithium is unavoidable.

Angiotensin Converting Enzyme (ACE) inhibitors and Angiotensin II Receptor antagonists (-sartans): decreases lithium excretion and therefore may increase lithium levels and the risk of toxicity.

Loop diuretics e.g. frusemide: may increase lithium levels and the risk of toxicity. Avoid combination where possible.

Non-Steroidal Anti-inflammatory Drugs (NSAIDs) e.g. ibuprofen, diclofenac: decrease lithium excretion and therefore may increase lithium levels and the risk of toxicity. Avoid the combination where possible. Low dose aspirin is safe to use.

Thiazide diuretics e.g. hydrochlorothiazide: may increase lithium levels and the risk of toxicity. Avoid the combination where possible.

Medicines that may contribute to serotonin toxicity e.g. antidepressants, some opioids, stimulants, linezolid: Lithium can contribute to serotonin toxicity therefore consumers who are prescribed a combination of these medicines should be made aware of the symptoms and closely monitored.

Antipsychotics: High doses or rapid dose increases of lithium and antipsychotics together may cause neurotoxicity.

2.6 Dosing (Lithium Carbonate)[1,2,3,4,5]

The recommendations below are a guide and not a standardised dosing schedule. Doses should be individualised to the consumer and titrated based on serum lithium levels (see therapeutic drug monitoring). Doses of lithium are not recommended to exceed 2500 mg daily. Slower titrations may be used according to the prescriber's clinical judgement.

Acute Mania[1]

- 750 mg – 1000 mg in daily divided doses. Increase dose by 250 - 500 mg daily if necessary. Adjust according to serum levels.

Prophylaxis of Bipolar Disorder[1]

- 250 mg – 500 mg twice daily for two weeks. Adjust according to serum lithium levels.

Practice points

- Doses above have been given in immediate release increments. The SR preparation may be used to its nearest dose increment e.g. 450 mg as a twice daily dose (12 hours apart). Slow-release tablets may be halved if necessary (tablets are scored). Crushing, chewing or taking the SR tablets with a hot beverage will counteract the slow-release properties.
- After a consumer's dose has been stabilised, single nightly doses may be prescribed, where possible, to facilitate morning blood tests and improve compliance.
- Reduce doses and monitor closely in the elderly and in consumers with renal impairment.
- It may take two to three weeks to observe significant therapeutic effect.
- Post-acute manic phase– consumers may tolerate higher doses of lithium while acutely manic. Signs of toxicity should be monitored, and doses adjusted after this stage as tolerability may be reduced.
- Ceasing lithium therapy should occur over at least a month if possible.

2.7 Therapeutic Drug Monitoring[1,2,3,4,6,7]

Levels should be assessed 5 - 7 days after starting treatment and after each dose change. Steady state is expected to be achieved in 5 - 7 days but this may be longer in the elderly or renally impaired (7 - 10 days).

Target ranges are as follows:

- Prophylaxis of bipolar disorder[7]: 0.4 -1 mmol/L
- Acute Mania[7]: 0.8 - 1.2 mmol/L

Aim for target concentrations in the upper end of the therapeutic range if the consumer is prescribed a single night-time dose of lithium as 12-hour serum levels can be 10-25% greater than levels observed for daily divided doses.

Maintenance monitoring is recommended every three months. More frequent monitoring is required in certain situations such as illness (particularly if febrile or vomiting), acute mania or depression, changes in diet, pregnancy, concurrent use of other medications (e.g. diuretics) or where there are signs of toxicity.

If a consumer is taking lithium on admission to hospital for any reason, it is recommended that a level be taken to ensure a current level is available to guide clinical decisions.

2.8 Monitoring[1,4,6]

Baseline tests to be conducted prior to treatment commencement include: full blood picture, electrolytes, creatinine, fasting blood sugar levels, body mass index, thyroid function tests, calcium and phosphate, ECG and pregnancy test (if appropriate).

Table 1 outlines the minimum recommended monitoring schedule once lithium therapy has commenced. Certain tests may need to be conducted more frequently depending on individual consumer factors e.g. impaired renal function. Monitor for clinical signs and symptoms of adverse effects.

Table 1: minimum recommended monitoring once lithium therapy has commenced.

Lithium level	5 - 7 days after commencement and after any dose change Repeat 3 monthly after establishing stable dose
Full blood picture, thyroid function tests	Repeat 3 months after establishing stable dose and then every 6 months
Renal function and electrolytes	Repeat every 3 to 6 months
Fasting blood sugar levels and body mass index	Repeat every 6 to 12 months
Calcium and phosphate	Repeat every 12 months
ECG	Repeat every 12 months
Pregnancy test	Ensure adequate contraception

Where the consumer declines to comply with monitoring requirements, this must be documented in the health care record and the prescriber notified.

2.9 Adverse effects[1,2,3,4,6,7]

Very Common Adverse effects
Gastrointestinal disturbances (nausea, diarrhoea, dry mouth, metallic taste), fine tremor, polyuria, polydipsia.

Many of these effects are minor, transient and often dose-related, and can be managed by minor dose adjustments and ensuring lithium levels remain in the therapeutic range.

Less Common Adverse Effects
Weight gain, fluid retention, acne or psoriasis flares, hypothyroidism and nephrotoxic effects.

The nephrotoxic effects of lithium are varied and often associated with more long-term use (although acute injury can occur), high dosing and advanced age. Nephrogenic diabetes insipidus, reduced glomerular filtration rate leading to end-stage renal disease, tubular atrophy, focal interstitial nephropathy and, rarely, nephrotic syndrome have been associated with lithium therapy.

Some renal insults may be irreversible upon cessation of lithium.

Lithium Toxicity
Symptoms of toxicity are commonly experienced at serum lithium levels above 1.5 mmol/L. This may be lower in elderly consumers or those with neurological damage, even occurring within the usual therapeutic ranges.

Mild to moderate toxicity:
- Blurred vision, increasing diarrhoea, nausea, vomiting, anorexia, muscle weakness, drowsiness, apathy, ataxia, flu-like illness.

Severe toxicity:
- Increased muscle tone, hyper-reflexia, myoclonic jerks, coarse tremor, dysarthria, disorientation, psychosis, seizures, renal failure, coma, death.

Acute on chronic poisoning may also occur. Chronic poisoning is associated with significant morbidity and mortality. It has an insidious onset and a toxicologist should be consulted if poisoning is suspected.

Management of Toxicity
Refer to hospital if an outpatient.

Withhold medication, order urgent bloods – lithium, serum creatinine, urea and electrolytes. There may be a delay in maximal toxicity so levels should be taken regularly (every 6 hours) to identify peak and monitor elimination.

Intravenous (IV) rehydration will help bring down the lithium level. Haemodialysis may be required for very severe acute lithium poisoning.

2.10 Consumer Education

Verbal and written information must be provided to every consumer that is commenced on lithium therapy. Use the Lithium medicine information leaflet from the Choice and Medication intranet site to support verbal counselling.[7] Document education provision in the consumer's health care record.

Education materials should be provided in a language and format that is understood by the consumer when available. This includes the use of an interpreter when required, in line with the WA Health System Language Services Policy (and Guidelines).

Due to the high-risk nature of lithium, emphasis must be placed on:
- the need for regular blood tests and monitoring
- the signs and symptoms of lithium toxicity especially during times of physical illness, excessive sweating or low fluid intake and the need to seek medical review urgently
- the importance of maintaining a normal diet without excessive salt, alcohol or low fluid intake
- avoiding over the counter medications such as anti-inflammatories, indigestion medications and urinary alkalisers, unless in consultation with a health professional
- taking medication regularly. Abrupt stopping can lead to relapse. If lithium is to be stopped, it should be withdrawn slowly if possible.

3. Roles and Responsibilities

The **Medical Officer** is responsible for:
- completing orders for medication on the appropriate medication chart or PBS prescriptions for outpatient consumers
- documenting a comprehensive monitoring plan
- reviewing recorded observations and monitoring parameters regularly and adjusting treatment where required
- documenting the reason for therapy changes
- conducting comprehensive consumer education regarding lithium therapy
- communicating a comprehensive handover at transitions of care. It is the responsibility of the Health Service Team (inpatient or community) to ensure routine monitoring is completed until care has been formally handed over to a general practitioner (GP) service

The **Registered Nurse / Midwife / Enrolled Nurse** is responsible for:

- recording observations and escalating abnormal readings for review
- monitoring the consumer for symptoms of lithium toxicity and escalating for review
- accurately recording the time of administration of each dose to ensure that blood drawn for therapeutic drug monitoring occurs at the appropriate time
- conducting consumer education regarding lithium therapy
- liaising with the consumer carer/case worker/GP to arrange required follow up appointments or blood tests to ensure continuity of care.

The **Pharmacist** (where available) is responsible for:

- endorsing medication as suitable to administer
- escalating any issues with regards to prescription or administration
- providing clinical information regarding prescribing and administration of lithium
- ensuring supply arrangements.

All staff are required to work within policies and guidelines to make sure that WACHS is a safe, equitable and positive place to be.

4. Monitoring and Evaluation

4.1 Monitoring

Managers of clinical areas, health sites and services are responsible for monitoring compliance with this policy.

Clinical incidents involving issues relating to lithium are monitored via the DATIX Clinical Incident Management reporting processes. SAC 1 events are reviewed by Regional Drug and Therapeutics Committees and the WACHS Safety and Quality Steering Committee.

Any incident that meets the criteria for a notifiable incident as defined by the *Mental Health Act 2014* (WA), must be reported to the Chief Psychiatrist in accordance with the Policy for Mandatory Reporting of Notifiable Incidents to the Chief Psychiatrist.

4.2 Evaluation

This guideline is to be reviewed every two (2) years.

Evaluation of this guideline is to be carried out by WACHS Mental Health directorate in consultation with WACHS Pharmacy Service and regional WACHS Health Services.

Policy evaluation methods and tools may include:

- staff feedback / consultation
- carer and consumer feedback / consultation
- survey
- compliance monitoring
- benchmarking
- reporting against organisational targets.

5. Compliance

Guidelines are designed to provide staff with evidence-based recommendations to support appropriate actions in specific settings and circumstances. As such, WACHS guidelines should be followed in the first instance. In the clinical context, where a consumer's management should vary from an endorsed WACHS guideline, this variation and the clinical opinion as to reasons for variation must be documented in accordance with the Documentation Clinical Practice Standard.

6. References

1. Australian Medicines Handbook Pty.Ltd. (2022) online (Lithium). [Accessed 10/2022] Available from: http://www.amh.net.au
2. Lithicarb® (Approved Product Information) [accessed from MIMS Australia internet database] [Accessed 10/2022]
3. Quilonum SR® (Approved Product Information) [accessed from MIMS Australia internet database]. [Accessed 10/2022]
4. Taylor D., Barnes T.R.E and Young A.H (2021) The Maudsley Prescribing Guidelines in Psychiatry. 14th Edition. John Wiley & Sons
5. Society of Hospital Pharmacists Australia, Don't Rush to Crush [accessed from MIMS Australia internet database] 4th edition 2022 [Accessed 10/2022]
6. Graylands Hospital Drug Bulletin (2014) Using Lithium Safely Vol 21 No.4 available from Using Lithium Safely (health.wa.gov.au) [Accessed 10/2022]
   Therapeutic Guidelines Pty Ltd. (2020). Psychotropic Guidelines
7. Bazire S et al Choice and Medication [Internet]. Mistura Enterprise Ltd. [Accessed 10/2022]

7. Definitions

Nil

8. Document Summary

Coverage	WACHS wide
Audience	Medical, nursing and pharmacy staff involved in prescribing, administration or monitoring of lithium
Records Management	Clinical: Health Record Management Policy
Related Legislation	• *Medicines and Poisons Act 2014* • *Mental Health Act 2014* (WA)
Related Mandatory Policies / Frameworks	• Clinical Governance, Safety and Quality Framework • Mental Health Framework • Consent to Treatment Policy - MP 0175/22 • High Risk Medication Policy - MP 0131/20 • Medication Chart Policy - MP 0078/18 • Medicines Handling Policy - MP 139/20 • Medication Review Policy - MP 0104/19 • Statewide Medicines Formulary Policy - MP 0077/18 • Recognising and Responding to Acute Deterioration (RRAD) Policy - MP 0171/22 • Clinical Incident Management Policy - MP 0122/19
Related WACHS Policy Documents	• Adults with Impaired Decision Making Capacity Procedure • Clinical Observation and Assessments Clinical Practice Standard • Documentation Clinical Practice Standard • High Risk Medications Procedure • Medication Prescribing and Administration Policy • Recognising and Responding to Acute Deterioration (RRAD) Policy • Recognising and Responding to Acute Deterioration (RRAD) Procedure
Other Related Documents	• WA Health Guidelines for Managing Specific High Risk Medications Relevant to the Organisation • WA Chief Psychiatrist Policy for Mandatory Reporting of Notifiable Incidents to the Chief Psychiatrist
Related Forms	• MR140A WACHS Adult Observation and Response Chart • MR170A National Inpatient Medication Chart – Adult Short Stay • MR171 National Inpatient Medication Chart – Adult Long Stay
Related Training Packages	• High Risk Medications: Introduction (HRMINT EL2)
Aboriginal Health Impact Statement Declaration (ISD)	ISD Record ID: 2157
National Safety and Quality Health Service (NSQHS) Standards	4.01, 4.03, 4.04, 4.11, 4.13, 4.15, 5.01, 5.11, 5.12, 5.13, 5.33, 5.34, 8.04 – 8.13

Aged Care Quality Standards	N/A
National Standards for Mental Health Services	1.2, 1.3, 1.6, 1.10, 1.12, 2.4, 6.7, 6.8, 6.9, 8.4, 8.10, 10.4.8, 10.5

9. Document Control

Version	Published date	Current from	Summary of changes
3.00	11 July 2023	11 July 2023	• Title • Division of absolute and relative contraindications • Addition of Electroconvulsive Therapy interactions • Division of adverse effects into common and less common • Addition of management of toxicity

10. Approval

Policy Owner	EDMH
Co-approver	EDMS
Contact	Director of Psychiatry – Clinical Governance
Business Unit	WACHS Mental Health
EDRMS #	ED-CO-15-78977

This document can be made available in alternative formats on request.