



Lithium Shortage

For the current status of drug shortages and discontinuations, refer to Drug Shortages Canada at www.drugshortagescanada.ca.

The information presented here is designed to assist health professionals in managing a drug shortage and in selecting alternative products for patients already receiving a specific treatment. It is not a comprehensive review or a clinical practice guideline for this condition. Patient assessment requires professional knowledge and judgment beyond the scope of this document. Consult CPS Full Access or other references if required.

TABLE 1: Lithium products marketed in Canada¹

Product	Strength	DIN	Manufacturer
Lithmax	300 mg	02266695	AA Pharma Inc.
Apo-Lithium Carbonate	150 mg	02242837	Apotex Inc.
	300 mg	02242838	
Carbolith	150 mg	00461733	Bausch Health, Canada Inc.
	300 mg	00236683	
	600 mg	02011239	
pms-Lithium Carbonate	150 mg	02216132	Pharmascience Inc.
	300 mg	02216140	
Lithane	150 mg	02013231	Searchlight Pharma Inc.
	300 mg	00406775	

Health Canada-approved indications for lithium:²

- Management of acute manic episodes and maintenance treatment of bipolar disorder

Common off-label uses of lithium:²

- Management of depressive episodes in bipolar disorder
- Augmentation therapy in patients with treatment-resistant unipolar depression
- Prophylaxis of chronic cluster headache

Management options:³

- Avoid starting patients on lithium while the shortage persists.
- Encourage patients to limit refill prescriptions to a 30-day supply and contact their pharmacy or health-care provider in advance of depleting their current supply.
- The information presented here is generalized, and patients should be evaluated on an individual basis with appropriate clinical monitoring and consideration of drug coverage options.

Lithium treatment requires therapeutic drug monitoring (“drug levels”).² Lithium levels are usually not required when changing brands, but levels should be monitored in the following situations:

- 5 days after a dose change
- A potentially interacting drug is added or discontinued
- There are signs and symptoms of toxicity or decreased effectiveness
- The patient’s renal function changes

Bipolar disorder is a complex, recurrent mood disorder characterized by either a manic episode (with or without a history of major depressive episode) or a hypomanic episode (with a current or past history of major depressive episode). These mood swings can significantly impact the patient’s daily functioning. Pharmacologic therapy varies according to the type and stage of the episode being treated; however, lithium is a first-line option for all types and stages. Since treatment for bipolar disorder is lifelong, it is crucial to engage the patient in collaborative decision-making.

Specific medication strategies for **mania** generally depend on whether the patient is already on maintenance therapy and is experiencing a breakthrough episode or adverse effects. First-line agents for mania include lithium, divalproex and second-generation (“atypical”) antipsychotics (see Table 2). Medication selection should balance the side effect profile with key clinical factors, including previous responses and patient preferences.

Treatment options for **depression** depend on whether the patient is on medication and has had a breakthrough episode or adverse effects. In an unmedicated patient, therapy may begin with any of the first-line treatments (see Table 3). Lamotrigine is the best-tolerated option, although it may take the longest to work and may be slightly less efficacious. The efficacy of lurasidone as monotherapy or in combination with lithium or valproate for adults with bipolar depression has been demonstrated in randomized controlled trials.

The **maintenance** phase occurs when the patient recovers from an acute episode and remains well (with no or minimum symptoms) for at least 2 months. Many patients who are doing well on current therapy but must change due to a drug shortage will need to receive maintenance treatment. Table 4 list several effective options for relapse prevention.

TABLE 2: **First-line drug therapy for mania in bipolar disorder**³

Drug	Dosage	Adverse Effects
Aripiprazole	Initial: 15 mg/day PO in monotherapy or 10-15 mg/day PO if combined with lithium or divalproex Maximum: 30 mg/day	Akathisia, dizziness, orthostatic hypotension, headache, gastrointestinal complaints, tremor, sedation
Asenapine	Initial: 5 mg BID SL Maximum: 10 mg BID SL depending on response and tolerability	Sedation, orthostasis, hypotension, dizziness, weight gain, extrapyramidal symptoms (EPS)
Cariprazine	Initial: 1.5 mg PO once daily Maximum: 6 mg/day	Akathisia, nausea, restlessness, EPS
Lithium	Initial: 300 mg BID PO (150 mg BID PO in the elderly) Usual dose: 900-2100 mg/day PO, guided by serum concentrations	Highly toxic in overdose (signs and symptoms of toxicity include ataxia, tremor, sedation or agitation, diarrhea, vomiting)
Paliperidone	Initial: 3-6 mg/day PO Maximum: 12 mg/day	Insomnia, headache, weight gain, orthostasis, rhinitis, anxiety, dose-related hyperprolactinemia, EPS
Quetiapine	Initial: 50 mg BID PO Usual dose: 200-400 mg PO twice daily	Weight gain, sedation, orthostasis, metabolic disturbances
Risperidone	Initial: 2-3 mg/day PO Usual dose: 3-6 mg/day in a single daily dose or 2 divided doses	Weight gain, orthostasis, dose-related EPS, metabolic disturbances
Valproic acid/divalproex	Initial: 250 mg TID PO Usual dose: 750-2000 mg/day PO, adjusted according to serum levels	Nausea, alopecia, tremor, weight gain, teratogenic, inhibition of hepatic enzymes

TABLE 3: First-line drug therapy for depression in bipolar disorder³

Drug	Dosage	Adverse Effects
Cariprazine	Initial: 1.5 mg PO once daily Maximum: 3 mg/day	Akathisia, nausea, restlessness, extrapyramidal symptoms (EPS)
Lamotrigine	Initial: 25 mg/day PO Usual maintenance: 100–300 mg/day PO in 2 divided doses	Rash (slow titration required), insomnia
Lithium	Initial: 300 mg BID PO (150 mg BID PO in the elderly) Usual dose: 600–1800 mg/day PO, guided by serum concentrations	Highly toxic in overdose (signs and symptoms of toxicity include ataxia, tremor, sedation or agitation, diarrhea, vomiting)
Lurasidone	Initial: 20 mg/day PO with food (at least 350 calories) Usual dose: 20–60 mg/day PO Maximum: 120 mg/day	Akathisia, anxiety, EPS, insomnia, nausea/vomiting, somnolence
Quetiapine	Initial: 50 mg/day PO Usual dose: 300 mg/day PO twice daily Maximum: 600 mg/day	Weight gain, sedation, orthostasis, metabolic disturbances

TABLE 4: First-line maintenance therapy for bipolar disorder³

Drug	Dosage	Adverse Effects
Aripiprazole	15 mg/day PO Maximum: 30 mg/day	Akathisia, dizziness, orthostatic hypotension, headache, gastrointestinal complaints, tremor, sedation
Aripiprazole injection	400 mg once monthly by deep IM injection Dose can be reduced to 300 mg once monthly if adverse reactions occur	Akathisia, dizziness, orthostatic hypotension, headache, gastrointestinal complaints, tremor, sedation
Asenapine	5 mg BID SL Maximum: 10 mg BID SL depending on response and tolerability	Sedation, orthostasis, hypotension, dizziness, weight gain, extrapyramidal symptoms (EPS)
Lamotrigine	100–300 mg/day PO	Rash (slow titration required), insomnia
Lithium	600–1800 mg/day PO, guided by serum concentrations	Highly toxic in overdose (signs and symptoms of toxicity include ataxia, tremor, sedation or agitation, diarrhea, vomiting)
Quetiapine	Usual: 300 mg/day PO Maximum: 600 mg/day	Weight gain, sedation, orthostasis, metabolic disturbances
Valproic acid/ divalproex	Usual dose: 750–2000 mg/day PO, adjusted according to serum levels	Nausea, alopecia, tremor, weight gain, teratogenic, inhibition of hepatic enzymes

References

1. Health Canada. *Drug product database online query* [internet]. Available from: <https://health-products.canada.ca/dpd-bdpp/index-eng.jsp>. Accessed July 17, 2024.
2. CPS: Drug Information. *Lithium* [drug monograph]. Canadian Pharmacists Association; 2020. Available from: <https://cps.pharmacists.ca>. Subscription required. Accessed July 17, 2024.
3. Parikh SV. *Bipolar disorder* [internet]. June 18, 2024. Available from: <https://cps.pharmacists.ca>. Subscription required. Accessed July 18, 2024.