Canadian Pharmacists Association | Association des pharmaciens du Canada

Carbamazepine Controlled-Release (CR) 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: **Carbamazepine products marketed in Canada**[1]

Product	Strength	DIN	Manufacturer
Mint-Carbamazepine	200 mg tablet	02541238	Mint Pharmaceuticals Inc.
Tegretol	200 mg tablet	00010405	Novartis Pharmaceuticals Canada Inc.
	200 mg CR tablet	00773611	
	400 mg CR tablet	00755583	
	100 mg/5 mL oral suspension	02194333	
Sandoz-Carbamazepine	200 mg CR tablet	02261839	Sandoz Canada Inc.
	400 mg CR tablet	02261847	
Taro-Carbamazepine	100 mg/5 mL oral suspension	02367394	Taro Pharmaceuticals Inc.
	100 mg chewable tablet	02244403	
	200 mg chewable tablet	02244404	
Teva-Carbamazepine	200 mg tablet	00782718	Teva Canada Ltd.

Health Canada–approved indications for carbamazepine:[2]

- For use as an anticonvulsant drug either alone or with other anticonvulsant drugs
- For symptomatic relief of pain of trigeminal neuralgia only during periods of exacerbation of true or primary trigeminal neuralgia
- May be used alone or as adjunct therapy to lithium in the treatment of acute mania or prophylaxis of bipolar disorders in patients who are resistant or intolerant of conventional antimanic drugs

Management options:

Carbamazepine is a first-line monotherapy for treating focal or tonic-clonic seizures.[3] The Canadian League Against Epilepsy (CLAE) has provided some practical tips online to help manage the shortage.[4] Some recommendations include:

- Consider starting new patients on medications other than carbamazepine CR
- Consider switching patients from CR formulation to immediate-release (IR) formulations
- Review pharmaco-equivalences between different anticonvulsants (see Table 2)

Treatment strategies in **seizure disorder** depend on the seizure type, potential for drug interactions and side effects, desired titration speed, comorbidities, cost, and patient preferences. See Table 3.

Trigeminal neuralgia usually responds to carbamazepine. Oxcarbazepine, a derivative of carbamazepine, may be more advantageous in that it is given twice daily and may have fewer side effects and drug interactions. Gabapentin, pregabalin, clonazepam and valproic acid may be tried if other strategies fail.[5] See Table 4.

Treatment strategies for mania in **bipolar disorder** depend on whether the patient is on maintenance therapy and experiencing a breakthrough episode or if they are not on any medication. First-line options for manic episodes include lithium, divalproex or second-generation antipsychotics. See Table 5. Carbamazepine is a second-line agent for managing bipolar disorder. Other second-line agents include olanzapine, ziprasidone and haloperidol. In medication selection, consider whether the patient has previously tried first-line agents, along with factors such as side effects, past responses and patient preferences.[6] See Table 5.

TABLE 2: **Pharmaco-equivalences between anticonvulsants**[4]

Carbamazepine CR PO 100 mg = carbamazepine IR PO 90–100 mg
Carbamazepine PO 100 mg = oxcarbazepine PO 110–150 mg
Carbamazepine PO 100 mg = eslicarbazepine PO 130 mg
Oxcarbazepine PO 100 mg = eslicarbazepine PO 100 mg

TABLE 3: **Antiepileptic agents for focal or unclassified tonic-clonic seizures**[3]

Drug	Dosage	Adverse Effects
Brivaracetam	Initial: 100 mg/day PO in 2 divided doses Usual maintenance: 100–200 mg/day PO in 2 divided doses	Sleepiness, nausea, decreased energy, dizziness, irritability, depression
Eslicarbazepine	Initial: 400 mg once daily PO × 1 wk Usual maintenance: 800 mg PO once daily Maximum: 1200 mg/day	Dizziness, fatigue, nausea, vomiting, blurred vision, headache, abnormal coordination
Gabapentin	Initial: 300 mg once daily PO Usual maintenance: 900–3600 mg/day PO divided Q6–8H	Tremor, vision changes, gastrointestinal upset
Lacosamide	Initial: 50–100 mg/day PO in 2 divided doses Usual maintenance: 200–400 mg/day PO in 2 divided doses	Dizziness, nausea, ataxia, sedation, PR interval prolongation
Lamotrigine	Initial: 25 mg/day PO Usual maintenance: 100–400 mg/day PO in 2 divided doses	Rash (slow titration required), insomnia
Levetiracetam	Initial: 1000 mg/day PO in 2 divided doses Usual maintenance: 1000–3000 mg/day PO in 2 divided doses	Sleepiness, decreased energy, headache, irritability, depression, psychiatric and behavioural abnormalities
Oxcarbazepine	Initial: 300 mg BID PO Usual maintenance: 1200–2400 mg/day PO in 2 divided doses	Drowsiness, ataxia, dizziness, nausea, hyponatremia
Valproic acid/divalproex	Initial: 250 mg BID PO Usual maintenance: 750–1000 mg/day PO in 2–4 divided doses	Nausea, alopecia, tremor, weight gain, teratogenic, inhibits hepatic enzymes

TABLE 4: **Alternative agents for trigeminal neuralgia**[5]

Drug	Dosage	Adverse Effects
Clonazepam	Initial: 1.5 mg/day PO Maximum: 20 mg/day	Sedation, serum levels potentially increased by CYP3A4 inhibitors
Gabapentin	Initial: 300–400 mg/day PO HS Maximum: 3600 mg/day in divided doses	Tremor, vision changes, gastrointestinal upset
Oxcarbazepine	Initial: 75–150 mg BID PO Maximum: 1200 mg/day	Drowsiness, ataxia, dizziness, nausea, hyponatremia
Pregabalin	Initial: 50–150 mg daily PO in 2 divided doses Usual effective dose: 300–600 mg/day Maximum: 600 mg/day	Sedation, ataxia, edema, diplopia, weight gain, dry mouth
Valproic acid/ divalproex	Initial: 125 mg BID PO; increase by 250 mg/day every 1–2 wk as necessary Usual maintenance: 750–1000 mg/day in 2–4 divided doses	Nausea, alopecia, tremor, weight gain, teratogenic, inhibits hepatic enzymes

TABLE 5: **First-line agents for mania in bipolar disorder**[6]

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, inhibits hepatic enzymes

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