

Clobazam (Frisium®)

Clobazam Products Available in Canada ¹			
Product Name	DIN	Manufacturer	Available on Sask Formulary? ²
Apo-Clobazam	02244638	APX	Y
Clobazam-10	02248454	PRO DOC LImitee	N
Dom-Clobazam	02247230	DOM	Y
Frisium	02221799	LUD	N
Novo-Clobazam	02238334	NOP	Y
PMS-Clobazam	02244474	PMS	Y

In Canada, clobazam is approved for “adjunctive therapy in patients with epilepsy who are not adequately stabilized with their current anticonvulsant therapy.”³

It is considered an add-on for all seizure types: tonic-clonic; absence; myoclonic and atonic; and partial (simple or complex) with or without secondary generalization.^{4,5}

Considerations:

- There are no drugs available which will provide an antiepileptic substitution for clobazam in all patients. This shortage calls for highly **individualized assessment**.
- We have two concerns: **seizure control** afforded by clobazam as well as **benzodiazepine withdrawal** in the event of abrupt withdrawal.
- Generally, clobazam is used in patients who have been **refractory** to other antiepileptics so it is likely seizure control may be challenging and several options may already have been trialed; all previous antiepileptic use needs to be gathered and, if possible, the reason for discontinuation.

To address withdrawal:

- Benzodiazepine withdrawal can manifest as status epilepticus as well as insomnia, agitation, anxiety, dysphoria, headache, muscle aches, twitches, tremors and myriad other symptoms.⁶ Protocols vary but long-term users may expect discontinuation to take two to three months.^{6,7} Since most facilities and pharmacies will have a few days' therapy at most of clobazam, **an appropriate taper will not take place**.
- **Benzodiazepine substitution will be required** to prevent withdrawal. **Clonazepam** has the closest kinetic profile to clobazam so is a reasonable choice for benzodiazepine substitution.⁸
- Usual seizure dose range clobazam: 10 mg BID; 30 mg HS; (20-30 mg per day)⁵
Usual seizure dose range clonazepam: 0.5 mg PO TID; 1 mg TID; 2 mg TID (1.5-8 mg/day)⁵

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To address seizure:

- As mentioned above, the choice of antiepileptic will need to be made on an **individual patient basis**. **Table 1** provides alternatives for the different seizure types.
- Rivotril’s product monograph includes the following statement: Clonazepam is “useful alone or as an adjunct in the management of myoclonic and akinetic seizures and petit mal variant (Lennox-Gastaut syndrome). RIVOTRIL may be of some value in patients with absence spells (petit mal) who have failed to respond to succinimides.”⁹ However, **clonazepam does not appear in therapeutic references** as an alternative for any type of seizure. (See Table 1)
- To minimize adverse effects, **titrate new antiepileptic at recommended rate**.¹⁰
- Be cognizant of **drug interactions**.

Table 1. Effective Anti-Epileptic Agents by Seizure Type^{4,7}		
Seizure Type	First Line Therapeutic Alternative *	Second Line Therapeutic Alternative
Tonic-Clonic	carbamazepine, lamotrigine, VPA** phenytoin, oxcarbazepine	levetiracetam, topiramate
Partial (Simple or Complex)	carbamazepine, lamotrigine, levetiracetam <i>oxcarbazepine, phenytoin, VPA</i>	<i>gabapentin, lacosamide oxcarbazepine, phenobarbital, primidone, topiramate, VPA, vigabatrin</i>
Absent	ethosuximide <i>lamotrigine, VPA</i>	<i>lamotrigine, levetiracetam, topiramate, VPA</i>
Myotonic	VPA <i>levetiracetam, topiramate</i>	<i>lamotrigine, levetiracetam, topiramate</i>
Atonic	VPA	<i>lamotrigine, levetiracetam, topiramate</i>

*Use bolded agents preferentially followed by italicized. **VPA = valproic acid/divalproex sodium

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References:

1. Health Canada. Drug Product Database Online Query. Ottawa, ON: Health Canada; [cited 2013 Jan 13]. Available from: <http://webprod.hc-sc.gc.ca/dpd-bdpp/index-eng.jsp>
2. Saskatchewan Formulary. Drug Plan and Extended Benefits Branch [homepage on the Internet]. Government of Saskatchewan; [cited 2013 Jan 13]. Available from <http://formulary.drugplan.health.gov.sk.ca/>
3. Frisium product monograph. Lundbeck, Inc. Deerfield, IL 60015 USA. 2011 Dec 9. (Distributed by Accuristix Mississauga, ON L5R 3Y4)
4. Moeller JJ, Sadler RM. Seizures and epilepsy. In: Gray Jean, editor. e-Therapeutics+ [Internet]. Ottawa (ON): Canadian Pharmacists Association; c2013 [updated 2011 May; cited 2013 Jan 13]. Available from: <http://www.e-therapeutics.ca>. Also available in paper copy from the publisher.
5. Jensen B. Antiepileptics (Antiseizure). RxFiles drug comparison charts. 9th ed. Saskatoon, SK: Saskatoon Health Region; 2012. p. 84. Available from: www.RxFiles.ca. Accessed 2013 Jan 13.
6. Virani AS, Bezchlibnyk-Butler KZ, Jeffries JJ, editors. Clinical handbook of psychotropic drugs. 18th ed. Toronto: Hogrefe & Huber Publishers; 2009.
7. DynaMed [Internet]. Ipswich (MA): EBSCO Publishing. 1995 - 2013. Epilepsy in adults. [updated 2012 Oct 2; cited 2013 Jan 14]; [about 24 screens]. Available from <http://search.ebscohost.com/login.aspx?direct=true&site=dynamed&id=113862>. Registration and login required.
8. e-CPS [Internet]. Ottawa (ON): Canadian Pharmacists Association; c2013 [updated 2012 Sep; cited 2013 Jan 13]. Benzodiazepines [CPhA monograph]. Available from: <http://www.e-cps.ca>. Also available in paper copy from the publisher.
9. Rivotril product monograph. Hoffman-La Roche Limited. Mississauga ON. L5N 6L7. Revised July 8, 2009)
10. (UpToDate - Overview of the management of epilepsy in adults. Schachter S. Updated 2012 Nov 26; cited 2013 Jan 15. Available from uptodate.com. Login and password required.