

## Clobazam (Frisium®)

Clobazam Products Available in Canada <sup>1</sup>			
Product Name	DIN	Manufacturer	Available on Sask Formulary? <sup>2</sup>
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.”<sup>3</sup>

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.<sup>4,5</sup>

### 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.<sup>6</sup> Protocols vary but long-term users may expect discontinuation to take two to three months.<sup>6,7</sup> 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.<sup>8</sup>
- Usual seizure dose range clobazam: 10 mg BID; 30 mg HS; (20-30 mg per day)<sup>5</sup>  
Usual seizure dose range clonazepam: 0.5 mg PO TID; 1 mg TID; 2 mg TID (1.5-8 mg/day)<sup>5</sup>

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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.”<sup>9</sup> 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**.<sup>10</sup>
- Be cognizant of **drug interactions**.

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

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

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## References:

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