

Clobazam (Frisium®)

Please note: As of June 9, 2016, Apotex expects to have stock available June 17, 2016
McKesson states an availability date of June 24, 2016

Clobazam Products Available in Canada ¹			
Product Name	DIN	Manufacturer	DPEBB ² /NIHB ³ Benefit?
Apo-Clobazam	02244638	APX	Y/Y
Clobazam-10	02248454	PRO DOC Limitee	N/Y
Frisium	02221799	LUD	Y/Y
Teva-Clobazam	02238334	TEV	Y/Y

DPEBB=Drug Plan and Extended Benefits Branch; NIHB= Non-Insured Health Benefits

In Canada, clobazam is approved for “adjunctive therapy in patients with epilepsy who are not adequately stabilized with their current anticonvulsant therapy.”⁴ 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.^{5,6}

Considerations:

There are no drugs available which will provide an antiepileptic substitution for clobazam in all patients. This shortage calls for highly **individualized assessment**.

- There are two concerns: **seizure control** afforded by clobazam and **benzodiazepine withdrawal** in the event of abrupt discontinuation.
- 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.⁷ Protocols vary but long-term users may expect discontinuation to take two to three months.^{7,8} 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.⁹
- Usual seizure dose range clobazam: 10 mg BID; 30 mg HS; (20-30 mg per day)⁶
- Usual seizure dose range clonazepam: 0.5 mg PO TID; 1 mg TID; 2 mg TID (1.5-8 mg/day)⁶

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. **Consult the patient's neurologist if at all possible**.
- 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.”¹⁰ 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.**¹¹
- Be cognizant of **drug interactions.**

Table 1 Effective Anti-epileptic Agents by Seizure Type ^{5,8}		
Seizure Type	First Line Therapeutic Alternatives*	Second Line Therapeutic Alternatives
Tonic-Clonic	CBZ, lamotrigine, VPA phenytoin, oxcarbazepine	levetiracetam, topiramate
Partial (Simple or Complex)	CBZ, lamotrigine, levetiracetam <i>oxcarbazepine, phenytoin, VPA</i>	gabapentin, lacosamide, phenobarbital, primidone, topiramate, vigabatrin
Absent	ethosuximide <i>lamotrigine, VPA</i>	levetiracetam, topiramate
Myotonic	VPA <i>levetiracetam, topiramate</i>	lamotrigine
Atonic	VPA	lamotrigine, levetiracetam, topiramate

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

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References:

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