



# B.C. INTER-PROFESSIONAL PALLIATIVE SYMPTOM MANAGEMENT GUIDELINES

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# TWITCHING/ MYOCLONUS/ SEIZURES

## DEFINITIONS<sup>3</sup>

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**Twitching** refers to an involuntary muscle contraction; it tends to be repetitive, unwanted, and lacking obvious cause.

**Myoclonus** is defined as involuntary single or irregularly repetitive movement of one part of the body associated with either brief, shock-like muscle contractions or jerks (positive myoclonus), or brief loss of muscle tone (negative myoclonus). Hiccough is a type of myoclonus. Myoclonus may precede onset of opioid-induced neurotoxicity.<sup>33</sup>

**Opioid-induced neurotoxicity** is due to the accumulation of toxic metabolites. Impaired renal function, dehydration and electrolyte imbalances contribute to this condition. It may cause myoclonus and seizures.<sup>33</sup>

**Seizures** may be varying in intensity and type and may include an absent stare, muscle rigidity, cyanosis, and an altered state of consciousness. They may last from 1-4 minutes.

**Status epilepticus** is a seizure lasting 5 minutes or longer, or repeated seizures one after another without regaining consciousness.

## PREVALENCE

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**Myoclonus** occurs more commonly (2.8-87%) in patients on higher doses of opioids,<sup>1</sup> or in the presence of renal failure<sup>2</sup>; however, causes can be multifactorial.

**Seizures** may be the first indication of a brain tumour. They occur in up to 50% of palliative patients with a primary brain tumour,<sup>3</sup> and in 20-45% of patients with brain metastases.<sup>4,5</sup>

## IMPACT

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Twitching and myoclonus may be misinterpreted as seizure activity. Seizures can be frightening for the patient and family. Indicators of neurotoxicity may require switching of opioids.<sup>33</sup>

## STANDARD OF CARE

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### Step 1 | Goals of care conversation

Determine goals of care in conversation with the patient, family and inter-disciplinary team. Refer to additional resources ([Additional resources for management of seizures](#)) for tools to guide conversations and required documentation. Goals of care may change over time and need to be reconsidered at times of transition, e.g., disease progression or transfer to another care setting.

### Step 2 | Assessment

**Twitching, myoclonus and seizures assessment:  
Using Mnemonic O, P, Q, R, S, T, U and V<sup>32</sup>**

<b>Mnemonic Letter</b>	<b>Assessment Questions</b> <i>Whenever possible, ask the patient directly. Involve family as appropriate and desired by the patient.</i>
<b>O</b> nset	When did it begin? How long does it last? How often does it occur?
<b>P</b> rovoking /Palliating	What brings it on? What makes it better? What makes it worse? Have you recently started any new medications or treatments?
<b>Q</b> uality	What does it feel like? Can you describe it? How do you feel afterwards?
<b>R</b> egion/Radiation	Does your entire body move? Is the movement only in a part of your body? Ask family or caregivers to describe what happens.
<b>S</b> everity	How severe is this symptom? What would you rate it on a scale of 0-10 (0 being none and 10 being the worst possible)? Right now? At worst? On average? How bothered are you by this symptom? Are there any other symptom(s) that accompany this symptom?

*Twitching, myoclonus and seizures assessment: using mnemonic O, P, Q, R, S, T, U and V continued on [next page](#)*

## Twitching, myoclonus and seizures assessment: Using Mnemonic O, P, Q, R, S, T, U and V *continued*

<b>Treatment</b>	What medications and treatments are you currently using? Are you using any non-prescription treatments, herbal remedies, or traditional healing practices? How effective are these? Do you have any side effects from the medications and treatments? What have you tried in the past? Do you have concerns about side effects or cost of treatments? Have you recently changed a dose or type of treatment? Have you stopped or started alcohol or other substances?
<b>Understanding</b>	What do you believe is causing this symptom? How is it affecting you and/or your family? What is most concerning to you?
<b>Values</b>	What overall goals do we need to keep in mind as we manage this symptom? What is your acceptable level for this symptom (0-10)? Are there any beliefs, views or feelings about this symptom that are important to you and your family?

**Symptom Assessment:** Physical assessment as appropriate for symptom

**Diagnostics:** consider goals of care before ordering diagnostic testing

Degree of investigation depends on severity and goals of care, including desired location.<sup>16</sup> May reveal more than one cause.

- CBC and biochemical tests may reveal reversible causes.
- CSF culture for infectious causes.
- Radiologic: CAT scan or MRI.
- Electroencephalogram if suspect seizure activity, but may not be needed.<sup>8</sup>

## Step 3 | Determine possible causes and reverse as possible if in keeping with goals of care

- Identifying the underlying etiology of the myoclonus, twitching or seizures is essential in order to provide the appropriate treatment.<sup>3,6</sup>
- Opioid-induced myoclonus is often misinterpreted as seizure activity by caregivers and clinicians.<sup>1</sup> This is important as myoclonus tends to respond to correction of the underlying reversible causes.<sup>7</sup>
- Terminal delirium can also be misinterpreted as seizure.<sup>1</sup>
- Impaired excretion of opioids and their metabolites may cause myoclonus.
- Most prevalent in renal impairment with morphine, codeine, meperidine and, to a lesser extent, hydromorphone.<sup>1</sup> Liver impairment also a risk factor.<sup>9</sup> Methadone or fentanyl rarely cause myoclonic neurotoxicity.<sup>1,7,10,11</sup>
- Drug causes are extensive and include: tricyclic antidepressants, serotonin reuptake inhibitors, anticonvulsants, ertapenem, pregabalin, trazodone, and levodopa.<sup>12,13</sup>
- Assess for drug interactions that may contribute to neurotoxicity, e.g., from antipsychotics, antidepressants, and other central nervous system drugs.<sup>13,14</sup>
- Fully review drugs recently introduced, discontinued, or dosing altered. Especially assess benzodiazepines, alcohol, opioids, anticonvulsants, smoking, caffeine, and complementary or alternative medicines.
- Dehydration may be a contributing factor.<sup>7</sup>
- Other causes may include: pinched nerve, nerve injury, stimulant abuse, epilepsy, Parkinson's disease, amyotrophic lateral sclerosis, and benign fasciculation syndrome.<sup>3</sup>

### Seizure

- Seizures may be caused by primary or metastatic brain tumours.<sup>3</sup>
- Metabolic causes: hypoglycemia (most common metabolic cause), hyperglycemia, hyponatremia, renal or hepatic failure, and hypercalcemia.
- Hypoglycemia can also be caused by prolonged seizure activity.<sup>3</sup>
- A wide variety of other causes may be identified including stroke, sepsis or late onset epilepsy.

## PRINCIPLES OF MANAGEMENT

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When considering a management approach, always balance burden of a possible intervention against the likely benefit (e.g., does the intervention require transfer to another care setting?)





- Lorazepam is the first-line for all 3 conditions.
- Ensure patient safety and comfort during and following a seizure.
- Twitching/myoclonus is frequently related to opioids and is often reversible.
- Educate patient and family to discern between myoclonus and seizure activity, and to report to their health care team.

### Step 4 | Interventions

## LEGEND FOR USE OF BULLETS

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Bullets are used to identify the type or strength of recommendation that is being made, based on a review of available evidence, using a modified GRADE process.

	<b>Use with confidence:</b> recommendations are supported by moderate to high levels of empirical evidence.
	<b>Use if benefits outweigh potential harm:</b> recommendations are supported by clinical practice experience, anecdotal, observational or case study evidence providing low level empirical evidence.
	<b>Use with caution:</b> Evidence for recommendations is conflicting or insufficient, requiring further study
	<b>Not recommended:</b> high level empirical evidence of no benefit or potential harm

## Non-pharmacological interventions

### Interventions available in the home and residential care facilities

- Recognize that myoclonus or seizures can increase pain, fatigue, and other distressing symptoms. **Follow-up assessment and appropriate intervention.**<sup>15</sup>
- Myoclonus generally responds to **conservative treatment**: correct dehydration and renal function, if possible; and reduction and/or rotation of opioid.<sup>7, 12</sup>
- Seizure treatment will vary** according to the frequency and duration of convulsions, and whether there is a reversible underlying cause.<sup>8</sup>
- Position HOB** 30° above level of heart if increased cerebral pressure.<sup>5</sup>

### Prevention/risk reduction

- Screen for recent history of recreational drug and alcohol use.
- Review medication for those that reduce seizure threshold, or reduce effectiveness of current meds. Adjust medications and doses appropriately.<sup>22, 23</sup> Monitor drug levels as required for patient status and location of care.
- Prevent, monitor for, and minimize adverse effects.

### Physiotherapy and occupational therapy

- Mobility and transfer safety. Referral for assessment, patient/family education and recommendations.<sup>15</sup>

## Interventions that may require additional equipment or transfer to acute care


### Environment – injury prevention and maintenance of airway during a seizure.

- As per local seizure protocol.
- Ensure potential aggressive treatments align with patient goals of care and consider patient status and location: hydration; intubation and transfer to ICU.<sup>8</sup>


*Non-pharmacological interventions continued on [next page](#)*






## Non-pharmacological interventions *continued*

-  Some treatments may be more appropriate earlier in disease trajectory, for short durations to achieve symptom control, or to meet a specific goal.


### Hydration

-  Consider for reversible causes of myoclonus<sup>2</sup>. Depends on patient status, goals of care, and care location Limited evidence of benefit. Requires further study.<sup>17</sup>


### Surgical

-  Resection of lesion with clear margins has been successful in patients with primary, low grade brain tumours. Remission of seizures in 80% of patients.<sup>18</sup>
-  Careful consideration must be given to the life expectancy and appropriateness for patient.<sup>15</sup>
-  May allow eventual weaning from long-term anti-consultants after excision.<sup>8</sup>



### Radiation Therapy

-  Seizure control can be improved in primary tumors when radiation therapy is offered early, even if no survival benefit.<sup>19,20,21</sup>

### Oxygen

-  Status epilepticus patients benefit from oxygen,<sup>16</sup> if available and if patient is NOT actively dying. Hypoxia is a risk with longer seizures and can result in significant impairment.

## Pharmacological interventions





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**Lorazepam** is a first-line therapy for twitching, myoclonus and seizures. Advantages include: rapid onset, sustained duration of action, 85-89% response rate in tonic-clonic seizures, lower cardiorespiratory depression than diazepam, familiarity and availability throughout patient care settings.<sup>1,2</sup>
- 
 Use non-oral routes of administration often to ensure reliable effectiveness.

### Initial Management with Lorazepam<sup>3</sup>

Myoclonus/ Twitching	Partial Seizure	Tonic-Clonic Seizure	Status Epilepticus
0.5 to 2 mg SL or SC Q4H PRN	1 to 2 mg SL or SC stat then 1 to 2 mg Q4H to Q6H	4 to 8 mg IV or SC stat, then 2 to 4 mg Q4H to Q6H	2 to 8 mg IV, SC or SL stat, then q10min to q20min until controlled








## Management for Specific Symptoms Outlined in this Guideline

### 1) Twitching or Myoclonus Management




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 Stop the offending drug, whenever possible.<sup>12, 24, 25</sup> Often myoclonus gradually resolves in a few days.<sup>2, 12, 24</sup> Some medications require a gradually tapering to prevent complications, e.g., cardiovascular and central nervous system (CNS).<sup>26</sup>
- 
 Reduce the dose of the offending drug.<sup>1</sup> Reduce opioid dose by 20-30%<sup>11</sup> or 30-50% for high doses,<sup>28</sup> and reduce dosing interval as well with irreversible renal failure for renally excreted opioids.<sup>13</sup>
- 
 The benefit of a dose reduction over rotation may be less certain and only postpone the need to switch opioids.<sup>25</sup>
- 
 Do not use naloxone to treat opioid-induced myoclonus as it will not respond and may reverse symptom control for other symptoms.<sup>1, 10, 25, 27</sup>

*Pharmacological interventions continued on [next page](#)*



## Pharmacological interventions *continued*

-  Stop other non-essential medications.<sup>6</sup>
-  Switch (rotate) to a different opioid. If hyperalgesia accompanies the myoclonus, a switch is particularly helpful.<sup>24</sup>
-  Fentanyl or methadone are useful choices for experienced prescribers as both of these have minimal or no active neurotoxic metabolites.<sup>1, 10, 24</sup>
-  Maintain patient pain and symptom goals. Do not solely reduce opioid to control myoclonus.<sup>24</sup>
-  Consider use of non-opioid adjuvant analgesics, e.g., anticonvulsants, acetaminophen, and others.<sup>29</sup> Refer to Pain Management guideline.
-  Treat pharmacologically to resolve reversible causative metabolic abnormalities.
-  As evidence and topic management guidelines are not robust,<sup>30</sup> utilize further resources including palliative care physician consultants, medical specialists, or experienced multidisciplinary clinicians including clinical pharmacists.

## 2) Twitching or Myoclonus Drug Dosing

-  Choice of second-line anticonvulsants for management is uncertain. Benzodiazepines are commonly selected, in part based on suitability for patient setting, ease of administration, cost and familiarity. Options include:
  -  Midazolam, 1 to 5 mg IV, SC, buccal PRN (especially in uremic-induced).<sup>20</sup>
  -  Clonazepam, starting at 0.5 mg orally once or twice daily.<sup>13, 31</sup>

## 3) Seizure Management

-  Avoid starting anticonvulsants prophylaxis in brain tumor patients (primary or metastatic) if the patient has never had any seizures, due to lack of benefit and risk of drug burden.<sup>2, 21</sup>
-  Initiation of long-term anticonvulsants after a first time seizure may not be required.<sup>8, 23</sup>

*Pharmacological interventions continued on [next page](#)*

## Pharmacological interventions *continued*

- Assess and provide treatment if high risk of reoccurrence, e.g., in brain metastases from melanoma, choriocarcinoma, renal cell carcinoma or thyroid papillary cancer.<sup>21</sup>
- Review the current dose of corticosteroid; consider starting one adjunctively in those with intracranial tumour and seizure or scheduled cerebral radiotherapy.<sup>23</sup>













### 4) Seizure Drug Dosing

- Review individual seizure type and tailor monotherapy anticonvulsant to patient.<sup>27</sup>
- Midazolam via continuous subcutaneous infusion over 24 hours can be used<sup>23</sup>; however, review use and suitability with local palliative care team.

### 5) Status Epilepticus Management

- Status epilepticus should be controlled even in the unconscious patient near death because of the distress that continuous seizures cause to the patient's family.<sup>3</sup>
- First line: Lorazepam 2 to 8 mg IV or SC or SL STAT then q10 to 20 min until controlled. IV maximum infusion rate 2 mg per minute.<sup>3</sup>
- Alternatively: Midazolam 5 to 10 mg IV, buccally, or Diazepam 10 to 20 mg IV or rectally.<sup>3,27</sup>
- Phenytoin 50 mg per min IV until seizure stops or maximum 20mg per kg per 24 hours.<sup>3</sup>
- Valproic acid loading dose 20 mg per kg then 3 to 5 mg per kg per min infusion.<sup>3</sup>
- Failing control: Phenobarbital 120 mg SC or IV and titrating to control.<sup>3</sup>

## Patient and family education

-  **Myoclonus** is described as brief muscle jerks or spasms. They may appear before or during sleep. While common, they rarely need treatment. Help family members differentiate between myoclonus and seizure activity:
  -  Increased frequency or intensity may indicate an underlying problem; instruct patient and family to inform the care team of any changes.
-  **Seizures** are frightening to the patient and family. Take time afterward to explore concerns of the patient and family, and offer honest reassurance.<sup>23</sup> Address questions,<sup>3,16</sup> dispel fears and maximize comfort.
-  Primary focus is on safety during and after seizures, medication use, eliminating the underlying cause if feasible and knowing when to contact the health care provider.<sup>15</sup>
-  Ensure alternate medication routes have been made available if needed and instruct patient's family on how to provide medication for active management.<sup>8</sup>
-  Do not attempt to restrain the person; loosen tight clothing around the neck.
-  Do not shout at the person or expect verbal commands to be obeyed.
-  Do not try to force anything into the patient's mouth. Do not give any fluids or food by mouth until the person has fully recovered consciousness.
-  When the seizure stops, turn the person onto his/her side until fully alert. Expect a period of sleepiness after the seizure.
-  If the patient has been driving or operating machinery, they may not continue until cleared by a physician.
-  Contact your health care provider for additional support if needed (during office hours).
-  Call after hours **Nurse Line** if available in your region, as needed.

## ADDITIONAL RESOURCES FOR MANAGEMENT OF SEIZURES

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### Resources Specific to Seizures

- B.C. Epilepsy Society: information sheets on safety during seizures, diary templates, emotional support etc.
  - <http://www.bcepilepsy.com/resources/information-sheets>
- BC Cancer Agency: Brain and central nervous system cancer
  - <http://www.bccancer.bc.ca/health-info/types-of-cancer/brain-central-nervous-system>
- BC Cancer Agency: Headlines: a newsletter for brain tumor patients and their families
  - <http://www.bccancer.bc.ca/health-info/types-of-cancer/brain-central-nervous-system/headlines>

### General Resources

- **Provincial Palliative Care Line** – for **physician** advice or support, call **1 877 711-5757** In ongoing partnership with the Doctors of BC, the toll-free Provincial Palliative Care Consultation Phone Line is staffed by Vancouver Home Hospice Palliative Care physicians 24 hours per day, 7 days per week to assist physicians in B.C. with advice about symptom management, psychosocial issues, or difficult end-of-life decision making.
- BC Centre for Palliative Care: Serious Illness Conversation Guide
  - <http://www.bc-cpc.ca/cpc/>
- BC Guidelines: Palliative Care for the Patient with Incurable Cancer or Advanced Disease
  - <http://www2.gov.bc.ca/gov/content/health/practitioner-professional-resources/bc-guidelines/palliative-care>
- BC Palliative Care Benefits: Information for prescribers
  - <http://www2.gov.bc.ca/gov/content/health/practitioner-professional-resources/pharmacare/prescribers/plan-p-bc-palliative-care-benefits-program>

*Additional resources for management of seizures continued on [next page](#)*

## ADDITIONAL RESOURCES FOR MANAGEMENT OF SEIZURES *CONTINUED*

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- National Centre for Complementary and Alternative Medicine (NCCAM) for additional information on the use of non-pharmacological interventions  
→ <https://nccih.nih.gov/>
- Canadian Association of Psychosocial Oncology: Pan-Canadian Practice Guideline: Screening, Assessment and Management of Psychosocial Distress, Depression and Anxiety in Adults with Cancer  
→ [http://www.capo.ca/wp-content/uploads/2015/11/FINAL\\_Distress\\_Guideline1.pdf](http://www.capo.ca/wp-content/uploads/2015/11/FINAL_Distress_Guideline1.pdf)
- Fraser Health psychosocial care guideline  
→ <https://www.fraserhealth.ca/media/psychosocial%20care.pdf>

### Resources specific to health organization/region

- Fraser Health  
→ <http://www.fraserhealth.ca/health-professionals/professional-resources/hospice-palliative-care/>
- First Nations Health Authority  
→ <http://www.fnha.ca/>
- Interior Health  
→ <https://www.interiorhealth.ca/YourCare/PalliativeCare/Pages/default.aspx>
- Island Health  
→ [http://www.viha.ca/pal\\_eol/](http://www.viha.ca/pal_eol/)
- Northern Health  
→ <https://www.northernhealth.ca/Professionals/PalliativeCareEndofLifeCare.aspx>
- Providence Health  
→ <http://hpc.providencehealthcare.org/>
- Vancouver Coastal Health  
→ <http://www.vch.ca/your-care/home-community-care/care-options/hospice-palliative-care>

*Additional resources for management of seizures continued on [next page](#)*

## ADDITIONAL RESOURCES FOR MANAGEMENT OF SEIZURES *CONTINUED*

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### Resources specific to patient population

- ALS Society of Canada: A Guide to ALS patient care for primary care physicians  
→ <https://als.ca/wp-content/uploads/2017/02/A-Guide-to-ALS-Patient-Care-For-Primary-Care-Physicians-English.pdf>
- ALS Society of British Columbia 1-800-708-3228  
→ [www.alsbc.ca](http://www.alsbc.ca)
- BC Cancer Agency: Symptom management guidelines  
→ <http://www.bccancer.bc.ca/health-professionals/clinical-resources/nursing/symptom-management>
- BC Renal Agency: Conservative care pathway and symptom management  
→ <http://www.bcrenalagency.ca/health-professionals/clinical-resources/palliative-care>
- BC's Heart Failure Network: Clinical practice guidelines for heart failure symptom management  
→ <http://www.bcheartfailure.ca/for-bc-healthcare-providers/end-of-life-tools/>
- Canuck Place Children's Hospice  
→ <https://www.canuckplace.org/resources/for-health-professionals/>
  - 24 hr line – 1.877.882.2288
  - Page a Pediatric Palliative care physician – 1-604-875-2161 (request palliative physician on call)
- Together for short lives: Basic symptom control in pediatric palliative care  
→ <http://www.togetherforshortlives.org.uk/professionals/resources/2434-basic-symptom-control-in-paediatric-palliative-care-free-download>

## UNDERLYING CAUSES OF TWITCHING, MYOCLONUS AND SEIZURES

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Information on underlying causes contained within the body of the document.



## MEDICATIONS FOR MANAGEMENT OF TWITCHING, MYOCLONUS AND SEIZURES

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Information on medications for management contained within the body of the document.

Prices for prescription drugs may be obtained from BC PharmaCare. The British Columbia Palliative Care Benefits Plan <http://www2.gov.bc.ca/assets/gov/health/health-drug-coverage/pharmacare/palliative-formulary.pdf> provides province wide drug coverage for many of the recommended medications– check website to confirm coverage. **Consider price when choosing similarly beneficial medications, especially when the patient / family is covering the cost.**

## TWITCHING, MYOCLONUS AND SEIZURES MANAGEMENT ALGORITHM

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No management algorithm included in this document.

## TWITCHING, MYOCLONUS AND SEIZURES EXTRA RESOURCES OR ASSESSMENT TOOLS

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No extra resources or assessment tools included in this document.

## TWITCHING, MYOCLONUS AND SEIZURES REFERENCES

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*Twitching/myoclonus/seizures references continued on [next page](#)*

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