Clinical Resource Guide:
Seizure Management in the Hospice Setting

INTRODUCTION

Seizure management can be challenging in any patient population, but especially in the hospice patient, who is often without IV access and in the home or facility setting. While rare for a patient to have a seizure, it is a serious complication when experienced, requiring an action plan to address. The incidence of seizures in the hospice setting is unknown, but literature from the palliative care setting suggests up to 13% of patients may experience the condition, with 25-50% of these patients with a brain neoplasm. However, the prevalence of seizure activity in patients with a brain primary cancer is dependent upon diagnosis, as slow growing types (oligodendroglioma, low-grade astrocytoma) tend present with more seizure activity (70-100% of patients) as compared to more aggressive glioblastoma (10-20%). This Pharmacist Corner was designed to serve as a guide to help support hospice teams prepare for and effectively manage seizure disorder in their patient populations.

Pharmacist Corner Objectives

1.) Identify risk factors for seizure activity and appropriate patient selection for initiating/maintaining therapy
2.) Determine appropriate pharmacologic anticonvulsant therapy and route of administration based on patient-specific factors

PATHOPHYSIOLOGY

Seizures can be caused by structural damage to the brain or be a systemic insult to the brain. See examples in the table below:

POSSBLE CAUSES OF SEIZURE	
Structural Damage	**Systemic Insult**
• Primary tumor • Metastases • Abscesses • Paraneoplastic encephalitis	• Hypoxia • Hypoglycemia • Hypo- or Hypernatremia • Hypo- of Hypermagnesemia • Meds lowering the seizure threshold

Seizures are classified according to their level of origin in the brain. Anytime a seizure is accompanied by a loss of consciousness, there will follow a postictal state, which may include somnolence, confusion, or headache, and can last up to several hours.

CLASSIFICATION OF SEIZURE BY TYPE		
Seizure	**Characteristics**	**Type**
Partial or focal seizures	**Simple**: without loss of consciousness **Complex**: with loss of consciousness	Motor Sensory Autonomic Affective
Generalized	Primary or secondary (following partial seizure) with or without aura	*Nonconvulsive*: • Absence or petit mal *Convulsive*: • Grand mal or tonic-clonic • Clonic (upper limb, neck, face) • Myoclonic (limbs) • Tonic (rigidity and falls) • Atonic (sudden loss of muscle tone

HISTORY AND PHYSICAL EXAM

When a patient develops a seizure, a prompt history and physical examination are useful to determine the cause. A structural cause can be suspected if there was an aura before the seizure, if the seizure was focal, or if the physical examination revealed focal neurologic findings. These latter neurologic findings might disappear within a few hours after the seizure event.

SEIZURE PROPHYLAXIS

Anticonvulsant prophylaxis is not recommended in patients with brain tumors, whether primary or metastatic, if the patient has never had any seizures. This is because of the minimal risk of developing convulsions for most tumors, and the considerable potential burden of antiseizure side effects (drug-drug interactions, sedation, cognitive impairment). However, brain metastases from melanoma, choriocarcinoma, renal cell carcinoma, thyroid papillary

cancer, and cancer of the testis might be exceptions, as these cancers might have a higher risk of causing seizures owing to their increased risk of bleeding.

A study by Forsyth et al. **did not show any benefit of seizure prophylaxis**, as patients still developed convulsions due to tumor progression or subtherapeutic levels of anticonvulsants at similar rates as those not taking prophylaxis. Patients should take dexamethasone before, during, and immediately after cerebral radiotherapy to prevent the edema secondary to acute radiation toxicity, which could otherwise provoke seizures.

TREATMENT

The treatment of seizures will vary based on frequency, duration, and presence of a reversible cause. For example, a patient experiencing a seizure for the first time with a reversible cause does not require long-term anticonvulsant therapy, while a patient with a brain lesion presenting with their first episode should be considered.

ANTICONVULSANT RECOMMENDATIONS

TYPE	First-Line Treatment	Second-Line Treatment
PARTIAL	• Carbamazepine • Phenytoin • Oxcarbazepine • Valproic acid	• Phenobarbital • Gabapentin • Topiramate • Lamotrigine • Levetiracetam
ABSENCE	• Valproic acid • Clonazepam	• Topiramate • Lamotrigine
MYOCLONIC	• Valproic acid • Clonazepam	• Clobazam • Topiramate
TONIC-CLONIC	• Carbamazepine • Phenytoin • Valproic Acid	• Phenobarbital • Oxcarbazepine • Topiramate

For patients initiated or continued on anticonvulsant therapy, the table below provides guidance for initial doses, anticipated therapeutic doses, and additional considerations for each medication when reviewing patient-specific factors and creating a treatment plan.

ORAL ANTICONVULSANT DOSING AND CONSIDERATIONS			
Medication	**Initial Dose**	**Usual Effective Dose**	**Considerations/Side effects**
Levetiracetam	1000mg/day	1000-3000mg/day in two divided doses	May cause anxiety, agitation dizziness
Phenytoin	100mg po BID	200mg-500mg/day	Many drug-drug interactions
Carbamazepine	200mg/day; incr. by 200mg/wk	300-1600mg in 3-4 doses (IR) or in two divided doses (SR)	Many drug-drug interactions
Valproic acid	15mg/kg daily; 250-500mg/day	Up to 60mg/kg/day; 1000-3000mg/day	Dose reduce for hepatic failure
Oxcarbazepine	300-600mg/day	900-2400mg/day	Dose reduce for renal failure
Phenobarbital	60mg/day	60-250mg/day, max: 600mg/day (Adults: 1-5mg/kg/day): single or divided doses	CNS depressant, may cause respiratory depression, rash, somnolence

In patients who have lost the ability to take anticonvulsants orally, a rotation to a medication that can be administered via an alternative route should be considered by the hospice team. Medications commonly utilized for this clinical scenario in the hospice setting are listed in the table below

NON-ORAL ANTICONVULSANT DOSING AND CONSIDERATIONS			
Medication	**Route**	**Dosing**	**Therapy Cost***
Lorazepam	Sublingual (Lorazepam Intensol®)	0.5mg – 2mg Q8H; PRN	**$18.00-$68.00/30ml**
Diazepam	Diazepam tab rectally	SEE APPENDIX A: Diazepam	**$0.43/dose**
	Rectal gel (Diastat®)		**$350-$550/fill**
	Nasal spray (Valtoco®)		**$600-$800/fill**
Midazolam	Midazolam IV nebulized	SEE APPENDIX B: Midazolam	**$3.43/dose**
	Nasal spray (Nayzilam®)		**$650-$850/fill**

*Prices may vary depending upon dispensing pharmacy

SUMMARY

This Pharmacist Corner addresses the complexities of managing seizures in hospice patients and was designed to offer a comprehensive guide for the hospice care team to help with clinical decision-making. The recommendation against routine anticonvulsant prophylaxis in a patient with a brain neoplasm who has not previously experienced a seizure is emphasized, balancing the minimal risk of convulsions against the potential side effects of medication. Treatment approaches, including first and second-line anticonvulsants and their respective dosing considerations, are outlined. Additionally, this guide provides an overview of the non-oral alternatives for patients unable to take medications orally, providing insight into routes of administration and associated considerations. This resource equips hospice teams with practical insights and recommendations for effective seizure management in this specialized care setting. For questions regarding patient-specific scenarios, please call BetterRX for a Clinical Pharmacy Consultation.

APPENDIX A: Rectal Diazepam

Diastat® Dosing

Calculating Prescribed Dose

The diazepam rectal gel dose should be individualized for maximum beneficial effect. The recommended dose of diazepam rectal gel is 0.2-0.5 mg/kg depending on age. See the dosing table for specific recommendations.

Age (years)	Recommended Dose
2 through 5	0.5 mg/kg
6 through 11	0.3 mg/kg
12 and older	0.2 mg/kg

Because diazepam rectal gel is provided as unit doses of 2.5, 5, 7.5, 10, 12.5, 15, 17.5, and 20 mg, the prescribed dose is obtained by rounding upward to the next available dose. The following table provides acceptable weight ranges for each dose and age category, such that patients will receive between 90% and 180% of the calculated recommended dose. The safety of this strategy has been established in clinical trials.

2 - 5 Years 0.5 mg/kg		**6 - 11 Years** 0.3 mg/kg		**12+ Years** 0.2 mg/kg	
Weight (kg)	Dose (mg)	Weight (kg)	Dose (mg)	Weight (kg)	Dose (mg)
6 to 10	5	10 to 16	5	14 to 25	5
11 to 15	7.5	17 to 25	7.5	26 to 37	7.5
16 to 20	10	26 to 33	10	38 to 50	10
21 to 25	12.5	34 to 41	12.5	51 to 62	12.5
26 to 30	15	42 to 50	15	63 to 75	15
31 to 35	17.5	51 to 58	17.5	76 to 87	17.5
36 to 44	20	59 to 74	20	88 to 111	20

The rectal delivery system includes a plastic applicator with a flexible, molded tip available in two lengths. The DIASTAT® ACUDIAL™ 10 mg syringe is available with a 4.4 cm tip and the DIASTAT® ACUDIAL™ 20 mg syringe is available with a 6.0 cm tip. DIASTAT® 2.5 mg is also available with a 4.4 cm tip.

In elderly and debilitated patients, it is recommended that the dosage be adjusted downward to reduce the likelihood of ataxia or oversedation.

The prescribed dose of diazepam rectal gel should be adjusted by the physician periodically to reflect changes in the patient's age or weight.

The DIASTAT® 2.5 mg dose may also be used as a partial replacement dose for patients who may expel a portion of the first dose.

Additional Dose

The prescriber may wish to prescribe a second dose of diazepam rectal gel. A second dose, when required, may be given 4-12 hours after the first dose.

APPENDIX B: Intranasal Diazepam

Valtoco® Dosing

Dose Based on Age and Weight			Administration	
6 to 11 Years of Age (0.3 mg/kg)	12 Years of Age and Older (0.2 mg/kg)	Dose (mg)	Number of Nasal Spray Devices	Number of Sprays
Weight (kg)	Weight (kg)			
10 to 18	14 to 27	5	One 5 mg device	One spray in one nostril
19 to 37	28 to 50	10	One 10 mg device	One spray in one nostril
38 to 55	51 to 75	15	Two 7.5 mg devices	One spray in each nostril
56 to 74	76 and up	20	Two 10 mg devices	One spray in each nostril

Second Dose (if needed): A second dose, when required, may be administered after at least 4 hours after the initial dose. If the second dose is to be administered, use a new blister pack of VALTOCO.

Maximum Dosage and Treatment Frequency: Do not use more than 2 doses of VALTOCO to treat a single episode.

It is recommended that VALTOCO be used to treat no more than one episode every five days and no more than five episodes per month.

APPENDIX C: Intranasal Midazolam

Nayzilam® Dosing:

1.) Administer one spray (5mg/0.1ml) into one nostril
2.) One additional spray (5mg) into the opposite nostril may be administered after 10 minutes if the patient has not responded to the initial dose.
3.) Do not use more than two doses of Nayzilam® to treat a seizure cluster. It is recommended to not use more than for one episode every three days or no more than five episodes/month.

References

1.) Tradounsky G. Seizures in Palliative Care. *Canadian Family Physician*. September 2013: (59); 951-955.
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3.) Holsti M, Dudley N, Schunk J et al. Intranasal midazolam vs. rectal diazepam for home treatment of acute seizures in pediatric patients with epilepsy. *Arch Adolescent Med*. 2010; 164(8):747-753.
4.) Trinka E, Holfer J, Litinger M, Brigo F. Pharmacotherapy for status epilepticus. *Drugs*. 2015;75 (13)1499-1521.
5.) Diastat. Package insert. Valeant Pharmaceuticals North America, LLC. 12/2016
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7.) Nayzilam. Package insert. UCB, Inc. 1/2023.

