New Onset Afebrile Seizure
Inpatient

Nationwide Children's — When your child needs a hospital, everything matters.

Center for Clinical Excellence

Inclusion Criteria:
- Children ≥ 6 months of age with first presentation of unprovoked convulsive seizure

Exclusion Criteria:
- Status epilepticus
- Pre-existing epilepsy diagnosis
- Presence of intracranial hardware
- History of head trauma in past 48 hours
- Concern for non-accidental trauma
- Concurrent concern for CNS infection
- History or suspicion of brain tumor
- Current metabolic disturbance or oncologic processes
- Febrile seizure (simple & complex)
- Neurocutaneous disorders
- Psychogenic non-epileptic event (PNEE)

Considerations for Rescue Medications:
- Patient ≥ 6 months of age
- Family distance from medical facility
- Rescue medication was required during patient visit
- Family preference
- Seizure was >5 minutes
- Co-morbid medical diagnosis suggests greater risk for future seizure

Discharge Planning
- Verify that the Rx has been sent to the NCH or a local pharmacy
- Consider 2 doses of rescue medication (i.e. for home and daycare/school)
- Clarify whether Neurology Clinic follow up is required (appointments might not be scheduled before discharge); provide family with Neurology Clinic contact information if test results are pending
- Seizure Helping Hands; seizure teaching video; seizure Action Plan

Diagnostic Timeout
- Definition and Diagnosis
- Differential Diagnoses
- Red Flags and Risk Assessment

Seizure H&P Considerations

- Neurology consult
- MRI and labs if indicated
- Routine EEG (discuss with Neurology prior to ordering on a weekend)
- Order seizure rescue medication
- Vitals Q8H
- Neuro checks Q4H

Monitor for signs of deterioration:
- Decline in mental status
- Deterioration since previous neuro check
- Focal neurological deficits
- Recurrence of seizure

Escalation of care required? — Yes →

Escalation of Care
- Notify primary resident, neurology resident
- Consider supplemental oxygen if patient is actively seizing
- Place IV to ensure access
- ACT per clinical judgement

No ↓

Demonstrates anticipated improvement toward baseline mental status?

Yes ↓

- Review EEG and any imaging/ labs
- Reassess patient
- Provide caregiver CPR training

Meets discharge criteria? — No → **Off Pathway** Seek ongoing Neurology input

Yes ↓

Discharge when meeting criteria
- Seizure resolved
- Normal mental status/return to baseline mental status or continued progression to baseline
- Discussion and/or consultation with Neurology
- If indicated, daily anti-seizure and/or rescue medications have been prescribed and education provided
- Safe discharge plan and teaching including Sudden Unexpected Death of Someone with Epilepsy (SUDEP)

Definitions & Diagnosis

Is this a new onset afebrile seizure?

- Seizure- Transient event with clinical symptoms due to abnormal, excessive, and synchronous discharges of neurons residing primarily in the cerebral cortex. This abnormal paroxysmal activity is intermittent and usually self-limited, lasting seconds to a few minutes.
  - History- often includes a period of change in tone with unresponsiveness, rhythmic limb movements and eye deviation followed by post-ictal period

- This pathway covers only unprovoked seizures with the following considerations:
  - Does not meet criteria for febrile seizure
  - No suspicion of CNS infection
  - No suspicion of metabolic disturbance (vomiting, diarrhea, dehydration, persistent AMS)
  - No suspicion of ingestion
  - No suspicion of head trauma

- The clinician should diagnose seizures on the basis of history
  - Consider home video recording of suspected event
  - EEG may be obtained later and is not required to diagnose seizures

Consider other alternate clinical problem and diagnosis when:
Lack of above diagnostic features.

Consider a diagnostic timeout (“What else could this be?”) or using a diagnostic checklist.

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Differential Diagnoses

- **Psychogenic Non-Epileptic Events**

- **Consideration of vaso-vagal syncope**
  - Prodromal lightheadedness, vision changes
  - No loss of bowel or bladder control
  - No biting of tongue or limb jerking
  - Brief loss of consciousness followed by waking with a normal mental status (no prolonged post-ictal confusion)

- **Consideration of cardiovascular event**
  - Prodromal chest pain or heart palpitations
  - Event occurred with exertion/exercise
  - Family history cardiac death or long QT
  - Waking with a normal mental status (no post-ictal confusion)

- **Consideration of breath holding spells**
  - Six months to 6 years of age (majority occur before 18 months of age)
  - Loss of consciousness in the setting of crying

- **Consideration of reflux (Sandifer's)**
  - Infants through pre-school age
  - History of spit up
  - Classic arching back posturing after feeding
  - Episode with temporal relationship to feeding

*If considering meningitis, febrile seizure, ingestion, or other provoked seizure the patient should not be treated following this pathway

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Epileptic Seizures vs. Psychogenic Non-Epileptic Events (PNEE)

Signs Favoring PNEE	Signs Favoring Epileptic Seizures	Indeterminate Signs
• Long duration • Fluctuating Course • Asynchronous Movements* • Pelvic Thrusting* • Side-to-side Head or Body Movements** • Forced Eye Closure • Ictal Crying • Memory Recall	• Occurrence from Physiologic Sleep • Postictal Confusion • Stertorous Breathing	• Gradual Onset • Non-Stereotyped Events • Flailing or Thrashing Movements • Opisthotonos • Tongue Biting • Urinary Incontinence

*May not reliably differentiate between PNEE and frontal lobe partial epileptic seizures
** May only be helpful in distinguishing convulsive PNEE and epileptic seizures

Adapted from:

Avbersek A, Sisodiya S. Does the primary literature provide support for clinical signs used to distinguish psychogenic nonepileptic seizures from epileptic seizures? J Neurol Neurosurg Psychiatry. 2010; 81:719–725.

Perez DL, LaFrance WC. Nonepileptic seizures: an updated review. CNS Spectr. 2016 June;21(3:) 239-246.

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Return to Differential Diagnosis

Red Flags & Risk Assessment

- **Red Flags – Higher Risk**
  - Patient has seizure lasting >5 minutes, or recurrence of seizure
  - Focal neurological deficits
  - Patient continues to seize following administration of abortive medication
  - New or persistent fever
  - Failure to return to baseline mental status

- **Low risk**
  - Single seizure
  - Return to baseline
  - No focal neurological findings

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Diagnostic Evaluation – H&P

- The broad objective of the seizure history and physical exam is to characterize the event and determine whether the patient is high or low risk for seizure recurrence
- History should be taken from persons who directly observed the event and supplemented with video recording if possible
- History of Present Illness (ideally from the person who witnessed the event)
  - What did caregiver first notice (generalized/bilateral vs focal/unilateral onset)?
  - What was patient doing prior to seizure onset (sleeping, eating, playing)?
  - Make caregiver describe in detail or demonstrate limb movements
  - Describe any attempts (verbal, tactile) to gain attention of patient during seizure
  - Duration of seizure
  - Any focal features (such as eye deviation, asymmetric limb posturing or movements) during the seizure?
- History
  - Birth history
  - Developmental history and age at milestones
  - Family history of seizures or other neurological disorders
- Complete Neurological exam
- If history and/or exam reveals concerns for provoked seizure (i.e. electrolyte disturbance or infection), patient should be off pathway and evaluated per standard care processes

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Diagnostic Testing

- EEG should be considered for patients hospitalized with a new onset seizure. Discuss with the Neurology consult prior to ordering on the weekend. EEG should be ordered as routine unless otherwise directed by Neurology consultation. If not obtained during the hospitalization, EEG should be ordered by the PCP in a timely fashion in coordination with Neurology

- Consider non-urgent MRI- ordered by PCP or neurologist outpatient for patients:
  - Age <1 year
  - Focal onset seizure (consider more urgent imaging during hospitalization)
  - Abnormalities on EEG concerning for focal seizures and/or epilepsy

- Provoked seizure suspicion- patient moves off pathway
  - If failure to return to baseline, or reported symptoms present, then consider electrolytes or blood glucose
  - If considering LP due to concern for meningitis/encephalitis
  - If considering toxicology screen due to concern for ingestion

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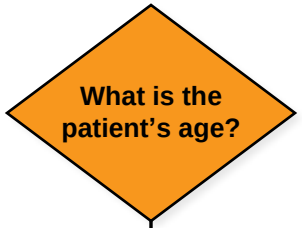
Seizure Rescue Medication Decision

^Midazolam kit includes:

- 5 mg/mL midazolam vial (1 mL or 2 mL)
- Syringe (1 mL or 3 mL)
- Cannula
- Atomizer

^Midazolam kit is not available at most community pharmacies. Please send these prescriptions only to NCH Pharmacies.

Cost considerations when selecting a medication	
Midazolam kit	$40
Nayzilam®	$800
Valtoco®	$800
Diazepam gel	$400



6 months – 5 years

Medication	Route	Weight Limit	Insurance Coverage	
			Medicaid	Commercial
Midazolam kit	Intranasal	None	✓	Out of pocket**
Valtoco®	Intranasal	10 kg	PA-required	Not covered
Nayzilam®	Intranasal	12.5 kg	PA-required	Not covered
Diazepam gel	Rectal	5 kg	✓	✓

6 – 11 years

Medication	Route	Insurance Coverage	
		Medicaid	Commercial
Valtoco®	Intranasal	✓	Identify coverage*
Midazolam kit	Intranasal	✓	Out of pocket**
Nayzilam®	Intranasal	PA-required	Not covered
Diazepam gel	Rectal	✓	✓

≥ 12 years

Medication	Route	Insurance Coverage	
		Medicaid	Commercial
Nayzilam®	Intranasal	✓	Identify if product covered*
Valtoco®	Intranasal	✓	
Midazolam kit	Intranasal	PA-required	Out of pocket**
Diazepam gel	Rectal	✓	✓

*** Prior Authorization (PA) may be required, co-pay card is available if pts ≥ 12yo with Nayzilam or ≥ 6yo with Valtoco (≥ 10kg) which MAY bring co-pay to ~$30/fill (NCH may not be contracted to use co-pay card)**

**** Cash price for the midazolam kit is likely cheaper than co-pay for Nayzilam (co-pay assistance is not available to patients < 12yo) or Valtoco (co-pay not available < 6yo)**

Note: Patients may not be able to refill existing prescription for non-preferred products and may need to be converted to insurance preferred product

Please order 2 doses so medication is available for home and school/daycare

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Midazolam

Midazolam 5 mg/mL injectable solution for NASAL use

Intranasal Midazolam (Versed®) Dosing Recommendations (by weight)	
Recommended dose = 0.2-0.4 mg/kg for all ages	
Weight (kg)	**Dose (mg)**
< 5	0.3mg/kg minimum
> 5 to 10	2 mg (0.2 mL each nostril)
> 10 to 18	4 mg (0.4 mL each nostril)
> 18 to 25	5 mg (0.5 mL each nostril)
≥ 25	10 mg (1 mL each nostril)

Rescue Medication Dosing

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Nayzilam

Nayzilam (midazolam 5 mg/0.1 mL nasal spray)

Nayzilam® (midazolam nasal spray) Dosing Recommendations (by weight)	
Recommended dose = 0.2-0.4 mg/kg for all ages	
Weight (kg)	**Dose (mg)**
≥ 12.5 to 25	5 mg (1 sp ray in 1 nostril) *
≥ 25	10 mg (1 sp ray in each nostril) *

Cost: ~$800/kit

Availability: Most retail pharmacies (may need 24 hours to order in)

Quantity limits: usually up to 3 kits/fill

FDA labeled indications: **≥ 12 years of age**: 5 mg in one nostril for cluster seizures. May repeat dose in 10 minutes in alternate nostril based on response and tolerability-our prescribing practices may differ from labeled instructions

Managed Care Plans: Covered by all if ≥ 12 years old; PA likely required if <12yo

Commercial Insurance: may need a PA, but may be a plan exclusion; co-pay varies with plan

*Off-label

Rescue Medication Dosing

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Valtoco

Valtoco® (diazepam nasal spray) Dosing Recommendations (by age and weight)					
Recommended dose by age 2 to 5 years = 0.5 mg/kg*		Recommended dose by age 6 to 11 years = 0.3 mg/kg		Recommended dose by age ≥ 12 years = 0.2 mg/kg	
Weight (kg)	**Dose (mg)**	**Weight (kg)**	**Dose (mg)**	**Weight (kg)**	**Dose (mg)**
10 to < 15	One 5 mg device (1 spray in 1 nostril)	10 to < 19	One 5 mg device (1 spray in 1 nostril)	14 to < 28	One 5 mg device (1 spray in 1 nostril)
15 to < 23	One 10 mg device (1 spray in 1 nostril)	19 to < 38	One 10 mg device (1 spray in 1 nostril)	28 to < 51	One 10 mg device (1 spray in 1 nostril)
≥ 23	15 mg as two 7.5 mg devices (1 spray in each nostril)	38 to < 56	15 mg as two 7.5 mg devices (1 spray in each nostril)	51 to < 76	15 mg as two 7.5 mg devices (1 spray in each nostril)
		≥ 56	20 mg as two 10 mg devices (1 spray in each nostril)	≥ 76	20 mg as two 10 mg devices (1 spray in each nostril)

Cost: ~$800/kit

Availability: Most retail pharmacies (may need 24 hours to order in)

Quantity limits: usually up to 3 kits/fill

FDA labeled indications: **≥ 6 years of age** for cluster seizures-May repeat dose in 4 hours-do not exceed 2 doses in 24 hours, 1 episode every 5 days and 5 episodes per month

Managed Care Plans: Covered by all if ≥ 6 years old; PA required if <6yo

Commercial Insurance: may be covered with PA, but may be a plan exclusion-co-pay varies with plan, co-pay assistance is available for patients ≥ 6 year old

*off-label for patients < 6yo

Rescue Medication Dosing

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Diazepam

Diazepam Rectal Gel (Diastat® AcuDial ™) Dosing Recommendations (by age and weight)					
Recommended dose by age 2 to 5 years = 0.5 mg/kg*		Recommended dose by age 6 to 11 years = 0.3 mg/kg		Recommended dose by age ≥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

Rescue Medication Dosing

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Metrics

Pathway Goal

- To aid in the identification, diagnosis and treatment of patients presenting with a new onset seizure. With specific guidance on the initial evaluation including considerations for EEG and MRI as well as indications for seizure rescue medications while ensuring proper discharge education and follow-up.

Quality Measures

Outcome Metrics

- Primary Outcome metric: Hospital length of stay
- Secondary Outcome metric: Percentage of pathway eligible patients ≥ 6 months of age with a seizure rescue medication prescription

Process Metrics

- Pathway Utilization: percent of pathway eligible patients who utilized the inpatient order set
- Seizure action plan completion: percent of pathway eligible patients who have a completed seizure action plan

Balancing Metrics

- Return to ED/Hospital within 7 and 30 days

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Origination Date: *June, 2020*

Last Revision Date: *May, 2023*

Next Revision Date: *May, 2026*

Clinical Pathway Development

This clinical pathway was developed using the process described in the NCH Clinical Pathway Development Manual Version 6, 2022. Clinical Pathways at Nationwide Children's Hospital (NCH) are standards which provide general guidance to clinicians. Patient choice, clinician judgment, and other relevant factors in diagnosing and treating patients remain central to the selection of diagnostic tests and therapy. The ordering provider assumes all risks associates with care decisions. NCH assumes no responsibility for any adverse consequences, errors, or omissions that may arise from the use or reliance on these guidelines. NCH's clinical pathways are reviewed periodically for consistency with new evidence; however, new developments may not be represented, and NCH makes no guarantees, representations, or warranties with respect to the information provided in this clinical pathway.

For more information about our pathways and program please contact:
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