New Onset
Afebrile Seizure
Emergency Department/Urgent Care

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)

History consistent with seizure (not actively seizing)

Diagnosis & Definition

Differential Diagnoses

PE with new neuro deficits?

Yes → **Off Pathway**: See Sudden Neurological Deterioration Protocol

No

Bilateral tonic-clonic (BTC) seizures lasting ≥ 5 minutes

or

≥ 2 discreet BTC seizures between which there is incomplete recovery of consciousness?

Yes → **Off Pathway**: See Generalized Convulsive Status Epilepticus Pathway

No

Diagnostic evaluation guided by history and physical exam

Diagnostic evaluation reveals underlying etiology of seizure?

Yes → **Off Pathway**: Treat according to accepted practice

No

Meets one or more Admission Criteria?

No → **Discharge Patient**

- Consider rescue medication
- Follow-up with Primary Care Physician in 2-3 days

Yes

- Call Neurology if not already consulted
- If in urgent care consider direct admission versus transfer to Main Campus ED

Admit Patient to Hospital Peds/Neurology

Diagnosis & Definition

- Seizure: Transient event with clinical symptoms due to abnormal excessive and synchronous neuronal activity in the brain. The history often includes a period of change in tone with unresponsiveness, rhythmic limb movements, and eye deviation followed by post-ictal period.
- This guideline covers only unprovoked seizures with the following conditions:
  - Afebrile
  - No suspicion of CNS infection
  - No suspicion of metabolic disturbance (vomiting, diarrhea, dehydration, persistent AMS)
  - No suspicion of ingestion
  - No suspicion head trauma within the past 48 hours
- The clinician should diagnose seizure on the basis of history
  - View home recording of event, if available
- EEG is not required to diagnose seizures and is not completed in the Emergency Department setting

Return to Algorithm

Differential Diagnoses

- **Psychogenic Non-Epileptic Events**

- **Vaso-vagal syncope**
  - Prodromal lightheadedness, vision changes
  - No loss of bowel or bladder control
  - No tongue biting
  - Brief (few seconds) of convulsions (convulsive syncope)

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

- **Breath holding spells**
  - Six months – 6 years of age (majority occur before 18 months of age)
  - Loss of consciousness in the setting of crying or pain

- **Gastroesophageal 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 concerned for provoked seizure (meningitis, febrile seizure, ingestion) the patient should not be treated by following this guideline

Return to Algorithm

Epileptic Seizures versus 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.

Return to Algorithm

Return to Differential Diagnosis

Diagnostic Evaluation

- 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
- History should be taken from persons who directly observed the event and supplemented with video recording if possible
- History of present illness
  - What was patient doing prior to seizure onset (sleeping, eating, playing)?
  - What did caregiver first notice?
  - Any focal features (e.g. eye deviation to the right or left, asymmetric posturing, asymmetric movements)?
  - Make caregiver describe in detail or demonstrate limb movements
  - Attempts (verbal, tactile, noxious) to gain attention of patient during seizure
  - Duration of seizure
- Past Medical History
  - Birth history
  - Developmental history and age at milestones
  - Family history of seizures or other neurological disorders
- Complete neurological exam to identify focal neurologic deficits (if identified, consider SND pathway)
- If history and/or exam reveals concerns for provoked seizure (electrolyte disturbance, or infection), off pathway and evaluate per standard care processes.

Return to Algorithm

Admission Criteria

- Multiple seizures within 24 hours of presentation
- Requiring multiple rescue medications (e.g. > 1 benzodiazepine or levetiracetam or fosphenytoin)
- Persistently altered mental status

Return to Algorithm

ED Discharge Criteria & Planning

- **Discharge criteria:**
  - Appropriate return to baseline mental status
- **Considerations for seizure rescue medications:**
  - Age ≥ 6 months
  - Family lives far distance from medical facility
  - Rescue medication was required during patient visit
  - Co-morbid medical diagnosis suggests greater risk for future seizure
- **Follow Up:**
  - Primary Care Physician (PCP) within 2-3 days
  - PCP to place referral to neurology clinic and can *consider*:
    - Outpatient EEG
    - Non-urgent outpatient MRI for the following:
      - Age < 1 year
      - Focal onset seizure

EEG and MRI at the discretion of the PCP.
These studies can be deferred until after neurology evaluation.

Rescue medication dosing

Return to Algorithm

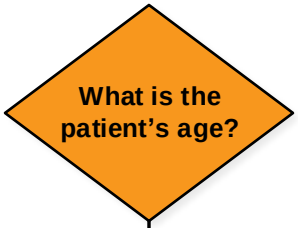
Seizure Rescue Medication Decision

^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.

Return to Algorithm

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	0.3 mg/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

Discharge Planning

Return to Algorithm

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

Discharge Planning

Return to Algorithm

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

Discharge Planning

Return to Algorithm

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

Discharge Planning

Return to Algorithm

Key References

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Return to Algorithm

Metrics

ED/UC Process Measure:

- Pathway Visualization
- Discharge smart set utilization

ED/UC Outcome measure:

- LOS from arrival to disposition
- Decrease in admission rate following first time seizure

Return to Algorithm

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Origination Date: *June, 2020*

Last Revised: *June 2023*

Next Revision Date: *June, 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.

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Return to Algorithm