

New Onset Afebrile Seizure Emergency Department

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)

[Diagnosis & Definition](#)

[Differential Diagnoses](#)

History consistent with seizure
(not actively seizing)

PE with new neuro deficits?

Yes

Off Pathway

See Sudden Neurological
Deterioration Protocol

No

Bilateral tonic-clonic (BTC)
seizures lasting ≥ 5 minutes
or
 ≥ 2 discrete 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?](#)

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**

No

Discharge Patient

- [Consider rescue medication](#)
- [Follow-up with Primary Care Physician in 2-3 days](#)

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 <i>Adapted from:</i> Avbersek A, Sisodiya S. Does the primary literature provide support for clinical signs used to distinguish psychogenic nonepileptic seizures from epileptic seizures? <i>J Neurol Neurosurg Psychiatry</i>. 2010; 81:719–725. Perez DL, LaFrance WC. Nonepileptic seizures: an updated review. <i>CNS Spectr</i>. 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 $\geq$ 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®	\$870
Valtoco®	\$2300
Diazepam gel	\$200

What is the patient's age?

< 2 years

2 – 11 years

≥ 12 years

Medication	Route	Weight Limit	Insurance Coverage	
			Medicaid	Commercial
Midazolam kit	Intranasal	None	✓	Out of pocket**
Valtoco®	Intranasal	6 kg	PA-required	Not covered
Nayzilam®	Intranasal	12.5 kg	PA-required	Not covered
Diazepam gel	Rectal	5 kg	✓	✓

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	✓	✓

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 ≥ 2yo with Valtoco (≥ 6kg) which MAY bring co-pay to ~\$20/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 < 2yo)

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)
6 to 11	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)
12 to 22	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 to 33	15 mg as two 7.5 mg devices (1 spray in each nostril)	38 to < 55	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)
≥ 34	20 mg as two 10 mg devices (1 spray in each nostril)	≥ 55	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: ~\$2300/kit (Only available in 5-dose kits. 5 mg and 10 mg kits contain 5 spray devices, and 15 mg and 20 mg kits contain 10 spray devices)

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

Quantity limits: usually up to 2 kits/fill

FDA labeled indications: **≥ 2 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 ≥ 2 years old; PA required if <2 years old

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 ≥ 2 years old

*off-label for patients < 2 years old

[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

1. Berg AT, Shinnar S, Levy SR, Testa FM. Newly diagnosed epilepsy in children: presentation at diagnosis. *Epilepsia*. 1999;40(4):445-452.
2. Gayatri NA, Morrall MC, Jain V, Kashyape P, Pysden K, Ferrie C. Parental and physician beliefs regarding the provision and content of written sudden unexpected death in epilepsy (SUDEP) information. *Epilepsia*. 2010;51(5):777-782.
3. Hirtz D, Ashwal S, Berg A, et al. Practice parameter: evaluating a first nonfebrile seizure in children: report of the quality standards subcommittee of the American Academy of Neurology, the Child Neurology Society, and the American Epilepsy Society. *Neurology*. 2000;55(5):616-623.
4. Hogan RE, Tarquinio D, Sperling MR, et al. Pharmacokinetics and safety of VALTOCO (NRL-1; diazepam nasal spray) in patients with epilepsy during seizure (ictal/peri-ictal) and nonseizure (interictal) conditions: a phase 1, open-label study. *Epilepsia*. 2020;61(5):935-943.
5. Howell CM, Davis MS, Callanan DL. Stepping outside the box: an adolescent with a new-onset seizure. *Pediatr Emerg Care*. 2013;29(9):1011-1012.
6. Kimia AA, Capraro AJ, Hummel D, Johnston P, Harper MB. Utility of lumbar puncture for first simple febrile seizure among children 6 to 18 months of age. *Pediatrics*. 2009;123(1):6-12.
7. Lateef TM, Tsuchida TN, Chang T, Johnson J, Gaillard WD, Nelson KB. Diagnostic value of lumbar puncture in afebrile infants with suspected new-onset seizures. *J Pediatr*. 2008;153(1):140-142.
8. Sofat P, Teter B, Kavak KS, Gupta R, Li P. Time interval providing highest yield for initial EEG in patients with new onset seizures. *Epilepsy Res*. 2016;127:229-232.
9. Strobel AM, Gill VS, Witting MD, Teshome G. Emergent diagnostic testing for pediatric nonfebrile seizures. *Am J Emerg Med*. 2015;33(9):1261-1264.
10. Huff JS, Murr N. Seizure. In: StatPearls. Treasure Island (FL): *StatPearls Publishing*; 2022.
11. Specchio N, Wirrell EC, et al. International League Against Epilepsy classification and definition of epilepsy syndromes with onset in childhood: position paper by the ILAE Task Force on Nosology and Definitions. *Epilepsia*. 2022;63:1398-1442.

[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](#)

Pathway Team & Process

Content Development Team:

Leaders:

Neurology:

Monica Islam, MD
Anup Patel, MD
Dara Albert, MD

Members:

Hospital Pediatrics:

Ryan Bode, MD, MBOE
Jillian Kunar, DO
Gerd McGwire, MD, PhD

Neurology:

Melissa Chung, MD
Megan Fredwall, MD
Adam Ostendorf, MD

Emergency Medicine:

Betsy Schmerler, MD
Kelli Mavromatis RN, BSN, CPEN

Neurodiagnostics:

Iris Karhoff

Pharmacy:

Daniel Rieck, PharmD
James Herbst, PharmD

Clinical Program Manager:

Kathy Moellman, MSN, RN

Quality Consultant:

Will Parker

Clinical Pathways Program:

Medical Director – Emergency Medicine:

Aarti Gaglani, MD

Medical Director – Hospital Pediatrics:

Gerd McGwire, MD, PhD

Medical Director – Clinical Informatics & Emergency Medicine:

Laura Rust, MD, MPH

Physician Informatics:

Kathy Nuss, MD

Juan D. Chaparro, MD

Business & Development Manager:

Rekha Voruganti, MBOE, LSSBB

Program Coordinators:

Tahje Brown, MBA

Tara Dinh, BS

Clinical Pathway Approved:

Medical Director – Associate Chief Quality Officer, Center for Clinical Excellence:

Ryan Bode, MD, MBOE

Origination Date: *June, 2020*

Last Revised: *June, 2023*

Next Revision Date: *June, 2028*

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 associated 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.

Copyright © 2023. Nationwide Children's Hospital. All rights reserved. No part of this document may be reproduced, displayed, modified, or distributed in any form without the express written permission of Nationwide Children's Hospital.

**For more information about our pathways and program please contact:
ClinicalPathways@NationwideChildrens.org**

[Return to Algorithm](#)