

INCLUSION CRITERIA

- Infants less than 30 days of age presenting with probable clinical seizures (focal clonic or focal tonic seizures) or confirmed clinical seizures

EXCLUSION CRITERIA

- Known or suspected metabolic disease or genetic disorder
- Infants less than 32 weeks gestation

MEASURES

- Appropriate second-line antiseizure medication selection
- Percent intubation within 6 hours of antiseizure medication administration

LABS AND DIAGNOSTICS

- Obtain CMP, Calcium, Magnesium
- Obtain head ultrasound
- Obtain brain MRI when stable
- Obtain head CT if trauma is a concern
- Consider ammonia and lactate
- Recommend workup and treatment for presumed neonatal infection

FURTHER MANAGEMENT

Acute symptomatic seizures- seizures provoked by injury to the central nervous system

Further Management

- If seizure continues consider giving the alt. second line or proceed with midazolam drip
- Discuss maintenance ASM with neurology within 6 hours of seizure onset. **See page 3.**
- Discuss discontinuation of maintenance ASM with neurology after 72 hours of seizure freedom if there is no increased risk for continued seizures

Medications

Medication	Dosage
Lorazepam	0.1 mg/kg/dose IV
Phenobarbital	20 mg/kg/dose IV
Fosphenytoin	First Dose: 20 mg PE/kg/dose IV Second Dose: 10 mg PE/kg/dose IV
Levetiracetam	First Dose: 60 mg/kg/dose IV Second Dose: 40 mg/kg/dose IV
Midazolam	Loading Bolus Dose: 0.1 mg/kg/dose IV Continuous Infusion Dose: 0.05 - 0.1 mg/kg/hr IV

INITIAL ASSESSMENT

- Note seizure onset time in RN seizure flowsheet
- Assess airway, breathing, circulation
- Place on CR monitor and pulse ox
- Obtain point of care glucose and ISTAT
- Obtain vascular access
- Consult Neurology
- If in ED, consult Neonatology. If in Acute Care, consult Neonatology or Critical Care Medicine. Consider admission to unit.
- Initiate EEG within one hour if possible
- If patient is hemodynamically unstable, may consider administering Lorazepam IV. Reassess after 5 minutes then resume pathway.

First Line Medication

- **ADMINISTER** first Phenobarbital IV dose after EEG confirmation or probable clinical seizures

30 min

Continued seizures?

No

Yes

Repeat First Line Medication

- **ADMINISTER** second Phenobarbital IV dose

30 min

Continued seizures?

No

Yes

Yes

Second Line Medication

- **ADMINISTER** First Fosphenytoin dose IV (Preferred for acute symptomatic seizures¹) See page 2

30 min

Continued seizures?

Yes

Repeat Second Line Medication

- **ADMINISTER** Second Fosphenytoin dose IV

No

Second Line Medication

- **ADMINISTER** First Levetiracetam dose IV (Preferred agent in children with congenital cardiac anomaly or hemodynamic instability) See page 2

Yes

Continued seizures?

No

Yes

Repeat Second Line Medication

- **ADMINISTER** Second Levetiracetam dose IV

Alternative Option

Further management per **Neurology.** See page 2.

Go to
pg 2

Second Line Medications

Drug	Indications	Contraindications & Cautions
Fosphenytoin	Acute symptomatic seizures	- Significant hypotension - Bradycardia, heart block - Drug interactions
Levetiracetam	- Congenital heart anomaly - Hemodynamic instability	Reduce dose in end-stage renal disease

Continued Management of Neonatal Seizures, NICU/Neurology

INCLUSION CRITERIA

- Infants less than 30 days of age on maintenance antiseizure medication

EXCLUSION CRITERIA

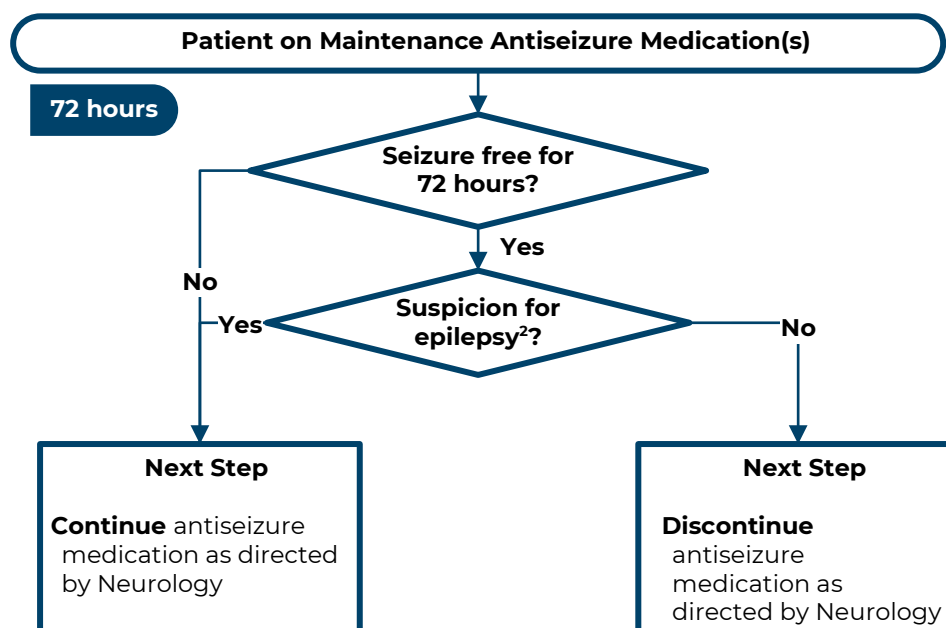
- None

MEASURES

- Increase frequency of Phenobarbital as first line agent
- Decrease duration of antiseizure medication to less than 10 days
- Reduce percentage of patients discharged home on antiseizure medication

²SUSPICION FOR EPILEPSY

- Absence of a known neurologic insult
- Atypical seizure pattern
- Signs of underlying genetic syndrome or congenital brain malformation



Disclaimer: The clinical pathways are based upon publicly available medical evidence and/or a consensus of medical practitioners at Nemours Children's Health ("Nemours") and are current at the time of publication. These clinical pathways are intended to be a guide for practitioners and may need to be adapted for each specific patient based on the practitioner's professional judgment, consideration of any unique circumstances, the needs of each patient and their family, and/or the availability of various resources at the health care institution where the patient is located.

VERSION MANAGEMENT

- Version 1.0 (6/27/2023): Go Live.
- Version 2.0 (2/27/2026): Look back review completed

Questions about this pathway should be directed to clinicalpathways@nemours.org.

AUTHORS & REFERENCES

Central Florida Authors: Marcella Escoto Ventura (Critical Care), Melanie Ortiz (Neurology), Ju Tang (Neurology)

Delaware Valley Authors: Daniel Dirnberger (Neonatology), Elizabeth Wright-Jin (Neurology), Lynn Fuchs (Neonatology), Rodney Scott (Neurology)

North Florida Autor: Fernando Galan (Neurology)

- Alix V, James M, Jackson AH, Visintainer PF, Singh R. Efficacy of Fosphenytoin as First-Line Antiseizure Medication for Neonatal Seizures Compared to Phenobarbital. *J Child Neurol*. 2021;36(1):30-37. doi:10.1177/0883073820947514
- Benedetti GM, Vartanian RJ, McCaffery H, Shellhaas RA. Early Electroencephalogram Background Could Guide Tailored Duration of Monitoring for Neonatal Encephalopathy Treated with Therapeutic Hypothermia. *J Pediatr*. 2020;221:81-87.e1. doi:10.1016/j.jpeds.2020.01.066
- Fitzgerald MP, Kessler SK, Abend NS. Early discontinuation of antiseizure medications in neonates with hypoxic-ischemic encephalopathy. *Epilepsia*. 2017;58(6):1047-1053. doi:10.1111/epi.13745
- Fitzgerald MP, Massey SL, Fung FW, Kessler SK, Abend NS. High electroencephalographic seizure exposure is associated with unfavorable outcomes in neonates with hypoxic-ischemic encephalopathy. *Seizure*. 2018;61:221-226. doi:10.1016/j.seizure.2018.09.003
- Glass HC, Shellhaas RA, Wusthoff CJ, et al. Contemporary Profile of Seizures in Neonates: A Prospective Cohort Study. *J Pediatr*. 2016;174:98-103.e1. doi:10.1016/j.jpeds.2016.03.035
- Glass HC, Soul JS, Chang T, et al. Safety of Early Discontinuation of Antiseizure Medication After Acute Symptomatic Neonatal Seizures [published correction appears in *JAMA Neurol*. 2021 Jul 1;78(7):882]. *JAMA Neurol*. 2021;78(7):817-825. doi:10.1001/jamaneurol.2021.1437
- Hnaini M, Darwich M, Koleilat N, et al. High-Dose Levetiracetam for Neonatal Seizures: A Retrospective Review. *Seizure*. 2020;82:7-11. doi:10.1016/j.seizure.2020.08.030
- Keene JC, Morgan LA, Abend NS, et al. Treatment of Neonatal Seizures: Comparison of Treatment Pathways From 11 Neonatal Intensive Care Units. *Pediatr Neurol*. 2022;128:67-74. doi:10.1016/j.pediatrneurol.2021.10.004
- Kharoshankaya L, Stevenson NJ, Livingstone V, et al. Seizure burden and neurodevelopmental outcome in neonates with hypoxic-ischemic encephalopathy. *Dev Med Child Neurol*. 2016;58(12):1242-1248. doi:10.1111/dmcn.13215
- Le VT, Abdi HH, Sánchez PJ, et al. Neonatal Antiepileptic Medication Treatment Patterns: A Decade of Change. *Am J Perinatol*. 2021;38(5):469-476. doi:10.1055/s-0039-1698457
- Osmond E, Billetope A, Jary S, Likeman M, Thoresen M, Luyt K. Neonatal seizures: magnetic resonance imaging adds value in the diagnosis and prediction of neurodisability. *Acta Paediatr*. 2014;103(8):820-826. doi:10.1111/apa.12583
- Pressler RM, Cilio MR, Mizrahi EM, et al. The ILAE classification of seizures and the epilepsies: Modification for seizures in the neonate. Position paper by the ILAE Task Force on Neonatal Seizures. *Epilepsia*. 2021;62(3):615-628. doi:10.1111/epi.16815
- Qiao MY, Cui HT, Zhao LZ, Miao JK, Chen QX. Efficacy and Safety of Levetiracetam vs. Phenobarbital for Neonatal Seizures: A Systematic Review and Meta-Analysis. *Front Neurol*. 2021;12:747745. Published 2021 Nov 18. doi:10.3389/fneur.2021.747745
- Sharma D, Hussain AM, Sharma SS. Efficacy of Levetiracetam in neonatal seizures: a systematic review. *J Matern Fetal Neonatal Med*. 2022;35(20):3923-3930. doi:10.1080/14767058.2020.1844651
- Sharpe C, Reiner GE, Davis SL, et al. Levetiracetam Versus Phenobarbital for Neonatal Seizures: A Randomized Controlled Trial [published correction appears in *Pediatrics*. 2021 Jan;147(1)]. *Pediatrics*. 2020;145(6):e20193182. doi:10.1542/peds.2019-3182
- Shellhaas RA, Chang T, Tsuchida T, et al. The American Clinical Neurophysiology Society's Guideline on Continuous Electroencephalography Monitoring in Neonates. *J Clin Neurophysiol*. 2011;28(6):611-617. doi:10.1097/WNP.0b013e31823e96d7
- Slaughter LA, Patel AD, Slaughter JL. Pharmacological treatment of neonatal seizures: a systematic review. *J Child Neurol*. 2013;28(3):351-364. doi:10.1177/0883073812470734
- Wietstock SO, Bonifacio SL, Sullivan JE, Nash KB, Glass HC. Continuous Video Electroencephalographic (EEG) Monitoring for Electrographic Seizure Diagnosis in Neonates: A Single-Center Study. *J Child Neurol*. 2016;31(3):328-332. doi:10.1177/0883073815592224
- Wusthoff CJ, Dlugos DJ, Gutierrez-Colina A, et al. Electrographic seizures during therapeutic hypothermia for neonatal hypoxic-ischemic encephalopathy. *J Child Neurol*. 2011;26(6):724-728. doi:10.1177/0883073810390036
- Wusthoff CJ, Sundaram V, Abend NS, et al. Seizure Control in Neonates Undergoing Screening vs Confirmatory EEG Monitoring. *Neurology*. 2021;97(6):e587-e596. doi:10.1212/WNL.0000000000012293