Status Epilepticus Management

Mark Schomer, MD
Jennifer Madan-Cohen, MD

What is a Clinical Pathway?

An evidence-based guideline that decreases unnecessary variation and helps promote safe, effective, and consistent patient care.

Objectives of Pathway

- Decrease time to benzodiazepine administration and subsequent anti-epileptic treatments for patients in status epilepticus
- Decrease length of hospital stay for patients in status epilepticus
- Decrease morbidity and mortality of status epilepticus

Why is Pathway Necessary?

- This population makes up 18-41 per 100,000 children presenting to emergency rooms each year
- Chart review of seizures in Connecticut Children's' ED from January 2017 through June 2018 (18 months)
  - Benzodiazepines being administered as quickly as 15 seconds into seizures
  - Many are being underdosed
  - Many are getting multiple doses at subtherapeutic dosing
- There has been large variability in time to 1st benzodiazepine administration as well as subsequent therapies for refractory status epilepticus

Background

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- Status epilepticus is defined as a continuous seizure for 30 minutes or more[1]
    - Seizures lasting longer than 5 minutes are less likely to self-terminate
- One adult study showed no self-terminating seizure lasted longer than eleven minutes[2]

[1]American Epilepsy Society. (n.d.). Retrieved February 2, 2019, from https://www.aesnet.org/
[2]Jenssen, S., Gracely, E. J., & Sperling, M. R. (2006). How Long Do Most Seizures Last? A Systematic Comparison of Seizures Recorded in the Epilepsy Monitoring Unit. *Epilepsia,47*(9), 1499-1503. doi:10.1111/j.1528-1167.2006.00622.

Background

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- Multicenter observational cohort of patients admitted with refractory SE between 2011 and 2016[3]
  - 103 patients were broken down into three groups
    - –Lower dose lorazepam (<0.05 mg/kg)
    - –Medium dose lorazepam (0.05 to 0.1 mg/kg)
    - –Higher dose lorazepam (>0.1 mg/kg)
- For all seizure types
  - Median seizure resolution time
    - –Lower dose: 350 minutes
    - –Medium dose: 160 minutes
    - –Higher dose: 93 minutes
- For convulsive seizures
  - Median seizure resolution time
    - –Lower dose: 120 minutes
    - –Higher dose: 67 minutes

[3]Smith, D., Mcginnis, E., Walleigh, D., & Abend, N. (2016). Management of Status Epilepticus in Children. *Journal of Clinical Medicine,5*(4), 47. doi:10.3390/jcm5040047.

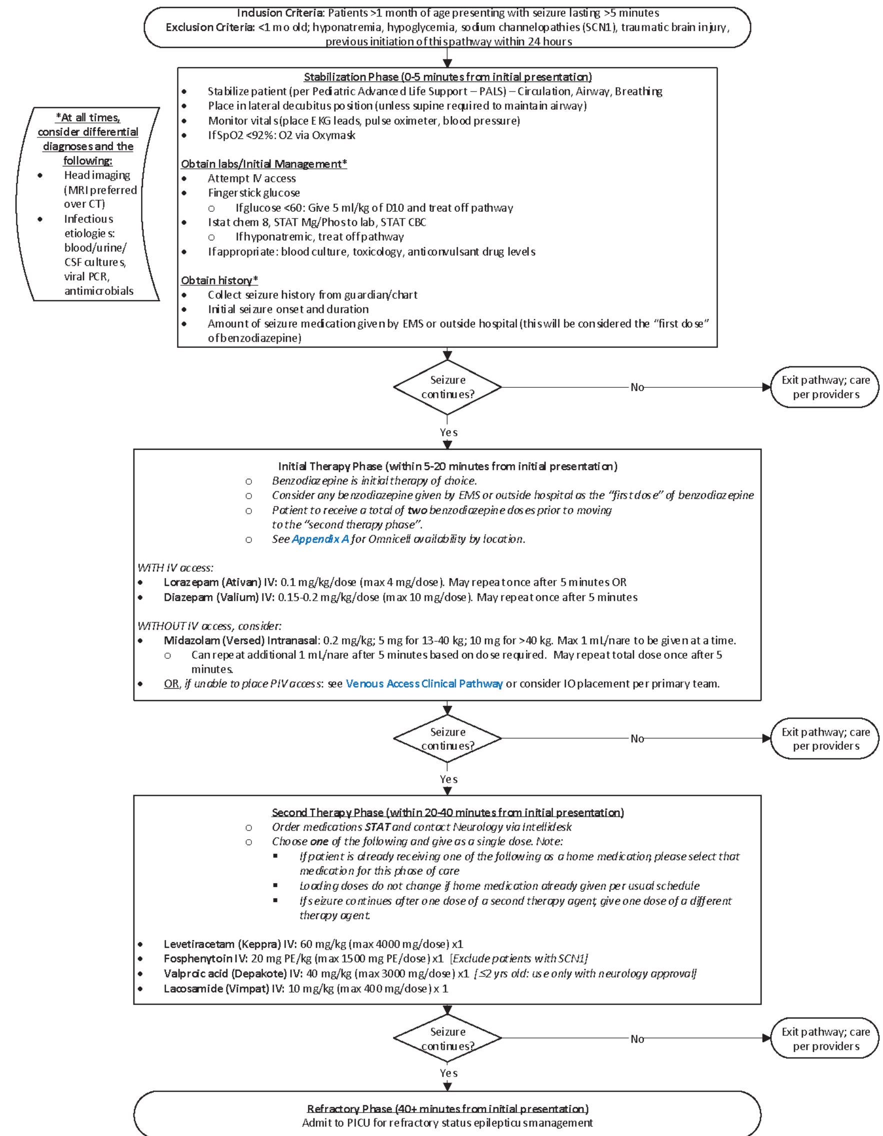
This is the Status Epilepticus Management Clinical Pathway.

We will be reviewing each component in the following slides.

CLINICAL PATHWAY:

Status Epilepticus Management

THIS PATHWAY SERVES AS A GUIDE AND DOES NOT REPLACE CLINICAL JUDGMENT.



Inclusion Criteria: Patients >1 month of age presenting with seizure lasting >5 minutes
Exclusion Criteria: <1 mo old; hyponatremia, hypoglycemia, sodium channelopathies (SCN1), traumatic brain injury, previous initiation of this pathway within 24 hours

Stabilization Phase (0-5 minutes from initial presentation)

- Stabilize patient (per Pediatric Advanced Life Support – PALS) – Circulation, Airway, Breathing
- Place in lateral decubitus position (unless supine required to maintain airway)
- Monitor vitals (place EKG leads, pulse oximeter, blood pressure)
- If SpO2 <92%: O2 via Oxymask

Obtain labs/Initial Management*

- Attempt IV access
- Finger stick glucose
  - If glucose <60: Give 5 ml/kg of D10 and treat off pathway
- Istat chem 8, STAT Mg/Phos to lab, STAT CBC
  - If hyponatremic, treat off pathway
- If appropriate: blood culture, toxicology, anticonvulsant drug levels

Obtain history*

- Collect seizure history from guardian/chart
- Initial seizure onset and duration
- Amount of seizure medication given by EMS or outside hospital (this will be considered the "first dose" of benzodiazepine)

***At all times, consider differential diagnoses and the following:**

- Head imaging (MRI preferred over CT)
- Infectious etiologies: blood/urine/CSF cultures, viral PCR, antimicrobials

Seizure continues? — No → Exit pathway; care per providers — Yes ↓

Initial Therapy Phase (within 5-20 minutes from initial presentation)

- *Benzodiazepine is initial therapy of choice.*
- *Consider any benzodiazepine given by EMS or outside hospital as the "first dose" of benzodiazepine*
- *Patient to receive a total of* ***two*** *benzodiazepine doses prior to moving to the "second therapy phase".*
- *See Appendix A for Omnicell availability by location.*

WITH IV access:

- **Lorazepam (Ativan) IV:** 0.1 mg/kg/dose (max 4 mg/dose). May repeat once after 5 minutes OR
- **Diazepam (Valium) IV:** 0.15-0.2 mg/kg/dose (max 10 mg/dose). May repeat once after 5 minutes

WITHOUT IV access, consider:

- **Midazolam (Versed) Intranasal:** 0.2 mg/kg; 5 mg for 13-40 kg; 10 mg for >40 kg. Max 1 mL/nare to be given at a time.
  - Can repeat additional 1 mL/nare after 5 minutes based on dose required. May repeat total dose once after 5 minutes.
- OR, *if unable to place PIV access:* see Venous Access Clinical Pathway or consider IO placement per primary team.

Seizure continues? — No → Exit pathway; care per providers — Yes ↓

Second Therapy Phase (within 20-40 minutes from initial presentation)

- *Order medications* ***STAT*** *and contact Neurology via Intellidesk*
- *Choose* ***one*** *of the following and give as a single dose. Note:*
  - *If patient is already receiving one of the following as a home medication, please select that medication for this phase of care*
  - *Loading doses do not change if home medication already given per usual schedule*
  - *If seizure continues after one dose of a second therapy agent, give one dose of a different therapy agent.*

- **Levetiracetam (Keppra) IV:** 60 mg/kg (max 4000 mg/dose) x1
- **Fosphenytoin IV:** 20 mg PE/kg (max 1500 mg PE/dose) x1 *[Exclude patients with SCN1]*
- **Valproic acid (Depakote) IV:** 40 mg/kg (max 3000 mg/dose) x1 *[≤2 yrs old: use only with neurology approval]*
- **Lacosamide (Vimpat) IV:** 10 mg/kg (max 400 mg/dose) x 1

Seizure continues? — No → Exit pathway; care per providers — Yes ↓

Refractory Phase (40+ minutes from initial presentation)
Admit to PICU for refractory status epilepticus management

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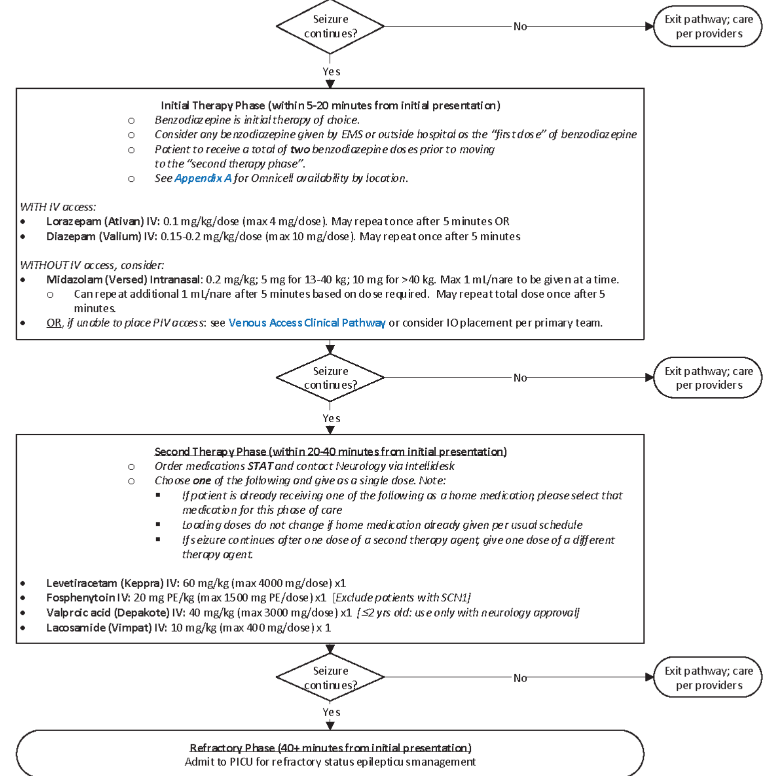
Inclusion Criteria: Patients >1 month of age presenting with seizure lasting >5 minutes
Exclusion Criteria: <1 mo old; hyponatremia, hypoglycemia, sodium channelopathies (SCN1), traumatic brain injury, previous initiation of this pathway within 24 hours

The status epilepticus pathway is intended for patients over 1 month of age who present with a seizure longer than 5 minutes.

Patients with hyponatremia, hypoglycemia, known sodium channelopathies, or TBI should be treated off pathway.

In addition, patients should not be treated on this pathway if the pathway has already been initiated for them within the past 24 hours.



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Ensure stabilization per PALS. Focus first on patient's circulation, airway and breathing.

Monitor vitals and provide supplemental oxygen as needed.

Inclusion Criteria: Patients >1 month of age presenting with seizure lasting >5 minutes
Exclusion Criteria: <1 mo old; hyponatremia, hypoglycemia, sodium channelopathies (SCN1), traumatic brain injury.

Stabilization Phase (0-5 minutes from initial presentation)

- Stabilize patient (per Pediatric Advanced Life Support – PALS) – Circulation, Airway, Breathing
- Place in lateral decubitus position (unless supine required to maintain airway)
- Monitor vitals (place EKG leads, pulse oximeter, blood pressure)
- If SpO2 <92%: O2 via Oxymask

Obtain labs/Initial Management*

- Attempt IV access
- Fingerstick glucose
  - If glucose <60: Give 5 ml/kg of D10 and treat off pathway
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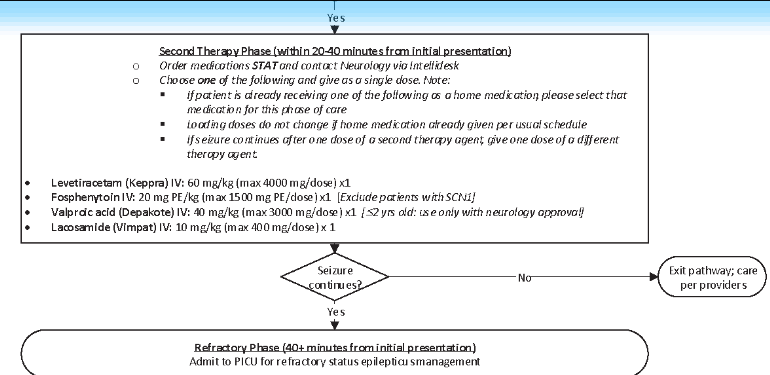
- If appropriate: blood culture, toxicology, anticonvulsant drug levels

Obtain history*

- Collect seizure history from guardian/chart
- Initial seizure onset and duration
- Amount of seizure medication given by EMS or outside hospital (this will be considered the "first dose" of benzodiazepine)



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While IV access is attempted, quickly obtain labs and obtain a history.

Always consider why the patient is seizing.

- Obtaining a fingerstick blood glucose and ISTAT chemistry within the first 5 minutes of the seizure can rule out hypoglycemia and/or hyponatremia as causes.
- Additional studies may also be considered.

Inclusion Criteria: Patients >1 month of age presenting with seizure lasting >5 minutes
Exclusion Criteria: <1 mo old; hyponatremia, hypoglycemia, sodium channelopathies (SCN1), traumatic brain injury,

Stabilization Phase (0-5 minutes from initial presentation)

- Stabilize patient (per Pediatric Advanced Life Support – PALS) – Circulation
- Place in lateral decubitus position (unless supine required to maintain air
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***At all times, consider differential diagnoses and the following:**

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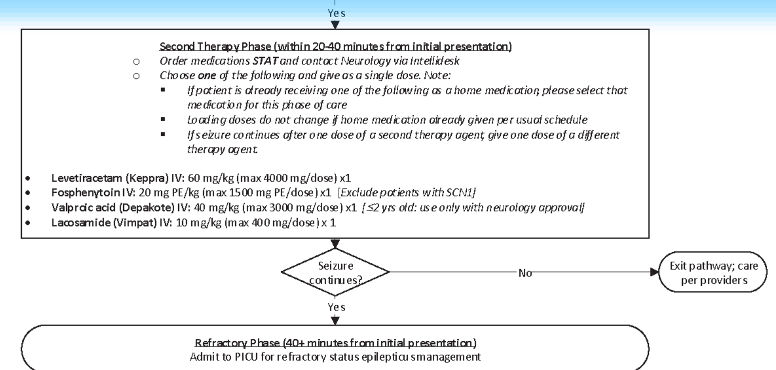

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When obtaining the history, note the type and amount of seizure medication that was given by EMS, outside hospital or parent.
- This is considered the "first dose" of benzodiazepine.

Also note the type of seizure medication the patient takes at baseline (as applicable).
- This will be useful in the second phase of therapy.

Inclusion Criteria: Patients >1 month of age presenting with seizure lasting >5 minutes
Exclusion Criteria: <1 mo old; hyponatremia, hypoglycemia, sodium channelopathies (SCN1), traumatic brain injury

Stabilization Phase (0-5 minutes from initial presentation)
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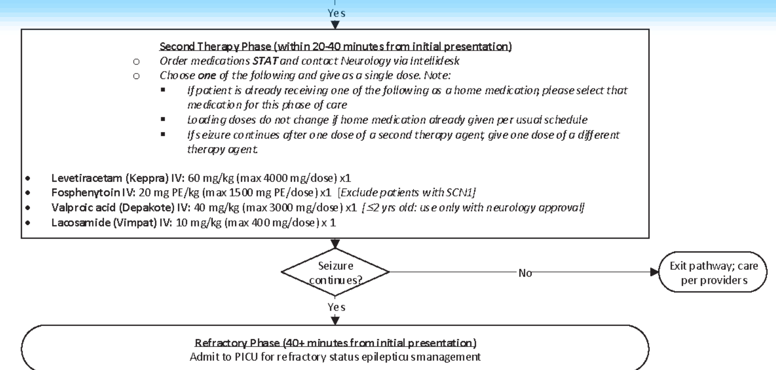

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If the seizure is continuing, it is important to give a benzodiazepine as the initial therapy, within 5-20 minutes of initial presentation.

Patients should receive TWO doses of benzodiazepines before moving on to the next, or "second", phase of therapy.

If the patient was already given benzodiazepines prior to arriving at the hospital, each dose is counted towards the total of TWO doses before moving on to the Second Therapy Phase.

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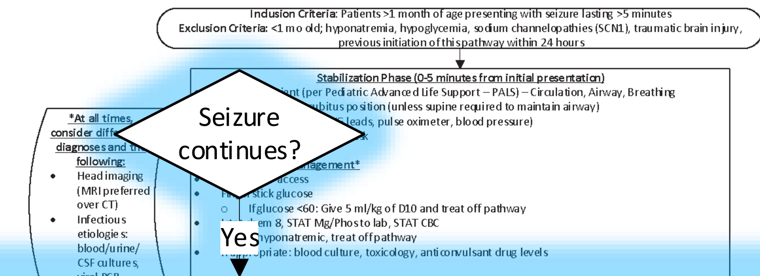


Initial Therapy Phase (within 5-20 minutes from initial presentation)

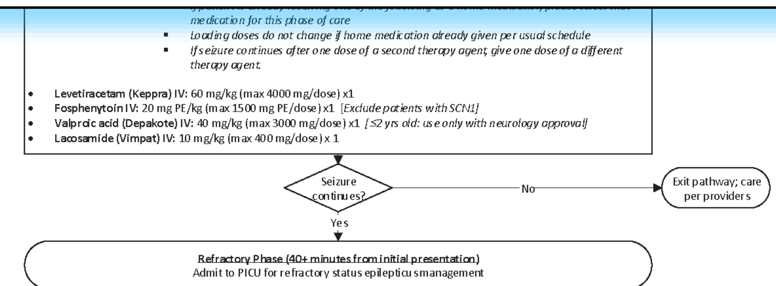
- *Benzodiazepine is initial therapy of choice.*
- *Consider any benzodiazepine given by EMS or outside hospital as the "first dose" of benzodiazepine*
- *Patient to receive a total of **two** benzodiazepine doses prior to moving to the "second therapy phase".*
- *See* **Appendix A** *for Omnicell availability by location.*

WITH IV access:

- **Lorazepam (Ativan) IV:** 0.1 mg/kg/dose (max 4 mg/dose). May repeat once after 5 minutes OR
- **Diazepam (Valium) IV:** 0.15-0.2 mg/kg/dose (max 10 mg/dose). May repeat once after 5 minutes

WITHOUT IV access, consider:

- **Midazolam (Versed) Intranasal**: 0.2 mg/kg; 5 mg for 13-40 kg; 10 mg for >40 kg. Max 1 mL/nare to be given at a time.
  - Can repeat additional 1 mL/nare after 5 minutes based on dose required. May repeat total dose once after 5 minutes.
- OR, *if unable to place PIV access*: see **Venous Access Clinical Pathway** or consider IO placement per primary team.



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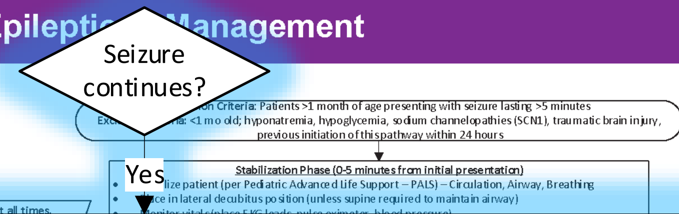

Appendix A shows which medications are directly available in the Omnicell.

Initial Therapy Phase (within 5-20 minutes from initial presentation)

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e PIV access: see **Venous Access Clinical Pathway** or consider IO placement per primary team.

CLINICAL PATHWAY: Status Epilepticus Appendix A: Omnicell Medication Availability by Location

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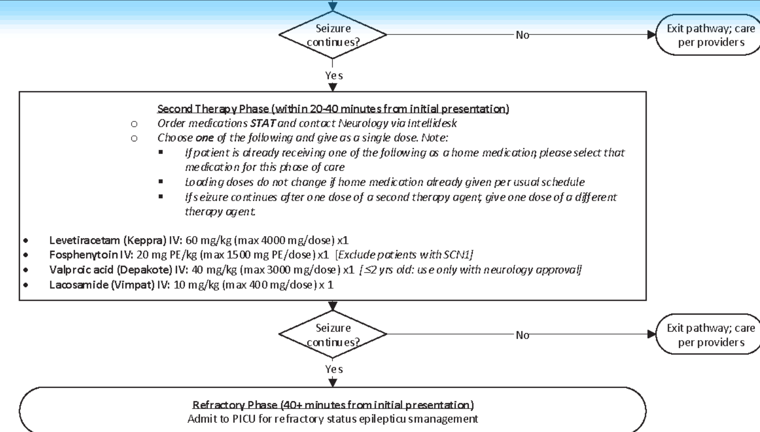
Medication	MS7A	ED	PICU
Levetiracetam 100 mg/ml 5ml injection	•	•	•
Diazepam Rectal gel 2.5 mg, 10 mg, 20 mg	•		
Diazepam 5 mg/1mL 2 mL syringe (IV formulation per rectum)	•	•	•
Lacosamide 10 mg/ml 10 or 20 ml injection	•	•	•
Phenobarbital 65 mg/ml 1 ml injection	•	•	•
Fosphenytoin 500 mg/10ml injection	•	•	•
Lorazepam 2 mg/1ml injection	•	•	•
Midazolam 5 mg/1ml injection	•	•	•



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Options for benzodiazepines are also given if IV access cannot be obtained.

Providers can choose to give midazolam intranasally, place an IO, or follow the Venous Access Clinical Pathway for help obtaining access while attempting to stabilize the patient.

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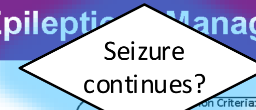

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WITH IV access:

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- **Midazolam (Versed) Intranasal**: 0.2 mg/kg; 5 mg for 13-40 kg; 10 mg for >40 kg. Max 1 mL/nare to be given at a time.
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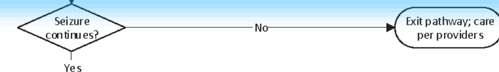

Second Therapy Phase (within 20-40 minutes from initial presentation)

- *Order medications **STAT** and contact Neurology via Intellidesk*
- *Choose **one** of the following and give as a single dose. Note:*
  - *If patient is already receiving one of the following as a home medication, please select that medication for this phase of care*
  - *Loading doses do not change if home medication already given per usual schedule*
  - *If seizure continues after one dose of a second therapy agent, give one dose of a different therapy agent.*

- **Levetiracetam (Keppra) IV:** 60 mg/kg (max 4000 mg/dose) x1
- **Fosphenytoin IV:** 20 mg PE/kg (max 1500 mg PE/dose) x1 *[Exclude patients with SCN1]*
- **Valproic acid (Depakote) IV:** 40 mg/kg (max 3000 mg/dose) x1 *[≤2 yrs old: use only with neurology approval]*
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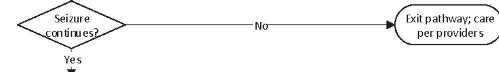

Refractory Phase (40+ minutes from initial presentation)
Admit to PICU for refractory status epilepticus management

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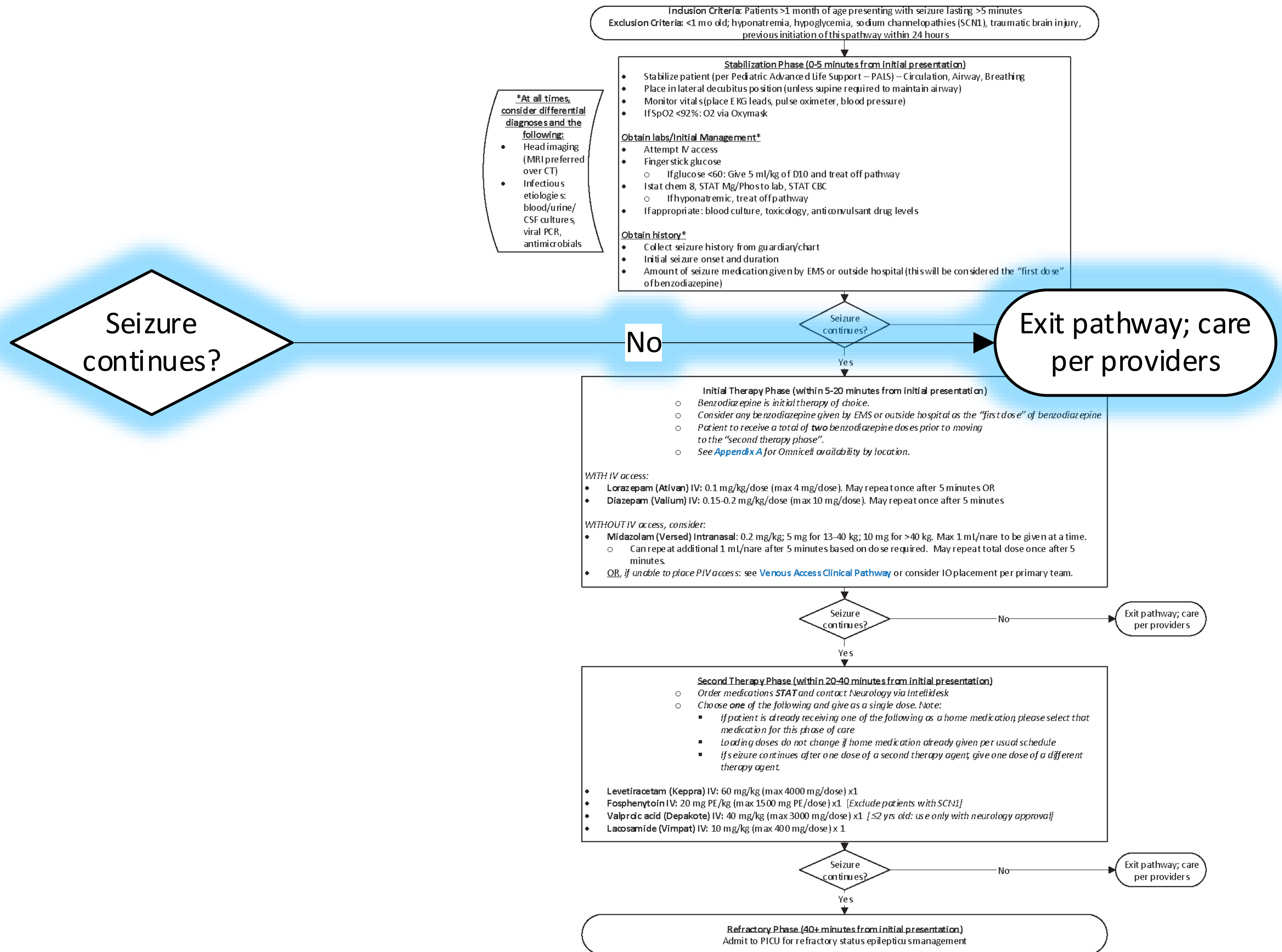
At any point in time, when the seizure stops, exit the status epilepticus management pathway and provide clinical care per patient's care providers.



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Inclusion Criteria: Patients >1 month of age presenting with seizure lasting >5 minutes
Exclusion Criteria: <1 mo old; hyponatremia, hypoglycemia, sodium channelopathies (SCN1), traumatic brain injury, previous initiation of this pathway within 24 hours

Stabilization Phase (0-5 minutes from initial presentation)
- Stabilize patient (per Pediatric Advanced Life Support – PALS) – Circulation, Airway, Breathing
- Place in lateral decubitus position (unless supine required to maintain airway)
- Monitor vitals (place EKG leads, pulse oximeter, blood pressure)
- If SpO2 <92%: O2 via Oxymask

Obtain labs/Initial Management*
- Attempt IV access
- Fingerstick glucose

*At all times, consider differential diagnoses and the following:
- Head imaging (MRI preferred over CT)

If the seizure continues despite two doses of benzodiazepines, initiate the Second Therapy Phase.

This should begin within 20-40 minutes from the patient's initial presentation with a seizure.

Second Therapy Phase (within 20-40 minutes from initial presentation)

- *Order medications **STAT** and contact Neurology via Intellidesk*
- *Choose **one** of the following and give as a single dose. Note:*
  - *If patient is already receiving one of the following as a home medication, please select that medication for this phase of care*
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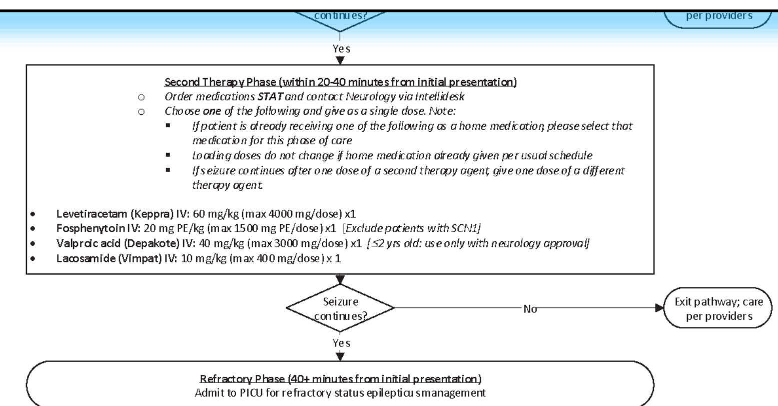

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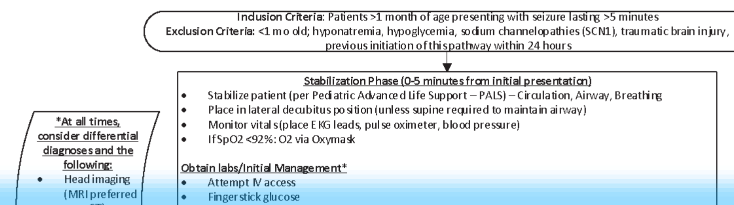
One of the following medications should be given STAT as a loading dose in the second therapy phase.

Preference is given to the medication that the patient is already on at home.

- **Note:** the loading dose will not change if the home seizure medication was given per their usual schedule

Depakote IV is only for those over 2 years of age. Anyone younger than this should be discussed with neurology first prior to administration.



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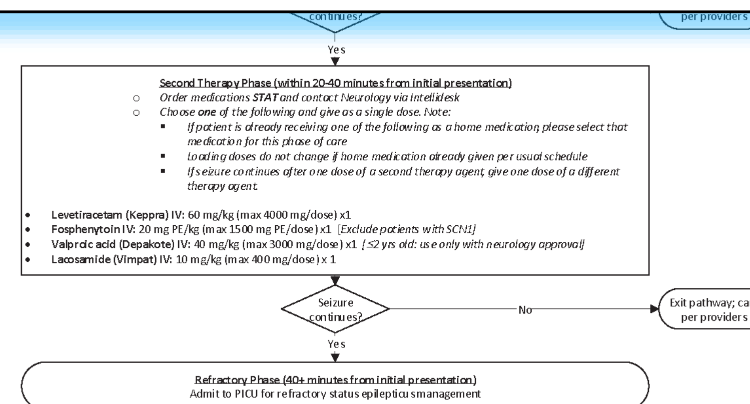

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CLINICAL PATHWAY:
Status Epilepticus Management

THIS PATHWAY SERVES AS A GUIDE AND DOES NOT REPLACE CLINICAL JUDGMENT.

Inclusion Criteria: Patients >1 month of age presenting with seizure lasting >5 minutes
Exclusion Criteria: <1 mo old; hyponatremia, hypoglycemia, sodium channelopathies (SCN1), traumatic brain injury, previous initiation of this pathway within 24 hours

Stabilization Phase (0-5 minutes from initial presentation)
- Stabilize patient (per Pediatric Advanced Life Support – PALS) – Circulation, Airway, Breathing
- Place in lateral decubitus position (unless supine required to maintain airway)
- Monitor vitals (place EKG leads, pulse oximeter, blood pressure)
- If SpO2 <92%: O2 via Oxymask

Obtain labs/Initial Management*
- Attempt IV access
- Fingerstick glucose

*At all times, consider differential diagnoses and the following:
- Head imaging (MRI preferred over CT)

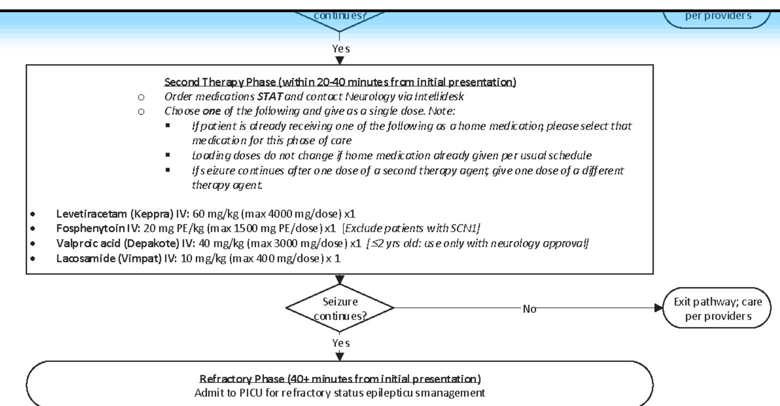
If the seizure is continuing at the 40 minute mark, give a single IV dose of an alternate Second Therapy Phase medication.

Neurology should be involved at this point to help direct care.

Second Therapy Phase (within 20-40 minutes from initial presentation)

- *Order medications* ***STAT*** *and contact Neurology via Intellidesk*
- *Choose* ***one*** *of the following and give as a single dose. Note:*
  - *If patient is already receiving one of the following as a home medication, please select that medication for this phase of care*
  - *Loading doses do not change if home medication already given per usual schedule*
  - *If seizure continues after one dose of a second therapy agent, give one dose of a different therapy agent.*

- **Levetiracetam (Keppra) IV:** 60 mg/kg (max 4000 mg/dose) x1
- **Fosphenytoin IV:** 20 mg PE/kg (max 1500 mg PE/dose) x1 *[Exclude patients with SCN1]*
- **Valproic acid (Depakote) IV:** 40 mg/kg (max 3000 mg/dose) x1 *[≤2 yrs old: use only with neurology approval]*
- **Lacosamide (Vimpat) IV:** 10 mg/kg (max 400 mg/dose) x 1



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Review of Key Points

- Exclude <1 month old and patients with documented SCN1a mutations and/or diagnosed Dravet syndrome
- Obtain a fingerstick blood glucose and Istat chemistry within the first 5 minutes to rule out hypoglycemia and/or hyponatremia as causes of the seizure.
- Initial Therapy medications are benzodiazepines.
- Patient should receive 2 doses of the appropriate benzodiazepine before proceeding to the “Second Therapy Phase”
  - If they received benzodiazepines prior to arrival in the hospital, each dose is counted as being appropriate.

Pathway Contacts

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Thank You!

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Clinical pathways guide the management of patients to optimize consistent use of evidence-based practice. Clinical pathways have been shown to improve guideline adherence and quality outcomes, while decreasing length of stay and cost. Here at Connecticut Children's, our Clinical Pathways Program aims to deliver evidence-based, high value care to the greatest number of children in a diversity of patient settings. These pathways serve as a guide for providers and do not replace clinical judgment.