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Inclusion Criteria
- ≥1 month corrected age
- Patient with seizure or history of seizure

Exclusion Criteria
- Non-epileptic seizure events (pseudoseizures)
- Toxic ingestion

Seizure Care

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Inclusion Criteria
- ≥1 month corrected age
- Patient with seizure or history of seizure

Exclusion Criteria
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- Toxic ingestion

On Arrival/First Seizure
- Order 1st Line and 2nd Line medication based on guidance in this pathway, then confirm with Neurology.
- If patient has established epilepsy, see Longitudinal Care Plan in Epic.

Dose 1:
- Begin at minute 15 (5 min after both doses of 1st Line are completed)

Dose 2:
- Begin 5 minutes after Dose 1 is finished infusing
- Order 3rd line medication
- Start EEG, call EEG tech

! Choose two different medications:

Dose 1:
- <2 months old<sup>a</sup>
- PB or LEV
- 1st time seizure<sup>b</sup>
- LEV or FOS
- Hypotension/myocardial dysfunction
- LEV
- History of seizure<sup>c</sup>
- LEV or FOS<sup>d</sup> or PB or VPA<sup>e</sup>
- Emergency department
- LEV

Dose 2:
- LEV or FOS or PB<sup>a</sup>
- LEV or FOS or PB
- LEV or FOS or PB
- LEV or FOS or PB
- FOS or PB or VPA<sup>d</sup>

Seizure continues

Definitions:
- Status Epilepticus: Seizures with motor manifestations longer than 5 minutes, or two or more seizures without return of consciousness between seizures
- Established status epilepticus (ESE): Seizure continues after benzodiazepine administration
- Refractory status epilepticus (RSE): Seizures continue after 1st and 2nd line therapy
- Febrile Seizure: Febrile Seizure Pathway
- EMU: Epilepsy Monitoring Unit

*Definition identified on Longitudinal Care Plan supersedes the information above

Seizure continues

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Seizure Pathway v5.0

Stop and Review

On Arrival/First Seizure
- Prepare 1st Line medication
- Secure IV access
- Support airway, breathing (O2), circulation
- Check glucose and sodium

Seizure continues

1st Line
- Dose 1: Lorazepam IV at 5 minutes
- If no IV access: midazolam IN
- If GRID/epilepsy monitoring: midazolam IV
- ! Request both 2nd Line drug doses
- Dose 2: Repeat benzodiazepine 5 minutes later if seizure continues
- Diagnostic tests and assess for risk of infection
- Consult neurology

1st Line medications based on guidance in this pathway, then confirm with Neurology.

2nd Line
- Acute Care: Call code blue for seizure ≥ 20 minutes

3rd Line
- Midazolam bolus and continuous infusion x 24 hours, see titration guide
- Continuous EEG monitoring
- Titrated baseline epilepsy medication
- Repeat AED levels (orders in PICU/CICU Seizure Plan)
- If persistent focal or clinical seizure on exam, consider diagnostic tests

3rd Line medications based on guidance in this pathway, then confirm with Neurology.

4th Line
- Consider transition to pentobarbital or ketamine from Seizure Acute Rescue Orderset
- Optimize adjunctive antiseizure medications
- Consider additional oral or IV medication (IVIG, steroids) or treatment (therapeutic hypothermia)

4th Line medications based on guidance in this pathway, then confirm with Neurology.

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For questions concerning this pathway, contact: SeizurePathway@seattlechildrens.org
If you are a patient with questions contact your medical provider.
Definitions

What are the most current definitions of status epilepticus and refractory status epilepticus?

- Based on the 2016 International League Against Epilepsy (ILAE) scheme, seizures are classified as **focal**, **generalized**, or **unknown onset**. Seizures are then subclassified as **motor** and **nonmotor**, and then further subclassified as **having awareness**, **impaired awareness**, or **unknown awareness** [LOE: guideline (Fisher 2016)].

- **Status epilepticus** (SE) is defined as convulsive, focal, or absence. Convulsive SE includes >5 minutes of ongoing generalized clinical seizure activity, recurrent seizure without recovery to clinical baseline, or electrographic seizure activity (Falco-Walter 2016; Brophy 2012; Trinka 2015).

- **Focal SE** with impaired consciousness is >10 minutes, and absence SE is >10-15 minutes (Falco-Walter 2016; Trinka 2015).

- **Established SE** is persistence beyond treatment with a benzodiazepine (Falco-Walter 2016). Refractory SE is defined as ongoing seizures after treatment with appropriate doses of first (benzodiazepine) and second line AEDs (Falco-Walter 2016; Brophy 2012).

What is a seizure cluster?

- A **seizure cluster** is a series of brief seizures with return to baseline in between. Refer to a patient's seizure action plan and/or longitudinal care plan for individualized seizure cluster treatment threshold and timing. (Jafarapour 2019)

How to Find Longitudinal Care Plan in Epic

The Longitudinal Care Plan can also be found by the following path/steps: Chart Review > Media > filter to Document Type > Care Plan > select the appropriate plan.

Type Care Plan in Search field and a list of all plans associated with patient will appear

The Longitudinal Care Plan* is linked to in the patient Storyboard

*Longitudinal Care Plan is not specific to Neuro. Need to look for the plan with content related to seizures for the patient

*If there is more than one Care Plan for the patient, type “Care Plan” in the Search field, and select the one with content related to seizures.

The Longitudinal Care Plan can also be found by the following path/steps: Chart Review > Media > filter to Document Type > Care Plan > select the appropriate plan.
Diagnostic Tests

Acute Status Epilepticus: Diagnostic Tests

Labs
- STAT glucose
- Full Electrolytes (with iCa, Mg, Phos)
- Liver and kidney function (LFTs, BUN, Cre)
- Anti-seizure medication levels

History
- Check Longitudinal Care Plan
- Check med rec for anti-seizure medications to inform 2nd agent choice

Imaging
- Consider CT (HASTE MRI in some cases) if emergent imaging indicated (e.g. new focal seizure, a symmetric EEG)

Infectious Workup
- Consider an LP in patients with seizure and fever at high risk of CNS infection
- Do not delay antimicrobials for infectious work up

Toxicology Testing
Consider toxicology testing in children with prolonged seizure/SE, when no apparent etiology is immediately identified, as the frequency of ingestion as a diagnosis was at least 3.6%. To detect a specific ingestion, suspected because of the clinical history, it should be noted that a specific serum toxicology level is required, rather than simply urine toxicology screening. [Very low quality] (Riviello, 2006)

Assess Risk of Meningitis or Intracranial Infection
Perform a lumbar puncture in any child with seizure and a fever who is felt to be at SIGNIFICANT RISK for meningitis/intracranial infection. Specific aspects of the history or exam that might suggest meningitis or intracranial infection are outlined in the table below:

### Assess Risk for Meningitis or Intracranial Infection

<table>
<thead>
<tr>
<th>History</th>
<th>Physical Signs</th>
<th>Complex Features</th>
<th>Meningitis Less Likely</th>
</tr>
</thead>
<tbody>
<tr>
<td>• &gt;3 days duration of illness</td>
<td>• Petechiae</td>
<td>• Focal seizures</td>
<td>• Prior febrile seizure</td>
</tr>
<tr>
<td>• Seen by primary MD in previous 24 hours</td>
<td>• Questionable nuchal rigidity</td>
<td>• Seizure duration &gt;15 minutes</td>
<td>• Pre-existing neurological findings</td>
</tr>
<tr>
<td>• Drowsiness or vomiting at home</td>
<td>• Drowsiness</td>
<td>• Multiple seizures in 24 hours</td>
<td>•</td>
</tr>
<tr>
<td>• Infant 6-12 months old deficient in Hib or pneumococcal vaccines or immunization status cannot be determined</td>
<td>• Convulsing on examination</td>
<td></td>
<td></td>
</tr>
<tr>
<td>• Pretreated with antibiotics</td>
<td>• Weakness or neurological deficit on examination</td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>• Signs of infection of head or neck with potential for intracranial extension (such as mastoiditis, sinusitis, etc.)</td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>• Bulging fontanelle</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

More detail on this subject can be found in the Febrile Seizure Pathway.
Benzodiazepines

Benzodiazepines (1st line: 2 doses)
Default benzodiazepine:
- Lorazepam 0.1 mg/kg (max 4mg/dose) IV if seizure lasts >3 minutes (> 5 minutes for partial seizure), repeat dose in 5 minutes if seizure continues

No IV Access
- Midazolam 0.2 mg/kg (max 10mg/dose) nasally, ½ dose in each nostril if seizure lasts >3 minutes (> 5 minutes for partial seizure), repeat dose in 5 minutes if seizure continues
- If no nares available: Midazolam 0.5 mg/kg (max 10mg/dose) bucally if seizure lasts >3 minutes (> 5 minutes for partial seizure), repeat dose in 10 minutes* if seizure continues

For patients in the Epilepsy Monitoring Unit or in hospital for GRID/Strip Monitoring
- Midazolam 0.1 mg/kg (max 5mg/dose) IV if seizure lasts >3 minutes, repeat dose in 5 minutes if seizure continues

*Rationale for every 10 minutes is that medication is not aerosolized so absorption may be slower (expert opinion)

Administer a maximum of two doses of first-line treatment (including pre-hospital treatment). More than two doses is associated with respiratory depression and subsequent doses are unlikely to be effective [Guideline (Friedman 2011)]

Administer intranasal OR buccal midazolam if unable to secure immediate IV access.

A meta-analysis suggests that buccal midazolam is more effective in seizure cessation than rectal or IV diazepam. Buccal and IM midazolam were found to be more effective in time to seizure stoppage than IV diazepam. The action of IV diazepam was faster, but time needed to start IV increased the time to seizure stoppage. The choice or route of benzodiazepine results in little to no difference in respiratory depression [LOE: +3 moderate to +1 very low certainty (McTague 2018)].

In two meta-analyses, the evidence suggests the choice of benzodiazepine results in little to no difference in seizure cessation, respiratory depression, ICU admission, time to seizure stoppage or seizure recurrence after 24h. Compared to diazepam, lorazepam has a lower incidence of respiratory depression, NNT 14 (95% CI 8 to 59) given a control event rate of 38% and ICU admission, NNT 6 (95% CI 5 to 277) given a control event rate of 24% (McTague 2018). [LOE: +3 moderate to +2 low certainty (McTague 2018; Zhang, 2020)].
### Table 1: First line convulsive SE treatment in children

<table>
<thead>
<tr>
<th>Intervention</th>
<th>Comparison</th>
<th>Seizure cessation</th>
<th>Respiratory depression</th>
<th>ICU admission</th>
<th>Time to seizure stoppage (sec)</th>
<th>Seizure recurrence</th>
</tr>
</thead>
<tbody>
<tr>
<td>McTague 2018</td>
<td>Lorazepam</td>
<td>Diazepam</td>
<td>No difference</td>
<td></td>
<td>Favors Lorazepam +2</td>
<td>No difference</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td>+3</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Zhang, 2020</td>
<td>Midazolam</td>
<td>Diazepam</td>
<td>No difference</td>
<td>+2</td>
<td>Favors Midazolam +3</td>
<td>No difference</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td>+3</td>
</tr>
</tbody>
</table>

### Table 2: First line convulsive SE treatment comparison by drug and route in children

<table>
<thead>
<tr>
<th>Intervention</th>
<th>Comparison</th>
<th>Seizure cessation</th>
<th>Time to seizure stoppage (sec or min)</th>
<th>Respiratory depression</th>
<th>Number Needed to Treat (NNT) and effect size</th>
</tr>
</thead>
<tbody>
<tr>
<td>McTague 2018</td>
<td>Intranasal lorazepam</td>
<td>IM paraldehyde</td>
<td>No difference +2</td>
<td>-</td>
<td>-</td>
</tr>
<tr>
<td></td>
<td>IV lorazepam</td>
<td>IV diazepam / phenytoin combo</td>
<td>No difference +3</td>
<td>-</td>
<td>No difference +3</td>
</tr>
<tr>
<td></td>
<td>IV lorazepam</td>
<td>Intranasal lorazepam</td>
<td>No difference +3</td>
<td>-</td>
<td>-</td>
</tr>
<tr>
<td></td>
<td>Buccal midazolam</td>
<td>Rectal diazepam</td>
<td>Favors midazolam +1</td>
<td>-</td>
<td>No difference +2</td>
</tr>
<tr>
<td></td>
<td>Buccal midazolam</td>
<td>IV diazepam</td>
<td>No difference +4</td>
<td>Favors midazolam +3</td>
<td>-</td>
</tr>
<tr>
<td></td>
<td>Intranasal midazolam</td>
<td>IV diazepam</td>
<td>No difference +3</td>
<td>No difference +2</td>
<td>-</td>
</tr>
<tr>
<td></td>
<td>Intranasal midazolam</td>
<td>Rectal diazepam</td>
<td>No difference +2</td>
<td>-</td>
<td>-</td>
</tr>
<tr>
<td></td>
<td>IM midazolam</td>
<td>IV diazepam</td>
<td>No difference +2</td>
<td>Favors midazolam +1</td>
<td>-</td>
</tr>
<tr>
<td></td>
<td>IM midazolam</td>
<td>Rectal diazepam</td>
<td>No difference +3</td>
<td>-</td>
<td>-</td>
</tr>
<tr>
<td></td>
<td>IV midazolam</td>
<td>IV diazepam</td>
<td>No difference +3</td>
<td>No difference +3</td>
<td>No difference +3</td>
</tr>
<tr>
<td></td>
<td>IV midazolam</td>
<td>IV lorazepam</td>
<td>No difference +3</td>
<td>No difference +3</td>
<td>-</td>
</tr>
</tbody>
</table>
Second line convulsive SE treatment

In a meta-analysis, the evidence suggests that choice of 2nd line agent (phenobarbital, phenytoin, fosphenytoin, levetiracetam, valproate) results in little to no difference in seizure cessation and seizure recurrence after 24h (Zhang 2020). A second meta-analysis found that compared to phenytoin, levetiracetam likely increases seizure cessation, NNT 36 (95% CI 22 to 95) given a control event rate of 68% and in a subgroup of children, NNT 41 (95% CI 23 to 248) with a control event rate of 71%. There are likely fewer adverse events in the levetiracetam group compared to the phenytoin group of adults and children (NNT 32, 95% CI 19 to 197, given a control event rate of 21%). There is little or no difference in the adverse events in the children subgroup, or admission to ICU or mortality for adults and children [LOE: +3 moderate to +2 low certainty (Xue 2020)].

Table 3: Second line treatment of convulsive SE in children

<table>
<thead>
<tr>
<th>Intervention</th>
<th>Comparison</th>
<th>Seizure cessation</th>
<th>Seizure recurrence</th>
<th>Adverse events</th>
<th>Admission to ICU</th>
<th>Mortality</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Zhang 2020 - Children</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Phenobarbital</td>
<td>Valproate</td>
<td>No difference +2</td>
<td>No difference +2</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Phenytoin</td>
<td>Valproate</td>
<td>No difference +2</td>
<td>No difference +2</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Fosphenytoin</td>
<td>Valproate</td>
<td>No difference +2</td>
<td>No difference +2</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Levetiracetam</td>
<td>Valproate</td>
<td>No difference +2</td>
<td>No difference +2</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td><strong>Xue 2020 – Adults and Children</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Levetiracetam</td>
<td>Phenytoin</td>
<td>Favors levetiracetam +3</td>
<td>Favors levetiracetam +3</td>
<td>No difference +3</td>
<td>No difference +3</td>
<td></td>
</tr>
<tr>
<td><strong>Xue 2020 – Children subgroup</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Levetiracetam</td>
<td>Phenytoin</td>
<td>Favors levetiracetam +3</td>
<td>No difference +2</td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

- For children already on an anti-seizure drug, consider a bolus dose of the anti-seizure drug the patient is already on prior to initiating an additional agent [Guideline (Brophy 2012)].
- Do not use valproic acid in patients with POLG-1 mutations who may present with refractory status epilepticus because it may cause fatal hepatitis; avoid valproic acid in patients under age 2 due to the risk of hepatitis.
3rd Line - Midazolam

Refractory status epilepticus: CEEG and titration of midazolam infusion

<table>
<thead>
<tr>
<th>Initiation</th>
<th></th>
</tr>
</thead>
<tbody>
<tr>
<td>• Bolus 0.15 mg/kg midazolam IV</td>
<td></td>
</tr>
<tr>
<td>• Initiate midazolam infusion at 100 mcg/kg/hr</td>
<td></td>
</tr>
<tr>
<td>• Q 15 minutes: Bolus 0.15 mg/kg midazolam IV AND increase infusion by 100 mcg/kg/hr for ongoing seizure (in communication with NEU) until burst suppression is achieved.</td>
<td></td>
</tr>
<tr>
<td>• Airway, hemodynamic support as clinically indicated.</td>
<td></td>
</tr>
<tr>
<td>• NPO</td>
<td></td>
</tr>
<tr>
<td>➢ If difficulty achieving burst suppression</td>
<td></td>
</tr>
<tr>
<td>• Consider ketogenic diet preparation (send labs; NS-based IVF) with Neurology</td>
<td></td>
</tr>
<tr>
<td>• By 24 hours: discuss alternatives</td>
<td></td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Stable burst suppression</th>
<th>Minimum 24h</th>
</tr>
</thead>
<tbody>
<tr>
<td>• Wean for over-suppression</td>
<td></td>
</tr>
<tr>
<td>• Titrate other antiseizure medications</td>
<td></td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Weaning</th>
<th></th>
</tr>
</thead>
<tbody>
<tr>
<td>• Wean by 100 mcg/kg/hr q 4 hours (in communication with NEU)</td>
<td></td>
</tr>
<tr>
<td>• Continue EEG until off of IV anesthetic x 24 hours</td>
<td></td>
</tr>
<tr>
<td>• Hold wean &amp; notify neurology for any clinical seizure</td>
<td></td>
</tr>
<tr>
<td>• If electrographic seizures: consider increase in maintenance antiseizure medications while continuing midazolam wean</td>
<td></td>
</tr>
</tbody>
</table>

Refractory seizures: 3rd and 4th line medications

• Begin 3rd line treatment after seizure duration of 40 minutes [Guideline (Glauser 2016)] to 45 minutes [Guideline (NICE 2012; Friedman 2011)]

• Use midazolam 3rd line because it may have a slightly better risk/benefit profile [Guideline (Friedman 2011)]

  Options include repeating 2nd line therapy, or anesthetic doses of thiopental, midazolam, pentobarbital, or propofol [Guideline (Glauser 2016, Brophy 2012, NICE 2012, Capovilla 2013)]

  Adults using midazolam infusion achieved a high rate of seizure control with the lowest rate of side effects and a low rate of withdrawal seizures compared to thiopental/phenobarbital or propofol (Ferlisi 2012)

• Give midazolam in normal saline solution to allow for possible addition of ketogenic diet

• Titrate anesthetic doses to burst suppression EEG pattern [Guideline (Brophy 2012)]

• If midazolam is ineffective, consider the following options: pentobarbital, ketamine, ketogenic diet, pyridoxine, plasmapheresis or steroids (for refractory status epilepticus caused by an autoimmune process), and therapeutic hypothermia

Return to Seizure Pathway
Admit and ICU Transfer Criteria

Admit Criteria (from ED)
- Unstable cardiorespiratory or neurologic status (not returning to baseline, very somnolent)
- Underlying infection requiring inpatient stay
- Disabling parental anxiety
- Lack of safe home or safe transport to home

Children who are clinically unstable neurologically (e.g., not returning to baseline, very somnolent following doses of anti-seizure medications) should be admitted for observation and support.
[Expert Opinion (E)] (Fetveit, 2008; Baumer, 2004)

Children who present with an underlying infection requiring inpatient stay (e.g., severe pneumonia, infection requiring intravenous antibiotics) should be admitted.
[Expert Opinion (E)] (BC, 2010)

Children whose parents have "disabling" anxiety following the seizure episode may require admission for observation and further parental education and reassurance. [Expert Opinion (E)](BC, 2010; Fetveit, 2008)

Children that lack a safe home or safe transportation home require admission and may require social work consultation. [Expert Opinion (E)] (Fetveit, 2008)

ICU Transfer Criteria
- Any unresolved hemodynamic or respiratory compromise following seizure cessation
- Ongoing status epilepticus despite 2nd line therapy
- Care exceeding floor RN/RT capacity or safety

Return to Seizure Pathway
Ketogenic Diet Preparation

**Labs**
- Plasma amino acids
- Urine organic acids
- Acylcarnitine profile
- Ammonia
- Lactate

**Actions**
- Consult nutrition (ketogenic dietician)
- Avoid dextrose infusions, medications in dextrose while decision-making
Continuous EEG

Seizure with lack of return to baseline (30 min)
OR
Ongoing seizure activity 10 minutes > 2nd line, 1st dose AED (30 min)

STAT EEG
*Temporary (fast) lead placement
*Immediate bedside read

- Established clinical seizure phenotype?
  - Reliable exam (no paralysis)?
  - Low risk condition?

YES

Clinical monitoring

NO

Continuous EEG
*Long-term (slower) lead placement
*EEG tech monitoring + read q2h/q4h
*Consider imaging/procedures before hookup*

Indications for continuous EEG (refer to CCEEG P&P)

<table>
<thead>
<tr>
<th>Definite</th>
</tr>
</thead>
<tbody>
<tr>
<td>Ongoing status epilepticus requiring IV anesthetic agent (e.g. midazolam infusion)</td>
</tr>
<tr>
<td>Increased ICP requiring IV anesthetic agent titrated to burst suppression (e.g. pentobarbital)</td>
</tr>
<tr>
<td>Any high risk patient (examples below) requiring frequent paralytic</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>High risk; consider use</th>
</tr>
</thead>
<tbody>
<tr>
<td>Events of unclear significance (hemodynamic/motor symptoms)</td>
</tr>
<tr>
<td>Encephalopathy, in the setting of CNS injury. Examples include:</td>
</tr>
<tr>
<td>Recent seizure (30 min)</td>
</tr>
<tr>
<td>Stroke</td>
</tr>
<tr>
<td>Trauma</td>
</tr>
<tr>
<td>Sepsis</td>
</tr>
<tr>
<td>CNS infection</td>
</tr>
<tr>
<td>Structural brain lesion/tumor</td>
</tr>
<tr>
<td>Ischemic/hypoxemic injury/cardiac arrest</td>
</tr>
<tr>
<td>ECLS</td>
</tr>
<tr>
<td>Therapeutic hypothermia</td>
</tr>
<tr>
<td>Postoperative neurosurgery</td>
</tr>
<tr>
<td>Post cardiac bypass</td>
</tr>
<tr>
<td>Liver or renal failure</td>
</tr>
<tr>
<td>Toxin ingestion</td>
</tr>
</tbody>
</table>

Process notes

- Assess need daily w/ NEU |
- Reorder q24h |
- Ongoing monitoring by EEG tech |
- Formal review by EEG reader based on priority score: |
  1: q2h |
  2: q4h |
  3: q8h |
- Concerns? Page NEU resident (will discuss with EEG reader PRN)

Return to Seizure Pathway

To Continuous EEG page 2
In children with status epilepticus, how (in which patients and for how long) should continuous EEG (cEEG) monitoring be used?

- Initiate continuous EEG within 60 minutes of seizure onset if ongoing seizures are suspected or the patient has not returned to baseline after administration of seizure medication \([+2 \text{ Low quality } \text{(Claasen 2013, Brophy 2012)}]\)
- Initiate cEEG monitoring in patients with unexplained abnormal mental status, or with abnormal mental status in the setting of high-risk clinical setting (including following seizure, acute supratentorial brain injury, and pharmacologic paralysis)
- Continuous EEG is required for the management of status epilepticus \([+1 \text{ Very low quality } \text{(Claasen 2013, Brophy 2012)}]\)
- For patients with refractory status epilepticus, continue cEEG for 24-48 hours of electrographic control, and during weaning of 3rd line antiepileptic agents
Summary of Version Changes

- **Version 1.0 (6/19/2012):** Go live.
- **Version 1.1 (6/24/2012):** Adaptation for android use.
- **Version 1.2 (6/11/2013):** Exclusion criteria updated; patients in ICU may be on pathway at discretion of attending MD.
- **Version 2.0 (5/11/2016):** Added value analysis with rationale supporting use of intranasal midazolam over rectal diazepam.
- **Version 2.1 (12/5/2016):** Changed name of inpatient order from orderset to powerplan.
- **Critical Care Pathway Version 1.0 (5/3/2017):** Go live.
- **Version 3.0 (8/3/2017):** Combined with critical care with acute care and ED phases, added 2nd to 4th line treatment options.
- **Version 3.1 (8/4/2017):** Fixed language in ED phase in arrow between benzodiazepine dose 1 and 2.
- **Version 3.2 (9/16/2019):** Changed units for midazolam infusion to mcg/kg/hr.
- **Version 4.0 (6/10/2021):** Periodic review go live. Updated 2nd line medications; removed propofol for refractory seizures; combined ED, Acute Care, and Critical Care algorithms into one; updated Inclusion/Exclusion criteria; converted document to new CSW algorithm template.
- **Version 4.1 (7/13/2021):** Added 1st Line timing caution triangle and defined the EMU (Epilepsy Monitoring Unit), changed “antiepileptic” to antiseizure”, and reported maximum dose in milligrams.
- **Version 5.0 (6/8/2022):** Corrected phenobarbital and valproic acid maximum doses; clarified Dose 1 and Dose 2 guidance on Seizure pathway page; added Seizure Cluster definition to Definitions page.
Approved by the CSW Seizure Pathway team for June 10, 2021 go-live

CSW Seizure Pathway Team:

Seizure CSW Owner: Lindsey Morgan, MD  
Pharmacy: Lindsay McNeely, PharmD BCPPS  
Pharmacy Informatics: Stacy Traxler, PharmD  
Clinical Nurse Specialist: Hector Valdivia, MN, RN, CCRN  
Clinical Nurse Specialist: Sara Fenstermacher, MSN, RN,CPN  
Clinical Nurse Specialist: Simeng Wang, BSN, RN, CPN  
Clinical Nurse Specialist: Angela Turner, DNP-PCNS, RN, CPN  
Neurology Stakeholder: Edward “Rusty” Novotny, MD  
Emergency Medicine Stakeholder: Heath Stanford Ackley, MD  
ICU Stakeholder: Leslie Dervan, MD

Clinical Effectiveness Team:

Consultant: Jen Hrachovec, PharmD, MPH  
Project Manager: Dawn Hoffer, SAPM  
EHR Informatician: Brian Cartin, MD  
EHR Informatician: Mark Lo, MD  
EHR Analyst: Gaurav Gupta, GA  
Librarian: Sue Groshong, MLIS  
Literature Reviewer: Lisa Abrams, RN, MSN, ARNP(ret)  
Program Coordinator: Ivan Meyer

Clinical Effectiveness Leadership:

Medical Director: Darren Migita, MD  
Operations Director: Jaleh Shafii, MS, RN, CPHQ

Retrieval Website: http://www.seattlechildrens.org/pdf/seizure-pathway.pdf

Please cite as:
Evidence Ratings

This pathway was developed through local consensus based on published evidence and expert opinion as part of Clinical Standard Work at Seattle Children’s. Pathway teams include representatives from Medical, Subspecialty, and/or Surgical Services, Nursing, Pharmacy, Clinical Effectiveness, and other services as appropriate.

When possible, we used the GRADE method of rating evidence quality. Evidence is first assessed as to whether it is from randomized trial or cohort studies. The rating is then adjusted in the following manner (from: Guyatt G et al. J Clin Epidemiol. 2011;4:383-94, Hultcrantz M et al. J Clin Epidemiol. 2017;87:4-13.):

Quality ratings are downgraded if studies:
- Have serious limitations
- Have inconsistent results
- If evidence does not directly address clinical questions
- If estimates are imprecise OR
- If it is felt that there is substantial publication bias

Quality ratings are upgraded if it is felt that:
- The effect size is large
- If studies are designed in a way that confounding would likely underreport the magnitude of the effect OR
- If a dose-response gradient is evident

Certainty of Evidence
★★★★ High: The authors have a lot of confidence that the true effect is similar to the estimated effect
★★★☆☆ Moderate: The authors believe that the true effect is probably close to the estimated effect
★★☆☆☆ Low: The true effect might be markedly different from the estimated effect
★☆☆☆☆ Very low: The true effect is probably markedly different from the estimated effect

Guideline: Recommendation is from a published guideline that used methodology deemed acceptable by the team
Expert Opinion: Based on available evidence that does not meet GRADE criteria (for example, case-control studies)
Literature Search Methods
Two reviewers independently screened abstracts and included guidelines and systematic reviews that addressed optimal diagnosis, treatment, and prognosis of patients who meet pathway inclusion/exclusion criteria. One reviewer extracted data and a second reviewer quality checked the results. Differences were resolved by consensus.

Literature Search Results
The searches of the 4 databases (see Electronic searches) retrieved 426 records. Our searches of other resources identified 0 additional records that appeared to meet the inclusion criteria.

Once duplicates had been removed, we had a total of 319 records. We excluded 270 records based on titles and abstracts. We obtained the full text of the remaining 49 records and excluded 38.

We combined these studies with those previously identified for prior versions of this pathway, and for this update we have included a total of 11 studies (11 new). The flow diagram summarizes the study selection process. Three comparative trials in pediatrics were obtained outside the structured search parameters and are listed under Additional References. These trials were used to inform antiseizure medication dosing.
Search Methods, Seizures ICU, Clinical Standard Work

Studies were identified by searching electronic databases using search strategies developed and executed by a medical librarian, Susan Groshong. Searches were performed in November 2016 in the following databases—on the Ovid platform: Medline and Cochrane Database of Systematic Reviews; elsewhere: Embase, National Guideline Clearinghouse, TRIP and Cincinnati Children’s Evidence-Based Care Recommendations. In Medline and Embase, appropriate Medical Subject Headings (MeSH) and Emtree headings were used respectively, along with text words, and the search strategy was adapted for other databases as appropriate. The concept of status epilepticus was searched; retrieval was limited to humans, English language and 2011 to current. A second search was performed concurrently in the databases listed above plus Ovid Cochrane Central Register of Controlled Trials for the concepts electroencephalography monitoring and cardiac surgery or extracorporeal membrane oxygenation. The search results were limited to humans, English language and 2006 to current. Retrieval for both searches were further limited to certain evidence categories, such as relevant publication types, index terms for study types and other similar limits. Additional articles were identified by team members and added to results.

**Identification**

- 318 records identified through database searching
- 12 additional records identified through other sources

**Screening**

- 295 records after duplicates removed
- 198 records excluded

**Eligibility**

- 97 records assessed for eligibility
  - 40 full-text articles excluded, 12 did not answer clinical question, 28 did not meet quality threshold

**Included**

- 57 studies included in pathway

Flow diagram adapted from Moher D et al. BMJ 2009;339:bmj.b2535
Included Studies 2021


Additional References 2021


Additional References 2021 continued

Included Studies 2017


Included Studies 2017 continued


Included Studies 2017 continued


Included Studies 2017 continued


Medical Disclaimer

Medicine is an ever-changing science. As new research and clinical experience broaden our knowledge, changes in treatment and drug therapy are required.

The authors have checked with sources believed to be reliable in their efforts to provide information that is complete and generally in accord with the standards accepted at the time of publication.

However, in view of the possibility of human error or changes in medical sciences, neither the authors nor Seattle Children’s Healthcare System nor any other party who has been involved in the preparation or publication of this work warrants that the information contained herein is in every respect accurate or complete, and they are not responsible for any errors or omissions or for the results obtained from the use of such information.

Readers should confirm the information contained herein with other sources and are encouraged to consult with their health care provider before making any health care decision.