Intended to guide treatment of seizure NOT due to toxicologic etiology. Contact poison center at 800-222-1222 if concern for tox-related seizures as management may differ.

≥5 minutes of continuous seizure activity or episodes without return to baseline

If seizure continues after benzodiazepine bolus therapy

Single bolus of 1 of the following:

- Fosphenytoin** IV 20 mg/kg, max 1500 mg
  Monitor for hypotension and arrhythmia
- Levetiracetam IV 60 mg/kg, max 4500 mg
- Valproic Acid IV 40 mg/kg, max 3000 mg
  Avoid for hepatic or metabolic diseases

If patient still seizing after 2nd line infusion completed

Intubate

Choose 1 of the following:

- Midazolam IV
  Bolus: 0.2 mg/kg
  Infusion: 1-10 mcg/kg/min
  titrate by 1 mcg/kg/hr by RN
  >10 mcg/kg/hr by physician
  No bolus restriction

- Propofol### IV
  Bolus: 1 - 2 mg/kg
  max 80 mcg/kg/min
  Infusion: 5 - 80 mcg/kg/min
  Titrate by 5-10 mcg/kg/min every 5-10 min by RN
  Bolus restricted to physician

If patient continues to seize, see Adult SE Guideline, Critical Care Unit

** Fosphenytoin can be given if fosphenytoin is not available, but ensure max rate is limited to 50 mg/min. If patient develops hypotension or arrhythmia, infusion should be slowed down.
### High dose, long duration propofol drips must be monitored for propofol-related infusion syndrome

Monitor:
- Airway, Breathing, Circulation
- Initiate airway protection:
  - Oxygen, lateral decubitus positioning and frequent suctioning
- Avoid intubation if possible

Workup:
- Fingerstick glucose
- STAT sodium
- CBC, CMP, magnesium, phosphorus, ABG
- Blood alcohol level, if indicated
- Anti-epileptic levels (or hold yellow tube if meds unknown)
- Urine tox screen, urine pregnancy test
- ECG, telemetry

If patient develops hypotension or arrhythmia, infusion should be slowed down.

High dose, long duration propofol drips must be monitored for propofol-related infusion syndrome

Monitor:
- Airway, Breathing, Circulation
- Continue airway protection measures
- Avoid intubation if possible

Workup:
- Serum AED levels
- Head CT for 1st time seizure, when no longer seizing
- If febrile, consider LP (CSF cell count, protein, glucose, HSV PCR, VDRL, cryptococcal Ag, Enterovirus PCR)
- Blood cultures

Intervention:
- Treat possible underlying etiology/correct metabolic disturbances
- Consult neurology

Monitor:
- Airway:
  - Intubate prior to initiating sedating anti-seizure medications
  - Breathing
  - Circulation

Order:
- 1 hour post-load levels for fosphenytoin or valproic acid

Intervention:
- Titrate drip for any ongoing clinical seizure activity
- Admit to ICU – Neurocritical care preferred
- Initiate eEEG as soon as possible following intubation as paralytics may mask seizure activity
- Ensure adequate access (consider central venous line)

This guideline was ratified by the Emergency Department faculty at Maine Medical Center in June 2022. It reflects our expert opinion and is not necessarily applicable to all institutions. It is intended to be a reference for providers caring for patients and is not intended to replace providers’ clinical judgment. Created by Cynthia Gaudet DO, Samantha L. Wood MD, Jane Morris MD, and Megan Selvitelli MD.
**Adult Status Epilepticus Guideline, Critical Care Unit**
Ongoing management of status epilepticus beyond the Emergency Department and into the Neurocritical care unit

### Refractory SE

#### 20 - 40 MIN

**Add 3rd line Agent:**
- Chose a different agent than the one used as a 2nd line agent:
  - Fosphenytoin** IV 20 mg/kg, max 1500 mg
  - Levetiracetam IV 60 mg/kg, max 4500 mg
  - Valproic Acid IV 40 mg/kg, max 3000 mg
  - Phenobarbital IV Bolus: 20 mg/kg
  - Additional fosphenytoin** IV 5-10 mg/kg for patients initially loaded with fosphenytoin

#### 40-60 MIN

**Patient admitted to Neurocritical Care**

cEEG initiated and shows ongoing seizure activity

**Initiate Burst Suppression**

- Pentobarbital 5-15 mg/kg IV load followed by 0.5-5 mg/kg/hr infusion, titrated to a burst suppression pattern on EEG
- Once pentobarbital started, discontinue midazolam or propofol, but continue other antiseizure medications
- Maintain burst suppression for 24 hours, then wean over 12-24 hours; If clinical or electrographic seizures recur, then burst suppression should be resumed

**If patient still seizing consider the following options**

**Additional anticonvulsants**: lacosamide, perampanel, topiramate, clobazam, etc.

**Ketogenic diet**

- Urgent vagal nerve stimulator placement and activation

**Epilepsy resection surgery** (if a single seizure focus is identified)

**Ketamine** 2 mg/kg bolus followed by 0.5-10 mg/kg/hr infusion

**Electroconvulsive therapy** (ECT)

If concern for possible paraneoplastic/autoimmune etiology, consider initiation of immunomodulation therapies:

- Methylprednisolone 1 g/day for 5 days IV
- IVIG 0.4 mg/kg/d x5 days
  - OR
  - Plasmapheresis qod x 5-7 exchanges
- Rituximab 375 mg/m² once weekly for 4 doses

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**Monitor:**
- Vital signs
- Ongoing vent management
- Telemetry

**Workup:**
- Continuous EEG
- Follow up on initial CSF results if LP done

**Intervention:**
- Continue to correct all underlying causes/metabolic disturbances
- Avoid/discontinue medications which are proconvulsant
- Initiate acyclovir if concern for HSV encephalitis
- Initiate antibiotics if concern for bacterial meningitis

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**Monitor:**
- Ongoing vent management
- Telemetry
- While on pentobarbital, monitor for myocardial suppression, loss of GI motility and absorption, and there is an increased risk of infections

**Work up:**
- Follow up on AED levels
- Consider: Tick panel, treponemal IgG/IgM, HIV

**Intervention:**
- Titrate pentobarbital to maintain burst suppression:
The EEG should be low voltage suppressed (flat) with rare (3-10) electrical bursts of higher amplitude mixed frequency activity per minute

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**Monitor:**
- Ventilator, telemetry
cEEG
- Monitor AED levels as needed
- Monitor for toxicity of AEDs

**Order:**
- Consider additional CSF studies as clinically indicated: repeat HSV PCR, MS panel, Epilepsy Autoimmune Evaluation, meningitis/encephalitis pathogen panel, VZV IgG/IgM, VZV PCR
- Arboviral panel, Powassan
- MRI brain (must be after seizures controlled so that cEEG can be removed)

**Intervention:**
- Discuss goals of care if seizures remain uncontrolled
- Consider Palliative Care consult

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*Phenytoin can be given if fosphenytoin is not available, but ensure max rate is limited to 50 mg/min. If patient develops hypotension or arrhythmia, infusion should be slowed down.*

*High dose, long duration propofol drips must be monitored for propofol-related infusion syndrome.*
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<tr>
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| 1 | Glauser, Tracy et al *Epilepsy currents* 2016 | Evidence Based Guideline: Treatment of convulsive status epileptics in children and adults: Report of the guideline committee of the American Epilepsy Society | Evidence based clinical practice guideline | NA | First line: A benzodiazepine (specifically IM midazolam or IV lorazepam) is recommended was the initial therapy of choice, given their demonstrated efficacy, safety, and tolerability.  
Second line: No evidence based second therapy of choice. Choose one of the following as a single loading dose:  
- IV forsyphenytion (20mg/kg, max 1500mg)  
- IV valproic acid (40 mg/kg, max 3000mg)  
- IV levetiracetam (60mg/kg, max 4500mg)  
Third Line: No clear evidence to guide therapy. If second therapy fails to stop seizure, treatment considerations should include intubation, sedation (midazolam or pentobarbital or propofol), neurology consult and cEEG monitoring. | - Strong evidence for 1st line recommendations  
- Insufficient evidence for 2nd and 3rd line recommendations |
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| 2 | Chamberland et al *Lancet* 2020 | Efficacy of levetiracetam, fosphenytoin and valproate for established status epilepticus by age group (ESETT): a double blind, responsive adaptive, randomized controlled trial. | RCT |  | No difference in primary outcome: absence of seizure with improved consciousness and without additional anti seizure medication at 1h from start of drug infusion. Choose one of the following as next line therapy for benzodiazepine-refractory status epilepticus:  
- IV levetiracetam (60mg/kg; max 4500mg): children (52%), adults (44%), older adults (37%)  
- IV Fosphenytoin (20mg/kg; max 1500mg): children (49%), adults (46%), older adults (47%)  
- IV Valproate (40mg/kg; max 3000mg): children (52%), adults (46%), older adults (47%) | Large RCT, second line therapy is equally effective |
| 3 | Teiman, David et al *NEJM* 1998 | A comparison of Four treatments for Generalized Convulsive Status Epilepticus | RCT | I | Control of SE at 20 min (p=0.02)  
IV lorazepam 0.1mg/kg (64.9%)  
IV phenytoin 18mg/kg (43.6%)  
IV phenobarbital 15 mg/kg (58.2%)  
IV diazepam 0.15 mg/kg (55.8%) | Large RCT, sufficient power |
| 4 | Silbergleit, R et al *NEJM* 2012 | Intramuscular versus intravenous therapy for prehospital status epilepticus | Non-inferiority RCT | I | Absence of seizure activity on arrival to ED (p < 0.001 FOR non-inferiority)  
IM midazolam 10mg (73.4%)  
IV lorazepam 4mg (63.4%) | Large RCT, sufficient power |
| 5 | Gujjar, Arunodaya et al *Seizure: European Journal of Epilepsy* 2017 | Intravenous levetiracetam versus phenytoin for status epilepticus and cluster seizures: A prospective, randomized study | Small RCT | II | Rate of seizure control in SE at 24h following second line agent (p=0.62)  
IV levetiracetam  
IV phenytoin |  |