# Status Epilepticus Treatment Algorithm

<table>
<thead>
<tr>
<th>Timing</th>
<th>Medication Recommendations</th>
<th>Comments</th>
</tr>
</thead>
</table>
| Within first 5 minutes          | **ADMINISTER BENZODIAZEPINE STAT***<sup>*</sup>  
Lorazepam 0.1 mg/kg IV (preferred)  
(max 4 mg/dose)  
or  
Midazolam 0.2 mg/kg IV or IM  
(max 10 mg/dose)  
+  
Fosphenytoin 20 mg PE/kg IVPB  
If still seizing in 5 minutes, repeat same dose of benzodiazepine | • **ABCs:** maintain airway protection  
  ○ O₂ via nasal cannula  
  ○ Intubation for compromised airway/gas exchange or elevated intracranial pressure  
  ○ Fluid resuscitation and vasopressor support if SBP < 90 mmHg or MAP < 70 mmHg  
  • Vital signs (SaO₂, BP, HR)  
  • Obtain peripheral IV access  
  • Finger-stick blood glucose: treat if BG < 70 mg/dl  
    ○ Thiamine 100 mg IV, then  
    ○ 50 mL dextrose 50% IV |
| Within 30 minutes (if still seizing) | Give additional fosphenytoin 5 mg PE/kg  
+  
Levetiracetam 1000-3000 mg IVPB  
(consider 20 mg/kg, max dose 3000 mg)  
or  
Valproate 20-40 mg/kg IVPB | • Consult neurology/neurocritical care  
• Send labs:  
  ○ CBC  
  ○ BMP  
  ○ Calcium (total, ionized)  
  ○ Magnesium  
  ○ AED levels (if taking previously)  
• Neurologic exam |
| If seizures persist ≥ 30 minutes | Midazolam infusion  
(0.2 mg/kg bolus, then 0.05 mg/kg/hr IV infusion titrated to achieve seizure control; max rate 2 mg/kg/hr)  
or  
Propofol infusion  
(1-2 mg/kg bolus, then 20 mcg/kg/min IV infusion titrated to achieve seizure control; max rate 50 mcg/kg/min)  
or  
Pentobarbital infusion  
(5-15 mg/kg bolus, then 0.5 mg/kg/hr titrated to achieve seizure control; max rate 5 mg/kg/hr, no higher than 50 mg/min)  
or  
Ketamine infusion  
(0.5-5 mg/kg bolus, then 0.5 mg/kg/hr titrated by 0.5-1 mg/kg/hr every 6-8 hours to achieve seizure control; max rate 10 mg/kg/hr) | **Note:** Patients MUST be intubated prior to initiation of continuous infusions  
Infusion rates should be titrated based on continuous EEG monitoring  
• Order continuous EEG  
• Diagnostic imaging including head CT  
• ICP monitoring if elevated ICP suspected  
• Foley catheter placement |

*If NO IV access: Midazolam 0.2 mg/kg IM up to maximum or 10 mg or Diazepam rectal gel 0.2 mg/kg PR
Definition / Background / Key Aspects of Care

Status Epilepticus (SE)
- Continuous clinical and/or electrographic seizures lasting \( \geq 5 \) minutes or
- Recurrent seizure activity without returning to baseline between seizures

Convulsive SE
- Convulsions associated with rhythmic jerking of the extremities

Nonconvulsive SE
- Seizure activity on electroencephalogram (EEG) without clinical findings associated with convulsive SE

Refractory SE
- Clinical or electrographic seizures that do not respond after adequate doses of an initial benzodiazepine (BZD) followed by a second acceptable antiepileptic drug (AED)

Diagnosis
All patients
- Consult Neurology/Neurocritical Care:
  - Consider transfer to the Neurosciences Critical Care Unit (NCCU)
- Finger-stick blood glucose to check for hypoglycemia
- Vital signs:
  - \( \text{O}_2 \) saturation/RR
  - BP
  - HR
- Head computed tomography (CT) scan to evaluate etiology of seizure
- Labs:
  - Blood glucose
  - Complete blood count
  - Basic metabolic panel
  - Calcium
    - Total
    - Ionized
  - Magnesium
  - AED levels (if taking AEDs previously)

Consider based on patient history, clinical presentation, and/or neurology recommendations:
- Brain magnetic resonance imaging (MRI)
- Lumbar puncture (LP)
- Comprehensive toxicology panel (IHIS order: Toxicology Drug Screen, Serum):
  - Isoniazid
  - Tricyclic antidepressants
  - Theophylline
  - Cocaine
  - Sympathomimetics
  - Alcohol
  - Organophosphates
  - Cyclosporine

Monitoring
- Immediately order spot electroencephalogram (EEG)
  - IHIS order: EEG Extended < 1 Hour
- Consider continuous EEG monitoring if clinically indicated (e.g., persistent encephalopathy)
  - IHIS order: EEG Extended > 1 Hour

Management
Goals of Treatment
- Rapid cessation of seizure activity while maintaining airway, breathing, and circulation
- Identification and treatment of underlying seizure etiology
- Long-term maintenance of seizure control

Within 5-10 minutes
- Maintain airway protection
  - Administer \( \text{O}_2 \) via nasal cannula or face mask to maintain \( \text{SaO}_2 > 92\% \)
  - Immediate intubation for compromised airway/gas exchange or suspected elevated intracranial pressure (ICP)
- Obtain peripheral IV access
  - Administer benzodiazepine STAT for emergent seizure control
    - Lorazepam
      - 0.1 mg/kg IV push up to maximum of 4 mg
      - Preferred due to longer duration of action
    - Midazolam
      - 0.2 mg/kg IV push up to maximum of 10 mg
  - Order fosphenytoin 20 mg PE/kg STAT for urgent seizure control
  - Fluid resuscitation
  - Treat hypoglycemia if \( \text{BG} < 70 \) g/dL
    - Administer thiamine 100 mg IV, then Administer 50 mL dextrose 50%
- If NO IV access
  - Midazolam 0.2 mg/kg IM up to maximum or 10 mg
  - Diazepam rectal gel 0.2 mg/kg PR
- Vasopressor support if \( \text{SBP} < 90 \) mm Hg or \( \text{MAP} < 70 \) mm Hg

Within 10 minutes
- Send laboratory tests listed above
- Neurologic exam
- Consult Neurology
FOR PATIENTS STILL SEIZING OR SUBCLINICAL SEIZURES SUSPECTED:

**Within 30 minutes:**
- Administer additional fosphenytoin 5 mg PE/kg and
- Administer either:
  - Levetiracetam 1000-3000 mg IV (consider 20 mg/kg, max 3000 mg)
  - Valproate (VPA) 20-40 mg/kg IV

**Within 60 minutes**
- Patient MUST be intubated prior to continuous infusion of an AED listed below
- Administer one of the following:
  - Midazolam 0.2 mg/kg IV bolus followed by 0.05-2 mg/kg/hr IV infusion
  - Propofol 1-2 mg/kg IV bolus followed by 20-50 mcg/kg/min IV infusion
  - Pentobarbital 5-15 mg/kg IV bolus followed by 0.5-5 mg/kg/IV infusion
  - Ketamine 0.5-5 mg/kg IV bolus followed by 0.5-10 mg/kg/hr IV infusion
- Infusion rates should be titrated by physician order only to achieve seizure control on continuous EEG or for clinical signs of active seizure
- See Appendix 1 for titration instructions of continuous infusion medications and breakthrough SE dosing

FOR ALL PATIENTS

**Within 60 minutes**
- Continuous EEG
- Diagnostic imaging
- ICP monitoring if suspected elevated ICPs
- Foley catheter placement for accurate documentation of intake and output

Continued Medical Care

Order Maintenance Drug Regimen
- Refer to Appendix 1 for drug dosing

Therapeutic Drug Level Monitoring:

Phenytoin (PHT)
- Consider free phenytoin level 2 hours after administration of the loading dose(s) if patient still actively seizing
- Order free phenytoin trough level approximately 24 hours after administration of loading dose(s)

<table>
<thead>
<tr>
<th>Free PHT Level* mcg/mL</th>
<th>No Seizure Activity</th>
<th>Ongoing Seizure Activity</th>
</tr>
</thead>
<tbody>
<tr>
<td>&lt; 0.5</td>
<td>Reload 20 mg/kg</td>
<td>Reload 20 mg/kg</td>
</tr>
<tr>
<td>0.5-1.0</td>
<td>Reload 10 mg/kg</td>
<td>Reload 10 mg/kg</td>
</tr>
<tr>
<td>1.0-2.0</td>
<td>No change</td>
<td>Mini-load according to the equation below to optimize level between 2-2.5**</td>
</tr>
<tr>
<td>2.0-2.5</td>
<td>No change or decrease maintenance regimen if AEs present</td>
<td>No change; Consider additional AED</td>
</tr>
<tr>
<td>&gt; 2.5</td>
<td>Decrease maintenance regimen</td>
<td>No change or decrease maintenance regimen if AEs present</td>
</tr>
</tbody>
</table>

**Phenytoin/Fosphenytoin mini-load (mg) =** (desired free level – actual free level ) x 10 x actual body weight (kg) x 0.7

Valproic acid and derivatives (VPA):
- Consider total valproic acid level 1 hour after administration of the loading dose(s) if patient still actively seizing
- Order total valproic acid trough level approximately 24 hours after administration of loading dose(s)

<table>
<thead>
<tr>
<th>Total VPA Level* mcg/mL</th>
<th>No Seizure Activity</th>
<th>Ongoing Seizure Activity</th>
</tr>
</thead>
<tbody>
<tr>
<td>&lt; 10</td>
<td>Reload 20-40 mg/kg</td>
<td>Reload 20-40 mg/kg</td>
</tr>
<tr>
<td>10-50</td>
<td>Reload 10-20 mg/kg</td>
<td>Reload 10-20 mg/kg</td>
</tr>
<tr>
<td>50-100</td>
<td>No change</td>
<td>Mini-load according to the equation below to optimize level between 100-150**</td>
</tr>
<tr>
<td>100-150</td>
<td>No change or decrease maintenance regimen if AEs present</td>
<td>No change; Consider additional AED</td>
</tr>
<tr>
<td>&gt; 150</td>
<td>Decrease maintenance regimen</td>
<td>No change or decrease maintenance regimen if AEs present</td>
</tr>
</tbody>
</table>

**VPA mini-load (mg) =** (desired level – actual level) x actual body weight (kg) x 0.2
## Disposition Planning
- Consider admission/transfer to Neurosciences Critical Care Unit
- Consult Social Worker and Case Manager to assist with long-term planning

## Nursing Pearls for SE
- Assess and document neurological assessment and seizure activity
- Implement and maintain standard seizure precautions
- Minimize time to administration of AEDs. For a patient in active SE, AEDs should be administered STAT
- Implement seizure care plan and patient educations
- Continuous infusions of AEDs should NOT be stopped to perform neurological exam and are NOT titrated to a sedation scale (e.g., RASS)

## References

## Quality Measures
- Percent of patients receiving benzodiazepines first-line
- Percent of patients who received continuous EEG
- Percent of patients who have electrographic seizure control maintained for 24-48 hours
- Mechanical ventilation > 72 hours
- Percent of patients who received more than one non-benzodiazepine AED representing “failure” or “escalation of care”

## Order Sets
- Status Epilepticus Order Set (IHIS order: “Status epilepticus”)
- Pentobarbital Coma Order Set (IHIS order: “Pentobarbital coma”)

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**Guideline Approved**

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# Appendix 1. Intermittent Dosing of Antiepileptic Drugs for Status Epilepticus

<table>
<thead>
<tr>
<th>Drug</th>
<th>Initial Dosing</th>
<th>Administration</th>
<th>Pharmacokinetics</th>
<th>Serious Adverse Events</th>
<th>Comments</th>
</tr>
</thead>
<tbody>
<tr>
<td>Lorazepam (Ativan®)</td>
<td>0.1 mg/kg IV (max 4 mg)</td>
<td>Dilute 1:1 with NS Up to 2 mg/min IV push May repeat in 5-10 min</td>
<td>~90% protein-bound Preferred in patients with hepatic impairment 88% excreted as inactive metabolite in urine $t_{1/2}$ ~ 14 hours</td>
<td>Hypotension Respiratory depression</td>
<td>Preferred BZD to be used 1&lt;sup&gt;st&lt;/sup&gt; line in the management of SE due to quick onset of action and longer duration of action than midazolam IV contains propylene glycol; prolonged high-dose infusion may lead to metabolic acidosis</td>
</tr>
<tr>
<td>Midazolam (Versed®)</td>
<td>0.2 mg/kg IV/IM (max 10 mg)</td>
<td>IV push over 2-5 min Repeat every 5-10 min to a max total dose of 2 mg/kg</td>
<td>Onset 3-5 min IV, 15 min IM Duration &lt; 2 hours $t_{1/2}$ 2-7 hours ~97% protein-bound Hepatic metabolism ~90% excreted in the urine as metabolites</td>
<td>Hypotension Respiratory depression</td>
<td>Quicker onset of action than lorazepam, but limited by shorter duration of action. May be used as an alternative to achieve initial seizure control IM midazolam may be considered for patients without IV access</td>
</tr>
<tr>
<td>Diazepam (Valium®/Diastat®)</td>
<td>0.15 mg/kg IV (max 10 mg) 0.2 mg/kg suppository PR</td>
<td>Up to 5 mg/min IV push Rectal suppositories</td>
<td>Onset: ~ 1 min ~95% protein bound $t_{1/2}$ ~40 hours for parent compound Hepatic metabolism Excreted in the urine as metabolites</td>
<td>Hypotension Respiratory depression</td>
<td>Diazepam suppositories may be considered for patients without IV access IV contains propylene glycol; prolonged high-dose infusion may lead to metabolic acidosis</td>
</tr>
<tr>
<td>Fosphenytoin (Cerebyx®)</td>
<td>Load: 20 mg/kg IVPB Maintenance: 5-7 mg/kg/day divided Q8H or Q12H</td>
<td>Up to 150 mg PE/min May give additional 5 mg PE/kg 10 min after load if still seizing Compatible in NS, dextrose, and LR</td>
<td>Onset ~15 minutes to become converted to phenytoin 95-99% protein-bound Hydrolyzed to active phenytoin, which is then metabolized by the liver Excreted in urine as inactive metabolites</td>
<td>Hypotension Arrhythmias Bradycardia Cardiac toxicity</td>
<td>Preferred over phenytoin for loading dose since it can be infused at a faster rate; however it takes time to convert from the prodrug to active drug Dosed in phenytoin equivalents (PEs)</td>
</tr>
</tbody>
</table>
| **Phenytoin (Dilantin®)** | Load: 20 mg/kg IVPB  
Maintenance: 5-7 mg/kg/day divided Q8H or Q12H | Up to 50 mg/min  
Dilute in **NS only**, avoid small veins; administer through 0.22 micron filter. **Cannot be administered via PICC line.** | Onset ~ 30-60 minutes  
~90-95% protein-bound  
Hepatic metabolism  
t1/2 7-42 hours  
Excreted in urine as inactive metabolites | Hypotension  
Arrhythmias,  
Bradycardia  
Cardiac toxicity  
Purple glove syndrome | IV contains propylene glycol; high doses may lead to metabolic acidosis |
|---|---|---|---|---|---|
| **Levetiracetam (Keppra®)** | Load: 1000-3000 mg IVPB  
(max 3000 mg)  
Maintenance: 3000-6000 mg/day divided Q12H  
(If > 4000 mg, divide Q8H) | 2-5 mg/kg/min  
Protein binding < 10%  
Not extensively metabolized, primarily by enzymatic hydrolysis to inactive metabolites  
t1/2 6-8 hours  
Excreted in urine (66% unchanged drug) | Onset ~ 1 hour to peak  
Somnolence  
Rare psychosis, aggression | Minimal drug interactions  
No adjustment in hepatic failure  
Therapeutic drug monitoring is NOT recommended. Send-out lab may take several days to return limiting utility of the results |
| **Valproate (Depakene®)** | Load: 20-40 mg/kg IVPB  
Maintenance: 15-60 mg/kg/day divided Q8H | Up to 6 mg/kg/min  
80-90% protein-bound  
Extensive hepatic metabolism  
t1/2 9-19 hours  
Excreted 30-50% in urine as glucuronide conjugate | Hepatotoxicity  
Hyperammonemia  
Encephalopathy  
Pancreatitis  
Thrombocytopenia and inhibition of platelet activity  
Pregnancy X | Carbapenem antibiotics significantly reduce VPA levels resulting in inability to achieve therapeutic serum concentrations of VPA and loss of seizure control. **If receiving carbapenem antibiotics, choose an alternative agent** |
## Appendix 2. Continuous Infusion Antiepileptic Drugs for Status Epilepticus

### Clinical Pearls for Continuous Infusions
- Patients **MUST** be intubated prior to initiation of continuous infusions
- Infusion rates should be titrated based on continuous EEG
- When converting from one continuous infusion AED to another, the drugs should be overlapped for a sufficient period of time to minimize periods without therapeutic levels of AEDs

<table>
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<tr>
<th>Drug</th>
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<th>Administration</th>
<th>Pharmacokinetics</th>
<th>Serious Adverse Events</th>
<th>Comments</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Midazolam</strong> (Versed®)</td>
<td>0.2 mg/kg bolus, followed by 0.05 mg/kg/hr IV infusion</td>
<td>For breakthrough seizures, give 0.2 mg/kg bolus, increase infusion rate by 0.5-1 mg/kg/hr</td>
<td>See chart above</td>
<td>Hypotension, Respiratory depression</td>
<td>Tachyphylaxis occurs after prolonged use</td>
</tr>
<tr>
<td><strong>Propofol</strong> (Diprivan®)</td>
<td>1-2 mg/kg bolus, followed by 20 mcg/kg/min IV infusion</td>
<td>For breakthrough seizures, increase rate by 5-10 mcg/kg/min. May consider 1 mg/kg bolus prior to increasing rate</td>
<td>Onset ~ 30 seconds, Duration 3-10 minutes, 97-99% protein-bound Hepatic metabolism 88% excreted in the urine as inactive metabolites</td>
<td>Hypotension (especially with bolus dose), Respiratory depression, Cardiac failure, Rhabdomyolysis, Metabolic acidosis, Renal failure (PRIS), Hypertriglyceridemia</td>
<td>Formulated in lipid emulsion – must adjust daily caloric intake (1.1 kcal/mL). Risk of PRIS and adverse events increase with higher doses of propofol administered for prolonged period of time (&gt; 48 hours). Consider alternative agent if serum triglycerides &gt; 500 g/dL or CK &gt; 500. Triglycerides and CK should be monitored at least every other day.</td>
</tr>
<tr>
<td><strong>Pentobarbital</strong> (Nembutal®)</td>
<td>5-15 mg/kg bolus, followed by 0.5 mg/kg/hr IV infusion</td>
<td>For breakthrough seizures, give 5 mg/kg bolus and increase rate by 0.5-1 mg/kg/h every 12 hours Do not administer faster than 50 mg/min</td>
<td>Onset within 3-5 minutes, Duration: variable, 45-70% protein-bound Hepatic metabolism t½ ~ 22 hours Excreted in the urine</td>
<td>Hypotension, Respiratory depression, Cardiac depression, Paralytic ileus, Complete loss of neurological function</td>
<td>IV contains propylene glycol; high doses or prolonged infusions may lead to metabolic acidosis. Paralytic ileus may occur; all patients should have standing orders for a bowel regimen and consideration should be given to prokinetic agents (e.g., erythromycin, metoclopramide) if no contraindications exist.</td>
</tr>
<tr>
<td><strong>Ketamine</strong> (Ketalar®)</td>
<td>0.5-5 mg/kg bolus, then 0.5 mg/kg/hr IV infusion</td>
<td>For breakthrough seizures, increase rate by 0.5-1 mg/kg/hr every 6-8 hours</td>
<td>Onset ~ 30 seconds, Duration ~ 5-10 minutes, Hepatic metabolism to active metabolite Excreted in the urine</td>
<td>Tachycardia, Hypertension, Emergence reactions (vivid dreams, hallucinations, delirium)</td>
<td>Tachyphylaxis may occur after several days of continuous infusion. Emergence reactions after stopping continuous infusion may be prevented by pre-treatment with a benzodiazepine</td>
</tr>
</tbody>
</table>