## Status Epilepticus Treatment Algorithm

<table>
<thead>
<tr>
<th>Timing</th>
<th>Medication Recommendations</th>
<th>Comments</th>
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</thead>
</table>
| **Within first 5 minutes**     | **ADMINISTER BENZODIAZEPINE STAT***: Lorazepam 0.1 mg/kg IV (preferred) (max 4 mg/dose) or Midazolam 0.2 mg/kg IV or IM (max 10 mg/dose) | • 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 |
|                                | Fosphenytoin 20 mg PE/kg IVPB                                    | • Consult neurology/neurocritical care  
  • Send labs:  
    - CBC  
    - BMP  
    - Calcium (total, ionized)  
    - Magnesium  
    - AED levels (if taking previously)  
  • Neurologic exam |
| **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 | |
| **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 ≥ 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:
  - O₂ 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 O₂ via nasal cannula or face mask to maintain SaO₂ > 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 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 SBP < 90 mm Hg or 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)

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

**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)

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

**VPA mini-load (mg) =**
(desired level – actual level) x actual body weight (kg) x 0.2

*Trough level or 2h post load level

**Trough level or 1h post load level

**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”)

Authors

- Michel Torbey, MD
- Justin Kaplan, Pharm.D.
- Sarah Adriance, Pharm.D., BCPS
- Guhan Rammohan, MD
- Dorina Harper, RN, CNS
### 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&lt;sup&gt;®&lt;/sup&gt;)</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 $t_{1/2} \sim 14$ 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&lt;sup&gt;®&lt;/sup&gt;)</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&lt;sup&gt;®&lt;/sup&gt;/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 $t_{1/2} \sim 40$ 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&lt;sup&gt;®&lt;/sup&gt;)</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>
<tr>
<td>Drug</td>
<td>Load</td>
<td>Maintenance</td>
<td>Rate</td>
<td>Onset</td>
<td>Protein Bound</td>
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<tr>
<td>Phenytoin (Dilantin®)</td>
<td>20 mg/kg IVPB</td>
<td>5-7 mg/kg/day divided Q8H or Q12H</td>
<td>Up to 50 mg/min</td>
<td>30-60 minutes</td>
<td>90-95%</td>
</tr>
<tr>
<td>Levitiracetam (Keppra®)</td>
<td>1000-3000 mg IVPB (max 3000 mg)</td>
<td>3000-6000 mg/day divided Q12H (if &gt; 4000 mg, divide Q8H)</td>
<td>2-5 mg/kg/min</td>
<td>1 hour to peak</td>
<td>10%</td>
</tr>
<tr>
<td>Valproate (Depakene®)</td>
<td>20-40 mg/kg IVPB</td>
<td>15-60 mg/kg/day divided Q8H</td>
<td>Up to 6 mg/kg/min</td>
<td>80-90%</td>
<td>Extensive hepatic metabolism</td>
</tr>
</tbody>
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**Dilute in NS only, avoid small veins; administer through 0.22 micron filter. Cannot be administered via PICC line.**
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

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<tbody>
<tr>
<td>Midazolam (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></td>
<td>Titrated to achieve seizure control (max 2 mg/kg/hr)</td>
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<tr>
<td>Propofol (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></td>
<td>Titrated to achieve seizure control (max 50 mcg/kg/hr)</td>
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<tr>
<td>Pentobarbital (Nembutal®)</td>
<td>5-15 mg/kg bolus, following 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></td>
<td>Titrated to achieve seizure control (max 5 mg/kg/hr, but no higher than 50 mg/min)</td>
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</tr>
<tr>
<td>Ketamine (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>
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<tr>
<td></td>
<td>Titrated to achieve seizure control (max rate 10 mg/kg/hr)</td>
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</table>