## Management of Status Epilepticus (SE)

### Initial Treatment

<table>
<thead>
<tr>
<th>Timing</th>
<th>Drug</th>
<th>Medications</th>
<th>Additional Treatment</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Emergent Initial Therapy:</strong> ADMINISTER BENZODIAZEPINE STAT&lt;br&gt;Within first 5 minutes</td>
<td>Lorazepam - OR -</td>
<td>0.1 mg/kg IV (IV route preferred) (max 4 mg/dose)</td>
<td>• Consult Neurology/ Neurocritical Care&lt;br&gt;• ABCs: maintain airway protection&lt;br&gt;  ○ O₂ via nasal cannula&lt;br&gt;  ○ Intubation for compromised airway/gas exchange or elevated intracranial pressure&lt;br&gt;  ○ Fluid resuscitation and vasopressor support if SBP &lt; 90 mmHg or MAP &lt; 70 mmHg&lt;br&gt;• Vital signs (SaO₂, BP, HR)&lt;br&gt;• Obtain peripheral IV access&lt;br&gt;• Finger-stick blood glucose: treat if BG &lt; 70 mg/dl&lt;br&gt;  ○ Thiamine 100 mg IV, then 50 mL dextrose 50% IV</td>
</tr>
<tr>
<td>If NO IV access Midazolam - OR -</td>
<td>0.2 mg/kg IM (max 10 mg/dose)</td>
<td><strong>If NO IV access and IM is not feasible</strong>&lt;br&gt;<strong>Diazepam rectal gel</strong>&lt;br&gt;<strong>Weight (kg)</strong></td>
<td>• If hypotension occurs, reduce rate of Fosphenytoin infusion.</td>
</tr>
<tr>
<td><strong>≤ 62</strong></td>
<td><strong>12.5</strong></td>
<td><strong>If seizures continue after Fosphenytoin loading dose escalate to Urgent Control Therapy below.</strong>&lt;br&gt;<strong>Levetiracetam</strong>&lt;br&gt;- OR -</td>
<td><strong>Give additional 5 mg PE/kg IVP (no faster than 150 mg/minute)</strong>&lt;br&gt;<strong>-PLUS ONE OF THE FOLLOWING AGENTS BELOW-</strong>&lt;br&gt;<strong>Valproate</strong>&lt;br&gt;- OR -</td>
</tr>
<tr>
<td><strong>63 – 75</strong></td>
<td><strong>15</strong></td>
<td><strong>Fosphenytoin Loading Dose</strong>&lt;br&gt;20 mg PE/kg IVPB (no faster than 150 mg/minute)</td>
<td><strong>Protoplasmic</strong>&lt;br&gt;- AND/OR -</td>
</tr>
<tr>
<td><strong>76 – 87</strong></td>
<td><strong>17.5</strong></td>
<td><strong>Propofol infusion</strong>&lt;br&gt;- AND/OR -</td>
<td><strong>2 mg/kg bolus, then 20 mcg/kg/min titrated by 5-10 mcg/kg/min every 5 min to achieve seizure control; max rate 120 mcg/kg/min</strong></td>
</tr>
<tr>
<td><strong>= 88</strong></td>
<td><strong>20</strong></td>
<td><strong>Pentobarbital infusion</strong>&lt;br&gt;- AND/OR -</td>
<td><strong>10 mg/kg bolus, then 0.5 mg/kg/hr titrated by 0.5-1 mg/kg/hr every 12 hours to achieve seizure control; max rate 5 mg/kg/hr, no higher than 50 mg/min</strong></td>
</tr>
<tr>
<td><strong>Ketamine infusion</strong>&lt;br&gt;- AND/OR -</td>
<td><strong>2.5 mg/kg bolus, then 0.5 mg/kg/hr titrated by 0.5-1 mg/kg/hr every 1 hours to achieve seizure control; max rate 10 mg/kg/hr</strong></td>
<td><strong>Ketamine infusion</strong>&lt;br&gt;- AND/OR -</td>
<td><strong>2.5 mg/kg bolus, then 0.5 mg/kg/hr titrated by 0.5-1 mg/kg/hr every 1 hours to achieve seizure control; max rate 10 mg/kg/hr</strong></td>
</tr>
</tbody>
</table>

### Advanced Management of Refractory and Super-refractory Status Epilepticus:

If seizures persist ≥ 30 minutes

**Midazolam infusion**<br>- AND/OR -

0.2 mg/kg bolus, then 0.05 mg/kg/hr titrated by 0.05-0.1 mg/kg/hr every 3-4 hours to achieve seizure control; max rate 2 mg/kg/hr

**Propofol infusion**<br>- AND/OR -

2 mg/kg bolus, then 20 mcg/kg/min titrated by 5-10 mcg/kg/min every 5 min to achieve seizure control; max rate 120 mcg/kg/min

**Pentobarbital infusion**<br>- AND/OR -

10 mg/kg bolus, then 0.5 mg/kg/hr titrated by 0.5-1 mg/kg/hr every 12 hours to achieve seizure control; max rate 5 mg/kg/hr, no higher than 50 mg/min

**Ketamine infusion**<br>- AND/OR -

2.5 mg/kg bolus, then 0.5 mg/kg/hr titrated by 0.5-1 mg/kg/hr every 1 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

Within 60 minutes:

- Order continuous EEG
- Diagnostic imaging including head CT
- ICP monitoring if elevated ICP suspected
- Foley catheter placement
- Medications may be used concomitantly
Definitions

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

Consider additional testing 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

Continued Medical Care

Order Maintenance Drug Regimen

- Refer to Appendix 1 for therapeutic drug monitoring and drug dosing

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

- Initial dosing order for first benzodiazepines
- Initial dosing order for first AED
- Mechanical ventilation > 72 hours
- Average time between first dose benzodiazepines and administration of first line AED
- Order Set Usage

Order Sets

- Status Epilepticus Order Set
- Pentobarbital Coma Order Set

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- Dorina Harper, RN, CNS

Guideline Approved


Disclaimer: Clinical practice guidelines and algorithms at The Ohio State University Wexner Medical Center (OSUWMC) are standards that are intended to provide general guidance to clinicians. Patient choice and clinician judgment must remain central to the selection of diagnostic tests and therapy. OSUWMC’s guidelines and algorithms are reviewed periodically for consistency with new evidence; however, new developments may not be represented.

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Appendix 1: Therapeutic Drug Monitoring and Intermittent Dosing of Antiepileptic Drugs for Status Epilepticus

Phenytoin (PHT)
- Free phenytoin level \textit{2 hours after} administration of the loading dose(s)
- Order free phenytoin trough level 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>

* Trough level or 2h post load level

**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):
- Total valproic acid level \textit{1 hour after} administration of the loading dose(s)
- Order total valproic acid trough level 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>

* Trough level or 1h post load level

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

<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>
</table>
| **Lorazepam** (Ativa®) | 0.1 mg/kg IV (max 4 mg)          | ▪ Dilute 1:1 with NS  
▪ Up to 2 mg/min IV push  
▪ May repeat in 5-10 min | ~90% protein-bound  
Preferred in patients with hepatic impairment  
88% excreted as inactive metabolite in urine  
t<sub>1/2</sub> ~ 14 hours | ▪ Hypotension  
▪ Respiratory depression | ▪ Preferred BZD to be used 1<sup>st</sup> 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 |
| **Midazolam** (Versed®) | 0.2 mg/kg IV/IM (max 10 mg)      | ▪ IV push over 2-5 min  
▪ Repeat every 5-10 min to a max total dose of 2 mg/kg | Onset 3-5 min IV, 15 min IM  
Duration < 2 hours  
t<sub>1/2</sub> 2-7 hours  
~97% protein-bound  
Hepatic metabolism  
~90% excreted in the urine as metabolites | ▪ Hypotension  
▪ Respiratory depression | ▪ 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 |
| **Diazepam** (Valium®/Diastat®) | 0.15 mg/kg IV (max 10 mg)        | ▪ Up to 5 mg/min IV push  
▪ Rectal gel | Onset: ~ 1 min  
~95% protein bound  
t<sub>1/2</sub> ~40 hours for parent compound  
Hepatic metabolism  
Excreted in the urine as metabolites | ▪ Hypotension  
▪ Respiratory depression | ▪ Diazepam rectal gel may be considered for patients without IV access and IM Midazolam not available  
▪ IV contains propylene glycol; prolonged high-dose infusion may lead to metabolic acidosis |
| **Fosphenytoin** (Cerebyx®) | Load: 20 mg/kg IVPB (max 3000 mg)  
Repeat Load: May give additional 5mg PE/kg 10 min after load if still seizing  
Maintenance: 5-7 mg/kg/day divided Q8H or Q12H | ▪ Up to 150 mg PE/min  
▪ Compatible in NS, dextrose, and LR | 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 | ▪ Hypotension  
▪ Arrhythmias  
▪ Bradycardia  
▪ Cardiac toxicity | ▪ 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)  
▪ Use actual body weight for dosing |
<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><strong>Phenytoin</strong></td>
<td>Load: 20 mg/kg IVPB</td>
<td>• Up to 50 mg/min</td>
<td>Onset ~ 30-60 minutes</td>
<td>Hypotension</td>
<td>IV contains propylene glycol; high doses may lead to metabolic acidosis</td>
</tr>
<tr>
<td>(Dilantin®)</td>
<td>Maintenance: 5-7 mg/kg/day divided Q8H or Q12H</td>
<td>• Dilute in <strong>NS only</strong>, avoid small veins; administer through <strong>0.22 micron filter</strong>.</td>
<td>~90-95% protein-bound Hepatic metabolism t₁/₂ 7-42 hours Excreted in urine as inactive metabolites</td>
<td>Arhythmias, Bradycardia Cardiac toxicity Purple glove syndrome</td>
<td>Use actual body weight for dosing</td>
</tr>
<tr>
<td></td>
<td></td>
<td>• Cannot be administered via PICC line.</td>
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<tr>
<td><strong>Levetiracetam</strong></td>
<td>Load: 60 mg/kg (max 4500 mg)</td>
<td>• 5 mg/kg/min</td>
<td>Onset ~ 1 hour to peak Protein binding &lt; 10% Not extensively metabolized, primarily by enzymatic hydrolysis to inactive metabolites t₁/₂ 6-8 hours Excreted in urine (66% unchanged drug)</td>
<td>Somnolence Psychosis, aggression Rare elevated CK</td>
<td>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</td>
</tr>
<tr>
<td>(Keppra®)</td>
<td>Maintenance: 3000-6000 mg/day divided Q12H (If &gt; 4000 mg, divide Q8H)</td>
<td></td>
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</tr>
<tr>
<td><strong>Valproate</strong></td>
<td>Load: 40 mg/kg IVPB</td>
<td>• Up to 6 mg/kg/min</td>
<td>80-90% protein-bound Extensive hepatic metabolism t₁/₂ 9-19 hours Excreted 30-50% in urine as glucuronide conjugate</td>
<td>Hepatotoxicity Hyperammonemia Encephalopathy Pancreatitis Thrombocytopenia and inhibition of platelet activity</td>
<td>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</td>
</tr>
<tr>
<td>(Depakene®)</td>
<td>Maintenance: 5-20 mg/kg Q8H</td>
<td></td>
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<tr>
<td><strong>Lacosamide</strong></td>
<td>Load: 400 mg IVP</td>
<td>• Slow IV push at a rate not to exceed 80 mg/min</td>
<td>Onset immediate after IV administration, and 1-4 hours after oral 15% protein-bound Hepatic metabolism to inactive metabolite T₁/₂ ~13 hours Excreted 95% in urine</td>
<td>Dose-dependent PR interval prolongation, use caution with other PR prolonging agents or known second- or third-degree AV block Hypotension Bradycardia</td>
<td>Minimal drug interactions Dose adjustment in mild to moderate hepatic impairment and in patients with end stage renal disease or CrCl &lt;30 mL/min</td>
</tr>
<tr>
<td>(Vimpat®)</td>
<td>Maintenance: 100-300 mg Q12H</td>
<td>• May be administered without further dilution</td>
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</tr>
</tbody>
</table>
**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>
<thead>
<tr>
<th>Drug</th>
<th>Initial Dosing</th>
<th>Breakthrough Seizure Dosing</th>
<th>Pharmacokinetics</th>
<th>Serious Adverse Events</th>
<th>Comments</th>
</tr>
</thead>
<tbody>
<tr>
<td>Midazolam (Versed®)</td>
<td>0.2 mg/kg bolus, followed by 0.05 mg/kg/hr IV infusion</td>
<td>▪ Give 0.2 mg/kg bolus, increase infusion rate by 0.05-0.1 mg/kg/hr every 3-4 hours</td>
<td>See Appendix 1 (page 3)</td>
<td>▪ Hypotension</td>
<td>▪ Tachyphylaxis occurs after prolonged use</td>
</tr>
<tr>
<td></td>
<td></td>
<td>▪ Max 2 mg/kg/hr</td>
<td></td>
<td>▪ Respiratory depression</td>
<td></td>
</tr>
<tr>
<td>Propofol (Diprivan®)</td>
<td>2 mg/kg bolus, followed by 20 mcg/kg/min IV infusion</td>
<td>▪ Consider 1 mg/kg bolus prior to increasing rate</td>
<td>Onset ~ 30 seconds</td>
<td>▪ Hypotension (especially with bolus dose)</td>
<td>▪ Green urine</td>
</tr>
<tr>
<td></td>
<td></td>
<td>▪ Increase rate by 5-10 mcg/kg/min every 5 minutes.</td>
<td>Duration 3-10 minutes</td>
<td>▪ Respiratory depression</td>
<td>▪ Formulated in lipid emulsion – must adjust daily caloric intake (1.1 kcal/mL)</td>
</tr>
<tr>
<td></td>
<td></td>
<td>▪ Max 120 mcg/kg/hr</td>
<td>97-99% protein-bound</td>
<td>▪ Cardiac failure</td>
<td>▪ Risk of PRIS and adverse events increase with higher doses of propofol administered for prolonged period of time (&gt; 48 hours)</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>Hepatic metabolism</td>
<td>▪ Rhabdomyolysis</td>
<td>▪ 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>
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<tr>
<td></td>
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<td></td>
<td>88% excreted in the urine as inactive metabolites</td>
<td>▪ Metabolic acidosis</td>
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<td></td>
<td></td>
<td></td>
<td></td>
<td>▪ Renal failure (PRIS)</td>
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</tr>
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<td></td>
<td></td>
<td></td>
<td></td>
<td>▪ Hypertriglyceridemia</td>
<td></td>
</tr>
<tr>
<td>Pentobarbital (Nembutal®)</td>
<td>10 mg/kg bolus, following by 0.5 mg/kg/hr IV infusion</td>
<td>▪ Give 5 mg/kg bolus, increase infusion rate by 0.5-1 mg/kg/h every 12 hours</td>
<td>Onset within 3-5 minutes</td>
<td>▪ Hypotension</td>
<td>▪ IV contains propylene glycol; high doses or prolonged infusions may lead to metabolic acidosis</td>
</tr>
<tr>
<td></td>
<td></td>
<td>▪ Do not administer faster than 50 mg/min</td>
<td>Duration: variable</td>
<td>▪ Respiratory depression</td>
<td>▪ 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></td>
<td>▪ Max rate 5 mg/kg/hr</td>
<td>45-70% protein-bound</td>
<td>▪ Cardiac depression</td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>Hepatic metabolism</td>
<td>▪ Paralytic ileus</td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>t½ ~ 22 hours</td>
<td>▪ Complete loss of neurological function</td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>Excreted in the urine</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Ketamine (Ketalar®)</td>
<td>2.5 mg/kg bolus, then 0.5 mg/kg/hr IV infusion</td>
<td>▪ Give 2 mg/kg bolus, increase infusion rate by 0.5-1 mg/kg/hr every 1 hour</td>
<td>Onset ~ 30 seconds</td>
<td>▪ Tachycardia</td>
<td>▪ Tachyphylaxis may occur after several days of continuous infusion</td>
</tr>
<tr>
<td></td>
<td></td>
<td>▪ Max 10 mg/kg/hr</td>
<td>Duration ~ 5-10 minutes</td>
<td>▪ Hypertension</td>
<td><strong>Emergence reactions after stopping continuous infusion may be prevented by pre-treatment with a benzodiazepine</strong></td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>Hepatic metabolism to active metabolite</td>
<td>▪ Emergence reactions</td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>Excreted in the urine</td>
<td>▪ (vivid dreams, hallucinations, delirium)</td>
<td></td>
</tr>
</tbody>
</table>