**MGH STATUS EPILEPTICUS TREATMENT protocol**

**DIAGNOSIS OF STATUS EPILEPTICUS:**

1) **Generalized convulsive status epilepticus**
   Continuous convulsive seizure activity lasting > 5 mins
   OR, ≥ 2 convulsive seizures without full return to baseline between seizures

2) **Non-convulsive status epilepticus (NCSE)**
   
   2a) NCSE by strict electrographic criteria (adapted from *J Clin Neurophysiol* 2005; 22:79-91)

   An EEG pattern lasting ≥ 10 secs and satisfying either of the following, qualifies as an electrographic seizure*:
   1) Repetitive generalized or focal spikes, sharp-waves, spike-&-wave, or sharp-&-slow wave complexes at ≥3 Hz.
   2) Sequential rhythmic, periodic, or quasiperiodic waves at ≥ 1 Hz & unequivocal *evolution* in frequency
      (gradually increases/decreases by ≥ 1 Hz), morphology, or location (gradual spread into or out of a region
      involving ≥ two electrodes). Evolution in amplitude alone or in sharpness without other change in morphology
      is not enough to satisfy evolution in morphology.


   2b) NCSE by electroclinical or electroradiologic criteria

   Rhythmic/periodic EEG activity without evolution and with at least one of the following, qualifies as NCSE:
   1) Benzodiazepine trial (see below) demonstrating electrographic or clinical improvement
   2) Clear correlation between rhythmic/periodic EEG activity and clinical symptoms
   3) CT-PET or MRI neuroimaging showing a pattern of hypermetabolism or diffusion restriction not clinically explained by
      another inflammatory or ischemic processes.

   **Benzodiazepine Trial** (adapted from *Clin Neurophys* 2007;118:1660-1670)

   **Indication:** rhythmic or periodic epileptiform discharges on EEG with concurrent neurological impairment
   **Monitoring required:** EEG, pulse ox, blood pressure, EKG, respiratory rate with dedicated nurse

   Give sequential small doses of rapidly acting, short-duration benzodiazepine (e.g., midazolam at 1mg/dose), or a
   nonsedating IV anticonvulsant (e.g., levetiracetam, valproic acid, fosphenytoin, or lacosamide). Between doses, repeat
   clinical & EEG assessment. Trial is stopped for any of the following:
   1) Persistent resolution of the EEG pattern (and examination repeated).
   2) Definite clinical improvement.
   3) Respiratory depression, hypotension, or other adverse effect.
   4) Maximum allowed dose is reached (e.g., 0.2 mg/kg midazolam)

   **Interpretation:** POSITIVE test (i.e., seizure) if the ictal EEG pattern resolves and there is improvement in the patient’s
   clinical state and/or appearance of previously absent normal EEG patterns (e.g., return of posterior dominant rhythm).
   EQUIVOCAL test if the ictal EEG pattern improves but the patient does not.

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**TREATMENT OF STATUS EPILEPTICUS:**

1) **Generalized convulsive status epilepticus:** Use protocol on next page

2) **Non-convulsive status epilepticus** by electrographic, electroclinical, or electroradiologic criteria: No strong evidence to guide
   treatment; decision must be made on a case-by-case basis, weighing potential benefits of aggressive treatment (e.g. intubation
   and high dose anesthetics) vs potential risks. Benefits: rapid termination of seizures, prevention of seizure-induced secondary
   brain injury. Risks: side effects of anesthetics (e.g. hypotension, propofol infusion syndrome), prolonged mechanical ventilation
   and ICU course, with attendant risks of infection.

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**Authors:** Alice Lam, MD, PhD; M. Brandon Westover, MD, PhD

**Approved by:** Eric Rosenthal, MD; Andrew Cole, MD; Sydney Cash, MD, PhD; Daniel Hoch, MD, PhD [Last reviewed: 1/9/2015]
# MGH STATUS EPILEPTICUS TREATMENT PROTOCOL

## ANTI-CONVULSANT THERAPY

### 1st line (seizures ongoing for 5-10 mins)

**STATUS EPILEPTICUS**

**Lorazepam** 4mg IV (push over 2mins),
If szs not controlled within 5mins, repeat 4mg IV x 1
If no IV access:
**Diazepam** 20mg rectally (using IV sol’n)
or, **Midazolam** 10mg intranasal/buccal/IM (using IV sol’n).

### 2nd line (10-30 mins)

Choose from the following (may be used in combination):
1) **Valproic acid** 40mg/kg/IV (max rate 6mg/kg/min)
2) **Levetiracetam** 20mg/kg/IV (max rate 100mg/min)
3) **Phenobarbital** 20mg/kg/IV (max rate 50-75mg/min)
4) **Phenobarbital** 20mg PE/kg/IV (max rate 150mg PE/min)
or, **Phenytoin** 20 mg/kg/IV (max rate 25-50mg/min)
   If no effect, can give additional dose:
   **Phenobarbital** 10mg PE/kg IV or **Phenytoin** 10 mg/kg IV
5) **Lacosamide** 400mg IV over 5 min (need EKG pre/post)

### 3rd line (30-60 mins)

Choose from the following (may be used in combination):
1) **Midazolam** (good choice if BP unstable)
   Load 0.2mg/kg/IV.
   Repeat q5mins until szs stop (max load 2mg/kg)
   Maint. infusion 0.1 – 2 mg/kg/hr
2) **Propofol**
   Load 2mg/kg/IV.
   Repeat q5mins until szs stop (max load 10mg/kg)
   Maint. infusion 1-10mg/kg/hr (< 5 if tx > 48hrs)
Tritrate infusion to stop seizures or induce burst suppression (currently no evidence to guide best depth / duration of suppression).
Use IV fluids and pressors to support BP (anesthetic doses required to tx refractory SE are much higher than doses used for routine sedation).
Once sz-free for >24-48hrs, start slow taper of 3rd line meds over 24hrs, while maintaining high therapeutic levels of AEDs to avoid recurrent szs. Continue EEG monitoring until sz-free off 3rd line meds for >24 hrs, to monitor for recurrence of non-convulsive szs or NCSE.

### 4th line (>72 hrs)

Choose from the following (may be used in combination):
1) Repeat burst suppression for 24-48hrs
2) Add other AEDs (consider CBZ, TOP, not listed above)
3) IV magnesium (bolus 4g, then infuse 2-6g/hr/)
4) Ketamine
   Load w/ 1.5mg/kg/IV
   Repeat q5mins until szs stop (max load 4.5mg/kg)
   Maint. infusion at 1.2-7.5mg/kg/hr
5) **Pentobarbital** (titrate to burst suppression)
   Load 5mg/kg/IV (max rate 50mg/min).
   Repeat q5mins until szs stop (max load 15mg/kg)
   Maint. infusion 1-10 mg/kg/hr
6) **IV pyridoxine** (200mg/day)
7) **Immune modulation**
   Steroids (methylprednisolone 1g IV qd x 3-5 days)
   and/or IVIG (0.4g/kg/day x 5 days)
   and/or plasma exchange (every other day x 5-7 days)
7) Ketogenic diet
8) Therapeutic hypothermia
9) Electroconvulsive therapy (ECT)

## CONCURRENT MANAGEMENT

1) Airway, Breathing, Circulation
2) Vital signs (cont. monitoring): HR, BP, O2, EKG
3) Finger stick blood glucose
   If glucose low/unk: give thiamine 100mg IV, then D50 (50mL IV)
4) Obtain IV access (≥2 IVs)
5) If febrile, tx w/ anti-pyretics, cooling, consider Abx
6) Labs: CBC, BMP, Ca, Mg, Phos, LFTs, troponin, ABG, tox screen (blood & urine), blood cxs (esp if febrile), AED levels (in pts w/ prior hx of epilepsy), HCG (females)

If seizures persist

Check anti-convulsant levels post-load and re-bolus if needed (see box below for therapeutic levels):
- PHT, VPA, PHB - send level 1hr after load
- FOS-PHT - send level 2hrs after load

### INTUBATE.
Start continuous EEG monitoring

Continue maintenance anticonvulsants and adjust doses for therapeutic level:

## MAINTENANCE DOSES & THERAPEUTIC LEVELS

<table>
<thead>
<tr>
<th>AED</th>
<th>Maintenance Dose</th>
<th>Therapeutic Level</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Valproic acid</strong></td>
<td>30-60 mg/kg/day (BID)</td>
<td>70-120 ug/mL</td>
</tr>
<tr>
<td><strong>Levetiracetam</strong></td>
<td>2-4 g/day (BID)</td>
<td>25-60 mg/L</td>
</tr>
<tr>
<td><strong>Phenobarbital</strong></td>
<td>1-4mg/kg/day (BID)</td>
<td>20-50 mg/mL</td>
</tr>
<tr>
<td><strong>Phenytoin</strong></td>
<td>5-7 mg/kg/day (TID)</td>
<td>Unknown</td>
</tr>
<tr>
<td><strong>Lacosamide</strong></td>
<td>400-600mg/day (BID)</td>
<td>Unknown</td>
</tr>
</tbody>
</table>

* Total dilantin level should be corrected for patient’s renal function and albumin:
http://www.mdcalc.com/phenytoin-dilantin-correction-for-albumin-or-renal-failure/
If there is significant renal dysfunction or hypoalbuminemia, check a free dilantin level.

Continue workup to determine underlying cause of SE
1) Neuroimaging - brain MRI (preferred) or head CT
2) Lumbar puncture - evaluate for infection, inflammatory, autoimmune causes

Treat underlying cause of status epilepticus.

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10) Neurosurgical treatment (eg, resection of focal lesion)
11) TMS
No strong evidence to guide best treatment here.