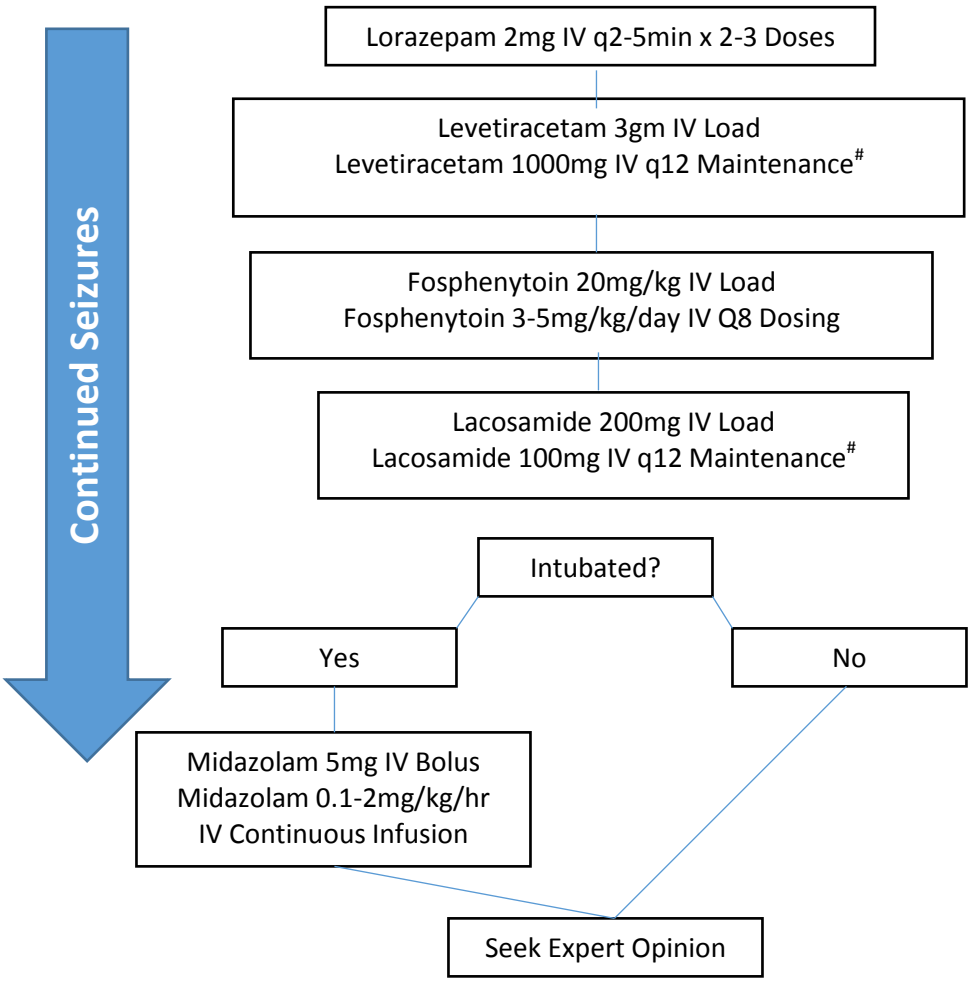
Section I: - Adult Guidelines for the Management of Status Epilepticus

-the following section has been approved by Dr. Matt Smith, Chair of Neuro Critical Care and Dr. John Brick, chair of Neurology

Status epilepticus (SE) is a life-threatening condition defined as ≥5 minutes of continuous clinical seizing or electroencephalographic (EEG) defined seizing. The disease state is associated with 9-21% mortality at hospital discharge if it is not treated emergently. Current guidelines exist that recommend the emergent and immediate treatment of SE and are summarized below. Additionally, these procedures make recommendations based on the most current literature on how to treat refractory SE, which is defined as SE that does not respond to the 1st and 2nd line therapies.

Initial Management



*Use actual body weight; adjusted body weight in obese. Phenytoin may be used alternatively
#Renal adjustments necessary

Emergent Considerations

Immediate (0-5 min)	Urgent (5-60 min)
• Airway, breathing circulation management • Establish Peripheral IV access • Emergent antiepileptic drug (AED)	• Basic metabolic panel, glucose point of care, blood cultures • Urgent AED administration (5-10 min) • Neurocritical care consultation • Diagnostic imaging (CT or MRI) • Refractory AED administration (20-60 min after urgent AED)

Medication Dosing (Not in order of Preference)

Emergent Therapy (1st Line)	
Diazepam	0.15mg/kg IV (maximum 10mg) Q5Min Rectal 0.2mg/kg Rectal (round to nearest 2.5mg)
Lorazepam	2-4mg IV push Q5-10Min (Max 4mg/dose; 12mg in an hour) 4mg IM Q5-10Min
Midazolam	0.2mg/kg IM (maximum 10mg)
Urgent Therapy (2nd Line)	
Fosphenytoin	20mg/kg IV (Actual body weight; use adjusted body weight in obesity) Loading dose Follow by 3-5mg/kg/day maintenance dose (divided into 2-3 doses) ***Peripheral or Central line available; Maximum rate 150mg/min** *May be given IM as single dose in 1-4 injection sites. (20mL/site tolerated in adults)
Phenytoin	20mg/kg IV (Actual body weight; use adjusted body weight in obesity) Loading dose Follow by 3-5mg/kg/day maintenance dose (divided into 2-3 doses) ***Central line preferred; Maximum rate 50mg/min**
Valproic Acid	20-40mg/kg IV Loading dose Followed by 15mg/kg/day maintenance dose (divided in 3 doses)
Ancillary Therapy (3rd Line)	
Clobazam	5-10 mg PO/gastric BID *Hepatic adjustments necessary; no IV formulation
Lacosamide	200mg IV Loading dose 100-200mg IV Q12H maintenance dose (Maximum daily dose of 400mg) *Renal adjustments necessary
Levetiracetam	1000-2000mg IV Loading dose 500-1000mg IV Q12H maintenance dose *Renal adjustments necessary
Topiramate	200-400 mg PO/gastric Loading dose 300-1600 mg/day divided 2-4 times daily *Renal adjustments necessary; no IV formulation
Refractory Therapies	
Ketamine	1.5mg/kg IV push Load Initiate 2mg/kg/hr continuous infusion; adjustments to be made per attending
Midazolam	0.1-0.2mg/kg IV Load or alternatively 5-10mg IV once Initiate 0.1mg/kg/hr infusion; if breakthrough seizures, repeat loading dose and increase infusion rate by 0.05-0.1mg/kg/hr (2mg/kg/hr max)
Pentobarbital	5-15mg/kg IV (maximum rate 50mg/min) Load

	Initiate 0.5-5mg/kg/hr continuous infusion; administer additional 5mg/kg and increase rate 0.5-1mg/kg/hour q12 hours for refractory status.
Propofol	1-2mg/kg IV Load Initiate 20mcg/kg/min infusion; increase 5-10mcg/kg/min q 5mins (80mcg/kg/min Max)

Medication Monitoring and Considerations

Drug	Special Considerations
Clobazam	• May cause fever, lethargy, and aggressive behavior • Case reports of angioedema
Diazepam	• Immediate onset, long half-life (20-50 hours) • Risk of propylene glycol toxicity with high doses
Fosphenytoin/ Phenytoin	• Monitor for bradycardia, hypotension, arrhythmia, nystagmus • Free phenytoin levels preferred over total (*see below*) • High drug-drug interaction potential (Cytochrome P450 Inducer) • Phenytoin preferred to be administered via central line (risk of phlebitis and extravasation/purple glove syndrome) • Only compatible with normal saline (NS)
Ketamine	• Emergence reactions include vivid dreams, hallucinations, delirium, and irritability. Hemodynamic instability may occur
Lacosamide	• Controlled substance (C-5) • Maximum 300mg daily in setting of severe renal impairment or moderate liver impairment
Levetiracetam	• Levels not correlated with outcome (only used to determine compliance) • May require renal adjustment

Lorazepam	• Onset of action
	  ○ 20-30 minutes IM
	  ○ 2-3 minutes IV
	• Risk of propylene glycol toxicity when given continuous infusion
	• Preferred benzodiazepine in setting of hepatic failure

Midazolam	• Onset of action
	  ○ 3-5 minutes IV
	• Accumulates in renal failure, hepatic failure, and prolonged infusion
	• High drug-drug interaction potential (Cytochrome P450 substrate)
	  ○ Prolonged sedation when used with other cytochrome p450 inhibiting medications.
	  ○ Active metabolites are renally eliminated

Pentobarbital	• Monitor for hypotension and ileus • High drug-drug interaction potential (Cytochrome P450 Inducer) • Goal drug level 20mcg/mL to achieve coma • Prolonged half life
Propofol	• Monitor for hypotension and bradycardia • Caution with high doses • Risk of propofol-related infusion syndrome (presents as metabolic acidosis and cardiovascular collapse) after long term use and high doses • Consider monitoring triglyceride levels weekly
Topiramate	• Monitor for metabolic acidosis

	• May cause fever • Monitor for hypotension
Valproic Acid	• Risk of severe hepatotoxicity, pancreatitis and DIC • Caution with use in acute bleeding • Goal drug levels 50-100mcg/mL

Phenytoin Level Monitoring

- Goal free level 1-2mcg/mL at steady state (total level 10-20mcg/mL)
    - Steady state levels achieved in 5-10 days
    - Consider higher levels when patient in status epilepticus
- Free levels preferred for monitoring
    - Free levels take into account circulating phenytoin not bound to albumin
    - Total levels must be corrected using following equations
        - Corrected total level = Measured total/[(0.2 x serum albumin) + 0.1]
        - Corrected total level for ESRD = Measured total/[(0.1 x serum albumin) + 0.1]
- When to get levels
    - 2-4 hours after completion of initial loading dose (expect to achieve goal level)
        - If <1 free level, reload with phenytoin 5-10mg/kg IV
        - If 1-1.5 free level, consider increasing maintenance dose
        - If 1.5-2.0 free level, continue maintenance dose
    - 5 days after initiation or change in maintenance dose
        - Trough level for best results

References:

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5. Madzar D, et al. Effects of clobazam for treatment of refractory status epilepticus. BMC Neurol. 2016; 16:202.

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