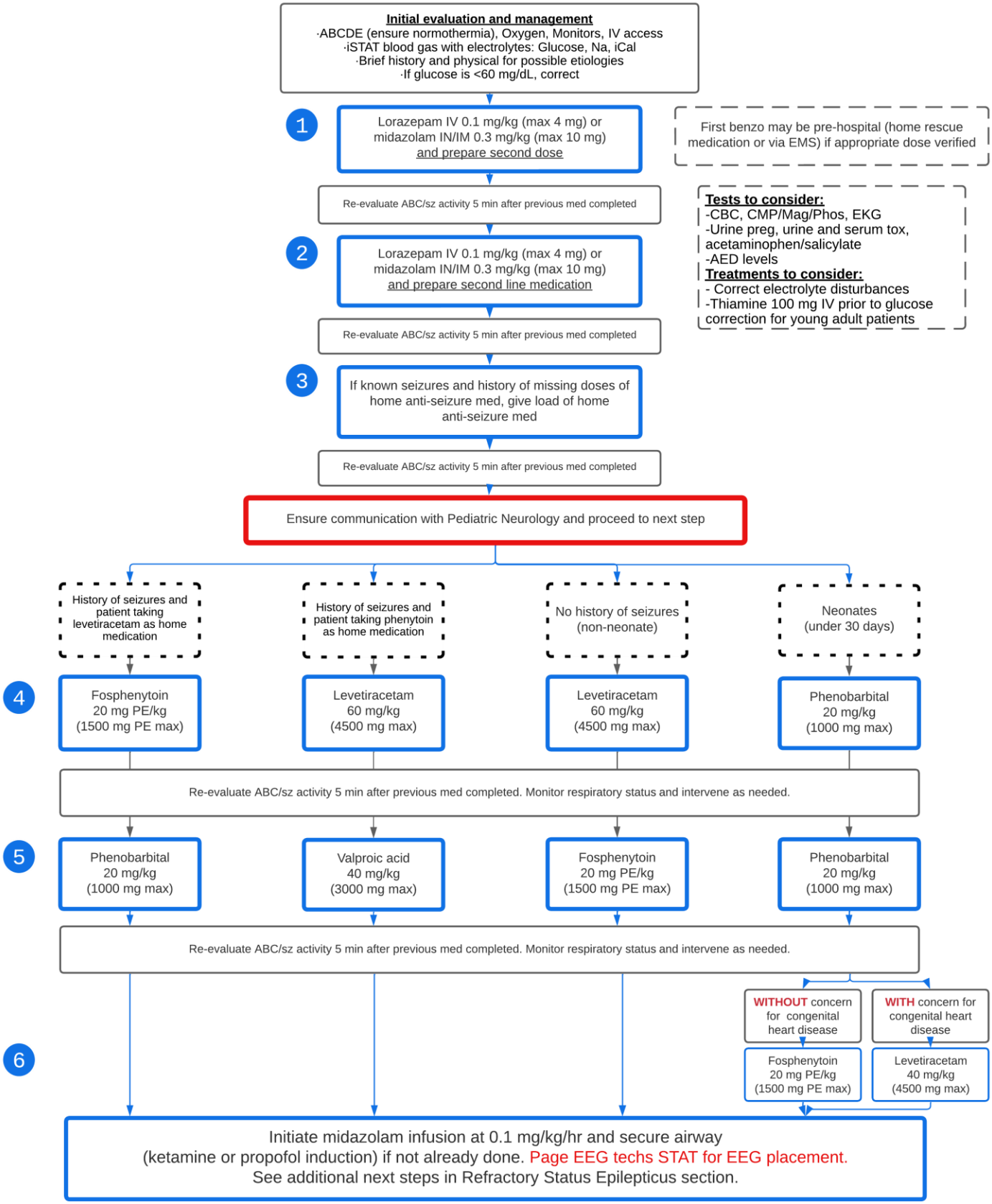
Hasbro Children's Hospital
Clinical Pathway for Evaluation and Treatment of Pediatric Status Epilepticus



Anti-Seizure Medication Dosing

Anti-seizure medication	Route for acute clinical scenarios	Dosing	Considerations	Infuse over	Time to onset
Lorazepam	IV	0.1 mg/kg/dose, max 4 mg		5 minutes	5-10 minutes
Midazolam	IV, IM, intranasal	IV: 0.2 mg/kg/dose, max 10 mg IM: 0.3 mg/kg/dose, max 10 mg Buccal: 0.3 mg/kg/dose, max 10 mg Intranasal: 0.3 mg/kg/dose, max 10 mg	Avoid intranasal midazolam in neonates	5 minutes	IV: 1-5 minutes IM: 5-10 minutes Buccal: 10-20 minutes Intranasal: Within 10 minutes
Diazepam	Rectal	0.2-0.5 mg/kg/dose, max 20 mg	Not generally utilized inpatient; dose is age and weight dependent		
Levetiracetam	IV	Loading dose: 60 mg/kg/dose, max 4500 mg		Infuse over 10 minutes for loading dose	5-30 minutes
Valproic acid	IV	Loading dose: 40 mg/kg/dose, max 3000 mg	Avoid in patients with hepatic dysfunction	Infuse over 10 minutes for loading dose	
Fosphenytoin	IV	20 mg PE (Phenytoin Equivalents)/kg/dose, max 1500 mg PE	Monitor for hypotension, arrhythmia. Avoid in patients with cardiac history.	Infuse over 10 minutes for loading dose Lab monitoring may include total and free levels	30-60 minutes
Phenobarbital	IV	Loading dose 20 mg/kg/dose, max 1000 mg	Monitor for hypotension	Infuse over 10 minutes for loading dose	5 minutes
Lacosamide	IV	Loading dose 10 mg/kg/dose, max 400 mg	Obtain EKG first; potential for bradycardia, PR prolongation	Infuse over 10 minutes for loading dose	1-4 hours to peak

Additional ED/Wards Management

- Discuss need for continuous EEG monitoring with Pediatric Neurology. If indicated, place order STAT for continuous EEG monitoring and contact EEG technician.
- Consider non-contrast CT brain for history concerning for trauma, hemorrhage, or increased intra-cranial pressure. Obtain Pediatric Neurosurgery consult if indicated.
- For neonates/infants to trial pyridoxine (200 mg IV load) in consultation with Pediatric Neurology, must 1) have CT head prior, 2) transfer to PICU and be on video EEG at the time of medication administration (risk of apnea).

Refractory Status Epilepticus

- Discuss goals of therapy with Pediatric Neurology Attending (termination of status epilepticus, versus termination of all electrographic seizures, versus burst suppression).
- **Midazolam** dosing and escalation (first line continuous infusion; may also choose ketamine as first line if there are contraindications to midazolam or hemodynamic considerations)
    - Loading dose: 0.1 mg/kg midazolam IV
    - Initiate continuous infusion at 0.1 mg/kg/hr
    - Give bolus dose of 0.1 mg/kg as frequently as every 15 minutes with evidence of ongoing seizure activity (clinical or non-convulsive)
    - After first hour, increase bolus dose to 0.2 mg/kg/dose and continuous infusion to 0.2 mg/kg/hr
    - After second hour, increase bolus dose to 0.4 mg/kg/dose and continuous infusion to 0.4 mg/kg/hr
    - After third hour, increase bolus dose to 0.6 mg/kg/dose and continuous infusion to 0.6 mg/kg/hr
    - If seizures persist with escalation of midazolam therapy, add ketamine infusion (see below). The timing of adding second infusion is at the discretion of the PICU and Pediatric Neurology attendings collaboratively.
    - May continue to increase midazolam infusion up to generally accepted maximum (secondary to saturation of GABA receptors) of 1.6 mg/kg/hr
- **Ketamine** dosing and escalation (may choose as first or second line continuous infusion)
    - If midazolam escalation has not ceased status epilepticus, add ketamine continuous infusion
    - Loading dose: 1 mg/kg ketamine IV over 10 minutes
    - Start infusion at 1 mg/kg/hr
    - Give bolus doses of 1 mg/kg every 30 minutes for ongoing status epilepticus
    - Titrate infusion by 1 mg/kg/hr every 2 hours to a maximum of 6 mg/kg/hr for a goal of seizure cessation
- **Additional guidance for neonates in refractory status**
    - Obtain phenobarbital level one hour after load
    - Continue to bolus with phenobarbital 20 mg/kg after initial level is obtained if remains in refractory status epilepticus
    - Goal phenobarbital level may be 40-60 or more in discussion with Pediatric Neurology
    - If refractory status epilepticus persists for a neonate, can continue to bolus phenobarbital as frequently as the time it takes to provide bolus, obtain level one hour after bolus, and discuss level with Pediatric Neurology
    - Continue to increase midazolam during this time with titration above
- **Pentobarbital** dosing and escalation
    - If midazolam and ketamine escalations have not met goal of seizure cessation, initiate goal of EEG burst suppression with pentobarbital
    - If not already in place, order vasopressor infusion given high likelihood of hemodynamic instability
    - Loading dose: 5 mg/kg pentobarbital
    - Give additional bolus doses of 5 mg/kg/dose every 15 minutes to attain burst suppression of 5-7 seconds
    - Often continuous infusion is not necessary given the prolonged half-life of pentobarbital
    - If continuous infusion is used, initiate at 1 mg/kg/hr and may increase by 1 mg/kg/hr every 12 hours to attain EEG flattening.
- If patient is in super refractory status epilepticus, alternatives may be considered such as metabolic and dietary therapies, hypothermia, and immunomodulatory therapy. FIRES/NORSE must be considered for all cases of

super refractory status epilepticus, and treatment such as steroids/IVIG should be considered. CSF should be obtained if not yet completed.

PICU Management

On arrival to the PICU (interventions as needed):

- Place cooling blanket for targeted temperature control under patient, and initiate controlled normothermia (36-37 C)
- Place esophageal temperature probe if advanced airway in place; consider rectal probe if contraindications to esophageal probe
- Complete history and physical exam, with focus on neurologic exam (recognizing that patient may be under neuromuscular blockade and significant sedation)
- Obtain CXR to confirm ETT placement if not confirmed in ED or requires adjustment
- Evaluate ventilator settings and ensure normocarbia, normoxia
- Ensure normotension
- Blood gas with lactate
- POCT glucose testing if previously hypoglycemic
- Communicate with Pediatric Neurology attending regarding continuous EEG monitoring (not available to initiate between 11 pm and 7 am) if not already decided
- Place order for STAT continuous EEG monitoring if within hours of 7 am – 10 pm

Evaluate need for:

- Airway support if not already in place
- Central venous access and/or arterial access; consider need for vasoactive support
- Vasoactive support
- Additional diagnostic procedures (LP, further lab workup), additional imaging such as MRI
- Antimicrobial treatment as indicated

Continuous EEG Monitoring

- **All patients meeting criteria of status epilepticus with ongoing stupor/coma require continuous EEG monitoring.**
- Discuss ordering STAT continuous EEG monitoring with Pediatric Neurology Attending (pending availability of tech and priority of studies such as MRI)
- Contact EEG technician as soon as order is placed
- Follow up with Pediatric Neurology Attending if tech does not arrive to PICU within established time frame
- If non-convulsive status epilepticus is suspected, Pediatric Neurology Attending will provide a preliminary EEG read to ER/PICU attending as soon as possible

Ongoing maintenance dosing and levels

- If phenobarbital is utilized:
    - Check level 1 hour after load and discuss goal level with Pediatric Neurology; patients in refractory or super refractory status may require higher levels
    - Start phenobarbital maintenance 6 hours after load at 5 mg/kg/day divided q 12 hours in discussion with Pediatric Neurology
- If fosphenytoin is utilized:
    - Check phenytoin free and total level 1 hour after load (free level will be affected by albumin/protein levels)
    - Start fosphenytoin maintenance 6 hours after load at 8-12 mg/kg/day divided q 8 hours in discussion with Pediatric Neurology
- If levetiracetam is used:
    - Start levetiracetam maintenance 12 hours after load at 40 mg/kg/day divided q 12 hours in discussion with Pediatric Neurology

Weaning of medications

- Duration of pharmacologic coma/continuous anti-seizure medication infusions should be discussed and determined between PICU and Pediatric Neurology; usually 24-28 hours
- Weaning period may also be 24-48 hours
- Patient should be maintained on continuous video EEG during infusion and weaning period, and in general until a period of 24 hours of seizure freedom is achieved.
- PICU and Pediatric Neurology Attendings must develop a plan to prevent recurrence of seizures during weaning phase (may require increasing scheduled anti-seizure medications, ketogenic diet, treatment of underlying cause, etc.).

Definitions and Metrics

Patients

- Patients being treated in Hasbro ED or pediatric inpatient units with status epilepticus

Definitions

- **Status epilepticus** (SE) is defined as ≥5 min of (1) continuous seizure or (2) two or more discrete seizures between which there is incomplete recovery of consciousness
- **Non-convulsive status epilepticus** (NCSE) is defined as ongoing electrographic seizures that may not be evident on physical exam, but identified with EEG monitoring, and suspected when a patient does not return to neurologic baseline
- **Refractory status epilepticus** (RSE) is defined as seizures that continue after administration of an appropriately dosed benzodiazepine and another anti-seizure medication
- **Super refractory status epilepticus** is defined as status epilepticus that continues for 24 hours or greater after the onset of treatment, or during the wean of continuous sedative/anesthetic agents

Clinical Goals

- Cessation of seizure as quickly as possible, **recognizing that ongoing SE lasting 30 minutes or more may cause long-term consequences (including neuronal injury, neuronal death, alteration of neuronal networks and functional deficits)**
- Preparation of the next anti-seizure medication while the current medication is infusing
- Re-evaluation of the patient (ABCs, including respiratory effort and bradypnea) **within 5 minutes of the completion of anti-seizure medication**

Metrics

- Time to administration of first anti-seizure medication
- Time to administration of second anti-seizure medication
- Time to EEG placement
- Time to termination of clinical/convulsive status epilepticus
- Time to termination of non-convulsive status epilepticus

References

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