

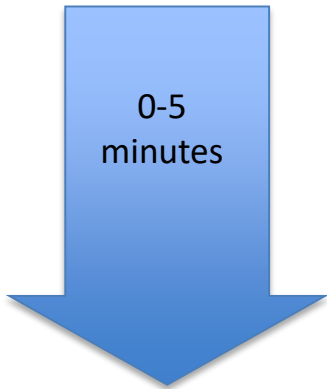
UNM Pediatric Status Epilepticus Pathway

Indication: children > 1 month - 18 years with:

- seizure > 5 minutes in duration OR
- recurrence of seizure without return to baseline

REFERENCES:

- ¹Glauser T, et al. Treatment of Convulsive Status Epilepticus in Children and Adults, *Epilepsy Currents* (2016)
- ²Alford E, et al. Treatment of Generalized Convulsive Status Epilepticus in Pediatric Patients, *J Pediatr Pharmacol Ther* (2015)

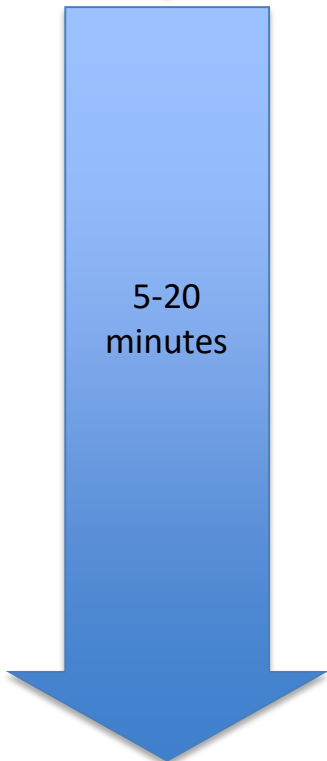


Stabilization Phase

POC Glucose

Order if applicable:

<input type="checkbox"/> iStat (VBG and electrolytes)	<input type="checkbox"/> Head CT or MRI
<input type="checkbox"/> Chem10	<input type="checkbox"/> Utox
<input type="checkbox"/> CBC	<input type="checkbox"/> LP (especially if <2 years, immune suppressed, or recent antibiotics)
<input type="checkbox"/> Calcium (total and ionized)	<input type="checkbox"/> Blood cx, UA, Urine cx
<input type="checkbox"/> Magnesium	
<input type="checkbox"/> AED Levels	



First Line Therapy

Did patient already receive appropriate 1st dose of benzodiazepine?

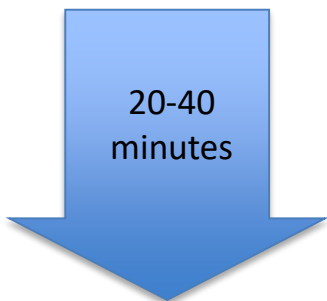
No

Route	Drug	Dose	Maximum
IntraMUSCULAR	midazolam	<ul style="list-style-type: none"> • 5 mg if 13-40 kg • 10 mg if > 40 kg 	10 mg
IntraNASAL	midazolam	0.2 mg/kg	10 mg
IntraVENOUS	lorazepam	0.1 mg/kg	4 mg
IntraVENOUS	diazepam	0.2 mg/kg	10 mg

If clinical seizure continues

Route	Drug	Dose	Maximum
IntraVENOUS	Lorazepam	0.1 mg/kg	4 mg
IntraVENOUS	diazepam	0.2 mg/kg	10 mg

Yes



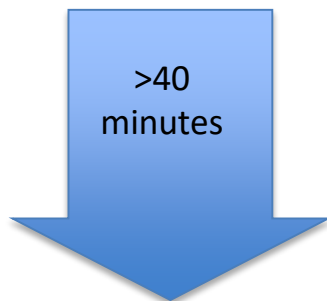
Second Line Therapy

If clinical seizure continues

NOTIFY NURSE TO DRAW MED FROM PIXIS

Route	Drug	Dose	Maximum
IntraVENOUS	Fosphenytoin	20 mg/kg	1500 mg
IntraVENOUS	Levetiracetam	60 mg/kg	4500 mg

Check Fosphenytoin level 2 hours after load



Third Line Therapy

If clinical seizure continues

- Consult Pediatric Neurology
- Consult PICU
- Order stat continuous EEG
- Proceed to Refractory Status Epilepticus Pathway

UNM Pediatric Status Epilepticus Pathway

Refractory Status Epilepticus

REFERENCES:

1. Brophy GM, et al. Guidelines for the evaluation and management of status epilepticus *Neurocritical Care* (2012)
2. Morrison G, et al. High-dose midazolam therapy for refractory status epilepticus in children. *Intens Care Med* (2006)
3. Abend NS and Loddenkemper T. Pediatric Status Epilepticus Management. *Current Opinion in Pediatrics* (2014)
4. Phelps S, *Pediatric Injectable Drugs*, 2013

TRANSFER TO PICU

There is no clear evidence to guide therapy in this phase. Select either of the following options.

ADDITIONAL ANTICONVULSANTS

- IV phenobarbital 20 mg/kg, max 1000 mg¹
 - IV valproic acid 20 mg/kg, max 1000 mg²
- ¹Check phenobarbital serum level 2 hours after load
 ²Valproic acid contraindicated if suspected or known metabolic disease, caution in children <2 years

WEAN:

- Decrease rate by 0.5 mg/kg/hr q 6 hours

Continue infusion until 24-48 hours seizure-free

MIDAZOLAM INFUSION

MIDAZOLAM INFUSION

- Bolus: 0.2 mg/kg¹ [Max 10 mg]
- Start infusion at 0.1 mg/kg/hour²

- Bolus: 0.15 mg/kg **AND** Increase infusion rate by 0.05-0.1 mg/kg/hr¹ [Repeat bolus and rate-increase q 15 minutes until seizure cessation]

Notes:

- If a rate of 1 mg/kg/hr fails to control seizures for >30 minutes, advance to next agent
- No max rate reported; note that rates above 2 mg/kg/hr (max 50 mg/hr) have been used in adults

If seizure continues

PENTOBARBITAL INFUSION

- Bolus: 5 mg/kg over 30 minutes.
- Repeat as needed to burst suppression IBI 10 seconds, up to 30 mg/kg (6 boluses total)⁴

ONCE BURST SUPPRESSION IS ACHIEVED:

- Start infusion at 1.0 mg/kg/hr⁴
- Stop midazolam infusion

- Increase infusion by 0.5 mg/kg/hr as needed to maintain BS

Notes:

- Monitor serum levels
- Max rate: 5 mg/kg/hr
- If IBI becomes prolonged, hold infusion until IBI < 20 seconds, then resume infusion at dose 0.5 mg/kg/hr less than previous dose

40-60 minutes

If seizure continues

If seizure continues

If seizure recurs

Seizure cessation

If seizure recurs

WEAN:

- Decrease rate by 0.5 mg/kg/hr q 6 hours

Continue infusion until 48 hours seizure-free

Seizure cessation

UNM Pediatric Status Epilepticus Pathway

Super refractory status epilepticus treatment options

KETAMINE INFUSION

(Continue midazolam infusion, see below)

- Bolus 2.5 mg/kg x2 q 5 minutes
- Start infusion at 8 mcg/kg/min (0.5 mg/kg/hr)
- Decrease midazolam infusion to 0.05 mg/kg/hr

- Increase rate by 8 mcg/kg/min (0.5 mg/kg/hr) every 15 minutes as needed to achieve resolution of clinical and/or electrographic seizures
- Continue Ketamine infusion until 48 hours seizure-free
- Wean by 8 mcg/kg/min (0.5 mg/kg/hr) q 6 hours

Notes

- Max rate: 55 mcg/kg/min (3.5 mg/kg/hr)
- Doses as high as 160 mcg/kg/min (10 mg/kg/hr) have been used in adults

Reference:

- Ilvento L, et al. Ketamine in refractory convulsive status epilepticus in children avoids endotracheal intubation *Epilepsy and Behavior* (2015)
- Gaspard N, et al. Intravenous ketamine for the treatment of refractory status epilepticus: a retrospective multicenter study, *Epilepsia* (2013)

LACOSAMIDE BOLUS

Weight <40 kg

- Bolus: 10 mg/kg
- Maintenance: 10 mg/kg/day div BID (start 12 hours later)

Weight >40 kg⁵

- Bolus: 200–400 mg
- Maintenance: 200mg bid

Notes

- Max maintenance dose: 14 mg/kg/day²⁻⁴
- Max infusion rate: 60 mg/min⁶

Reference:

- ²Grosso S, et al. Lacosamide in children with refractory status epilepticus. A multicenter Italian Experience, *European Journal of Paediatric Neurology* (2014)
- ³Poddar K, et al. Intravenous Lacosamide in Pediatric Status Epilepticus: An Open-Label Efficacy and Safety Study. *Pediatric Neurology* (2016)
- ⁴Arkilo D, et al. Clinical experience of intravenous lacosamide in infants and young children. *European Journal of Paediatric Neurology* (2016)
- ⁵Phelps S, *Pediatric Injectable Drugs*, 2013
- ⁶Hofler J, Intravenous lacosamide in status epilepticus and seizure clusters, *Epilepsia* (2011)

TOPIRAMATE BOLUS

- Bolus: 5 mg/kg
- Maintenance: 5 mg/kg/day div BID (start 12 hours later)

Notes

- Seizure-free after 24 hours: Continue 5 mg/kg/day div BID
- Seizures continue after 24 hours: Increase dose by 5 mg/kg/day q day
- Max dose reported in children: 25 mg/kg/day
- Max dose reported in adults: 1600 mg/day

- Monitor BMP daily

Reference:

- Akylidiz BN, et al. Treatment of pediatric refractory status epilepticus with topiramate, *Childs Nerv Syst* (2011)

PROPOFOL INFUSION

- Bolus: 3 mg/kg
- Start infusion at 50 mcg/kg/min (3 mg/kg/hr)
- Stop midazolam infusion

- Increase rate by 8 mcg/kg/min (0.5 mg/kg/hr) every 15 minutes as needed to achieve burst suppression (goal IBI 10 seconds)
- Once burst suppression is achieved → continue infusion for 24 hours → wean to 50% max rate for 6-12 hours → wean to 25% max rate for 6-12 hours → stop

- Monitor ABG, LFTs, CK q 6 x24 hours, then q12

Notes

- Max duration: 48 hours
- Max dose: 300 mcg/kg/min (18 mg/kg/hr)
- **Contraindications:** ketogenic diet, metabolic disorder, egg allergy

Reference:

- Phelps S, *Pediatric Injectable Drugs*, 2013
- Rossetti AO, et al. Propofol treatment of refractory status epilepticus: a study of 31 episodes, *Epilepsia* (2004)
- Van Gestel JP, et al. Propofol and thiopental for refractory status epilepticus in children, *Neurology* (2005)

VALPROIC ACID INFUSION

- Bolus: 20-40 mg/kg, then start infusion
 - Obtain level 1 hour after bolus
- Start infusion
 - Rate: 1 mg/kg/hr
 - With PHENobarbital or phenytoin, rate: 2 mg/kg/hr
 - With PENTobarbital, rate: 4 mg/kg/hr
- Increase rate by 1 mg/kg/hr as needed to achieve serum concentration (80-100 mg/L)
 - Obtain level 2 hours after rate increase

Notes

- Max rate: 6 mg/kg/hr
- Wean: 1 mg/kg/hr q 2 hours
- Contraindicated if suspected or known metabolic disease, caution in children <2 years

- Monitor CBC, CMP daily

Reference:

- Uberall R, et al. Intravenous valproate in pediatric epilepsy patients with refractory status epilepticus *Neurology* (2000)
- Hovinga CA, Use of intravenous valproate in three pediatric patients with nonconvulsive or convulsive status epilepticus, *Ann Pharmacother* (1999)
- Phelps S, *Pediatric Injectable Drugs*, 2013

UNM Pediatric Status Epilepticus Pathway

Super refractory status epilepticus treatment options

IMMUNOTHERAPY

METHYLPREDNISONE

- 30 mg/kg/day IV x 3 days

Notes

- Max: 1 gram/day
- Consider antiviral/antibiotic agents if infectious studies pending

IMMUNOGLOBULINS

- 1 gm/kg x 2 days

Notes

- Ensure all auto-antibody/infectious titers are drawn prior to administration

PLASMA EXCHANGE

- 5 exchanges
- Frequency: every other day

Notes

- Ensure all auto-antibody/infectious titers are drawn prior to administration

If an autoimmune or paraneoplastic etiology is confirmed and patient is not responding to above treatments, consider rituximab or cyclophosphamide.

Reference:

Abend N, et al. Status epilepticus and refractory status epilepticus management, *Semin Ped Neur* (2014)

KETOGENIC DIET

Step 1: Draw Screening Labs	Step 2: Develop a Feeding Plan	Step 3: Diet Initiation	Step 4: Diet Monitoring	Step 5: Discharge Planning														
-CBC -CMP -Mg and Phos -Plasma acylcarnitine profile -Urine organic acids -Plasma amino acids -Free and total carnitine -25-hydroxy vitamin D3 -Zn and Se	<p><u>Estimate caloric needs:</u> For <i>intubated</i> patients: Use the BMR (see below) For <i>extubated</i> patients: Use the BMR x 1.2-1.4</p> <p><u>Estimate fluid needs:</u> 0-10 kg: 100 mL/kg/day 10-20 kg: 1000mL + 50mL/kg/day 20-40 kg: 1500mL + 20mL/kg/day >40kg: use adult fluid needs</p> <p><u>Determine starting ratio:</u> <18 months: Initiate at 3:1 ratio and adjust as needed >18 months: Initiate at 4:1 ratio and adjust as needed</p> <p><u>Determine formula recipe:</u> Ketocal 4:1 liquid is 1.5 kcal/mL Ketocal 4:1 or 3:1 powder is 7 kcal/g (Displacement: 1mL/g)</p>	Remove all dextrose from fluids Change all medications to low-carbohydrate forms Slowly advance continuous feeds to goal and condense feeds further as tolerated	BMP, Mg, Phos daily UA q8hrs until 4+ ketones then q12hrs Blood glucose q4hrs until 4+ ketones then q8hrs <table border="1" style="width: 100%;"> <thead> <tr> <th>CO2 level</th> <th>Bicitra dosing (split BID)</th> </tr> </thead> <tbody> <tr> <td>If on carbonic anhydrase inhibitor</td> <td>1 mEq/kg</td> </tr> <tr> <td>16</td> <td>1 mEq/kg</td> </tr> <tr> <td>13-15</td> <td>2 mEq/kg</td> </tr> <tr> <td><12</td> <td>3 mEq/kg</td> </tr> </tbody> </table> <table border="1" style="width: 100%;"> <thead> <tr> <th>Blood sugar</th> <th>Intervention</th> </tr> </thead> <tbody> <tr> <td>< 40 mg/dL (with autonomic instability, jitteriness, sweating, dizziness or pallor)</td> <td>1. Give 15-30 mL of juice PO (or 3-5 oz unflavored Pedalyte via tube) 2. Wait 15 min & recheck blood sugar levels. If <40 mg/dL give an additional 15 mL juice (or 3 oz Pedalyte) & recheck blood sugar until >40 mg/dL</td> </tr> </tbody> </table>	CO2 level	Bicitra dosing (split BID)	If on carbonic anhydrase inhibitor	1 mEq/kg	16	1 mEq/kg	13-15	2 mEq/kg	<12	3 mEq/kg	Blood sugar	Intervention	< 40 mg/dL (with autonomic instability, jitteriness, sweating, dizziness or pallor)	1. Give 15-30 mL of juice PO (or 3-5 oz unflavored Pedalyte via tube) 2. Wait 15 min & recheck blood sugar levels. If <40 mg/dL give an additional 15 mL juice (or 3 oz Pedalyte) & recheck blood sugar until >40 mg/dL	If weaning diet, can decrease by 0.5:1 ratio every week until negative urine ketones then resume a regular diet If continuing diet, family needs a gram scale, urine ketone strips, glucometer, extensive dietitian education, and close follow-up as an outpatient
CO2 level	Bicitra dosing (split BID)																	
If on carbonic anhydrase inhibitor	1 mEq/kg																	
16	1 mEq/kg																	
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Reference:

Farias-Moeller R, et al. A practical approach to ketogenic diet in the pediatric intensive care unit for super-refractory status epilepticus, *Neurocrit Care* (20171)