

	<b>Recommendation</b>	<b>Source</b>	<b>Classification</b>	<b>Level of Evidence</b>	<b>Note</b>
<b>a</b>	Treatment algorithm for pediatric status epilepticus (SE) should include newer drugs such as fosphenytoin, levetiracetam, and valproic acid.	Abend et al. Anticonvulsant medications in the pediatric emergency room and intensive care unit. <i>Pediatr Emerg Care.</i> 2008 Oct;24(10):705-18	Review Article	IV	Suggested algorithm currently being used at Children's Hospital of Philadelphia. Basis of flow sheet.
<b>b</b>	IV lorazepam is at least as effective as IV diazepam, and is associated with fewer adverse events for treatment of acute tonic-clonic convulsive status epilepticus in children. If no IV access is available, buccal midazolam may be preferred.	Appleton et al. Drug management for acute tonic-clonic convulsions including convulsive status epilepticus in children. <i>Cochrane Database Syst Rev.</i> 2008 Jul 16;(3)	Systemic Analysis of RCTs	I	383 subjects from 4 RCTs studying efficacy and safety of antiepileptics in children.
<b>c</b>	IM or buccal midazolam is a safe and effective treatment for early SE in children when compared with IV or PR diazepam.	McMullan et al. Midazolam versus diazepam for the treatment of status epilepticus in children and young adults: a meta-analysis. <i>Acad Emerg Med.</i> 2010 Jun;17(6):575-82	Meta-Analysis of RCTs	I	774 subjects from 6 RCTs comparing Midazolam (IM, IN, Buccal) to Diazepam (IV, PR). 0 mo ~ 22 y/o. Midazolam with higher seizure control. Midazolam had 2 min shorter time to administration, and was less than 45s slower than IV diazepam after initiation. 0.8% respiratory complication vs 10.3% in diazepam. Dosing include 0.2mg/kg IM, 0.2mg/kg IN, 0.5mg/kg buccal, 10mg buccal.
<b>d</b>	Risk of respiratory depression is greater with more than two doses of benzodiazepines. Prehospital treatment should not be overlooked.	Chin et al. Inappropriate emergency management of status epilepticus in children contributes to need for intensive care. <i>J Neurol Neurosurg Psychiatry.</i> 2004 Nov;75(11):1584-8	Retrospective study	III	Cross-sectional retrospective study of 91 children who were admitted to PICU for status epilepticus. Those who had pre-hospital treatment with benzodiazepine were more likely to receive over 2 doses, and subsequently developed respiratory insufficiency.
<b>e</b>	LP, blood cultures, serum AED levels, toxicology screen and neuroimaging should be ordered only when clinically indicated.	Riviello et al. Practice parameter: diagnostic assessment of the child with status epilepticus (an evidence-based review): report of the Quality Standards Subcommittee of the American Academy of Neurology and the Practice Committee of the Child Neurology Society. <i>Neurology.</i> 2006 Nov 14;67(9):1542-50	Review Article	IV	A review by Am Acad of Neurology & Child Neurology Society.
<b>f</b>	IV Fosphenytoin is better tolerated and can be delivered faster than IV phenytoin. The cost difference between fosphenytoin and IV phenytoin is less than the medical cost to treat complications of status epilepticus or from potential malpractice costs due to complications secondary to IV phenytoin	DeToledo et al. Fosphenytoin and phenytoin in patients with status epilepticus: improved tolerability versus increased costs. <i>Drug Saf.</i> 2000 Jun;22(6):459-66	Review Article	IV	Author discusses safety profile of fosphenytoin vs phenytoin.
<b>g</b>	IV levetiracetam can be used adjunctively in children with status epilepticus.	Kirmani et al. Role of intravenous levetiracetam in acute seizure management of children. <i>Pediatr Neurol.</i> 2009 Jul;41(1):37-9	Retrospective Chart Review	III	Retrospective analysis using medical chart. 32 children 2mo~18y/o identified who received 50mg/kg bolus with 25mg/kg q12h maintenance. 16 patients had status epilepticus and 15 had acute exacerbation of seizures, and they had been given lorazepam & fosphenytoin prior. No serious side effects observed. All children responded to levetiracetam clinically and electrographically after 25~30min after initiating infusion.

h	IV levetiracetam may be effective in controlling status epilepticus in children, and is also well-tolerated in critically ill children.	Abend et al. Intravenous levetiracetam in critically ill children with status epilepticus or acute repetitive seizures. <i>Pediatr Crit Care Med.</i> 2009 Jul;10(4):505-10	Retrospective Case Series	III	10 children 0.08~14y/o in PICU received IV levetiracetam. Loading dose of 13~31mg/kg. All had temporary cessation, termination, or reduction in seizure activity. No acute adverse effects were noted.
i	IV valproic acid is as effective and has better tolerability than IV phenytoin when treating benzodiazepine-resistant status epilepticus.	Agarwal et al. Randomized study of intravenous valproate and phenytoin in status epilepticus. <i>Seizure.</i> 2007 Sep;16(6):527-32	RCT	Ia	100 patients (38 under 18y/o) with diazepam-refractory SE received either IV phenytoin or IV Valproic Acid loading dose of 20mg/kg at 40mg/min. 88% had control of SE vs 84% for phenytoin. No hypotension or respiratory depression was seen in valproate group, although mild elevation in liver enzymes were found in 4/50 pts. Phenytoin group had 6/50 hypotension and 2/50 respiratory depression. No difference in SE control between under 18 vs over 18y/o.
j	IV valproic acid bolus of 25mg/kg at 3mg/kg/min is safe and effective for the treatment of SE in children.	Yu et al. Safety and efficacy of intravenous valproate in pediatric status epilepticus and acute repetitive seizures. <i>Epilepsia.</i> 2003 May;44(5):724-6	Retrospective Review	III	18 pediatric patients with lorazepam-resistant SE received 25mg/kg at 3mg/kg/min of valproic acid. All had seizure cessation within 20 minutes. No significant changes in blood pressure or heart rate were noted. One patient had transient tremor. No changes in LFT were noted among patients younger than 24 months.
k	IV sodium valproate is an effective alternative to diazepam in controlling refractory status epilepticus in children and is without complications of respiratory depression or hypotension.	Mehta et al. Intravenous sodium valproate versus diazepam infusion for the control of refractory status epilepticus in children: a randomized controlled trial. <i>J Child Neurol.</i> 2007 Oct;22(10):1191-7	RCT	Ia	Open-label RCT of 40 children with refractory SE (diazepam+phenytoin+phenytoin) received sodium valproate 30mg/kg over 2~5 minutes, repeat bolus of 10mg/kg after 10 min, and infused 5mg/kg/hr thereafter, or diazepam 10ug/kg/min increased q5min by 10ug/kg/min until controlled or max of 100ug/kg/min. Time to control was 5min in valproic acid vs 17min in diazepam. 80% control vs 85%, no hypotension or ventilation requirement vs 50%&60% in diazepam. No adverse LFT effects in valproate.
l	Lorazepam, phenobarbital, phenytoin, and phenytoin+diazepam was equally efficacious with respect to recurrence, adverse reactions, and 30-day outcome.	Treiman et al. A comparison of four treatments for generalized convulsive status epilepticus. Veterans Affairs Status Epilepticus Cooperative Study Group. <i>N Engl J Med.</i> 1998 Sep 17;339(12):792-8	RCT	Ia	Double-blind RCT of 384 adult patients in 4 groups (Lorazepam 0.1mg/kg/5min, Phenobarbital 15mg/kg/16min, Phenytoin 18mg/kg/33min, Diazepam 015mg/kg+Phenytoin18mg/kg/42min). Success: lorazepam 65%, phenobarbital 58%, Diazepam/Phenytoin 56%, Phenytoin 43%. In intention-to-treat analysis, difference among 4 groups were not significant for recurrence, adverse reactions, or 30-day outcome.
m	Midazolam may be a good choice for initial treatment of refractory status epilepticus in children.	Gilbert et al. Efficacy and mortality in treatment of refractory generalized convulsive status epilepticus in children: a meta-analysis. <i>J Child Neurol.</i> 1999 Sep;14(9):602-9	Meta-analysis of RCTs	I	Meta-analysis of 12 RCTs studies. 111 children with refractory SE treated with diazepam, midazolam, thiopental, pentobarbital, and isoflurane. 29 received midazolam, with 100% efficacy and 0% mortality.

n	IV midazolam may be highly effective for treating status epilepticus in children when initiated within 3 hours of onset of seizure.	Hayashi et al. Efficacy of intravenous midazolam for status epilepticus in childhood. <i>Pediatr Neurol.</i> 2007 Jun;36(6):366-72	Retrospective Review	III	358 children who received IV midazolam for status epilepticus. 0.25mg/kg bolus + 0.25mg/kg/hr infusion. 65% had seizure suppression. It was the first-line tx for 70, second-line for 115, and third-line for 94. Effectiveness lower if midazolam initiated more than 3 hours after onset. Adverse events included respiratory depression in 86 cases, with 9 attributed to causal from midazolam. 27 showed circulatory distress, but no causal relationship with midazolam suggested.
o	High-dose IV midazolam can be used to control refractory status epilepticus in children.	Morrison et al. High-dose midazolam therapy for refractory status epilepticus in children. <i>Intensive Care Med.</i> 2006 Dec;32(12):2070-6	Retrospective Review	III	17 children who received midazolam for refractory SE as part of a protocol. Dose was 0.5mg/kg IV bolus + 2mcg/kg/min infusion, 5 minutes later, bolus 0.5mg/kg + infusion increase to 4mcg/kg/min, 5 minutes later, bolus 0.1mg/kg + increase infusion by 4mcg/kg/min, repeat up to 24mcg/kg/min. 76% had control within 30min, and 88% eventual control. Breakthrough seizure in 47%, Relapse in 6%. No significant adverse effects.
p	Pentobarbital may be an appropriate treatment for refractory status epilepticus despite increased risk for hypotension.	Claassen et al. Treatment of refractory status epilepticus with pentobarbital, propofol, or midazolam: a systematic review. <i>Epilepsia.</i> 2002 Feb;43(2):146-53	Meta-Analysis	Ia	193 adults in 28 studies who received midazolam, propofol, or pentobarbital for refractory SE. Pentobarbital had lower frequency of short-term treatment failure and breakthrough seizures when compared to midazolam and propofol. There was a higher frequency of hypotension in the pentobarbital group.
q	Pentobarbital may control refractory status epilepticus in some, but failure to respond is associated with poor prognosis.	Kim et al. Neurologic outcomes of pediatric epileptic patients with pentobarbital coma. <i>Pediatr Neurol.</i> 2001 Sep;25(3):217-20	Retrospective study	III	23 children with refractory SE received pentobarbital at 5mg/kg loading dose with 1-3mg/kg/hour infusion. 12 responders, 6 non-responders, and 5 relapsers. Mortality was 0 for responders and 91% for the latter two groups. Survival was greater in toddlers vs neonates/older children.