Pharmacotherapy of Status Epilepticus

modified September 2024

Despite the availability of several new anticonvulsants in recent years, the treatment of status epilepticus still involves the old standbys, particularly the benzodiazepines. The chart below provides anticonvulsant dosing and place in therapy of convulsive status epilepticus. Administration rates, monitoring, and other practical information is also provided. The chart is largely based on the 2016 American Epilepsy Society guidelines for the treatment of convulsive status epilepticus. The complete guidelines are available at http://www.ncbi.nlm.nih.gov/pmc/articles/PMC4749120/pdf/i1535-7511-16-1-48.pdf. An associated treatment algorithm is available at https://www.aesnet.org/images/default-source/default-album/cse-treatment-chart-final_rerelease.jpg?sfvrsn=f9e6cfd5_2. Since publication of these guidelines, several new studies comparing fosphenytoin, levetiracetam, and valproate sodium for benzodiazepine-refractory status epilepticus have been published.[9] After a benzodiazepine, loading doses of these agents (levetiracetam 60 mg/kg, valproate sodium 40 mg/kg, or fosphenytoin 20 mg/kg [phenytoin equivalents]) are likely equally effective.[9] Consider levetiracetam for ease of use and safety (i.e., drug interactions, adverse effects).[14] Levetiracetam is a safer option than phenytoin or valproate sodium when past medication history is not readily available.

—***Dosing, administration rates, and other information may differ from product labeling***—

DRUG	DOSE[b]	COMMENTS
Initial Treatment Options if still seizing after stabilization (i.e., airway, breathing, circulation, blood glucose, etc addressed)[1]		
Diazepam, intravenous	0.15 to 0.2 mg/kg/dose, max 10 mg/dose; may repeat once,[1] in 5 minutes[2] Consider using actual weight in obese adults.[7]	• Max administration rate: 5 mg/min[2] • Contains propylene glycol.[2,a] • Monitor for hypotension and respiratory depression.[2]
Lorazepam, intravenous	0.1 mg/kg/dose, max 4 mg/dose; may repeat once,[1] in 5 to 10 minutes[2] Consider using actual weight in obese adults.[7]	• Max administration rate: 2 mg/min.[2] • Contains propylene glycol.[2,a] • Dilute 1:1 with saline.[2] • Monitor for hypotension and respiratory depression.[2]
Midazolam, intramuscular	10 mg if >40 kg, 5 mg if 13 to 40 kg; single dose[1] Consider using actual weight in obese adults.[7]	• Monitor for respiratory depression and hypotension.[2]

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Alternative Initial Treatment Options (if above options not available)[1]		
Diazepam, rectal	0.2 to 0.5 mg/kg, max 20 mg; single dose[1]	• Monitor for respiratory depression and hypotension.[2] • Rectal gel is commercially available (*Diastat*).
Diazepam, nasal (*Valtoco* [US])[13]	0.2 mg/kg (6 to 11 years of age), or 0.3 mg/kg (≥12 years of age), max 20 mg.[6]	• Divide dose equally between nostrils.[6] • There is little data on intranasal diazepam for status epilepticus.[25]
Midazolam, intranasal or buccal	**Intranasal**: most common dose 0.2 mg/kg to 0.3 mg/kg, with a max dose of 10 mg[5,16,17] **Buccal**: 0.2 to 0.5 mg/kg, max 10 mg[4,6]	• Monitor for respiratory depression and hypotension.[2] • Can use injection solution buccally or intransally.[3,6] • For intranasal use, administer with needleless syringe, or consider use of a nasal atomizer device for converting IV syringe for intranasal use.[5,6] Nasal spray (5 mg/spray) is commercially available in US (*Nayzilam*).[6] Divide dose equally between nostrils.[4] • Buccal: solution typically placed between gum and cheek; cheek can be massaged.[4] • Use 5 mg/mL concentration for fast onset.[19] • **Most studies performed in children**.[4,18]
Phenobarbital, intravenous	15 to 20 mg/kg/dose; single dose.[1,2] Max 1,000 mg/dose in pediatrics.[26]	• Administration rate: 50 to 100 mg/min.[2] Max 1 mg/kg/min in pediatrics.[26] • Contains propylene glycol.[2,a] • Monitor for hypotension and respiratory depression.[2]
Second-line Options if patient is still seizing after 20 minutes (or sooner).[1] Failing **one** option, moving to a third (refractory) agent is recommended.[2]		
Levetiracetam, intravenous	60 mg/kg, max 4,500 mg/dose[9]	• Available in premixed bags.[2] Multiple bags will often be needed (1,500 mg in 100 mL is the most concentrated available). ○ Doses ≤4,500 mg have been given IV push to adults over as little as two minutes.[24] ○ Keep in mind practical limitations. USP <797> compounding regulations for immediate-use medications at the bedside limit three vials (500 mg each) to one syringe (1,500 mg total per syringe).[27]

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		• Few drug interactions.[2] Good tolerability.[1]
Second-line Options, continued		
Fosphenytoin, intravenous (a phenytoin prodrug)	20 mg phenytoin equivalents/kg, max 1,500 to 2,000 mg phenytoin equivalents; single dose.[1,15] Consider using actual body weight for obese patients.[15] **Fosphenytoin** can be administered **intramuscularly**, although the intravenous route is preferred for status epilepticus.[13] Fosphenytoin is 100% bioavailable when given intramuscularly, but peak levels are lower than after intravenous administration, and pharmacokinetics are similar to orally administered phenytoin.[6]	• Max administration rate up to 150 mg phenytoin equivalents per minute in adults.[2] For pediatrics, up to 3 mg/kg phenytoin equivalents per minute, not to exceed adult max.[28] • Compatible with saline, dextrose, and Lactated Ringer's solution.[2] • Monitor for hypotension and arrhythmias.[2] • **Phenytoin** is an alternative, but causes more injection-site pain, serious tissue damage, and arrhythmias, and is compatible only with normal saline.[1-3] Contains propylene glycol.[2] Max administration rate 50 mg/min in adults, or 1 mg/kg/min in pediatrics, not to exceed adults max.[2,26] If diluted in a mini-bag of normal saline, dilute to **not less than** 5 mg/mL.[6] Infuse with 0.22 to 0.55 micron in-line filter.[6] Watch solution for precipitation.[6] Use central access, or healthy antecubital fossa vein (or similar or larger vein) with 20-gauge catheter or larger.[6] Administer through a free-flowing IV of normal saline.[6] Flush line with saline before and after administration.[6]
Valproate sodium, intravenous	40 mg/kg, max 3,000 mg (single dose)[1,9,10]	• Administration rate: 3 to 6 mg/kg/min.[2] A rate of 10 mg/kg/min may be as safe as 6 mg/kg/min.[22] Can dilute in 100 mL saline.[12] • Consider after benzo for patients with a history of generalized epilepsy.[2] • Hepatotoxicity is a concern, especially with children <2 years of age, and with rapid infusion.[11,22]
Alternative Second-line Options (if above options not available)		
Phenobarbital, intravenous	15 to 20 mg/kg/dose (single dose), if not already given.[1,2] Max 1,000 mg/dose in pediatrics.[26]	• Administration rate: 50 to 100 mg/min.[2] • Contains propylene glycol.[2,a] • Monitor for hypotension and respiratory depression.[2]
Lacosamide, intravenous[8]	**Adults**: 200 to 400 mg, single dose.[2,8] 400 mg is the most common dose, and may be more effective.[8] **Pediatrics**: Limited data. 3.3 to 10 mg/kg/dose has been used in children.[30] Do not exceed adult dose.	• Limited data in status epilepticus.[2] Max 1 mg/kg/min in pediatrics.[26] • Few drug interactions.[2] • Monitor for hypotension, PR prolongation, AV conduction disturbance, bradycardia, and asystole.[2,3,30]

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		• Give 200 mg over 15 minutes.[2] Doses of up to 400 mg have also been given IV push at a rate of 40 to 80 mg/min.[6,21]
Continuous Infusion Options for Refractory Patients require ventilatory assistance, electroencephalogram monitoring, and cardiac monitoring.[2] Try an alternative if the first one doesn't work.[2]		
Midazolam infusion	**Bolus**: 0.2 mg/kg at a rate of 2 mg/min[2] **Continuous infusion**: 0.05 to 2 mg/kg/h.[2] **For breakthrough**: consider a 0.1 to 0.2 mg/kg bolus and increasing rate by 0.05 to 0.1 mg/kg/h every three to four hours.[2]	• Can cause hypotension (less than propofol).[2] • Tolerance with prolonged use.[2]
Propofol	**Bolus**: 1 to 2 mg/kg[2] **Continuous Infusion**: 20 mcg/kg/min, initial.[2] Range: 30 to 200 mcg/kg/min.[2] **For breakthrough**: consider increasing rate by 5 to 10 mcg/kg/min every 5 minutes. Or give a 1 mg/kg bolus and increase infusion rate.[2]	• Can cause hypotension, especially with loading doses.[2] • Watch for cardiac depression, rhabdomyolysis, metabolic acidosis, and renal failure. Use special caution with doses >80 mcg/kg/min for >48 hrs.[2] In children, use caution with doses >65 mcg/kg/min.[2] • Provides 1.1 kcal/mL.[2]
Pentobarbital	**Bolus**: 5 to 15 mg/kg. May give an additional 5 to 10 mg/kg. Infuse at a rate ≤50 mg/min.[2] **Continuous infusion:** 0.5 to 5 mg/kg/hr.[2] **For breakthrough**: consider a 5 mg/kg bolus, then increasing continuous infusion by 0.5 to 1 mg/kg/h every 12 h.[2]	• May be more effective than midazolam initially, but has more side effects.[2] • Can cause hypotension.[2] • Watch for cardiac depression and paralytic ileus.[2] • Contains propylene glycol.[2]
Ketamine	**Bolus:** 1 to 2.5 mg/kg.[9] In a case series, the median bolus dose was 1.5 mg/kg (adults and children).[20] **Continuous infusion**: 1 to 10 mg/kg/h.[9,23] In a case series, the median dose was 2.75 mg/kg/h (adults and children).[20]	• Evidence limited.[11] Efficacy and optimal dose unclear.[11] Studies ongoing.[11] • Appears well-tolerated; serious cardiorespiratory adverse effects are uncommon.[11]

a. Propylene glycol-containing products pose a higher risk of hypotension.[2]
b. Unless otherwise specified, dosing recommendations are intended for both children and adults.

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