

## **Alternatives to Phenytoin for Treatment of Status Epilepticus (In order of preference):**

1. Fosphenytoin 20 mg/kg phenytoin equivalents IV at 150 mg/min  
Fosphenytoin (Cerebyx®, ERFA), is available.<sup>1</sup>
2. Lorazepam 1-2 mg/min IV to max 0.1 mg/kg<sup>2-4</sup>  
Lorazepam is effective as monotherapy; however because of risk of status epilepticus recurrence, it is generally combined with phenytoin or fosphenytoin.<sup>2</sup>
3. Midazolam 10 mg IV bolus, then 0.05 – 0.4 mg/kg/h or diazepam 5 mg/min IV to max dose of 0.25- 0.4 mg/kg OR diazepam 20 mg rectally if no IV access.<sup>3</sup>
4. Phenobarbital up to 20 mg/kg IV (50-75 mg/min)<sup>3,4</sup>  
Effective as monotherapy; however not used first line because of sedation, duration of administration and believed to cause more hypotension and hypoventilation than benzodiazepines.<sup>5</sup>
5. Propofol 2-5 mg/kg IV bolus followed by infusion at 2-10 mg/kg/h<sup>3,4</sup>  
Generally used for refractory status epilepticus.<sup>5</sup>

## **Alternatives to Injectable Phenytoin for Treatment of Tonic Clonic (TC) or Partial/focal (P) Epilepsy:**

### **1. Administer phenytoin orally**

- phenytoin suspension can be administered via enteral feeding tube if patient can't swallow.

The suspension may be administered through a nasogastric tube. If this is necessary, the suspension should be diluted (e.g., 2- to 3-fold) with a compatible diluent (e.g., sterile water) prior to administration, and the tube should be flushed with at least 20 mL of diluent before and after administration. Enteral feeds should be stopped 2 hours before and resumed 2 hours after phenytoin doses, to minimize reduction of phenytoin bioavailability.<sup>6</sup>

### **2. Administer alternatives orally.**

*Seizure type, Dosing, Number of Daily Doses*<sup>2,3</sup> - see table

Oral Alternatives to Phenytoin for Treatment of Tonic-Clonic or Partial Seizures				
Drug	Seizure Type	Usual Daily Maintenance Dose (Adults/Children)	Number of Doses per Day	NG Tube Administration Feasible?
Carbamazepine	Tonic Clonic	800-1200 mg	2 to 4	Yes
	Partial	10-40 mg/kg/day		
Lamotrigine	Tonic Clonic	300- 400 mg	2 to 3	Yes – Chewables/dispersibles
	Partial	10-12 mg/kg/day*		
Valproic Acid	Tonic Clonic	750-1000 mg	2	Yes - syrup
	Partial (2 <sup>nd</sup> line)	60-80 mg/kg/day		
Levetiracetam	Tonic Clonic (2 <sup>nd</sup> line)	750-1000 mg	2	Yes
	Partial	60 mg/kg/day**		
Oxcarbazepine	Partial (2 <sup>nd</sup> line)	1200-2400 mg	2	No
		20-50 mg/day <sup>†</sup>		
Topiramate	Tonic Clonic (2 <sup>nd</sup> line)	200-400 mg	2	Yes – tablets, not contents of capsules
	Partial (2 <sup>nd</sup> line)	4-10 mg/kg/day		

\*Lamotrigine not indicated in children (<16yo) except for seizures associated with Lennox-Gastaut syndrome; dose is based on monotherapy. \*\*Not indicated in children † See weight-based dosing in monograph

*Feasibility of feeding tube administration:*

Carbamazepine:

Tegretol tablets easily disintegrate into a coarse dispersion when placed in 10 ml of water. Need to be careful to maintain suspension otherwise risk blockage of fine bore tube may occur.<sup>7</sup>

Administration of suspension through NG tube has led to clinical improvements and therapeutic serum concentrations.<sup>8</sup>

The suspension may adsorb to the tubing; however, diluting with an equal volume of water immediately prior to administration seems to prevent adsorption.<sup>7,9</sup>

In one study in 8 healthy male volunteers, the relative bioavailability of carbamazepine suspension after NG administration compared to oral administration was 90% that of when administered orally. The carbamazepine was administered during enteral feeding.<sup>10</sup>

Lamotrigine:

Dispersible tablets disintegrate quickly in 10 ml water – dispersion flushes down an 8Fr NG tube without blockage.<sup>7</sup>

### Lamictal

Regular tablets - no information.<sup>7,11</sup> For chewable/dispersible tablets - add a small amount of liquid (5 ml or enough to cover the tablet); when tablet is completely dispersed (approximately 1 minute), swirl the solution and administer immediately.<sup>11</sup>

### Valproic Acid:

Red clear liquid resistant to flushing down 8 Fr NG tube – dilution with water reduces resistance.<sup>7</sup>

There has been one case reported where NG tube administration of valproic acid syrup in an infant was effective and there didn't seem to be any issues. In another report, when a child with a J-tube switched from parenteral to enteral, the child experienced lot of diarrhea and therapeutic concentrations were unachievable.<sup>12</sup>

### Levetiracetam:

500 mg tablets disperse in 10 ml water after 5 minutes of shaking – forms milky dispersion that flushes down 8Fr NG tube easily.<sup>7</sup>

There are reports of successful use of levetiracetam with NG tube administration of tablets and suspension. (Suspension is not available in Canada).<sup>13</sup>

### Oxcarbazepine:

No information.<sup>7,14</sup>

### Topiramate:

Topamax tabs are film coated – can crush and shake in 10 ml of water for 5 minutes – forms dispersion that will easily flush down 8 Fr NG without blockage. Do not use the sprinkle beads as they stick to the tube causing blockage.<sup>7</sup>

Topamax tablets can be crushed and suspended in water; administer immediately.<sup>15</sup>

## **3. If parenteral is required:**

Fosphenytoin- dose as phenytoin equivalents. For example, if dose of phenytoin had been 100 mg, dose of fosphenytoin will be 100 mg phenytoin equivalents.

Off-label : subcutaneous administration of phenobarbital based on palliative care experience.<sup>16,17</sup>

Starting dose: 60-90 mg qhs SC. Usual maintenance: 60-120 mg/day SC. Max recommended dose 180-300 mg/day. Daily doses can be divided into three equal doses. Sedating.

References:

1. Phone communication with ERFA Customer Service, (514) 931-3133 April 2, 2012.
2. UpToDate - Status epilepticus in adults
3. Moeller JJ, Sadler RM. Seizures and epilepsy. In: Gray Jean, editor. e-Therapeutics+ [Internet]. Ottawa (ON): Canadian Pharmacists Association; c2012 [updated May 2011; cited 2012 Apr 2]. Available from: <http://www.e-therapeutics.ca>. Also available in paper copy from the publisher.
4. - Mechem CC. Chapter 146. Seizures and Status Epilepticus in Adults. In: Ma OJ, Cline DM, Tintinalli JE, Kelen GD, Stapczynski JS, eds. Emergency Medicine Manual. 6th ed. New York: McGraw-Hill; 2004. <http://www.accessemergencymedicine.com/content.aspx?aID=2122>. Accessed April 1, 2012.
5. Lung DD, Catlett CL, Tintinalli JE. Chapter 165. Seizures and Status Epilepticus in Adults. In: Tintinalli JE, Stapczynski JS, Cline DM, Ma OJ, Cydulka RK, Meckler GD, eds. Tintinalli's Emergency Medicine: A Comprehensive Study Guide. 7th ed. New York: McGraw-Hill; 2011. <http://www.accessmedicine.com/content.aspx?aID=6366002>. Accessed April 1, 2012.
6. e-CPS [Internet]. Ottawa (ON): Canadian Pharmacists Association; c2012 [updated 2011 Nov; cited 2012 Apr 1]. Phenytoin [CPhA monograph]. Available from: <http://www.e-cps.ca>. Also available in paper copy from the publisher.
7. White R, Bradnam V, editors. Handbook of drug administration via enteral feeding tubes..2nd ed. Grayslake, IL: Pharmaceutical Press; 2010.
8. Miles MV, Lawless ST, Tennison MB, et al. Rapid loading of critically ill patients with carbamazepine suspensions. Pediatrics. 1990; 86(2): 263-266.
9. Clark-Schmidt AL. Garnett WR, Lowe DR, et al. Loss of carbamazepine suspension through nasogastric feeding tubes. Am J Hosp Pharm. 1990; 47: 2034-37)
10. Bass J, Miles MV, Tennison MB, et al. Effects of enteral tube feeding on the absorption and pharmacokinetic profile of carbamazepine suspension. Epilepsia. 1989; 30(3): 364-9.
11. Phone communication with Vicky, GSK Medical Information 1-800-387-7374, April 2, 2012.
12. Phone communication with Abbott Laboratories Medical Information 1-800-699-9948, April 2, 2012.
13. Written communication from UCB Canada, April 2, 2012. On file.
14. Written communication from Novartis Medical Information April 2, 2012. On file.
15. Phone communication with Janine, Janssen Medical Information 1-800-567-3331, April 2, 2012.
16. <http://www.palliative.org/PC/ClinicalInfo/Clinical%20Practice%20Guidelines/PDF%20files/Chronic%20Seizure%20Pharmacological%20Management%20in%20Palliative%20Care.pdf>
17. <http://www.palliative.org/PC/ClinicalInfo/ACB%20PC%20resource%20manual.pdf>