

## If a patient must limit food/water prior to surgery, when and how can their seizure medications be given?

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This information should not replace guidance from a health care professional managing the care of your child or loved one. Caregivers should use this guide to help inform conversations as part of the health care team, working with medical professionals to determine the best course of action given the individual patient's medical history and the specific procedure.

Often prior to a surgery or procedure a patient may need to restrict intake of food and water. This may be called "**NPO**" or "nothing by mouth," but also can include food or water administered through enteral feeding tubes. Some procedures allow some flexibility for administration of medications, while others are very strict and all oral intake must be limited. First, check with their physician to determine if oral medications are allowed prior to the procedure. If possible, give their anti-seizure medication just before their procedure.

Anti-seizure medications work best when doses are not missed. However, sometimes delays in doses may be unavoidable due to medical procedures or surgeries. Luckily, there are several options to optimize seizure therapy and reduce the risk of seizures. Each patient and each case are different. The most appropriate course of action will be individualized on a case-by-case basis by their physician/neurologist. The information provided is for your reference so a more informed discussion may be had with your medical care team.

## If the patient is unable to take anything by mouth, your physician may choose one of the options below:

- (1) Skip or delay a dose (dependent on the medication and how long it stays in the body)
- (2) Utilize the intravenous formulation, if available
- (3) Utilize alternative routes, if available and appropriate
- (4) Utilize IV benzodiazepines (i.e., diazepam, lorazepam, midazolam) in the interim
- If a patient has not previously tolerated or is unable to take a specific benzodiazepine, their physician may consider other IV alternatives such as valproic acid, phenobarbital, or levetiracetam.
- Several medications (e.g., carbamazepine, clobazam, lacosamide, levetiracetam, pregabalin, zonisamide, valproic acid) have information on alternative routes in animal studies or small case reports. While some of these are promising, human data is lacking and a recommendation for using an alternative route based on available information is not possible at this time.
- In instances where no alternative routes are available or if alternate routes available are inappropriate, use of IV lorazepam is reasonable.

The table below lists common anti-seizure medications and routes of administration that could be utilized if an oral dose must continue to be delayed, including intravenous (IV), intramuscular (IM), intranasal (IN) and rectal (PR). The table also provides insight on how long a dose could be delayed before an alternative route needs to be considered based on the medication half-life.

Medication	IV	IM	IN	PR	How long can a dose be <u>delayed</u> before an alternative route or medication may be needed? *
Acetazolamide ( <i>Diamox</i> <sup>®</sup> )	Yes				6 to 12 hours (duration 8 to12)
Baclofen (Gablofen <sup>®</sup> , Lioresal <sup>®</sup> , Ozobax <sup>®</sup> )					4 to 8 hours
Brivaracetam (Briviact <sup>®</sup> )	Yes				9 hours
Cannabidiol (Epidiolex <sup>®</sup> )					>24 hours
Cannabidiol (artisanal brands)					>24 hours
<b>Carbamazepine</b> ( <i>Carbatrol</i> <sup>*</sup> , <i>Equetro</i> <sup>*</sup> , <i>Tegretol</i> <sup>*</sup> , <i>Tegretol</i> XR <sup>*</sup> )				Yes	8 to 17 hours (active metabolite efficacious >24 hours)
Cenobamate (Xcopri <sup>®</sup> )					>24 hours
Clemizole					
Clobazam (Frisium <sup>®</sup> , Onfi <sup>®</sup> )	Yes**		Yes†		16 to >24 hours(active metabolite efficacious >24 hours)
Clonazepam (Klonopin <sup>®</sup> )	Yes**		Yes†	Yes	17 to >24 hours
Diazepam (Valium <sup>®</sup> , Valtoco <sup>®</sup> , Diastat <sup>®</sup> )	Yes	Yes	Yes	Yes	>24 hours
Eslicarbazepine (Aptiom <sup>®</sup> )					10 to 20 hours

Medication	IV	IM	IN	PR	How long can a dose be <u>delayed</u> before an alternative route or medication may be needed? *
Ethosuximide (Zarontin <sup>®</sup> )					17 to >24 hours
Felbamate (Felbatol <sup>®</sup> )					10 to 22 hours (dependent on other concomitant medications)
Fenfluramine (Fintelpa <sup>®</sup> )					20 hours
Gabapentin (Neurontin <sup>®</sup> )					5 to 7 hours
<b>Glycopyrrolate</b> ( <i>Cuvposa<sup>®</sup></i> , <i>Robinul<sup>®</sup></i> )	Yes	Yes			3 to 7 hours
Lacosamide (Vimpat <sup>®</sup> )	Yes				7 to 14 hours
Lamotrigine (Lamictal <sup>®</sup> , Lamictal XR <sup>®</sup> , Subvenite <sup>®</sup> )					7 to >24 hours (dependent on other concomitant medications)
Levetiracetam (Keppra <sup>®</sup> )	Yes	Yes		Yes	5 to 8 hours
Levocarnitine ( <i>Carnitor</i> <sup>*</sup> )	Yes				17 hours
Lorazepam (Ativan <sup>®</sup> )	Yes	Yes	Yes	Yes	6 to >24 hours
Lorcaserin					11 hours
Methsuximide ( <i>Celontin</i> <sup>®</sup> )					2 to 4 hours (active metabolite efficacious >24 hours)
Midazolam (Versed <sup>®</sup> , Nayzilam <sup>®</sup> )	Yes	Yes	Yes	Yes	1 to 12 hours (varies by age and route)
<b>Oxcarbazepine</b> ( <i>Trileptal<sup>®</sup></i> , <i>Oxtellar XR<sup>®</sup></i> )					5 to 9 hours
Perampanel (Fycompa <sup>®</sup> )					>24 hours
Phenobarbital	Yes	Yes		Yes	>24 hours
Phenytoin (Dilantin <sup>®</sup> , Phenytoin InfaTabs <sup>®</sup> )	Yes				14 to 22 hours
Prednisone/Prednisolone	Yes‡	Yes‡			4 hours (duration can last >24 hours)
Pregabalin (Lyrica <sup>®</sup> )					3 to 6 hours
Primidone (Mysoline <sup>®</sup> )					5 to 22 hours
Rufinamide (Banzel <sup>®</sup> )					6 to 10 hours
Soticlestat					
Stiripentol (Diacomit <sup>®</sup> )					5 to 23 hours (dependent on other concomitant medications)
<b>Topiramate</b> ( <i>Topamax<sup>®</sup></i> , <i>Qudexy XR<sup>®</sup></i> , <i>Trokendi XR<sup>®</sup></i> )				Yes	8 to 21 hours (dependent on other concomitant medications)
Tiagabine (Gabitril <sup>®</sup> )					5 to 9 hours

Medication	IV	IM	IN	PR	How long can a dose be <u>delayed</u> before an alternative route or medication may be needed? *	
Valproic Acid/Divalproex Sodium (Depakote <sup>®</sup> , Depakote ER <sup>®</sup> , Depakote Sprinkles <sup>®</sup> , Depakene <sup>®</sup> , Depacon <sup>®</sup> )	Yes			Yes	7 to 16 hours	
Vigabatrin (Vigadrone <sup>®</sup> , Sabril <sup>®</sup> )					6 to 10 hours (duration can last >24 hours)	
Zonisamide (Zonegran <sup>®</sup> )					>24 hours	
Abbreviations: intravenous (IV); intramuscular (IM); intranasal (IN); rectal (PR)						
*Approximate estimations based on half-life of medication and duration of action of immediate release formulations in adult and pediatric patients with						
normal renal and hepatic function						
**Use of IV lorazenam reasonable						

**†**Use of IN midazolam reasonable

**‡**Use methylprednisolone

## Questions? Email: veronica@dravetfoundation.org

## **References:**

- 1) Lexicomp Online [Internet]. Hudson(OH): Lexicomp; c1978-2015. Available from: http://online.lexi.com/lco/action/home/switch
- 2) Micromedex Solutions [Internet]. Truven Health Analytics Inc; c2015. Available from: http://www.micromedexsolutions.com/micromedex2/librarian/
- 3) USP DI: drug information for the health care provider. 24th ed. Micromedex, Inc; 2004. Available from: http://www.micromedexsolutions.com/micromedex2/librarian/
- 4) AHFS<sup>®</sup>DI Essentials [Internet]. Bethesda (MD): American Society of Health-System Pharmacists, Inc.; c2004-2015. [revised 2010 Apr 1; cited 2015 Apr 2]. Available from: <u>http://online.lexi.com/lco/action/index/dataset/complete\_ashp</u>
- 5) Birnbaum AK, Kriel RL, Burkhardt RT, Remmel RP. (2000) Rectal absorption of lamotrigine compressed tablets. Epilepsia 41:850–853.
- 6) Graves NM, Kriel AL. AEDs for rectal administration [Internet]. Landover (MD): Epilepsy Foundation; 2004 Jan. Available from: https://www.epilepsy.com/learn/professionals/resource-library/tables/aeds-rectal-administration
- 7) Graves NM, Kriel AL. (1987) Rectal administration of antiepileptic drugs in children. Pediatric Neurol 3:321-326.
- 8) Leppik IE, Patel SI. (2015) Intramuscular and rectal therapies of acute seizures. Epilepsy Behav. 49:307-12.
- 9) Koppel BS. Surgery and anesthesia [Internet]. Landover (MD): Epilepsy Foundation; 2004 Feb 29. Available from: https://www.epilepsy.com/learn/professionals/diagnosis-treatment/drugs-their-contribution-seizures/surgery-and-anesthesia

- 10) Koppel BS. (2002) Contribution of drugs and drug interactions (prescribed, over the counter, and illicit) to seizures and epilepsy. In: Ettinger AB and Devinsky O, eds. Managing epilepsy and co-existing disorders. Boston: Butterworth-Heinemann 155–173.
- 11) Leppik IE, Goel V, Rarick J, Nixdorf DR, Cloyd JC. (2010) Intramuscular and intravenous levetiracetam in humans: safety and pharmacokinetics. Epilepsy Res 91(2-3):289-92.
- 12) Conway JM, Birnbaum AK, Kriel RL, Cloyd JC. (2003) Relative bioavailability of topiramate administered rectally. Epilepsy Res 54(2-3):91-6.
- 13) Gonçalves J, Alves G, Fonseca C, Carona A, Bicker J, Falcão A, Fortuna A. (2021) Is intranasal administration an opportunity for direct brain delivery of lacosamide? Eur J Pharm Sci 157:105632.
- 14) Gonçalves J, Bicker J, Gouveia F, Liberal J, Oliveira RC, Alves G, Falcão A, Fortuna A. (2019) Nose-to-brain delivery of levetiracetam after intranasal administration to mice. Int J Pharm 564:329-39.
- 15) Serralheiro A, Alves G, Fortuna A, Falcão A. (2014) Intranasal administration of carbamazepine to mice: a direct delivery pathway for brain targeting. Eur J Pharm Sci 60:32-9.
- 16) Wermeling DP. (2009) Intranasal delivery of antiepileptic medications for treatment of seizures. Neurotherapeutics. (2):352-8.
- 17) Kriel RL, Krach LE, Hoff DS, Gormley M, Jones-Saete C. (2007) Failure of absorption of baclofen after rectal administration. Pediatr Neurol. (4):351-2.
- 18) Doddrell C, Tripathi SS. (2015) Successful use of pregabalin by the rectal route to treat chronic neuropathic pain in a patient with complete intestinal failure. BMJ Case Rep 2015: bcr2015211511.
- 19) Eskandari S, Varshosaz J, Minaiyan M, Tabbakhian M. (2011) Brain delivery of valproic acid via intranasal administration of nanostructured lipid carriers: in vivo pharmacodynamic studies using rat electroshock model. Int J Nanomedicine 6:363-71.