Lancashire and South Cumbria Network

June 2022

Managing convulsive (tonic-clonic) status epilepticus (adults)

Professor S Chhetri
Clinical Professor and Consultant Neurologist
Clinical Director for Neurology
Co-Director, Lancashire and South Cumbria MND Care and Research Centre
Royal Preston Hospital

Hannah Sheridan
Lead Pharmacist - Emergency Department
Blackpool Victoria Hospital (BVH)
Blackpool Teaching Hospitals NHS (BTH)

Shaun Morgan
Lead Pharmacist - Critical Care
Royal Blackburn Teaching Hospital (EHLT)
East Lancashire Hospitals NHS Trust

Lauren Kilifin
Lead Pharmacist- ED & Admissions (RLI) & IVIG and Homecare (UHMB) Pharmacist Practitioner in acute medicine

Jenny Oakley
Lead Pharmacist - Surgery, Critical Care and WACS
Royal Lancaster Infirmary
University Hospitals of Morecambe Bay (UHMB)

Sean Connell
Advanced Acute and Emergency Medicine Pharmacist
Royal Preston Hospital
Lancashire Teaching Hospitals NHS Foundation Trust (LTH)

CONTENTS

Automatic Contents page. Place cursor onto Contents page above and press F9 Return to update. All procedural documents with 10 or more pages must utilise a contents page. The template has been designed with an 'automatic' contents page.

1 Introduction / Purpose

This is a guide for the in-hospital care drug management of adult patients with status epilepticus. It is aimed at all staff involved with caring for patients.

2 General Principles / Target Audience

Adult patients with convulsive (tonic-clonic) status epilepticus

Excludes
- All paediatric cases
- Adults in whom a different approach or an alternative care plan has been put in place e.g., patients in the last days/weeks of life

3 Definitions and Abbreviations

ABCDE – Airway, Breathing, Circulation, Disability, Exposure
AED's – Anti-epileptic drugs
BNF – British National Formulary
BTH- Blackpool Teaching Hospitals
ECG – electrocardiogram
EDC – Emergency Drug Cupboard
ELTH- East Lancashire Hospitals NHS Trust
IV – intravenous
IM – intramuscular
LTH – Lancashire Teaching Hospitals
MHRA –Medicines and Healthcare products Regulatory Agency
PNES - Psychogenic nonepileptic seizures
PR – per rectal
SE – status epilepticus
SPC – Summary of product characteristics
UHMB - University Hospitals of Morecambe Bay

4 References and Associated Documents

- Barsan W, Cloyd J, Pharm D, et al. Randomized Trial of Three Anticonvulsant Medications for Status Epilepticus. N Engl J Med Published Online First: 2019. doi:10.1056/NEJMoa1905795
- Chamberlain JM, Kapur J, Shinnar S, et al. Efficacy of levetiracetam, fosphenytoin, and valproate for established status epilepticus by age group (ESETT): a double-blind, responsive-adaptive, randomised controlled trial. Lancet. 2020;395(10231):1217-1224. doi:10.1016/S0140-6736(20)30611-5
- eBNF – accessed 06/07/2020.
- Kinney, M. O., Brigo, F., & Kaplan, P. W. (2020). Optimizing status epilepticus care during the COVID-19 pandemic. Epilepsy and Behavior, 109, [107124]. https://doi.org/10.1016/j.yebeh.2020.107124
- Injectable Medicines Guide NHS. Last updated 18/06/2020. Phenytoin Sodium Monograph on http://medusa.wales.nhs.uk/ available via Medicines Management Site free access, via free password/username, accessed 06/07/2020.

- Injectable Medicines Guide NHS. Last updated 21/08/2018. Levetiracetam Monograph on http://medusa.wales.nhs.uk/ available via Medicines Management Site free access, via free password/username, accessed 06/07/2020.
- Injectable Medicines Guide NHS. Last updated 01/06/2016. Sodium Valproate Monograph on http://medusa.wales.nhs.uk/ available via Medicines Management Site free access, via free password/username, accessed 06/07/2020.
- Intrapharm Laboratories Ltd. 2020. Levetiracetam 100 mg/ml concentrate for solution for infusion. Accessed 06/07/2020. https://www.medicines.org.uk/emc/product/11035/smpc
- Mercury Pharmaceuticals Limited. 2020. Phenytoin Sodium 50mg/ml Solution for Injection. Accessed 06/07/2020. https://www.medicines.org.uk/emc/product/4326
- MHRA. 2018. Valproate use by women and girls. Accessed 06/07/2020. https://www.gov.uk/guidance/valproate-use-by-women-and-girls
- Wrexham Maelor Hospital Pharmacy Department. Last updated June 2020. The NEWT Guidelines for administration of medication to patients with enteral feeding tubes or swallowing difficulties. Accessed 06/07/2020 with username and password https://access.newtguidelines.com/index.html
- NHS Improvement. (09/11/2016). Risk of death and severe harm from error with injectable phenytoin - NHS/PSA/W/2016/010. Accessed 06/07/2020. https://improvement.nhs.uk/news-alerts/risk-death-and-severe-harm-error-injectable-phenytoin/
- NICE guideline. NG 217 Epilepsies in children, young people and adults. Published: 27 April 2022. Accessed 27/06/2022
- NICE Epilepsies: diagnosis and management Clinical Guideline 137. Last updated 11/02/2020. Accessed 06/06/2020. https://www.nice.org.uk/guidance/cg137/chapter/Appendix-F-Protocols-for-treating-convulsive-status-epilepticus-in-adults-and-children-adults-published-in-2004-and-children-published-in-2011
- The Renal Drug Database. 2018. Phenytoin Monograph. Last updated 22/02/2018. Accessed 28/07/2020 via: https://renaldrugdatabase.com/monographs/phenytoin
- UKMi Medicines Q&A 444.4: How to minimise the risks to patients when using intravenous phenytoin in status epilepticus (SE)?, accessed 06/07/2020. https://www.sps.nhs.uk/articles/how-can-we-minimise-the-risks-to-patients-when-using-intravenous-phenytoin-in-status-epilepticus-se/
- UpToDate. Last updated 01/06/2020. Psychogenic nonepileptic seizures. Accessed 06/07/2020. https://www.uptodate.com/contents/psychogenic-nonepileptic-seizures?search=PNES&source=search_result&selectedTitle=1~38&usage_type=default&display_rank=1
- Wockhardt UK Ltd. 2020. Sodium Valproate 100mg/ml Solution for Injection or Infusion. Accessed 06/07/2020. https://www.medicines.org.uk/emc/product/1209

5 Main Part of the Procedural Document

Status Epilepticus (SE) is prolonged, uncontrolled seizure activity that is life threatening and if left untreated, mortality approaches 30%. It is a medical emergency that requires immediate anti-convulsive therapy to terminate the seizure and limit neurological damage. Validated treatment algorithms have been proven to improve outcomes in these patients. Convulsive seizures lasting longer than 5 minutes or recurring without recovery should be treated as SE.

Phenytoin has been the first line choice after benzodiazepines in SE for many years. However, NICE published updated guidance in April 2022 regarding the choice of second line antiepileptic drug if benzodiazepines had failed to terminate seizures.

"The committee agreed that the evidence for further antiseizure medication, if seizures continue after 2 doses of a benzodiazepine, showed a benefit for the intravenous administration of levetiracetam, phenytoin or valproate, but did not favour 1 specific medication over the others. However, based on their experience, the committee agreed that levetiracetam can be quicker to prepare, easier to administer and may be associated with fewer adverse effects than the alternative options, so it is likely to become the preferred second-line treatment. However, because the evidence showed no difference in efficacy, the committee agreed that phenytoin or valproate can also be considered. If status epilepticus does not respond to 1 of these medications, the committee agreed that another second-line medication should be considered."

This guidance will advise how to administer all three drugs (levetiracetam, phenytoin, and sodium valproate); in addition to important safety alerts and monitoring that must be done.

MHRA warning for women regarding sodium valproate:

Perform a pregnancy test for all female patients with childbearing potential if able when assessing (and treating) for seizures.

Refer to local trust guidelines regarding the use of sodium valproate in women of childbearing age.

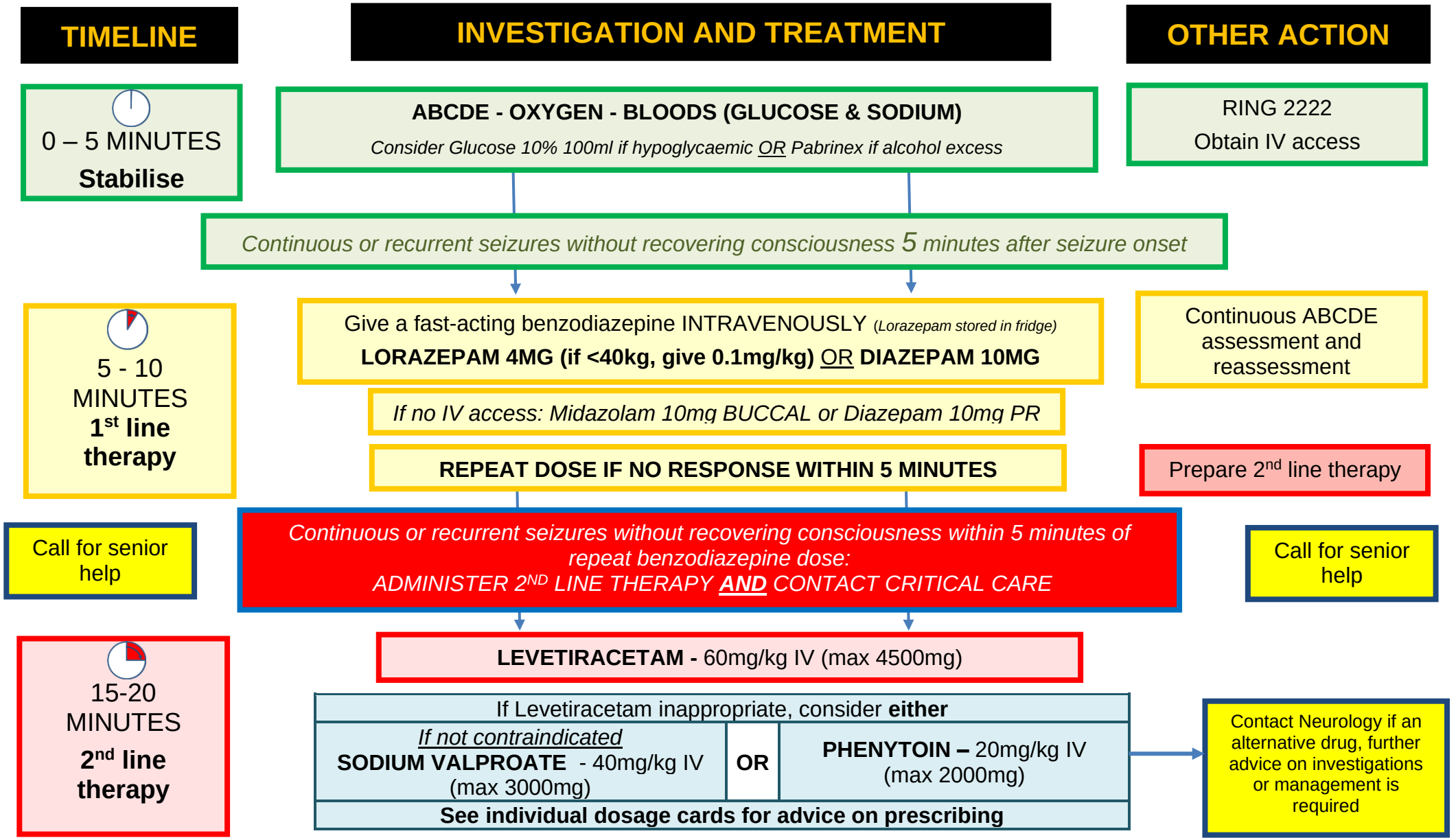
For all medication, strict aseptic techniques must be used throughout the procedure of preparation and administration.

Appropriate reversal agents must be available with staff able to administer them appropriately, i.e. medication for anaphylaxis, and flumazenil for benzodiazepine reversal.

If seizure activity continues beyond administration of the loading dose, ensure critical care are involved in the management of the patient as the patient may require an anaesthetic in order to terminate seizure activity.

NOTE: prescription and administration of loading doses (for the management of status epilepticus) of Sodium Valproate or Levetiracetam is "off-label".

5.1 Quick algorithm to follow for managing status epilepticus



5.2 Initial management – investigations and monitoring

- Assess and treat the patient using ABCDE approach
    - Airway
    - Breathing
    - Circulation
    - Disability
    - Exposure

Assess and monitor the patient as per relevant observation scoring system:
National Early Warning Score (NEWS2) or Modified Early Obstetric Warning Score (MEOWS) if the patient is pregnant and Neurological Observation Chart:

- Heart rate
- Respiratory rate
- Blood pressure
- Temperature
- Oxygen saturation
- Blood glucose – if hypoglycaemic (blood glucose <4mmol/l) consider Glucose 10% 100ml stat
- Glasgow Coma Score (GCS)
- Ensure adequate oxygenation
    - Administer oxygen to ensure SPO_2 is maintained >94% (if appropriate, 88-92% in patients at risk of type 2 respiratory failure)
    - Ensure this is prescribed (even if retrospectively as not to delay administering oxygen to a patient with reduce oxygen saturations) on the drug chart as this is a prescription only medication
    - Contact critical care immediately if the patient cannot maintain their own airway
- Establish peripheral venous access
- Pregnancy test if the patient is female and of childbearing potential
- Establish a detailed drug history and check for any serum levels of anti-epileptics
- Identify potential causes of seizure activity

Care must be taken when identifying potential causes of seizure activity. It is important to bear in mind the risks associated with administration of benzodiazepines in patients who are not having a true epileptic seizure. Clinical judgment must be used at the time to determine the risk of administering a drug that could potentially cause respiratory depression versus not administering it.

Consider questions such as:

- Is the patient known to have epilepsy?

- Is the patient known to have non-epileptic seizures?
- Does the patient already have a plan in place for the management of seizures?

See the below tables to aid differentiation between potential causes of seizures (table 1)

Table 1 - Potential causes of seizures	
Infection	Infection/sepsis, encephalitis (most commonly herpes virus), meningitis and cerebral abscess • Refer to the Trust antimicrobial formulary
Vascular	Ischaemic stroke, intracerebral or subarachnoid haemorrhage, cerebral venous sinus thrombosis, hypertensive encephalopathy, posterior reversible encephalopathy syndrome (PRES)
Inflammatory	Limbic encephalitis, demyelinating diseases or immune-mediated disorders
Metabolic	Acute metabolic disturbances (most commonly sodium, calcium, magnesium and glucose), hypoxia/cardiac arrest
Trauma	Head injury
Neoplasia	Cerebral tumour (primary or secondary)
Paraneoplastic	Some types of encephalitis
Degenerative	All dementia syndromes
Congenital:	Idiopathic epilepsy, developmental anomalies of cerebral structure (e.g. focal cortical dysplasias)
Iatrogenic	Non-concordance (forgetting or omitting medication)
Lifestyle	Alcohol, illicit drugs, 'legal highs' • Consider treatment with intravenous *Pabrinex*® 2 pairs in 100mL sodium chloride 0.9% or glucose 5% as an intravenous infusion over 30 minutes • Refer to Trust Alcohol Withdrawal pathway for further management • Refer to TOXBASE if necessary
Pregnancy	Pre-eclampsia

- Post seizure: request biochemical investigations

  - Arterial Blood Gas (ABG)
  - Renal function (including U&Es)
  - Liver Function Tests (LFTs)

- Electrolytes (including calcium, magnesium, phosphate)
- Full Blood Count
- ECG – compare with previous ECGs if available
- Coagulation studies
- Antiepileptic drug concentrations (if prescribed regular antiepileptic medicines, see below)
- Consider toxicology (blood and urine) if suspicion of overdose or use of illicit substances
- Pregnancy test if not already performed

When to contact neurology

Neurology should only be contacted in the following circumstances:

1. The patient is unable to have any of the 3 suggested medications (phenytoin, levetiracetam or sodium valproate) due to allergies, contraindications or another reason
2. The patient is in refractory status and specialist advice is required
3. Advice regarding further investigations is required
4. Advice regarding the initiation of regular antiepileptic medication is required

Neurology registrars can be contacted via Royal Preston Hospital switchboard (01772 716565).

5.3 Prescribing and administration of medication

First line therapy – CHECK IF A PREVIOUS DOSE HAS BEEN GIVEN ALREADY (E.g., by paramedics or other health care professional)

<table>
<tr><td colspan="2">Prescribe and administer a STAT dose of benzodiazepine as a first line therapy:</td></tr>
<tr><td>Intravenous access available</td><td>Lorazepam 4mg injection as an intravenous (IV) bolus injection – (stored in the fridge)

- Dilute a 4mg/mL ampoule with an equal volume of sodium chloride 0.9% or water for injection and administer immediately with the aim to control the seizure
- Dose is 0.1mg/kg – usual dose for patients >40kg is 4mg, however consider lower doses for patients at an increased risk of respiratory depression (e.g. frail patients), or administer the dose over 1 minute whilst monitoring the patients airway.

OR

Diazepam 10mg emulsion injection or Diazepam 10mg solution for injection are intravenous alternatives to lorazepam for the initial control of status epilepticus if lorazepam injection is unavailable

- Administer undiluted as a slow intravenous bolus injection over 2 minutes
- Note: diazepam solution for injection is an irritant and associated with increased risk of thrombophlebitis more than diazepam emulsion for injection. Diazepam solution for injection should be administered into a large vein of the antecubital fossa</td></tr>
<tr><td>NO intravenous access available</td><td>Diazepam 10mg rectal tubes

- 10mg administered rectally (PR)

OR
Midazolam 10mg/2mL oromucosal syringe

- 10mg administered into the buccal cavity

The full amount of solution should be inserted slowly into the space between the gum and the cheek. Avoid the back of the throat to prevent accidental aspiration of the solution. If necessary (for larger volumes and/or smaller patients), approximately half the dose should be given slowly into one side of the mouth, then the other half given slowly into the other side.</td></tr>
<tr><td colspan="2">If seizure activity continues for more than 5 minutes after the first dose, a second dose of benzodiazepine can be administered.
If there is no response observed or seizure activity remains uncontrolled after two doses, continue to treatment of established status epilepticus, continue to monitor the patient. and ensure critical care have been contacted.</td></tr>
</table>

Second line therapy

First line choice	**LEVETIRACETAM**

Contraindications: *known allergies to drug and excipients*
Note this list is not exhaustive – please refer to the BNF/SPC for further information

Dose: 60 mg/kg (max 4500mg) - see table below
Diluent: add required dose to a 100ml Sodium Chloride 0.9% bag (or Glucose 5%)
Route: IV
Rate: over 10 minutes

Flush vein PRE and POST injection with Sodium Chloride 0.9%

Weight (Kg)	Dose (grams)	Volume of 500mg/5ml
Less than 35	2g	20ml
35 – 44	2.5g	25ml
45 – 54	3g	30ml
55 – 64	3.5g	35ml
65 – 74	4g	40ml
Greater than 75	4.5g	45ml

Restart regular AED's at the usual time the patients takes them. If the patient is not on regular AED's and it is deemed necessary for the patient to have further investigations with the initiation of a maintenance dose, this should be started 12 hours after the loading dose.

- If switching between enteral or IV route, keep the same dose and frequency of administration
- The maintenance dose will depend on eGFR or creatinine clearance (using cockcroft and gault equation)

eGFR (ml/min/1.73m^2)	**Levetiracetam IV/PO maintenance doses (start 12 hours after loading dose)**
≥80ml/min	1500mg BD
50-79	1000mg BD
30-49	750mg BD
<30	500mg BD
Dialysis patients	500mg BD; supplemental dose of 250mg after each dialysis

Second line if Levetiracetam contraindicated

SODIUM VALPROATE

CONTRAINDICATIONS:

Note this list is not exhaustive – please refer to the BNF/SPC for further information

- women of childbearing potential* unless the conditions of "Prevent"– the valproate pregnancy prevention programme - are fulfilled
- acute or severe liver failure
- mitochondrial disorder

*any biological female up to the age of 55 years who is capable of becoming pregnant

Dose: 40mg/kg (max 3000mg) - see table below
Diluent: add required dose to a 100ml Sodium Chloride 0.9% or Glucose 5% bag
Route: IV
Rate: over 10 minutes

Flush vein PRE and POST injection with Sodium Chloride 0.9%

Weight (Kilograms)	Dose (milligrams)	Volume of 100mg/ml
Less than 35 Kg	900 mg	9ml
35-44 Kg	1200 mg	12ml
45-54 Kg	1500 mg	15ml
55-64 Kg	1800 mg	18ml
65-74 Kg	2100 mg	21ml
75-84 Kg	2400 mg	24ml
85-94 Kg	2700 mg	27ml
Greater than 95 Kg	3000 mg	30ml

Restart regular AED's at the usual time the patients takes them. If the patient is not on regular AED's and it is deemed necessary for the patient to have further investigations with the initiation of a maintenance dose, prescribe:

600mg TDS (IV or oral) starting 8 hours after the loading dose

- Renal impairment: no dose adjustments required. But can be dialysed out if on dialysis (discuss with pharmacist).

Third line if Levetiracetam and Sodium Valproate are contraindicated

PHENYTOIN

Contraindications *include: allergy to drug, heart block, sinus bradycardia, Adams-Stokes syndrome*

Note this list is not exhaustive – please refer to the BNF/SPC for further information

Is the patient already on Phenytoin?

No – see table below

Yes* – see appendix 2

*if there are any concerns regarding compliance – give full loading dose

Dose: 20mg/kg*
Route: IV (undiluted)
Rate: Max 50mg/minute
For >65 years/frail adults, or if history of cardiac disease, consider reduced rate to25mg/minute

Phenytoin injection has a high pH and may cause venous irritation and tissue damage in cases of extravasation. Administer via a large peripheral vein monitoring the insertion site for phlebitis. Re-site cannula at first signs of inflammation.

Flush vein PRE and POST injection with 10ml Sodium Chloride 0.9%

Cardiac monitoring must be in place

***If >80kg** – calculate Ideal Body Weight

- For males: IBW (kg) = 50kg + 2.3kg x (height [in]-60).
- For females: IBW (kg) = 45.5kg + 2.3kg x (height [in]-60).

Weight (Kilograms)	Dose (milligrams)	Volume of 250mg in 5mL vial
Less than 35 kg	Calculate dose - 20mg/kg	
35 – 44 kg	800 mg	16mL
45 – 54 Kg	1000 mg	20mL
55 – 64 Kg	1200 mg	24mL
65 – 74 Kg	1400 mg	28mL
75 – 84 Kg	1600 mg	32mL
85 – 94 Kg	1800 mg	36mL
Greater than 95 Kg	2000 mg	40mL

A Phenytoin level MUST be checked within 2 to 4 hours after the loading dose. If required, a maintenance dose of 100mg TDS IV must be prescribed to start 8 hours post loading dose or restart regular AED's at the usual time the patients takes them.

Appendix 1: Nil by mouth/swallowing difficulties and taking anti-epileptics

Anti-epileptics are time critical medicines and are available 24/7. Contact the pharmacy team as soon as possible to prevent delayed administration.

If a patient is unable to take an oral form of their medication, contact your ward pharmacist or the on-call pharmacist (via switchboard) for advice on alternative formulations of an antiepileptic drug. If an alternative form of a drug is not available, the pharmacist will tell you to speak to neurology; they are the speciality to provide advice on changing medication for the management of epilepsy.

NOTE: not all doses between different dosage forms are equivalent – always check before prescribing

The following anti-epileptic medications can be given intravenously if there is no oral route:

DRUG	BIOEQUIVALENT? (IV=ORAL)	COMMENTS
Brivaracetam	✓	*Stocked at BTH only*
Lacosamide	✓	
Levetiracetam	✓	
Phenobarbitone	✓	*Controlled Drug*
Phenytoin	**CHECK**	***Capsule/tablet = IV*** *If changing from capsule/tablet to IV, consider dose and frequency. IV total dose is usually prescribed in three doses.* *e.g., if patient on 300mg nocte (capsule/tablet), then prescribe IV as 100mg three times daily* ***Liquid ≠ IV & tablet/capsule*** *92mg Phenytoin base in liquid = 100mg phenytoin base in IV formulation.* *e.g. if patient prescribed '15ml three times daily' of liquid (30mg/5ml), dose of IV should be 100mg three times daily*
Sodium Valproate	✓	*Give IV dose in divided doses depending on type of preparation:* *- liquid/normal release tablets: divide dose and give 3-4 times per day* *- M/R (Chrono tablets): divide dose and give 2 times per day*

The following medications have alternative formulations which could be considered for patients unable to take standard tablets / capsules by the oral route. If a tablet is crushed or another method is used to change a licensed formulation, this makes the product 'unlicensed'. Therefore, it is important to bear in mind that bioavailability may be affected. Not all hospitals stock each formulation, and neither are

Appendix 1: Nil by mouth/swallowing difficulties and taking anti-epileptics

they all easily obtained. Consult the table below for your hospital, contact your pharmacy team and liaise with neurology if the specific formulation is not stocked locally.

DRUG	Alternative to tablet/capsule?	*COMMENTS*	BTH	UHMB	ELTH	LTH (Neuro centre)
Brivaracetam	Liquid (50mg/5ml)		Yes	No	No	No
Carbamazepine	Rectal suppositories	*100mg tablet = 125mg suppository* *e.g., tablet dose 200mg three times daily = suppository dose 250mg three times daily* *Max dose of suppositories: Up to 1 g daily in 4 divided doses for up to 7 days*	Yes	Yes	Yes	Yes
Clobazam	Tablets may be dispersed in water		Yes – restricted drug	Yes	Yes	Yes
Clonazepam	Tablets may be dispersed in 30ml of water		Yes – restricted drug	Yes	Yes	Yes
Eslicarbazepine	Liquid (50mg/ml)	*'specials' product*	No	No	No	Yes(tablets)
Ethosuximide	Liquid (250mg/5ml)	*Can dilute with water to reduce viscosity*	Yes	No	Yes	Yes(tablets)
Gabapentin	Capsules can be opened and contents mixed with water	*Controlled Drug*	Yes	Yes	Yes	Yes
Lacosamide	Liquid (50mg/5ml)		Yes	Yes	Yes	Yes
Lamotrigine	Use dispersible tablets		Yes	Yes	Yes	Yes
Levetiracetam	Liquid (500mg/5ml)		Yes	Yes	Yes	Yes
Oxcarbazepine	Liquid (300mg/5ml)		Yes	300mg tabs only	Yes	No
Perampanel	Liquid (0.5mg/ml)	*'specials' product*	2mg & 6mg tabs only	2mg tabs only	Yes (restricted)	No
Phenobarbitone/ Phenobarbital	Liquid (50mg/5ml) Or Liquid (15mg/5ml) - NOT for paediatrics	*Phenobarbital 15mg/5mL Elixir contains* ***38% v/v ethanol (alcohol).*** *Therefore should not be used in paediatrics.* *(Controlled Drug)*	Yes	Yes	Yes	Yes (25mg/5ml Alc free)
Phenytoin	Liquid (30mg/5ml)	***Liquid ≠ IV & tablet/capsule*** *92mg Phenytoin base in liquid = 100mg phenytoin base in IV formulation.* *e.g. if patient prescribed 100mg three times daily with tablets, when changing to liquid (30mg/5ml), prescribe:* *90mg (15ml) three times daily*	Yes	Yes	Yes	Yes
Pregabalin	Capsules can be opened and contents mixed with water	*Controlled Drug*	Yes	Yes	Yes	Yes

Appendix 1: Nil by mouth/swallowing difficulties and taking anti-epileptics

Primidone	Tablets may be crushed and mixed with water		Yes	Yes	Yes	Yes
Rufinamide	Liquid (40mg/ml)	*'specials' product*	No	No	No	No
Sodium Valproate	Liquid (200mg/5ml)		Yes	Yes	Yes	Yes
Stiripentol	Powder sachets	*Sachets not bioequivalent to capsule so changes must be done under specialist supervision*	Yes	No	Yes (restricted)	No
Tiagabine	Tablets may be crushed and mixed with water		No	No	No	No
Topiramate	Tablets may be crushed and mixed with water	*Alternatively, sprinkle capsules can be used*	Yes	Yes	Yes	Yes
Vigabatrin	Tablets may be crushed and mixed with water or sachets may be used		Yes	Yes	Yes (sachet)	Yes
Zonisamide	Capsules can be opened and contents mixed with water or apple juice.	*Alternatively, sprinkle capsule contents on to chocolate pudding or apple sauce.*	Yes	Yes	Yes	Yes

Appendix 2: Phenytoin loading dose when a patient is already on Phenytoin

Failure to take into account existing phenytoin levels may lead to toxicity

Is a phenytoin level available?

Note: Initiating treatment should not be delayed for phenytoin blood concentration results

YES

- Is the Phenytoin level sub-therapeutic, allowing a 'top up' dose to be given?

Ensure the adjusted phenytoin level is calculated for patients with hypoalbuminemia (<32g/L)

$$\text{Corrected Phenytoin level (mg/L)} = \frac{\text{reported level (mg/L)}}{(0.02 \times \text{serum albumin(g/L)}) + 0.1}$$

	Body Weight			
	50 kg	**60 kg**	**70 kg**	**80 kg**
Top-up Dose (IV)	**Phenytoin level increased by (with top-up dose):**			
250 mg	7 mg/L	6 mg/L	5 mg/L	4.5 mg/L
500 mg	14 mg/L	12 mg/L	10 mg/L	9 mg/L
750 mg	21 mg/L	18 mg/L	15 mg/L	13.5 mg/L

NO

OPTION 1

Administer HALF the recommended loading dose until levels are available

OPTION 2

Limit the loading dose to 500mg IV

After the loading dose, prescribe a maintenance dose: 100mg TDS IV

A Phenytoin level MUST be checked 18-24 hours after the loading dose and consideration given to increasing the usual maintenance dose (check compliance)