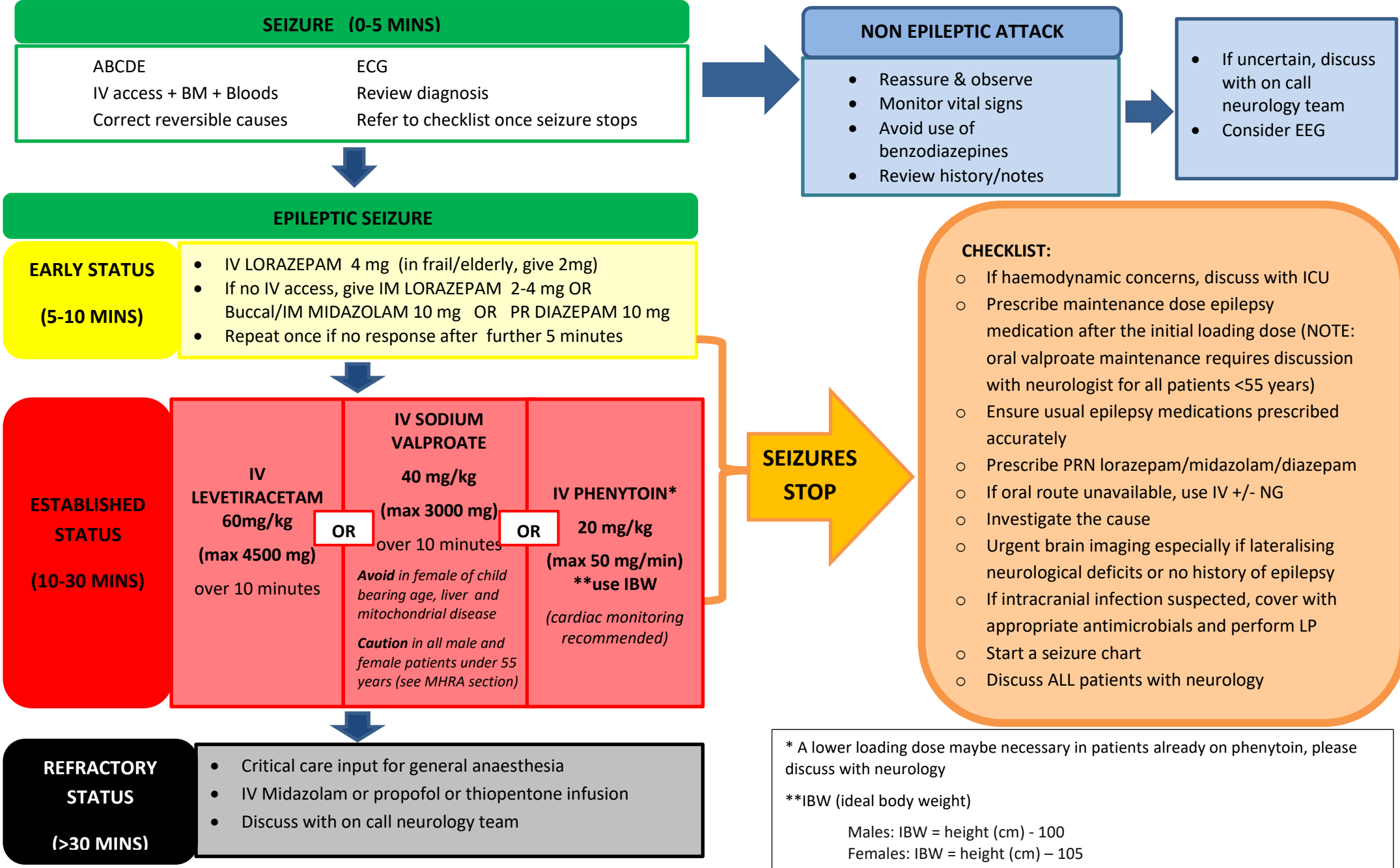


Neurology Department Royal Derby Hospital

## Status Epilepticus in Adults - Full Clinical Guideline

Ref. No.: CG-NEURO/2016/001 V 2.1.0

**A guideline for the management of convulsive status epilepticus**



## Introduction

Epilepsy is one of the most common neurological conditions. Recurrent seizures can adversely affect mood and cognition, and may even lead to injuries, or death. In the UK, there are an estimated 1000 deaths per year related to epilepsy<sup>1</sup>. Therefore, effective seizure management is essential. Convulsive status epilepticus is a clinical emergency. It is defined as continuous or recurrent seizures without recovery of consciousness for more than 5 minutes. It carries a high risk of mortality and morbidity. Early recognition and treatment are keys to minimising complications.

## Key Points:

- **Not all that shakes are epileptic in nature. Consider the possibility of non epileptic attacks.**
- All patients presenting with seizures require IV access, and are prescribed PRN IV/IM Lorazepam 2-4 mg or Buccal/IM Midazolam 10 mg or PR 10 mg diazepam.
- For patients with known epilepsy, please prescribe their usual epilepsy medications correctly. Missed doses is a common causes of uncontrolled or breakthrough seizures in the hospital.
- Prescribe and start maintenance dose of epilepsy medication 4-8 hours post loading dose.
- If oral route is unavailable, please use alternative routes, such as IV +/- NG route. Please refer to the list of epilepsy medication below for additional information or consult pharmacy.
- Always investigate for the cause of the seizures, for example:
  - Alcohol withdrawal (start Pabrinex as per hospital protocol)
  - Electrolyte abnormalities (watch out for hypoglycaemia – treat according to hospital guideline)
  - Infection
  - CNS tumours/inflammation
  - Non compliance
  - Toxins/illicit drugs
  - Venous sinus thrombosis
- Discuss all patients in status epilepticus with the on call neurology team.
- Record all seizures that have been witnessed in the case notes or seizure chart. Describe them as accurately as possible.
- Collateral history regarding seizure semiology and frequency is very helpful. Try your best to gather this information.
- Urgent brain imaging is required if there are lateralising neurological deficits or no prior history of epilepsy.
- Cover with the appropriate antimicrobials if concerned re: CNS meningitis/encephalitis/abscess.
- Maintain a seizure chart on the ward.
- Basic blood investigations should include FBC, UE, LFT, calcium, glucose, CRP, ABG/VBG +/- drug level (if concerned on non-compliance; phenytoin blood level is helpful to guide whether top up dose is required).

**First Line Treatment in Early Convulsive Status Epilepticus<sup>2,3,4</sup>**

- IV Lorazepam 4 mg is the drug of choice (use a lower dose of 2 mg in elderly/frail patients)
- If IV route not available, Lorazepam can be given IM or use Buccal/IM Midazolam 10 mg or PR diazepam 10 mg.
- These medications can be repeated once after further 5 minutes if seizure is persisting.
- If seizure stops, always review further management plan and investigate for possible causes. Refer to checklist.

**Second Line Treatment in Established Convulsive Status Epilepticus<sup>4,5,6</sup>**

- There is no difference in efficacy between IV Levetiracetam, Sodium Valproate or Phenytoin for treatment of established status epilepticus<sup>7</sup>.
- **For IV Levetiracetam:**
  - Give 60 mg/kg loading dose (maximum dose of 4500 mg), can infused over 10 minutes.
  - A maintenance dose is required starting at 750 mg BD.
  - If patient has renal impairment, a reduced maintenance dose is required. Please consult pharmacist.
- **For IV Sodium Valproate :**
  - Give 40 mg/kg loading dose (maximum dose of 3000 mg), infused over 10 minutes.
  - A maintenance dose is required starting at minimum 500 mg BD; alternatively 20-30mg/kg daily.
  - Sodium Valproate should be avoided in female of child bearing age (unless the conditions of “PREVENT” are fulfilled – refer to the last paragraph), patients with liver failure or mitochondrial disease.
  - For other male and female patients under 55 years, emergency intravenous treatment may be necessary if other agents are contraindicated. It is essential to refer to neurology to consider appropriateness of maintenance continuation as this requires two neurology specialists to agree initiation of therapy using national Risk Acknowledgement Forms (RAF).
- **For IV Phenytoin:**
  - Give 20 mg/kg loading dose (maximum rate of infusion 50 mg/minute), followed by maintenance dose. Prescribe 100 mg TDS for IV phenytoin or 300 mg once a day for PO phenytoin (use a dose 270 mg/day if using liquid Phenytoin).
  - A lower loading dose maybe required for patients who are taking phenytoin regularly. Please take a baseline phenytoin blood level and consult on call neurology team.
  - Please administer IV Phenytoin via a large bore cannula using a 0.22 micro in line filter.
  - During IV phenytoin loading dose, continuous cardiac monitoring should be used unless it is likely to lead to significant delay.
  - Be watchful of the side effects of IV Phenytoin: cardiac arrhythmias, rash, hypotension, purple glove syndrome
  - Please check phenytoin level 12-24 hours post loading dose as top up dose maybe needed.
  - Recheck pre-dose phenytoin level 5-7 days after starting maintenance dose.

- Alert all patients in status epilepticus to the ICU and neurology team.
- If seizure stops, always review further management plan and investigate for possible causes. Refer to checklist.
- If seizure does not stop, review your diagnosis. Consider possibility of non epileptic attacks. Move on to the next stage of treatment.

### **Refractory Convulsive Status Epilepticus**<sup>2,3</sup>

- Patients who have failed to respond to second line treatment are in refractory convulsive status epilepticus.
- They will require ICU input for GA, and treated with third line agents, such as IV midazolam/propofol/thiopentone infusions.
- Always involve the on call neurology team.

### **Non Convulsive Status Epilepticus**

It can be difficult to detect non convulsive status epilepticus, as the patient's presentation can be varied. The management is less urgent compared to the convulsive status epilepticus. About 8% of patients in coma are found in non convulsive status<sup>7</sup>. Consider this possibility if the patient has:

- a recent convulsive status epilepticus
- persistent altered behaviour
- failure to wake up appropriately post sedation wean
- subtle limb jerks, facial twitches, nystagmoid eye movements, eye deviation, speech arrest

EEG in these cases is helpful. Always ensure that these patients have their usual epilepsy medications prescribed accurately and/or maximised, consider loading doses of second line agents. Consider use of IV benzodiazepine under EEG control if diagnosis is not clear<sup>3</sup>. Discuss these patients with the on call neurology team.

### **Non Epileptic Attacks**

Not all that shakes are seizures. Consider the possibility of non epileptic attacks. Approximately, 20% of patients with epilepsy also experience non epileptic attacks<sup>8</sup>. And, nearly one quarter of patients who were admitted to the intensive care unit for apparent status epilepticus turn out to be non epileptic in nature<sup>9</sup>. Non epileptic attacks should not be treated with epilepsy medications, and the use of benzodiazepines to stop an attack must be avoided. It can be difficult to differentiate between a seizure and a non epileptic attack. If uncertain, always discuss the case with the on call neurology team. Here are a few commonly seen features in non epileptic attacks<sup>9</sup>:

- Waxing and waning
- Eyes closed
- Violent, thrashing, asynchronous movements
- Side to side head movements
- Prolonged duration of attacks

- Pelvic thrusting
- Back arching

The following websites can be recommended to these patients for additional support and understanding:

- [www.neurosymbols.org](http://www.neurosymbols.org)
- [www.nonepilepticattacks.info](http://www.nonepilepticattacks.info)

**Medicinal Forms of Common Epilepsy Medications<sup>10</sup>**

Please consult hospital pharmacist if uncertain.

Oral Formulations Only		Oral and IV Formulations
<ul style="list-style-type: none"> <li>• Lamotrigine</li> <li>• Carbamazepine (+ per rectal )</li> <li>• Eslicarbazepine</li> <li>• Oxcarbazepine</li> <li>• Zonisamide</li> <li>• Perampanel</li> <li>• Clonazepam</li> <li>• Clobazam</li> <li>• Ethosuximide</li> <li>• Topiramate</li> <li>• Pregabalin</li> </ul>	<ul style="list-style-type: none"> <li>• Gabapentin</li> <li>• Primidone</li> <li>• Rufinamide</li> <li>• Vigabatrin</li> </ul>	<ul style="list-style-type: none"> <li>• Levetiracetam</li> <li>• Sodium Valproate</li> <li>• Lacosamide</li> <li>• Phenytoin (oral suspension 90 mg equivalent to 100 mg tablet/IV)</li> <li>• Midazolam (+ buccal)</li> <li>• Lorazepam</li> <li>• Diazepam (+ per rectal)</li> <li>• Phenobarbitone</li> </ul>

**MHRA Valproate Alert<sup>11</sup>**

- Oral Valproate should not be used in male or female patients under 55 years girls and women of childbearing potential unless other treatments are ineffective or not tolerated.
- Initiation of oral valproate in male and female patients under 55 requires agreement of two specialists who will document this on a risk acknowledgement form [see links to MHRA templates below]
- Valproate is contraindicated in pregnancy unless there is no suitable alternative treatment.
- Valproate may only be initiated in women & girls under 55 years if the conditions of “Prevent – the valproate pregnancy prevention programme” [PPP] are fulfilled.
- Please refer to the [Healthcare Professional Guide](#) regarding this
- All other resources including the Risk Acknowledgment Forms (RAF/ARAF) and the Patient Guides can be found on the [MHRA pages](#):

<https://www.gov.uk/drug-safety-update/valproate-belvo-convulex-depakote-dyzantil-epilim-epilim-chrono-or-chronosphere-episenta-epival-and-syonellv-new-safety-and-educational-materials-to-support-regulatory-measures-in-men-and-women-under-55-years-of-age>

**Documentation Controls**

<b>Reference Number</b> CG-NEURO/2016/001	<b>Version:</b> 2.1.0		<b>Status</b> Final	
<b>Version / Amendment History</b>	<b>Version</b>	<b>Date</b>	<b>Author</b>	<b>Reason</b>
	1.1.0	2016	Clinical Pharmacists Group	To include Kings Lodge, LRCH
	1.2.0	2017	Clinical Pharmacists Group	Update to phenytoin
	2.0.0	2021	Dr Ling Toh	Review to update with Nottingham Neurology advice
	2.1.0	2024	James Hooley - Med Safety	Updated valproate sections to align with national MHRA regulatory changes.
<b>Intended Recipients:</b> Clinicians treating adult patients				
<b>Training and Dissemination:</b> <i>How will you implement the Clinical Guideline, cascade the information and address training</i> <ol style="list-style-type: none"> <li>1. Consider sending out a trust notification of the new guideline to all doctors (medicine and surgery).</li> <li>2. Participate in education days for junior doctors</li> </ol>				
<b>Development of Guideline:</b> Dr S L Toh, Consultant Neurologist, Alison Holmes, Epilepsy Specialist Nurse, Amanda Simmons, Epilepsy Specialist Nurse				
<b>Consultation with:</b> Thomas Morley, Lead Medicines Information Pharmacist, James Kerr, Divisional Pharmacist for Medicine, Dominic Moore, Lead Pharmacist – Commissioning & High Cost Medication  <b>Version 2.1.0 James Hooley</b> , Medication Safety Officer in consultation with authors and the Sodium Valproate Short Life Working Group (led by Richard Faleiro / Lara Raworth)				
<b>Linked Documents:</b> Nil				
<b>Keywords:</b> <b>Status epilepticus   Valproate   Valproic   Phenytoin   Levetiracetam   seizure   Epilepsy</b>				
<b>Business Unit Sign Off</b>			<b>Group:</b> n/a for interim update 2.1.0 <b>Date:</b>	
<b>Divisional Sign Off</b>			<b>Group:</b> Medical Division <b>Date:</b> V2.0.0 18/06/2021  <b>Version 2.1.0</b> amendments Signed off via Sodium Valproate Short Life Working Group. Future versions will revert to Medical Division oversight.	
<b>Date of Upload</b>			25/03/2024	
<b>Review Date</b>			July 2024	
<b>Contact for Review</b>			Dr Ling Toh	

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