NHS Greater Glasgow and Clyde

CLINICAL GUIDELINE

Generalised Convulsive Status Epilepticus in Adults

A guideline is intended to assist healthcare professionals in the choice of disease-specific treatments.

Clinical judgement should be exercised on the applicability of any guideline, influenced by individual patient characteristics. Clinicians should be mindful of the potential for harmful polypharmacy and increased susceptibility to adverse drug reactions in patients with multiple morbidities or frailty.

If, after discussion with the patient or carer, there are good reasons for not following a guideline, it is good practice to record these and communicate them to others involved in the care of the patient.

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Important Note:

The online version of this document is the only version that is maintained.
Any printed copies should therefore be viewed as 'Uncontrolled' and as such, may not necessarily contain the latest updates and amendments.

NHSGGC Management of Generalised Convulsive Status Epilepticus in Adults

Introduction

Convulsive status epilepticus (continuing or recurrent seizures over 5 minutes, or without recovery) is a medical emergency with a 16–39% mortality rate. There is a risk that seizures will cause cerebral damage if not controlled within 30 minutes of onset.

This guideline outlines the general management of convulsive status epilepticus in adults (those ≥ 16 years old) and is based on the SIGN guideline for diagnosis and management of epilepsy in adults and up-to-date trial information. Treatment may differ in individual clinical circumstances. Consult specialist guidelines for advice on the management of status epilepticus in pregnant patients.

The management of convulsive status epilepticus is outlined in the treatment pathway below, more detail regarding choice, dosage and administration of antiepileptic drugs can be found by following the relevant links throughout the document.

1. Treatment Pathway

Stage 1

0 – 5 minutes

Immediate Measures:

- Open and maintain airway
- Assess cardiac and respiratory function
- Check blood glucose
- Time seizure from onset
- Give oxygen
- Secure IV access in large veins
- Check temperature

Stage 2

> 5 minutes

Give ONE of the following drugs depending on local availability. Do not mix benzodiazepines:

- **Lorazepam** up to 4mg IV, given as 2mg IV over 1 minute, if seizure not terminating give a further 2mg IV after 2-3 minutes
- **Diazepam** 10 mg IV or rectally. Maximum rate 5mg/minute. Risk of respiratory depression. Give 5mg of Diazepam in the elderly or patients less than 50kg
- **Midazolam** 10 mg buccally, intranasally* or intramuscularly** (off-label). Give 5mg of Midazolam in the elderly or patients less than 50kg.
  *Intranasal midazolam: Use the buccal preparation. Half the dose in each nostril. **Intramuscular administration: use 10mg/2ml ampoules (stored in CD cupboard)

Administer a repeat dose of benzodiazepine at 10 minutes if there is no response

Determine aetiology

- Any suggestion of hypoglycaemia: give 100ml of glucose 20% IV. If no IV access 1mg IM glucagon. Check blood glucose again after 10 minutes.
- Any suggestion of alcohol abuse or impaired nutritional status: give thiamine IV (as 2 pairs of Pabrinex® ampoules)
- Give usual antiepileptic drug (AED) treatment if not already given – can be given via nasogastric tube if airway secured (see GGC NBM epilepsy guideline)
- Consider appropriate antibiotic/antiviral if any concern about CNS infection
- Take bloods: U+Es, LFTs, FBC, Coagulation screen, Glucose, CK, Calcium, Magnesium, Blood culture, Blood gas, Alcohol and toxicology screen, AED levels.

Stage 3

10 - 30 minutes

If status persists, give ONE of the following AED loading doses:

- **Intravenous Levetiracetam** (off-label) 60mg/kg, max: 4500mg/dose. See here (p4) for dosage and administration instructions OR
- **Intravenous Phenytoin** 18mg/kg, max: 1800mg/dose. See here (p5) for dosage and administration instructions OR
- **Intravenous Sodium valproate** (off-label) 25mg/kg, max: 2500mg/dose (**reproductive risks in all patients <55 years old – see below***). See here (p6) for dosage and administration instructions

Status Epilepticus is a clinical emergency and management is time critical, choice of AED should be according to local availability and information in Appendix 1 on indications and cautions.

If seizure is not terminating call ICU to inform them of the patient and contact neurology via switchboard for advice.

If seizures continue or reoccur in patients who are haemodynamically stable then consider another stage 3 AED.

*Sodium Valproate Reproductive Risks: **The primary aim in status epilepticus management is termination of seizures and preservation of life.** The MHRA have issued advice on use of sodium valproate in female and male patients under 55 years. Decisions regarding ongoing treatment once seizures are controlled must be in line with MHRA advice.

Stage 4

30 – 60 minutes

If status persists at 30 – 60 minutes, induce general anaesthesia in an appropriate setting with **midazolam, propofol, thiopentone or phenobarbital (unlicensed)** according to local protocols and continue management in ICU setting

Note: Anaesthetic agents MUST only be prescribed by doctors with training, skills and experience in their use (anaesthetists, intensivists or emergency physicians). If ongoing non-convulsive seizures a possibility (e.g. persistent low GCS) then consider contacting Neurophysiology (ggc.neurophysoncall@nhs.scot) for advice regarding the need for EEG.

Over next 24-48 hours optimize doses and levels of non-anaesthetic anti-epileptic drugs and, if no electrical or clinical evidence of ongoing seizures, withdraw anaesthesia to assess response.

2. Ongoing Management once seizures controlled

Seek neurology advice regarding ongoing management but do not delay starting maintenance therapy if advice not immediately available.

Drug	Usual Starting Dose	Time after loading dose to start first maintenance dose	Considerations
Levetiracetam	IV/PO 1000mg TWICE a day (if eGFR >50ml/min)	If eGFR (ml/min): • >50 = 6 hours • 30-50 = 12 hours • <30 = 24 hours	- Reduce dose in renal impairment. If eGFR (ml/min): • >50 = 1000mg TWICE a day • 30-50 = 750mg TWICE a day • <30 = 500mg TWICE a day Renal replacement therapy: 500-1000mg once daily – contact renal team to discuss timing of dialysis. - Check interactions in the BNF
Phenytoin	IV/PO 3 - 5mg/kg ONCE a day Usual starting dose IV/PO 300mg ONCE a day	12 - 24 hours	- Check level 2-4 hours post IV loading dose, if subtherapeutic a top up dose may be required - see link on how to interpret level for albumin - Seek pharmacy advice for patients requiring liquid or NG administration - Check interactions in the BNF
Sodium Valproate	IV/PO 5 - 7 mg/kg TWICE a day Usual starting dose IV/PO 300-400mg TWICE a day	4 - 8 hours	- **Reproductive risks in female and male patients <55 years.** Ongoing prescribing must adhere to Valproate Pregnancy Prevention Programme, link - Check interactions in the BNF - **AVOID** in combination with carbapenems e.g. meropenem – leads to a marked reduction in sodium valproate effect - Increases lamotrigine levels – seek neurology/pharmacy advice

Levetiracetam Dosage and Administration Advice in Status Epilepticus

Levetiracetam IV 60mg/kg, single dose; infuse over 15 minutes. Maximum dose 4500mg.

Cautions: Renal impairment (no reduction in loading dose is necessary – see page 3 for reduced maintenance doses in renal impairment).

Levetiracetam			
Weight (kg)	**Dose (mg) (60mg/kg)**	**Volume of 500mg/5ml injection**	**Administration**
35-44	2100	21	Give in 100ml NaCl 0.9% Give over 15 minutes For doses greater than 3000mg, remove and discard 30mls of NaCl 0.9% from the bag prior to adding levetiracetam.
45-54	2700	27	
55-64	3300	33	
65-74	3900	39	
75-84	4500	45	
85-95	4500	45	
>95	4500	45	

Use of levetiracetam in status epilepticus is ‘off-label’ but is approved for use in this way within NHSGGC, an unlicensed medicine form does not need to be completed for use in this indication.

Please state the infusion time when prescribing on the kardex or HEPMA.

Phenytoin Dosage and Administration Advice in Status Epilepticus

Phenytoin 18mg/kg IV, single dose, maximum dose 1800mg.
Contraindications: Heart block, bradycardia, porphyria.
Cautions: liver disease, check drug interactions (phenytoin is an enzyme inducer).

Table 1: Phenytoin IV loading dose (if no phenytoin present)

Phenytoin			
Weight (kg)	**Dose (mg) (18mg/kg)**	**Volume of IV phenytoin (ml) (vial = 250mg/5ml)**	**Administration**
35-44	700	14	Infuse through large vein. Flush well with sodium chloride 0.9% before and after phenytoin infusion **Rate:** Give over 30-40 minutes (<50mg/min). In elderly or known heart disease give over 60minutes **Dilution:** Ideally give undiluted via syringe pump. If dilution essential, dilute doses <1g in 100ml and doses >1g in 250ml NaCl 0.9%. Give through an in-line filter (0.22 -0.5 microns) via infusion pump* **Monitoring**: Continuous BP, ECG and RR monitoring required (risk of hypotension/bradycardia)
45-54	900	18	
55-64	1100	22	
65-74	1250	25	
75-84	1450	29	
85-95	1600	32	
>95	1800	36	

*Administration of diluted solution should commence immediately after the mixture has been prepared and be completed within 1 hour.

Check level (target: 10-20mg/L): 2-4 hours post IV loading dose, if subtherapeutic a top up dose may be required.

'Top up' loading dose of phenytoin for status epilepticus

If phenytoin is already present but the patient is still not controlled, a 'top-up' loading dose may be useful.

Phenytoin sodium top up dose (mg) = (20 – measured concentration (mg/L)) x 0.7 x wt (kg)

Table 2 gives the approximate increase in concentration following doses of 250 – 750mg.

Table 2: Phenytoin 'top-up' doses

Concentration increase with 'top-up' dose				
Dose/Weight	**50kg**	**60kg**	**70kg**	**80kg**
250mg	7mg/L	6mg/L	5mg/L	4.5mg/L
500mg	14mg/L	12mg/L	10mg/L	9mg/L
750mg	21mg/L	18mg/L	15mg/l	13.5mg/L

ALBUMIN: albumin level can affect the interpretation of phenytoin concentrations– see **link** or contact pharmacy for advice

Sodium Valproate Dosage and Administration Advice in Status Epilepticus

Sodium Valproate 25 mg/kg IV, single dose, infuse over 15 minutes. Maximum dose 2500mg.

Contraindications:

- Reproductive risk in all patients < 55 years **see below
- mitochondrial disease or metabolic disorder predisposing to hepatotoxicity
- concurrent use with carbapenems e.g. meropenem (major interaction resulting in markedly reduced sodium valproate levels and therapeutic effects)
- active liver disease
- porphyria

Cautions:

- Check concomitant drugs (valproate is an enzyme inhibitor, with immediate effect on half-life of other drugs e.g. lamotrigine)

Sodium Valproate			
Weight (kg)	**Dose (mg) (25mg/kg)**	**Volume of 100mg/1ml injection (ml)**	**Administration**
35-44	1000	10	Give in 50ml–100ml NaCl 0.9% Give over 15 minutes*
45-54	1250	12.5	
55-64	1500	15	
65-74	1750	17.5	
75-84	2000	20	
85-95	2250	22.5	
>95	2500	25	

*please note this is a faster infusion rate than specified in the current IV monograph but has been approved for administration in this way in NHSGGC

Use of sodium valproate in status epilepticus is 'off-label' but is approved for use in this way within NHSGGC, an unlicensed medicine form does not need to be completed for use in this indication.

Please state the infusion time when prescribing on the kardex or HEPMA.

Sodium Valproate Reproductive Risks: **The primary aim in status epilepticus management is termination of seizures and preservation of life. The MHRA have issued advice on use of sodium valproate in female and male patients under 55 years. Decisions regarding ongoing treatment once seizures controlled must be in line with MHRA advice.

Appendix 1: Indications and cautions for stage 3 antiepileptic drugs in the treatment of status epilepticus

Drug	May be preferred:	Cautions to consider:
Levetiracetam	• Already taking Levetiracetam and suspected poor adherence • Alternatives contraindicated or previously ineffective • Favourable side effect and interaction profile	• Known allergic reaction • Reduce maintenance dose in renal impairment • Mood or behavioural disorder (may worsen symptoms)
Phenytoin	• Already taking Phenytoin and suspected poor adherence • Alternatives contraindicated or previously ineffective	• Bradycardia • Heart block • Porphyria • Known allergic reaction • Caution in liver disease • Administration via enteral tubes can be problematic • Therapeutic drug monitoring required
Sodium Valproate	• Already taking Sodium valproate and suspected poor adherence • Genetic generalised epilepsy • Mood disorder • Alternatives contraindicated or previously ineffective	• Reproductive risks in female and male patients <55 years *see below • Pre-existing liver disease or pancreatitis • Known metabolic disorder predisposing to hepatotoxicity • Known allergic reaction • Mitochondrial disease • Avoid in patients prescribed carbapenem antibiotics • Porphyria

***** Sodium Valproate Reproductive Risks: **The primary aim in status epilepticus management is termination of seizures and preservation of life.** The MHRA have issued advice on use of sodium valproate in female and male patients under 55 years. Decisions regarding ongoing treatment once seizures controlled must be in line with MHRA advice.

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