MANAGEMENT of GENERALISED CONVULSIVE STATUS EPILEPTICUS in ADULTS

TARGET AUDIENCE	Secondary Care
PATIENT GROUP	This guideline outlines the general management of convulsive status epilepticus in adults (those ≥ 16 years old)

Clinical Guidelines Summary

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.

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.

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.

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Management of generalised convulsive status epilepticus in adults

Stage 1
0-5 minutes

Immediate Measures

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

Stage 2
> 5 minutes

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

- **Lorazepam** up to 4mg Intravenously, given as 2mg intravenously over 1 minute, if seizure not terminating give a further 2mg intravenously after 2-3 minutes
- **Diazepam** 10mg Intravenously or rectally. Maximum rate 5mg/minute. Risk of respiratory depression. Give 5mg of Diazepam in the elderly or patients less than 50kg
- **Midazolam** 10mg 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% intravenously. If no intravenous access 1mg intramuscularly glucagon. Check blood glucose again after 10 minutes
- Any suggestion of alcohol abuse or impaired nutritional status: give thiamine intravenously (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
- 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 page 4 for dosage and administration instructions

OR

- **Intravenous phenytoin** 18mg/kg. max 1800mg/dose. See page 5 for dosage and administration instructions

See Appendix a for guidance on indications/cautions to guide AED choice

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

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

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 for advice regarding the need for EEG.
Over next 24-48 hours optimise doses and levels of non – anaesthetic anti-epileptic drugs and, if no electrical or clinical evidence of ongoing seizures, withdraw anaesthesia to assess response

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	Intravenous/ Oral 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	Intravenous/ Oral 3 - 5mg/kg ONCE a day Usual starting dose Intravenous/ Oral 300mg ONCE a day	12 - 24 hours	- Check level 2-4 hours post Intravenous loading dose, if subtherapeutic a top up dose may be required - see link how to interpret level for albumin - Seek pharmacy advice for patients requiring liquid or NG administration - Check interactions in the BNF

Levetiracetam Dosage and Administration Advice in Status Epilepticus

Levetiracetam Intravenous 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 NHSL, an unlicensed medicine form does not need to be completed for use in this indication.

Please state the infusion time when prescribing on the medicine chart or HEPMA

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Phenytoin Dosage and Administration Advice in Status Epilepticus
Phenytoin 18mg/kg Intravenous, single dose, maximum dose 1800mg.
Contraindications: Heart block, bradycardia, porphyria.
Cautions: liver disease, check drug interactions (phenytoin is an enzyme inducer).

Table 1: Phenytoin Intravenous (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 Intravenous 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)

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

Table 2 gives the approximate increase in concentration following doses of 250 – 750mg. Table 2: Phenytoin 'top-up' dose

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

Appendix a: 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 contraindication 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 contraindication or previously ineffective	• Bradycardia • Heart Block • Porphyria • Known allergic reaction • Caution in liver disease • Administration via NG tubes can be problematic • Therapeutic drug monitoring required

References/Evidence

1. Scottish Intercollegiate Guidelines Network (SIGN). Diagnosis and management of epilepsy in adults. Edinburgh: SIGN;2015. (SIGN publication no.143). [may 2015, updated September 2018].
2. Kapur J, Elm J, Chamberlain JM et al. Randomised trial of three anticonvulsant medications for status epilepticus. NEJM 2019;381:2103-13
3. Jones S, Pahl C, Trinka E et al. A protocol for the in hospital emergency drug management of convulsive status epilepticus in adults. Pract Neurol 2014;14:194-197
4. Misra DM, Kalita J, Patel R. Sodium valproate vs phenytoin in status epilepticus: A pilot study. Neurology 2006;67:340-342
5. Glauser T, Shinnar S, Gloss D, et al. Evidence-based guideline: Treatment of convulsive status epilepticus in children and adults: Report of the Guideline Committee of the American Epilepsy Society. Epilepsy Currents 2016:16(1):48-61
6. Cock H. Status Epilepticus in Adults (convulsive seizures in patients aged >16 years old). Available from: https://www.stgeorges.nhs.uk/wp-content/uploads/2016/12/Status-epilepticus.pdf

Appendices

1. Governance information for Guidance document

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Date	**Lead Author**	**Change**	**Version No.**
1/12/2022	Jennifer Murphy		1
16/1/2024	Jennifer Murphy	Updated guidance on use of valproate in patients under 55 following MHRA patient safety alert	2
			3
		.	4
			5

2.You can include additional appendices with complimentary information that doesn't fit into the main text of your guideline, but is crucial and supports its understanding.