1. Introduction and Who Guideline applies to

Convulsive seizures are characterised by generalized tonic-clonic movements and impaired awareness. The accepted *operational* definition of convulsive status epilepticus (CSE) is '≥5 min of (1) continuous seizure or (2) two or more discrete seizures between which there is incomplete recovery of consciousness'. [1] (For a *conceptual* definition, see 2015 ILAE taskforce report. [2])

Since the duration of CSE that may lead to permanent neuronal injury by itself is believed to be around 30 minutes, every effort must be made to control seizures during that time window. The approach described here - rapid, step-wise administration of antiseizure medications (ASMs) with *simultaneous* preparation for the next step - is consistent with the established practice in children [3] that has also been adopted by some adult centres. [4]

Phenytoin has now been replaced by levetiracetam as the preferred 2nd-line ASM. While a major study in 2019 found that phenytoin, sodium valproate and levetiracetam are equally effective to control CSE, [5] and despite levetiracetam use in CSE still being off-label, NICE recognises that it 'may be quicker to administer and have fewer adverse effects than the alternative options'. [6]

This guideline applies to all University Hospitals of Leicester (UHL) staff involved in managing adult patients with CSE from the time of diagnosis until seizure activity has either stopped or general anaesthesia (GA) been induced. It also covers a number of actions that together represent good aftercare. Outside the scope of this guideline are

- Other types of SE – including focal motor, tonic, hyperkinetic, myoclonic and non-convulsive
- Drugs used to induce GA and further CSE management in the Intensive Care Unit (ICU)
- Decisions regarding long-term ASMs following CSE, which requires neurological expertise
- Eclampsia, for which the separate UHL obstetric guideline should be followed [7]

2. Guideline Standards and Procedures

2.1 Overall management of CSE

- A separate guideline in the shape of a proforma containing all elements of this document relevant to the Emergency Department is available for ED clinicians [8]
- In all other UHL areas, clinicians should follow the algorithm shown in **Appendix A** and the sections below

2.2 Antiseizure medications (ASMs)

A. Prescribing

- Easy-to-use dose sentences for all ASMs mentioned in this guideline can be found in Nervecentre Meds > Emergency Medicine > Common scenarios > Seizures
- A prescribing aid for levetiracetam, sodium valproate and phenobarbital for reference and use if Nervecentre Meds is offline can be found in **Appendix B**
- A prescribing aid for phenytoin is available separately [10]

B. 1st-line ASM (benzodiazepine)

- Intravenous (IV) lorazepam and buccal midazolam are both acceptable as the first benzodiazepine dose and appear to be equally effective
- If midazolam is chosen, use either the specifically formulated oromucusal solution (where available) or draw up a 10mg-in-2mL IV ampoule using a blunt filter needle
- Lorazepam should always be diluted with 0.9% NaCl to a concentration of 1mg/mL. Give a 1mg bolus, followed by a large flush, every minute until seizure has stopped or the full 4mg have been given This ensures that the smallest effective dose of lorazepam is administered and minimises the risk of respiratory depression.
- If a repeat dose of benzodiazepine is required, this should always be lorazepam

C. Intraosseous (IO) access

- IO access must be established immediately if IV cannulation has not been successful at the second attempt / before the next ASM dose is due
- The Deteriorating Adult Response Team (DART) will bring the required equipment and skills to deliver this intervention
- Follow the UHL LocSSIP for intraosseous cannulation in adults [9]

2.3 Aftercare bundle

- Place patient in recovery position if possible while postictal
- Monitor for, and manage, any respiratory depression during the postictal period
- If CSE had stopped after benzodiazepine only, now load with one appropriate 2nd-line ASM (levetiracetam, sodium valproate or phenytoin) to prevent seizure recurrence
- Look for and manage any potential causes and precipitants (see section 2.4 below)
- Identify, and appropriately manage, any injuries (e.g. shoulder dislocations)
- Wean off oxygen once target SpO_2 maintained
- Consider obtaining a CT-head if indicated (see section 2.5 below)
- Consider obtaining a chest radiograph (CXR) to exclude aspiration
- Depending on response to treatment, rate of recovery once seizures controlled and any causes identified, consider need to transfer patient to a higher level of care (such as a high-dependency area or ICU)
- Document the need to create an agreed emergency management plan during this admission for all patients with epilepsy who do not already have one in place
- Request same-day (next-day if CSE occurred out-of-hours) Neurology specialist review (see also section 2.6 below)

2.4 Causes

- Metabolic derangements, as listed in **Appendix A**
- Non-adherence to ASMs (in all patients with epilepsy, document plasma levels)
- Acute intracerebral process (see section 2.5 below for CT-head indications)
  - Stroke
  - Drugs and toxins, e.g. cocaine, local anaesthetics and isoniazid (INH) poisoning
  - CNS infection, including malaria and HIV
  - Sepsis-associated encephalopathy
  - Head injury
  - Hypoxic-ischemic brain injury
- Remote brain injury (post-traumatic, post-encephalitic, post-stroke etc.)
- Intracranial tumour
- Uncommon causes
  - Autoimmune
  - Genetic - e.g. fragile X syndrome
  - Mitochondrial disorders
  - Hyperammonaemia (e.g. in liver failure)
- Unknown; includes ‘cryptogenic new-onset refractory status epilepticus’ (C-NORSE)

The most common underlying causes of CSE are cerebrovascular disease (e.g. stroke) and low ASM plasma levels. While CSE caused by low ASM levels or alcohol misuse has a relatively good prognosis, poorer outcomes are seen in CSE due to cerebrovascular disease, particularly hypoxic-ischemic brain injury. [11]

2.5 Indications for CT-head

Only patients meeting one or more of the following criteria should undergo CT-head:

- Absence of a previous epilepsy history
- New focal neurological signs
- Recent head injury
- Known intracranial tumours
- Refractory CSE – i.e. requiring alternative 2nd-line or more ASMs to control seizures

2.6 Neurology specialist review

This should be timely and address the following aspects of care:

- Any further investigations that might be required to identify possible causes
- Initiation or adjustment of long-term treatment with ASMs
- For all patients with epilepsy, creation of an agreed emergency management plan or review of the existing plan as applicable

3. Education and Training

No additional skills are required to apply this guideline.

4. Monitoring Compliance

What will be measured to monitor compliance	How will compliance be monitored	Monitoring Lead	Frequency	Reporting arrangements
Compliance with drug choice and timeliness of CSE control	Audit	Neurology HOS to delegate	Annually	To ESM Q&S board

5. Supporting References

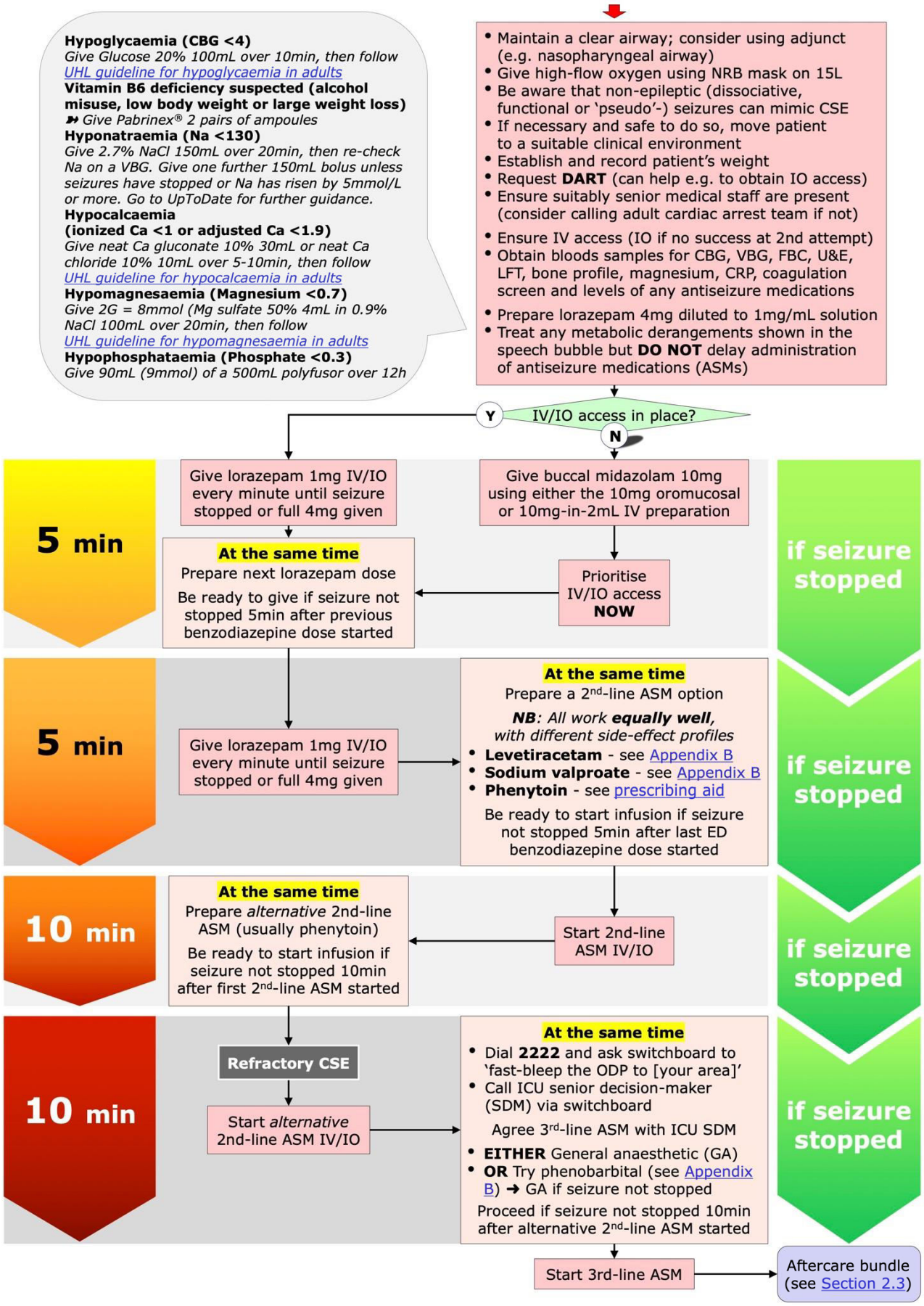
1. LowensteinDH, BleckT and MacdonaldRL. It's time to revise the definition of status epilepticus. Epilepsia 1999;40:120–122.
2. TrinkaE, CockH, HesdorfferD et al. A definition and classification of status epilepticus--Report of the ILAE Task Force on Classification of Status Epilepticus. Epilepsia. 2015;56:1515-23.
3. Advanced Life Support Group (ALSG). Advanced Paediatric Life Support: A Practical Approach to Emergencies (7th edition). Manchester: ALSG; 2023.
4. The Walton Centre NHS Foundation Trust (2020) Status epilepticus guideline [Accessed 03 Sep 2023].
5. KapurJ, ElmJ, ChamberlainJM et al. Randomized Trial of Three Anticonvulsant Medications for Status Epilepticus. N Engl J Med 2019;381:2103-13.
6. NICE (2022) Epilepsies in children, young people and adults. NG217. London: National Institute for Health and Care Excellence.
7. University Hospitals of Leicester NHS Trust (2022) Pre Eclampsia and Eclampsia – severe UHL obstetric guideline (C3/2001) [Accessed 03 Sep 2023].
8. University Hospitals of Leicester NHS Trust (2023) Convulsive status epilepticus in adults UHL Emergency Department guideline (C55/2023) [Accessed 31Oct23].
9. University Hospitals of Leicester NHS Trust (2023) Intraosseous Cannulation for Emergency Intravascular Access UHL LocSSIP (B33/2017) [Accessed 10 Sep 2023].
10. University Hospitals of Leicester NHS Trust (2023) Phenytoin IV prescribing aid UHL Emergency Department guideline (C69/2016) [Accessed 03 Sep 2023].
11. NeliganA and ShorvonSD. Frequency and prognosis of convulsive status epilepticus of different causes: A Systematic Review. Arch Neurol. 2010;67:931–40.

6. Key Words

Status epilepticus, SE, convulsive, convulsion, epilepsy, epileptic, seizure, levetiracetam, valproate, phenytoin, phenobarbital, lorazepam, midazolam, antiseizure medication, ASM, C-NORSE, hyponatraemia, alcohol, hypocalcaemia, hypomagnesaemia, hypoglycaemia, hypophosphataemia, Pabrinex, metabolic

CONTACT AND REVIEW DETAILS	
Guideline Lead (Name and Title) Martin Wiese, Emergency Physician	**Executive Lead** Andrew Furlong, Medical Director
Details of Changes made during review: • Guideline completely rewritten • Title change from 'status epilepticus' to 'convulsive status epilepticus'	

Appendix A. CSE in adults – management algorithm. Back to 1st page



Appendix B. Antiseizure medication prescribing aid

Back to 1st page

For reference and use if Nervecentre Meds is offline

Levetiracetam loading dose

- *Safe to use in patients already taking levetiracetam*
- *Find applicable weight range*
- *If NC offline, prescribe infusion on a paper drug chart*

Ideally avoid (but* NOT *contraindicated) if

- eGFR known to be <30 from previous U&E (**NB**: *CAN* still be given if no results available)
- History of intentional OD / suicidal ideation

Patient weight (kg)	Add required amount of levetiracetam to a 100 mL bag of sodium chloride 0.9% **Levetiracetam 60mg/kg** *ampoules contain 500mg in 5mL (100mg/mL)*		
	Dose	Volume	Rate
	mg	mL	mL/h
40 – 44	2500	25	750
45 – 49	2800	28	768
50 – 54	3100	31	786
55 – 59	3400	34	804
60 – 64	3700	37	822
65 – 69	4000	40	840
70 – 74	4300	43	858
> 74	4500	45	870

All infusions will complete in 10min

Sodium valproate loading dose

- *Find applicable weight range*
- *If NC offline, prescribe infusion on a paper drug chart*

Avoid if

- Already taking sodium valproate regularly
- Woman of childbearing potential
- Acute liver failure, known clotting disorder, active bleeding or recent neurosurgical procedure
- Mitochondrial disorders and aminoacidopathies

Patient weight (kg)	Add required amount of sodium valproate to a 100 mL bag of sodium chloride 0.9% **Sodium valproate 40mg/kg** *ampoules contain 400mg in 4mL (100mg/mL)*		
	Dose	Volume	Rate
	mg	mL	mL/h
40 – 44	1700	17	1000
45 – 49	1900	19	1000
50 – 54	2100	21	1000
55 – 59	2300	23	1000
60 – 64	2500	25	1000
65 – 69	2700	27	1000
70 – 74	2900	29	1000
> 74	3000	30	1000

All infusions will complete in a little under 8min

Phenobarbital loading dose

- *Use only if agreed with ICU SDM*
- *Tick applicable weight range*
- *If NC offline, prescribe infusion on a paper drug chart*

Avoid if

- Porphyria
- Older people / high risk of respiratory depression

Patient weight (kg)	Add required amount of phenobarbital to a 100 mL bag of sodium chloride 0.9% **Phenobarbital 10mg/kg** *ampoules contain 60mg in 1mL*		
	Dose	Volume	Rate
	mg	mL	mL/h
40 - 42	420	7	1000
43 - 48	480	8	1000
49 - 54	540	9	1000
55 - 60	600	10	1000
61 - 66	660	11	951
67 - 72	720	12	840
73 - 78	780	13	847
79 - 84	840	14	760
85 - 90	900	15	766
91 - 96	960	16	696
> 96	1020	17	638

Infusions will complete within 6 – 11min (infusion rate = 100mg/min)

ASM example prescriptions for use if Nervecentre is offline *for a 64kg patient*

Date	Infusion fluid		Additions to infusion		IV or SC	Line	Start Time	Time to run or ml/hr	Fluid Batch No.	
	Type/strength	Volume	Drug	Dose						Prescriber
DD/MM/YY	Sodium chloride 0.9%	100mL	Levetiracetam	3700mg = 37mL	IV		HH:MM	822 mL/h (i.e. runs over 10min)		Dr.'s Name
DD/MM/YY	Sodium chloride 0.9%	100mL	Sodium valproate	2500mg = 25mL	IV		HH:MM	1000 mL/h		Dr.'s Name
DD/MM/YY	Sodium chloride 0.9%	100mL	Phenobarbital	660mg = 11mL	IV		HH:MM	951 mL/h		Dr.'s Name

For phenytoin, see separate prescribing aid [10]