Worcestershire NHS
Acute Hospitals NHS Trust

Status Epilepticus Guideline in Adult Patients (17 years and over)

This guidance does not override the individual responsibility of health professionals to make appropriate decision according to the circumstances of the individual patient in consultation with the patient and /or carer. Health care professionals must be prepared to justify any deviation from this guidance.

Introduction

The purpose of this guideline is to standardise the treatment of generalised convulsive status epilepticus in adult patients aged 17 years and over requiring acute admission to hospital.
For patients 16 years and younger see Paediatric Status guidelines (WAHT-TP-052)

This guideline is for use by the following staff groups:

All qualified healthcare professionals involved in the management of Status Epilepticus in Adult patients.

Lead Clinician(s)

Stephen Pearson	ST6 Anaesthetics and ICM
Sarah Pittaway	Pharmacist Practitioner
Keith Hinton	Clinical Lead Pharmacist, Critical Care, Surgery and Anaesthetics
James France	Consultant Emergency Medicine (A&E)

Approved by Urgent Care on: July 2023

Approved by Medicines Safety Committee on: 9th August 2023

This guideline should not be used after end of: 9th August 2026

Key amendments to this guideline

Date	Amendment	Approved by:
January 2022	Writing of Guidance	See above

1. Introduction

Status epilepticus (SE) is a medical emergency. The mortality rate can be as high as 20% with first presentation of generalised convulsive status epilepticus. Many causes of SE are associated with significant morbidity and complications such as hypoxia, cardiac arrhythmias, and neurological insult can be life threatening.

2. Definitions

Convulsive status epilepticus

- A convulsive seizure that continues for more than 5 minutes, or convulsive seizures that occur one after the other with no recovery between

Generalised tonic-clonic seizure

- A seizure of sudden onset involving generalised stiffening and subsequent rhythmic jerking of the limbs, the result of rapid widespread engagement of bilateral cortical and subcortical networks in the brain

Non-convulsive status epilepticus

- A change in mental status or behaviour in absence of convulsions but with continuous seizure activity on EEG

3. Common causes of SE

- Acute structural brain injury – stroke, trauma, bleed, infection, tumour, abscess
- Long standing structural brain injury – post surgery or stroke
- Poor anticonvulsant therapy adherence
- Withdrawal syndrome – alcohol, medications, illicit drugs
- Metabolic abnormalities
    - Hypoglycaemia
    - Hepatic encephalopathy
    - Uraemia
    - Hyponatraemia
    - Hypocalcaemia
    - Hypomagnesaemia
- Use of or overdose of drugs that lower seizure threshold

4. Treatment Algorithm

4.1. Initial Management (0-5mins)

- ABCDE approach
- Protect patient from injuries but do not restrain
- Give oxygen 15l/min via non-rebreathe mask
- Consider the oropharyngeal or nasopharyngeal airway (Nasopharyngeal contraindicated in head injury)
- Place patient in recovery position with head down to prevent aspiration (in absence head or spinal injury)
- Routine observations – HR, BP, SpO2, RR, Temperature, GCS
- Gain IV access. Consider IO if unable.
- Check blood glucose
- If hypoglycaemic – give 75-100ml 20% glucose or 150-200ml 10% glucose

- Consider subsequent empirical IV vitamin B and C replacement (eg. Pabrinex®) in those at risk of Wernicke-Korsakoff syndrome, such as malnourished patients, hyperemesis gravidarum, or those with a possible history of alcohol abuse.

4.2. First line drug treatment (5-15minutes)

- If seizure persists at 5 minutes – give 4mg IV/ IO lorazepam (0.1mg/kg if <40kg)
  - If not available 10mg diazepam IV / IO
- If seizure persists at 10 minutes – give further 4mg IV / IO lorazepam
- If no IV or IO access any of these maybe considered:
  - 10mg buccal / IM midazolam
  - 4mg IM lorazepam
  - 10mg rectal diazepam

4.3. Second line drug treatment (15-30 minutes)

- If seizure persists at 15 minutes:
  - IV / IO Levetiracetam 60mg/kg (max 4500mg) in 100ml 0.9% sodium chloride. Flush the giving set post dose with 50ml to 100ml sodium chloride 0.9% to ensure the full dose is administered. (unlicensed dosing)

Weight (kg)	Dose Levetiracetam (500mg/5ml)	Administration
45-54	3000mg (30ml)	5 minutes
55-64	3600mg (36ml)	15 minutes (However, some studies have given over 5-10 minutes but increased risk of side effects)
65-74	4200mg (42ml)	
>75	4500mg (45ml) max dose	

- If **unable** to take Levetiracetam use Lacosamide:
  - IV/IO Lacosamide 400mg Give over 30 to 60 minutes, using an infusion pump.
  - **Contraindicated in Second- or third-degree AV block**
  - Lacosamide may be administered undiluted or may be diluted in a suitable volume of sodium chloride 0.9% or glucose 5%. There is no recommended final volume/concentration for dilution; for adults, it is usually convenient to dilute in 50mL or 100mL, but smaller or larger infusion volumes can be used if necessary.
  - This medicine has a low pH and may cause venous irritation and tissue damage in cases of extravasation. If a central venous access device is unavailable, administer via a large peripheral vein monitoring insertion site closely using a recognised phlebitis scoring tool. Re-site cannula at first signs of inflammation.

- **Alternatives** (if 1st two contra-indicated)
  - IV / IO phenytoin 20mg/kg (max **2000mg**) at a maximum rate of 50mg/min
  - Give undiluted using wide bore IV access
  - Do not load if already taking phenytoin

Phenytoin Dose - IV loading
Requires continuous ECG monitoring
No filter required
If significant ↓ BP or ↓ HR half the IVI rate 25mg/min

Weight (kg)	Phenytoin Dose (250mg/5ml)	Administration Time
45-54	1000mg (20ml)	20 minutes
55-64	1200mg (24ml)	24 minutes
65-74	1400mg (32ml)	28 minutes
75-84	1600mg (36ml)	32 minutes
85-94	1800mg (36ml)	36 minutes
>95	2000mg (40ml) max dose	40 minutes

- **Other alternatives -** IV valproate 40mg/kg (max 3g) in 100ml 0.9% sodium chloride over 5 minutes

Sodium Valproate is contra-indicated in:

- Women of child bearing potential (any biological female up to the age of 55 years who is capable of becoming pregnant) unless the conditions of "Prevent" – the valproate pregnancy prevention programme are fulfilled
- Severe liver failure or mitochondrial disorder

Sodium valproate should not be prescribed to anyone under the age of 55 unless two specialists independently consider and document that there is no other effective or tolerated treatment.

Although preparation for RSI is indicated at 15-30mins, induction of anaesthesia is to be considered (in the absence of other ABCDE concerns) once medical management/optimisation has been completed and medication fully loaded at the discretion of the senior Anaesthetic/ICI decision maker available.

4.4. Third line drug treatment (Beyond 30 minutes)

- Induction of general anaesthesia followed by infusion of:

	Induction	Maintenance
Propofol	1-2.5mg/kg	1-4mg/kg/hr
Thiopental sodium	3-5mg/kg	3-5mg/kg/hr
Ketamine	0.5-2mg/kg	2mg/kg/hr initially 0.3-7.5 mg/kg/hr
Midazolam	0.1-0.2mg/kg	0.05-0.5mg/kg/hr

5. Ongoing management

Investigations (should not delay drug treatment)

- Bloods:
  - Blood gas
  - Blood glucose
  - Full blood count and clotting
  - U&Es, LFTS, Calcium, Magnesium
  - CRP
  - Anti-epileptic drug levels if already taking
  - Blood culture if any suspicion of infective component
- Urine:
  - Toxicology (if toxic cause suspected e.g. TCAs, Amphetamines, Cocaine, Tramadol, mefenamic acid)
  - Pregnancy test (in all women of child bearing age)
- Lumbar puncture if indicated and no evidence of raised intracranial pressure on clinical examination and CT head.
  - Microbiology:
    - Cell count
    - Culture and sensitivity
    - Viral PCR (HSV 1 and 2, VZV and enterovirus)
    - Consider AFB/TB PCR
  - Biochemistry:
    - Protein
    - Glucose (with paired serum glucose for comparison)
- Consider auto-immune encephalitis screen (serum/CSF) if cause remains unclear.
- Imaging
  - CXR (if suspected aspiration)
  - CT head – if no immediately apparent cause for seizure
- Septic screen as guided by clinical features
- ECG
- EEG
- Consider antibiotics if febrile/features of systemic infection
- Consider non-epileptic attacks.
- Neurology referral/discussion
- Neurology referral trust email address
- Phone - WRH 38933/Alex 44674 or on call via switchboard
- Out of hours QEHB Neurology SpR on call

6. Maintenance anti-epileptic drugs

Continue patients existing ant-epileptic medications

- Levetiracetam:
  - Commence 10-14 hours after loading dose
  - 1g BD PO/NG/IV
  - Reduce in renal impairment
    - eGFR 50-80 - 1g BD
    - eGFR 30-50 - 750mg BD
    - eGFR <30 - 500mg BD

- Lacosamide:
  - 200mg BD to be given 12 hours after initial loading

- Phenytoin
  - Commence 6-8 hours after loading dose
    - 300mg OD PO
    - 270mg OD NG (liquid)
    - 100mg TDS IV (given neat over > 2 minutes)

  - **Check level 2-4 hours after IV loading dose or 12-24 hours after oral dose**
    - Level needs correcting for serum albumin concentration
    - Phenytoin interacts with oral or enteral feed and feeding tube. This is not applicable when given IV.

- Sodium valproate
  - Commence 10-14 hours after loading dose
  - 1000mg BD PO/NG/IV

Sodium Valproate is contra-indicated in:
- Women of child bearing potential (any biological female up to the age of 55 years who is capable of becoming pregnant) unless the conditions of "Prevent" – the valproate pregnancy prevention programme are fulfilled
- Severe liver failure or mitochondrial disorder

Sodium valproate should not be prescribed to anyone under the age of 55 unless two specialists independently consider and document that there is no other effective or tolerated treatment.

Critical Care:

Consider ICU admission in the following:
- Failure to terminate seizures despite 1st and 2nd line treatments
- Low conscious level after seizures terminated
- Respiratory depression that cannot be safely managed on the ward
- Cardiovascular instability that cannot be safely managed on the ward

Continuous EEG monitoring is not available at this trust. If this is required then consider transfer to another unit.

If using high dose Propofol infusion – monitor for Propofol infusion syndrome (PRIS)

- Features:
  - Metabolic acidosis
  - Rhabdomyolysis
  - Renal failure
  - Hypertriglyceridemia
  - Bradycardia
  - Cardiac failure

- Monitoring:
  - Monitor dose given – ensure <4mg/kg/hr
  - CK
  - Triglyceride levels.
  -
- Management:
  - Change to another agent
  - Supportive – organ support as required

Rationale for choice

ESETT(a) was a prospective, randomised, double-blinded, adaptive comparative-effectiveness trial of levetiracetam (60mg/kg max 4.5g), fosphenytoin (20mg/kg max 1.5g), and valproate (40mg/kg max 3g) in adults and children aged >2 years.
It found no statistically significant difference in the effectiveness or safety amongst the three agents. Seizure cessation and improved alertness occurred at 60 minutes in approximately 50% of patients.

ConSEPT (b) and EcLiPSE (c) are multi-centre RCTs in New Zealand/Australia and UK, respectively, comparing levetiracetam to phenytoin in paediatric status epilepticus. They found levetiracetam was not superior to phenytoin.

1st line – levetiracetam
- Safe in women of childbearing potential
- Doesn't require cardiac monitoring
- Fewest drug side effects/interactions
- Routine drug level monitoring not required
- 100% bioavailability when given enterally – reduced drug errors

2nd line – lacosamide
- Simple loading schedule

3rd line – phenytoin
- Familiarity
- Safe in women of childbearing potential
- Needs cardiac monitoring
- Risk of extravasation and tissue necrosis
- Lots of drug interactions
- Phenytoin interacts with oral and enteral feed and feeding tubes. This is not applicable when administered IV.

4rd line – valproate
- Contra-indicated in women of childbearing potential (MHRA)
- Avoid in liver disease

0-5 minutes **STABILISE**	ABCDE assessment, OXYGEN, BM Tilt trolley head down, turn patient onto left lateral side IV or IO Access, Senior Help Consider Pabrinex in Alcoholic and other at risk groups
5-15 minutes **1st Line Therapy**	**IV Lorazepam 4mg** (0.1mg/kg if <40kg) (Diazepam 10mg IV if no lorazepam) No IV access consider IM Lorazepam 4mg or PR Diazepam 10mg or Buccal Midazolam 10mg If no response **REPEAT DOSE** within 5-10 mins
15-30 minutes **2nd Line Therapy**	Continuous or recurrent seizures without recovering consciousness 20 minutes after seizure onset **IV LEVETIRACETAM 60mg/kg** (max 4500mg) over 5 to 15 minutes (see box) or **IV Lacosamide 400mg** if allergic to Levetiracetam See guideline for further information
Beyond 30 minutes	Continuous or recurrent seizures without recovering consciousness **30 minutes** after **ICU**
Post Status	●**Identify and Treat cause** Consider: CT scan / CSF examination (if no obvious cause), Anti-epileptic drug levels, Septic screen, CXR (?aspiration), Pregnancy test, alcohol levels, EEG ●**Regular Anti-Epileptic Drugs** within 4-8hrs of loading (see box)

Causes of Status Epilepticus
-Acute Structural brain injury – stroke, trauma, bleed, infection, tumour, abscess
-Long standing structural brain injury – post surgery or stroke
-Anti seizure medication non adherence
-Withdrawal syndrome
- Alcohol , medication, illegal highs

-Metabolic abnormalities
- Hypoglycaemia
- Hepatic Encephalopathy
- Uraemia
- Hyponatraemia, hypocalaemia and hypomagnesaemia

-Hypoxia/Cardiac Arrest
-Demyelinating diseases

Complications Status Epilepticus
Hypoxia
Hypoglycaemia
Rhabdomyolysis
Cerebral oedema
Electrolyte disturbance
Hypotension / Hypertension
Lactic acidosis
Dysrhythmias
Pulmonary oedema
DIC

Investigations
FBC, Coag, U&Es, LFTs, Mg, Ca
ABG, ECG, βhCG (♀)
Consider CT Head , Anticonvulsant levels
SEE FULL GUIDELINE

Treatment Hypoglycaemia
If BM <4.0
Give 75-100ml 20% glucose or 150-200ml 10% glucose

Maintenance Anti-Epileptic Drugs

Within 4-8hrs of loading. Always continue patient's existing anti-epileptic drugs. See guideline for further information

Levetiracetam Dosing – IV Loading

If allergic reaction – Lacosamide / phenytoin / sodium valproate
Loading dose of 60mg/kg in 100ml of 0.9% sodium chloride 0.9% or 5% Glucose over 5 - 15 minutes

Weight (kg)	Loading Dose of Levetiracetam (500mg/5ml)	Administration
45-54	3000mg (30ml)	5 minutes
55-64	3600mg (36ml)	15 minutes (However, some studies have given over 5-10 minutes but increased risk of side effects)
65-74	4200mg (42ml)	
>75	4500mg (45ml) max dose	

Lacosamide

IV/IO Lacosamide 400mg Give over 15 to 60 minutes, using an infusion pump. For doses greater than 200mg it is preferable to give over at least 30 minutes

Contraindicated in Second- or third-degree AV block

Monitoring Tool

This should include realistic goals, timeframes and measurable outcomes.

How will monitoring be carried out?

Who will monitor compliance with the guideline?

Page/ Section of Key Document	Key control:	Checks to be carried out to confirm compliance with the policy:	How often the check will be carried out:	Responsible for carrying out the check:	Results of check reported to: *(Responsible for also ensuring actions are developed to address any areas of non-compliance)*	Frequency of reporting:
	WHAT?	**HOW?**	**WHEN?**	**WHO?**	**WHERE?**	**WHEN?**
Page 2-4	Management of Status Epilepticus as per guideline	Review of Prescribing	Contemporaneously	Patient's consultant and clinical pharmacist review	Inappropriate prescribing reported on Datix	Contemporaneously
Page 4	Sodium valproate should not be prescribed to anyone under the age of 55 unless two specialists independently consider and document that there is no other effective or tolerated treatment.	Review of Prescribing	Contemporaneously	Patient's consultant and clinical pharmacist review	Inappropriate prescribing reported on Datix	Contemporaneously

References

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 Apr 11;395(10231):1217-24.

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Status epilepticus - Symptoms, diagnosis and treatment | BMJ Best Practice

Contribution List

This key document has been circulated to the following individuals for consultation;

Name	Designation
Tom Heafield	Consultant Neurologist
Sian Bhardwaj	Consultant in Anaesthesia & Intensive Care Medicine Clinical Director Intensive Care Medicine
Nick Fitton	Consultant in Anaesthetics & ICM
James France	Consultant in Emergency Medicine
Michael McAlindon	Consultant
Andrew Gallagher	Consultant Paediatrician Lead for Epilepsy

This document has been circulated to the following CDs heads of department for comment from their directorate

Name	Directorate / Department
James France	Emergency Department

This document has been circulated to the chair(s) of the following committees / groups for comments;

Name	Committee
Alison Smith	Medicines Safety Committee

Supporting Document 1 - Equality Impact Assessment Tool

To be completed by the key document author and included as an appendix to key document when submitted to the appropriate committee for consideration and approval.

Please complete assessment form on next page;

Herefordshire & Worcestershire STP - Equality Impact Assessment (EIA) Form
Please read EIA guidelines when completing this form

Section 1 - Name of Organisation (please tick)

Herefordshire & Worcestershire STP		Herefordshire Council		Herefordshire CCG	
Worcestershire Acute Hospitals NHS Trust	x	Worcestershire County Council		Worcestershire CCGs	
Worcestershire Health and Care NHS Trust	▪	Wye Valley NHS Trust		Other (please state)	

Name of Lead for Activity	

Details of individuals completing this assessment	**Name**	**Job title**	**e-mail contact**
	Keith Hinton	**Clinical team lead Pharmacist**	**keith.hinton1@nhs.net**
Date assessment completed	**8.02.2023**		

Section 2

Activity being assessed (e.g. policy/procedure, document, service redesign, policy, strategy etc.)	**Title:** Management status epilepticus in adult inpatients				
What is the aim, purpose and/or intended outcomes of this Activity?	As per title				
Who will be affected by the development & implementation of this activity?	X X ❑ ❑	Service User Patient Carers Visitors	X ❑ ❑ ❑	Staff Communities Other _____	
Is this:	❑ New activity Planning to withdraw or reduce a service, activity or presence?				
What information and evidence have you reviewed to help inform this assessment? (Please name sources, eg demographic information for patients / services / staff groups affected, complaints etc.	See references				
Summary of engagement or consultation undertaken (e.g. who and how have you engaged with, or why do you believe this is not required)	See circulation list				
Summary of relevant findings					

Section 3

Please consider the potential impact of this activity (during development & implementation) on each of the equality groups outlined below. **Please tick one or more impact box below for each Equality Group and explain your rationale**. Please note it is possible for the potential impact to be both positive and negative within the same equality group and this should be recorded. Remember to consider the impact on e.g. staff, public, patients, carers etc. in these equality groups.

Equality Group	Potential positive impact	Potential neutral impact	Potential negative impact	Please explain your reasons for any potential positive, neutral or negative impact identified
Age		X		
Disability		X		
Gender Reassignment		X		
Marriage & Civil Partnerships		X		
Pregnancy & Maternity		X		
Race including Traveling Communities		X		
Religion & Belief		X		
Sex		X		
Sexual Orientation		X		
Other Vulnerable and Disadvantaged Groups (e.g. carers; care leavers; homeless; Social/Economic deprivation, travelling communities etc.)		x		
Health Inequalities (any preventable, unfair & unjust differences in health status between groups, populations or		x		

Equality Group	Potential positive impact	Potential neutral impact	Potential negative impact	Please explain your reasons for any potential positive, neutral or negative impact identified
individuals that arise from the unequal distribution of social, environmental & economic conditions within societies)				

Section 4

What actions will you take to mitigate any potential negative impacts?	Risk identified	Actions required to reduce / eliminate negative impact	Who will lead on the action?	Timeframe
		.		
How will you monitor these actions?				
When will you review this EIA? (e.g in a service redesign, this EIA should be revisited regularly throughout the design & implementation)				

Section 5 - Please read and agree to the following Equality Statement

1. Equality Statement

1.1. All public bodies have a statutory duty under the Equality Act 2010 to set out arrangements to assess and consult on how their policies and functions impact on the 9 protected characteristics: Age; Disability; Gender Reassignment; Marriage & Civil Partnership; Pregnancy & Maternity; Race; Religion & Belief; Sex; Sexual Orientation
1.2. Our Organisations will challenge discrimination, promote equality, respect human rights, and aims to design and implement services, policies and measures that meet the diverse needs of our service, and population, ensuring that none are placed at a disadvantage over others.
1.3. All staff are expected to deliver services and provide services and care in a manner which respects the individuality of service users, patients, carer's etc, and as such treat them and members of the workforce respectfully, paying due regard to the 9 protected characteristics.

Signature of person completing EIA	Keith Hinton
Date signed	9/02/2023
Comments:	
Signature of person the Leader Person for this activity	
Date signed	
Comments:	

Supporting Document 2 – Financial Impact Assessment

To be completed by the key document author and attached to key document when submitted to the appropriate committee for consideration and approval.

	Title of document:	Yes/No
1.	Does the implementation of this document require any additional Capital resources	No
2.	Does the implementation of this document require additional revenue	No
3.	Does the implementation of this document require additional manpower	No
4.	Does the implementation of this document release any manpower costs through a change in practice	No
5.	Are there additional staff training costs associated with implementing this document which cannot be delivered through current training programmes or allocated training times for staff	No
	Other comments:	

If the response to any of the above is yes, please complete a business case and which is signed by your Finance Manager and Directorate Manager for consideration by the Accountable Director before progressing to the relevant committee for approval