Emergency protocols

Introduction & Acknowledgement

We proudly present to you Emergency Protocols in various specialties, compiled and reviewed under the supervision of **Prof. Dr. Muhammad Mustafa Abdel Ghaffar**, Chairman of General Organisation for Teaching hospitals and institutes, and **Prof. Dr. Sherif Mohamed Safwat**, Vice President of the Organization for Technical Affairs.

We would like to express the deepest gratitude and all the appreciation to all who made this project a reality, to each one of the great advisory committee doctors in various specialties for the effort expended in these protocols, Whose collaborative efforts brought these protocols to fruition.

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ACUTE STROKE PRACTICE GUIDELINES
For The Emergency Department

OUTCOMES / GOAL

1. Rapid identification of stroke events.
2. Manage acute stroke appropriately and efficiently according to recent guidelines.
3. Evaluate in a cost-effective manner.

TRIAGE STAFF (ER DEPARTMENT)

1. Triage physician to see patient rapidly upon arrival. If presenting with stroke signs/symptoms, notify emergency neurology physician.
2. Stoke symptoms include:
   - Sudden onset of numbness or weakness of the face, arm or leg, especially on one side of the body;
   - Confusion, trouble speaking or understanding speech;
   - Trouble seeing in one or both eyes;
   - Trouble walking, dizziness, or loss of balance or coordination;
   - Severe headache with no known cause or "worst headache of my life.")

EMERGENCY DEPARTMENT EVALUATION

1. Anticipate initial patient assessment for:
   - History: age, time of symptom onset (when last normal), duration, type of symptoms, medications (antiplatelet and anti-coagulants), past medical history (CAD, HTN, DM, previous TIA/stroke, PVD, seizures/epilepsy, tobacco, illicit drug use.
   - Exam: visual fields, extraocular muscles, speech impairment, weakness or sensory deficits, incoordination, ataxia.
2. Anticipate orders for:
   - Emergency CT brain without contrast
   - Labs for CBC, RBS, INR, PTT, troponin and Chemistry
   - 12 lead ECG
   - CXR (if clinically indicated)

HYPERACUTE STROKE CARE

A. Ischemic Stroke:

1. Consider thrombolytics for all ischemic stroke patients who present with symptom onset of 3 hours or less. Select patients may be considered for thrombolytics between 3-4.5 hours of onset. Follow international practice standard for intravenous administration of rT-PA in acute ischemic stroke as appropriate with goal of door to thrombolytics less than 60 minutes.
2. Consider interventional thrombectomy maneuvers for onset of symptoms of 24 hours or Less if clinically / radiologically in candidate patients.
3. Arrange for ICU / Stroke Unit admission

B. Hemorrhagic stroke:

1. If CT subsequently shows intracranial hemorrhage (subarachnoid or intracerebral), refer international Practice Guidelines for the Inpatient Management of Patients with Intracerebral and Subarachnoid Hemorrhage.
2. Arrange for ICU / Stroke Unit admission

ADMISSION CRITERIA

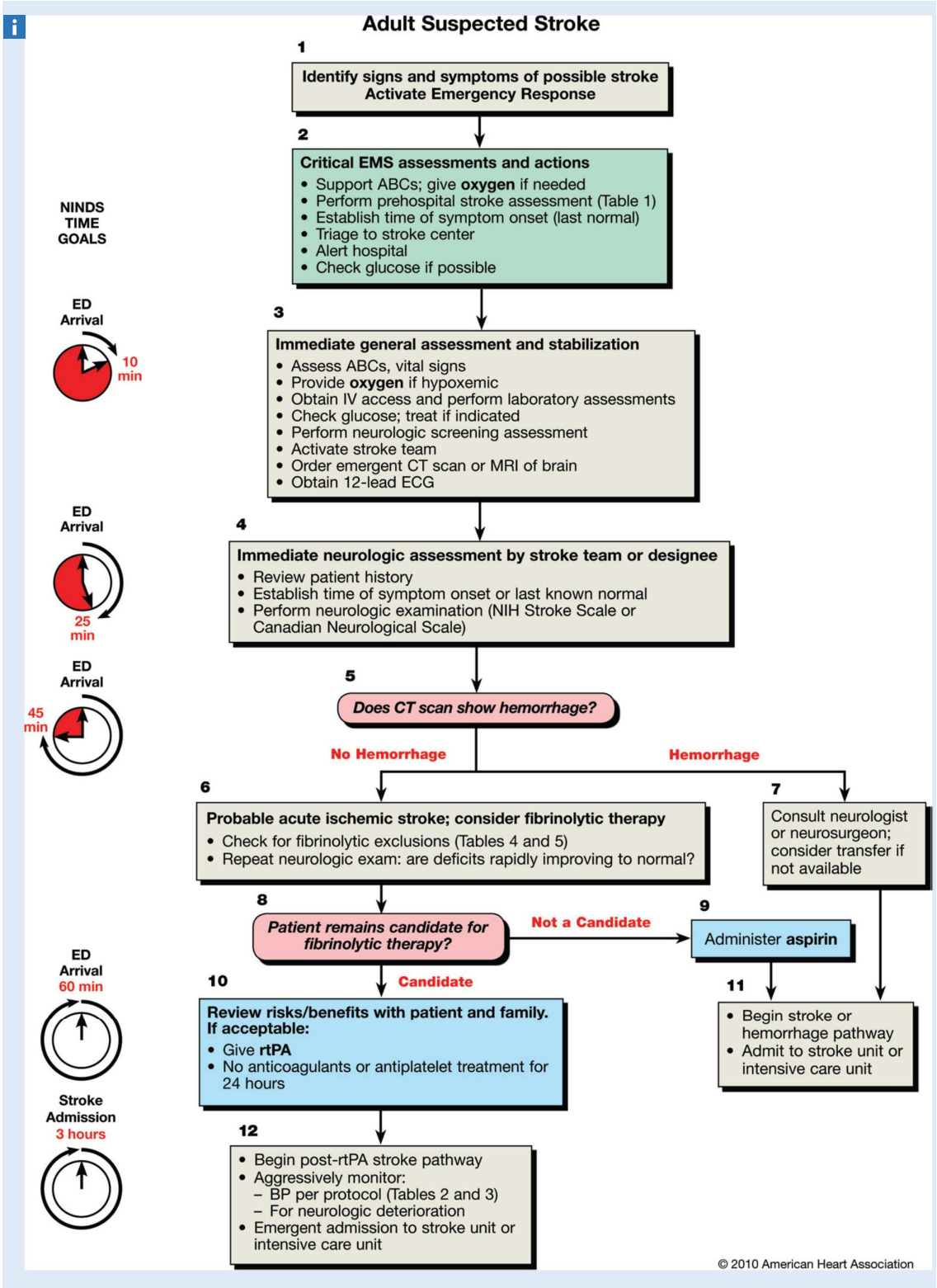
A. Criteria for admission to Neurosciences ICU / Stroke Unit:

- Acute ischemic stroke candidate for thrombolysis / thrombectomy.
- Patients with hemispheric stroke in whom impending mental status decline and loss of protective airway reflexes is of concern.
- Patients with basilar thrombosis or tip of the basilar syndrome.
- Patients with crescendo TIAs.
- Patient requiring blood pressure augmentation for a d ocumented area of hypoperfusion.
- Patients requiring IV blood pressure or heart rate control.
- Patients requiring every 1-2 hour neurological evaluation depending on symptom fluctuation or if ongoing ischemia is suspected.
- Patients with worsening neurological status.

B. Criteria for Admission to Neurology Ward

- Acute stroke symptom onset > 24 hours and not meeting above criteria.
- Non-crescendo TIAs for ischemic stroke workup.

PATIENT FLOWCHART

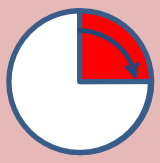


Treatment algorithm for tonic-clonic status epilepticus in adults

Timeline

t=0

t=5



t=15

t=15

Initial patient management 0-5 minutes

- Protect the patient. Do not restrain.
- Consider **airway** adjunct.
- Administer **oxygen**.
- Place patient in a semi-prone position, head down
- Gain **IV access**
- Obtain BM. **If hypoglycaemic** →

Give 150-200ml 10% glucose IV stat.

If seizures continue repeat this step AND commence 10% glucose infusion at 100ml/hr.

If suspicion of alcohol excess or malnutrition commence 1 pair Pabrinex IV BEFORE glucose replacement.

1st line treatment 5-15 minutes

If IV access

DOSE 1 – IV lorazepam 4mg bolus

Wait 5 minutes

DOSE 2 – IV lorazepam 4mg bolus

Wait 5 minutes

If no IV access

DOSE 1 – Buccal midazolam 10mg
(Alternative IM midazolam 10mg)

Wait 5 minutes

DOSE 2 – Buccal midazolam 10mg
(Alternative IM midazolam 10mg)

Wait 5 minutes

2nd line treatment 15 minutes onwards

IV or IO access
Escalate to Critical Care as per local policy

DOSE 3

IV Levetiracetam 60mg/kg, maximum 4500mg (in 100ml sodium chloride 0.9% over 10 minutes)

OR IV Phenytoin 20mg/kg, maximum 2g (rate 50mg/min, 25mg/min for elderly or patients with cardiac history, give undiluted)

OR IV Valproate 40mg/kg, maximum 3000mg (in 100ml sodium chloride 0.9% over 5 minutes)

Caution – phenytoin administration requires cardiac monitoring and wide bore IV access due to risk of extravasation and phlebitis.

	Preferred if	Avoid if
Levetiracetam (Keppra)	- Polypharmacy (fewest drug interactions)	- Mood or behavioural disorder (may worsen symptoms)
Phenytoin		- Cardiac monitoring not available - Known or suspected generalised epilepsy (genetic epilepsy) - Hypotension/bradycardia/heart block - Porphyria - Known or suspected overdose of recreational drugs / alcohol withdrawal.
Valproate	- Known or suspected idiopathic generalised epilepsy (genetic epilepsy) - Co-morbid mood disorder/migraines	- Women of childbearing potential (consider pregnancy test) - Liver disease - Pancreatitis - Known or suspected metabolic disorder/mitochondrial disease (risk of hepatotoxicity)

If ongoing seizures following the completion of the infusion **consider** 2nd IV antiepileptic drug infusion of a **different drug from the same list** (levetiracetam, phenytoin, valproate as above) **OR phenobarbital**.

Phenobarbital can be given 15mg/kg as a single dose, max. rate 100mg/min.
If at any point >30 minutes since seizure onset move to 3rd line treatment.

Ongoing management

Regular observations

12 lead ECG

Obtain FBC, U&Es, LFTs, Ca^{2+}, Mg^{2+}, clotting studies and if applicable antiepileptic drug levels and blood gas.

Treat acidosis if severe (discuss with critical care)

Determine if diagnosed epilepsy, medication history and acute seizure care plan

Consider neuroimaging and EEG

Consider possibility of non-epileptic seizures

Consider and treat potential causes:

- Medication related (poor compliance, poor absorption, recent antiepileptic drug changes, medication interactions or subtherapeutic levels)
- Infection
- Electrolyte disturbance
- Toxicity or drug withdrawal (including alcohol withdrawal)
- CNS pathology (tumour, stroke, encephalitis, PRES, neurodegenerative diseases etc.)

Seizure terminated

ABCDE assessment of patient at regular intervals.

Consider escalation to Critical Care setting if indicated

Start supportive medical care and look for underlying cause of status epilepticus

Caution when using multiple agents with similar mechanism of action in view of potential adverse effects. See Appendix 2.

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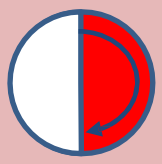
Treatment algorithm for tonic-clonic status epilepticus in adults (cont.)



t=30

t=24hrs+

24hrs+

The following stages must occur with anesthetic input, airway support and early arrangements for transfer to ITU.

3rd line treatment 30 minutes onwards (Refractory Status)

General anesthesia – induction and maintenance.

The properties of each drug should be considered when selecting induction and maintenance agents (these may be different).

	Induction	Maintenance
Propofol	1-2mg/kg bolus	up to 4mg/kg/hour titrated to effect, continuous infusion for min. 24 hours
Thiopental sodium	3-5mg/kg bolus	3-5mg/kg/hour titrated to effect, continuous infusion for min. 24 hours
Ketamine	3mg/kg bolus	1mg/kg/hour titrated to effect maximum 10mg/kg/hour, continuous infusion for min. 24 hours
Midazolam	0.2mg/kg bolus	0.05-0.5mg/kg/hour titrated to effect, continuous infusion for min. 24 hours

- General anaesthesia maintenance is typically with propofol and/or midazolam in the first instance.
- If first maintenance agent is unsuccessful at terminating seizures a second anaesthetic agent should be used.
- As a minimum, intermittent **EEG** to be performed aiming for suppression of electrographic epileptic activity.
- Maintenance doses of **antiepileptic drugs** (commence 10-14 hours after loading dose to allow regular ongoing dosing).

4th line treatment 24+ hours (Super-Refractory Status)

Seizures that continue or recur 24 hours after third line treatment are considered Super Refractory Status Epilepticus. Treatment at this stage should be guided by specialists using an MDT approach. There is no high quality randomised controlled trial evidence to guide treatment decisions.

- Look for an **underlying cause and treat** (e.g. infectious/autoimmune encephalitis, systemic infection, electrolyte disturbance, toxicity)
- **Neurosurgical intervention** (e.g. lesional resection)
- If no underlying cause identified in a first presentation of seizures, **immunotherapy** can be considered: high dose steroids, IVIG and /or therapeutic plasmapheresis
- **Alternative treatments** at this stage include therapeutic hypothermia, ketogenic diet and magnesium infusion.

Treatments considered to be ineffective should be discontinued to minimise risk of adverse effects.

Ongoing management in Critical Care Unit

At point of admission to ITU all patients should have an up-to-date ECG.

Ensure regular antiepileptic drugs are prescribed alongside any additional treatment as part of this pathway.

It is important to document why treatment decisions have been made and ensure detailed communication with next of kin regarding treatment plan and prognosis.

Caution

midazolam exhibits multiple drug interactions which should be considered: See appendix 2

Patients on **propofol** should be monitored for PRIS - propofol infusion syndrome (metabolic acidosis, rhabdomyolysis, renal failure, hypertriglyceridaemia, refractory bradycardia and cardiac failure)

Interpretation of processed EEG monitoring such as bispectral index (BIS) may become unreliable when using **ketamine** infusion.

Caution when using multiple agents with similar mechanism of action in view of potential adverse effects. See Appendix 2.

1. Introduction

Status epilepticus is a life-threatening neurological condition defined as five or more minutes of continuous seizure activity or repetitive seizures without regaining consciousness between episodes. On average, 20% of cases are fatal, although studies have reported mortality rates as high as 57% in adults [1]. Most patients have a background of epilepsy, however a number of secondary causes should be considered including stroke, infections, trauma, metabolic disorders, inflammatory conditions, CNS tumours and drug overdose.

Most convulsive seizures terminate spontaneously within three minutes and do not need emergency treatment. After five minutes of continuous seizure activity, the sooner treatment is initiated, the better the chances of seizure termination, and the lower the risk for adverse consequences.

1.1 Definitions and scope

Status epilepticus can be classified based on a number of clinical features [2]:

1) Tonic-clonic status epilepticus (generalised or focal evolving)

   Paroxysmal or continuous tonic-clonic motor activity that may be symmetrical or asymmetrical with impaired awareness. This variant of status epilepticus is the most common and has the highest associated morbidity and mortality. As a result most of the evidence for treatment interventions has focused on this patient group.

2) Focal aware motor status epilepticus

   Motor seizures localised to one side of the body with retained consciousness.

3) Status epilepticus without prominent motor symptoms

   These include a number of variants: impaired awareness cognitive status epilepticus (coma, obtundation, confusion, disorientation, confusion, disorientation, behavioural disturbance etc.), absence status epilepticus and focal impaired awareness status epilepticus.

This guideline will focus on the management of tonic-clonic status epilepticus.

The management of patients with focal aware motor status epilepticus OR status epilepticus without prominent motor symptoms (previously referred to as non-convulsive status epilepticus) have a lower risk of morbidity and mortality. The diagnosis and management of such cases can be complex and should be discussed with the on-call neurology registrar (contactable via the switchboard).

2 Treatment algorithm

2.1 Initial Management (t=0-5 minutes)

1. Protect the patient by using padded bed rails if in a bed or surrounding the patient with padding if on the ground. Do not restrain.
2. Insert an airway adjunct if safe to do so and administer oxygen.
3. Place patient in a semi-prone position with the head down to prevent aspiration.
4. Attempt to establish IV access.
5. Determine duration of seizure episode.
6. Obtain blood glucose. If the patient is hypoglycaemic give 150-200ml of 10% glucose rapidly, or equivalent dose of 20% glucose infusion. If there is any suspicion of alcohol excess or impaired nutrition commence intravenous infusion of Pabrinex 1 pair **before** glucose. If patient is hypoglycaemic and still fitting despite first glucose administration repeat IV glucose bolus then start a glucose infusion (10% glucose at 100ml/hr) [3].

Whilst continuing with the treatment pathway, the following should be considered **but should not delay drug administration**:

1. Commence regular monitoring of observations (respiratory rate, oxygen saturations, pulse rate, blood pressure and temperature).
2. Perform a 12 lead ECG for all patients.
3. Check blood glucose, full blood count, renal profile, liver function tests, corrected calcium, magnesium and clotting profile.
4. Consider treating acidosis if severe.
5. Determine epilepsy and medication history and acute seizure care plan
6. Check levels of anti-epileptic medication
7. Consider potential causes:
    a. Medication related (poor compliance, poor absorption, recent antiepileptic drug changes, medication interactions or subtherapeutic levels)
    b. Infection
    c. Electrolyte disturbance
    d. Toxicity or drug withdrawal (including alcohol withdrawal)
    e. CNS pathology (tumour, stroke, encephalitis, PRES, neurodegenerative diseases etc.)
8. Organise cross sectional neuroimaging and EEG where appropriate
9. Consider the possibility of non-epileptic seizures.

2.2 First Line Drug Treatment (t=5 minutes)

If seizures persist, at 5 minutes first line benzodiazepine drug therapy should be administered. If the patient has IV access, 4mg of IV lorazepam should be administered (DOSE 1). If after a further 5 minutes the seizure has not terminated a second 4mg of IV lorazepam can be administered (DOSE 2).

In a patient without IV access 10mg of buccal midazolam can be administered (DOSE 1) and repeated after 5 minutes if the seizure has not terminated (DOSE 2). IM midazolam can be used as an alternative if unable to give buccal midazolam due to trismus.

Dose-dependent depression of consciousness and respiratory drive may result from benzodiazepine administration. This should be considered when monitoring the patient, even once the seizure has terminated.

Up-to a third of cases are resistant to benzodiazepines and will require second line drug therapy [4,5]. This should commence 5 minutes after DOSE 2 has been administered.

2.3 Second Line Drug Treatment (t=15 minutes)

If seizures continue, IV or IO access must be obtained and the on-call anaesthetist alerted. There is no evidence based preferred second line drug treatment for status epilepticus, so the drug used should be chosen based on the underlying diagnosis, previous antiepileptic drug therapy, comorbidity and drug interactions. The results of the recently published Established Status Epilepticus Treatment Trial (ESETT) have demonstrated no significant difference in efficacy or adverse events between Fosphenytoin, Levetiracetam and Valproic Acid [6].

DOSE 3
IV Levetiracetam 60mg/kg, maximum 4500mg in 100ml of sodium chloride 0.9% over 10 minutes
OR
IV Phenytoin 20mg/kg, maximum 2000mg at 50mg/min, reduce rate to 25mg/min in elderly or patients with cardiac disease. Give undiluted with cardiac monitoring
OR
IV Valproate 40mg/kg, maximum 3000mg in 100ml of sodium chloride 0.9% over 5 minutes

The varied rate of loading should be noted. For example, in a 70kg patient phenytoin loading would take 28 minutes, levetiracetam 10 minutes and valproate 5 minutes at the above recommended rates.

Please see table below to assist with second line drug treatment decision:

	Preferred if	Avoid if
Levetiracetam (Keppra)	- Polypharmacy (fewest drug interactions)	- Mood or behavioural disorder (may worsen symptoms)
Phenytoin		- Cardiac monitoring not available - Known or suspected generalised epilepsy (genetic epilepsy) - Hypotension/bradycardia/heart block - Porphyria - Known or suspected overdose of recreational drugs / alcohol withdrawal
Valproate (Valproic Acid)	- Known or suspected idiopathic generalised epilepsy (genetic generalised epilepsy) - Co-morbid mood disorder/migraines	- Women of childbearing potential (consider pregnancy test) - Liver disease - Pancreatitis - Known or suspected metabolic disorder/mitochondrial disease (risk of hepatotoxicity)

Phenytoin administration requires cardiac monitoring and should only be given via wide bore intravenous access given the risk of tissue necrosis and extravasation.

If seizures continue despite completion of the first infusion and when it is also less than 30 minutes since seizure commenced, a second IV anticonvulsant should be considered before anaesthesia. Either a drug from the same list (levetiracetam, valproate, phenytoin as above) OR phenobarbital should be used. Phenobarbital can be given 15mg/kg as a single dose, max. rate 100mg/min. It should be avoided in acute porphyria and caution should be taken in the elderly or those at risk of respiratory depression.

If at any point more than 30 minutes have elapsed since seizure onset, general anaesthesia should not be delayed and third line drug treatments commenced.

It should be noted that there is no clear good quality evidence to guide therapy at this stage, and treatment decisions should be guided by senior clinicians with experience in managing refractory status epilepticus.

2.4 Third Line Drug Treatment (Refractory Status Epilepticus)

If seizures continue despite second line therapy, the patient is considered to have refractory status epilepticus. Mortality rates are high and as a result rapid initiation of IV anaesthetic agent should be commenced, titrated to suppress epileptic activity on EEG (urgent EEG should be arranged).

The properties of each drug should be considered when selecting induction and maintenance agents. Note that drugs selected for induction may be different to those

chosen for maintenance (general anaesthesia maintenance is typically with propofol and/or midazolam in the first instance)

Maintenance doses of antiepileptic drugs should be continued in addition to the anaesthetic agent. The general anaesthetic agent should be tapered after a minimum of 24 hours and if seizures recur either clinically or electrographically the infusion re-commenced for a further 12-24 hours.

Suggested agents:

Propofol

Induction: 1-2mg/kg bolus.
Maintenance: up to 4mg/kg/hour titrated to effect, continuous infusion for a minimum of 24 hours.

Propofol has a rapid onset of action. It commonly causes hypotension, and vasopressor support is required in 22-55% of patients undergoing infusion [7,10]. Prolonged infusions can lead to propofol infusion syndrome (PRIS), which is a rare but life threatening complication characterised by metabolic acidosis, rhabdomyolysis, renal failure, hypertriglyceridaemia, refractory bradycardia and cardiac failure. The main risk factors are high infusion rate and infusion duration above 48 hours. Management is supportive, including discontinuation of propofol along with appropriate organ support [11,12,16].

OR

Thiopental sodium

Induction: 3-5mg/kg bolus.
Maintenance: 3-5mg/kg/hour titrated to effect, continuous infusion for a minimum of 24 hours.

Thiopental is a barbiturate anaesthetic agent with good efficacy and a tendency to lower body temperature which may be beneficial in status epilepticus. Thiopental does, however, have major disadvantages. Firstly, as infusion it exhibits zero order kinetics and therefore tends to accumulate and have a long half-life. This can lead to an increased duration of ventilator dependency. Secondly, it has potent hypotensive and cardiorespiratory depressive effects, commonly requiring additional vasopressor support [14]. Continuous ECG monitoring should be performed in all patients and senior colleagues involved with treatment decision making.

OR

Ketamine

Induction: 3mg/kg bolus.
Maintenance: 1mg/kg/hr titrated to effect up to maximum 10mg/kg/hr, continuous infusion for a minimum of 24 hours.

There is an increasing body of literature supporting the use of ketamine as a third line agent in the management of refractory status epilepticus, with two randomised controlled trials assessing the efficacy and safety profile of ketamine to conventional anaesthetic agents for refractory status epilepticus currently in progress. Ketamine has a short half-life, reducing the likelihood of toxic accumulation. Compared with other drugs used for the treatment of refractory status epilepticus, respiratory depression and hypotension requiring vasopressor support are rarely observed [13].

Note, interpretation of processed EEG monitoring such as bispectral index (BIS) may become unreliable when using ketamine infusion.

OR

Midazolam

Induction: 0.2mg/kg bolus.
Maintenance: 0.05-0.5mg/kg/hour titrated to effect, continuous infusion for a minimum of 24 hours. Occasionally higher doses up to 50mg/hr may be used on consultant intensivist advice. The rationale for using the doses above 0.5mg/kg/hr need to be documented in case notes.

Midazolam is short acting, reducing the likelihood of toxic accumulation. Caution should be taken in obese patients due to accumulation in the fat tissues and those with renal insufficiency. It commonly causes hypotension, and vasopressor support is required in 30-50% of patients [7,8]. A number of studies suggest that breakthrough seizures occur more commonly with midazolam compared to other drugs used during this stage [7,9].

2.5 Fourth Line Drug Treatment

Super Refractory Status Epilepticus is defined as ongoing or recurring seizures for 24 hours after third line treatment. Treatment at this stage should be guided by specialists using an MDT approach. There is no high quality randomised controlled trial evidence to guide treatment decisions.

A detailed history should be obtained, and investigations guided by the clinical picture (usually MRI, CSF examination, metabolic screen, drug screen and autoimmune screen). Any underlying cause should be treated.

Administration and continuation of two antiepileptic drugs of differing mechanism of action should be considered alongside anaesthetic agents.

If neuroimaging demonstrates evidence of lesional epileptogenic focus, resective neurosurgery can be considered.

If no underlying cause identified and this is a first presentation of seizures a trial of high dose steroids can be considered. IVIG and therapeutic plasmapheresis can be used if no response despite 2 days of high dose steroids.

Other therapeutic options at this stage include [14,15]:

- IV Magnesium
- Therapeutic hypothermia
- Ketogenic Diet
- Paraldehyde infusion (particularly if porphyria a possibility)
- Electroconvulsive therapy

When treating outside of recommended dosage and licensing indications it is important to document treatment rationale. Detailed communication with next-of-kin should focus on causes of status epilepticus, treatment decisions and prognosis.

2.6 Indications for Intensive Care Admission (including but not limited to)

Consider admission:

- seizures continue despite 1st line (benzodiazepine) treatment at recommended dose
- unstable cardiorespiratory state
- unstable neurological state

Definite admission:

- seizures continue despite 2nd line treatments

2.7 Ongoing AED treatment

If a patient requires 2nd line treatment, antiepileptics that have been loaded should be continued at maintenance doses and discussed with neurology. The first maintenance dose of levetiracetam or valproate should be given as close to 12 hours (10-14 hours is acceptable) after the loading dose as is practical in order to allow regular maintenance dose administration, ideally during daytime hours. The first maintenance intravenous dose of phenytoin should be prescribed after 6-8 hours after the loading dose.

Suggested doses:

Levetiracetam – continue to prescribe levetiracetam maintenance 1000mg twice daily, unless eGFR<50 ml/min/1.73m^2 whereby drug monograph should be consulted. Higher doses as advised by neurology. Wait for 10-14 hours after loading dose to prescribe maintenance therapy.

Valproate – continue IV treatment up to maximum 2.5g daily (unless advised by specialist) in 2–4 divided doses by injection over 5 minutes or continuous infusion, usual dose 1000mg twice daily. When switching to oral therapy use the same total daily dose as IV treatment in 2 divided doses.

Phenytoin - initially continue to prescribe phenytoin maintenance 100 mg IV every 6–8 hours adjusted according to plasma-concentration monitoring. When converting to oral therapy use 3-4 mg/kg/day (usually 150 – 300mg given once daily at night)

Phenobarbital – then continue at 60–180 mg once daily, dose to be taken at night and discuss with neurology.

Caution: For underweight patients (less than 50kg), doses may need to be adjusted. Please discuss with local pharmacy.

For all patients on regular therapy, ensure their usual regular antiepileptic drugs are prescribed alongside any additional treatment as part of this pathway. It may be necessary to review treatment doses and discuss with the on-call neurologist or epilepsy team.

Note: some drug recommendations outlined in this guidance are 'off label' indications and based on more recent evidence.