# Status Epilepticus And Prolonged Seizures: Guideline For Management In Adults

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**Issue 1.1**  
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Who should read this document?
- All staff who manage patients who may experience epileptic seizures, in particular those working in emergency department, neurosciences and intensive care unit

Key Messages
- Benzodiazepines are the first line treatment for prolonged convulsive seizures and status epilepticus. IV lorazepam, IM midazolam or buccal midazolam are the preferred options. IV diazepam may be used in patients with IV access if lorazepam is not available
- Sodium valproate is the second line treatment of choice, except in women of childbearing age who may be pregnant, who should receive levetiracetam. Phenytoin may also be used.
- Failure to take medication as prescribed is the commonest reason for patients with epilepsy developing status epilepticus. Therefore, choice of emergency medication does not vary depending on the patients long term AED treatment.
- Patients who continue to experience seizure in spite of second line therapy, and those who fail to regain consciousness should be admitted to ICU
- Remember: Non Epileptic Attack Disorder is at least as common as epilepsy in patients presenting with apparent status epilepticus

Background & Scope
Convulsive status epilepticus is a medical emergency requiring rapid diagnosis and management to prevent both immediate complications and long-term sequelae. This policy applies to management of prolonged seizures and status epilepticus in patients aged 16 and over.
Initial management

All patients experiencing generalised tonic clonic seizures (GTCS) should have ABC management, and high flow oxygen. GTCS that last longer than 5 minutes, or two minutes longer habitual seizures in patients known to have epilepsy, have a low chance of terminating spontaneously. Therefore, emergency intravenous antiepileptic medication should be administered to all patients who experience convulsive seizures lasting 5 minutes or longer. Benzodiazepines (lorazepam, midazolam and diazepam) are first line treatment. Second line treatments include sodium valproate, levetiracetam and phenytoin. Patients whose seizures continue in spite of second line treatment should be admitted to intensive care unit for intravenous general anaesthesia with ventilation.

Emergency antiepileptic medication for prolonged convulsive seizures

First line treatment:-

Benzodiazepines are first line treatment, and should be administered if seizure is ongoing at 5 minutes.

- For patients with intravenous access, IV Lorazepam 0.1 mg/kg (usually 4 mg bolus) is the drug of first choice. IV diazepam emulsion (5-10mg) may be used if lorazepam is not available\(^1\),\(^2\)

- For patients who do not have intravenous access Non IV buccal or IM Midazolam should be used.
  
  - Treatment of choice is 10mg buccal Midazolam\(^2\)

  - Intramuscular midazolam 10mg was shown to be non inferior to lorazepam in one trial, and could be used in patients where there are no contraindications to IM injections (eg:anticoagulation). Midazolam 10mg in 2ml solution should be used for IM injection

- Rectal diazepam emulsion 10 mg should be reserved for patients with refractory epilepsy, who have rectal diazepam prescribed as their usual rescue therapy in the community\(^1\).

- A second dose may be administered if seizure is not terminated 5 minutes after administration of the first dose.

Second line treatment:-

If seizure is not terminated 20minutes after onset, in spite of administration of benzodiazepines, second line treatment should be administered. There is no clear evidence of difference in efficacy between phenytoin, valproate and levetiracetam.
Therefore, choice of therapy should be made based on patient characteristics including age, gender, reproductive status and comorbidities

- IV Sodium valproate initially 10 mg/kg (usually 400–800 mg) over 3–5 minutes followed by 1.6g by intravenous infusion over 24 hours. This is the drug of choice for patients with traumatic brain injury and high grade primary brain tumours. Valproate should be avoided in women in the child bearing age group, who may be pregnant.

- IV Levetiracetam 2000mg infused over 15 minutes, followed by 1000mg BD in patients with normal renal function. This is least likely to have significant drug interactions, and is safe in pregnancy.

- IV Phenytoin 20 mg/kg, infused slowly (maximum rate 50 mg/min). Injectable phenytoin is a high-risk medicine with the potential to cause patient harm. It should be avoided in the elderly because of increased risk of cardiovascular complications, as well as in those at risk of drug interactions (including patients on chemotherapy or anticoagulated with warfarin). Please see Appendix 1 for detailed guidance on the safe administration of intravenous phenytoin.

**Treatment of refractory status:**

Patients whose seizures continue after 40 minutes, inspite of first and second line treatment have refractory status epilepticus, and require administration of general anaesthesia, and admission to ICU.

- Midazolam, propofol and thiopentone may be used to induce general anaesthesia

- Opioids (alfentanil, remifentanil) should be avoided, as they are generally proconvulsant

- Ideally, continuous EEG monitoring should be performed to ensure that seizure activity has been suppressed, and no breakthrough seizures occur. If this is unavailable, EEG should be performed as soon as possible after induction of anaesthesia, and at regular intervals (at least daily) for the duration of anaesthesia.

- Burst suppression is the commonly used EEG target of anaesthetic drug treatment, and should be maintained for a period of 24-48 hours.

- Additional treatment with antiepileptic drugs not mentioned above, ketamine, inhalational anaesthetics, hypothermia, magnesium, pyridoxine, immunotherapy, ketogenic diet, emergency neurosurgery, electroconvulsive therapy, cerebrospinal fluid drainage, vagal nerve stimulation and deep brain stimulation may be considered in consultation with the neurology / epilepsy team.

**Algorithms** for management of prolonged seizures and status epilepticus, as well as for management of refractory status epilepticus on ICU are shown below.
Algorithm for management of prolonged convulsive seizures and status epilepticus in adults

Convulsive seizure activity >5 minutes

- Airway, Breathing, Circulation
- Start high flow O2
- IV access*, Urgent bloods*
- BM Stix, SaO2, ECG, BP

Urgent bloods
- FBC, U&E, LFTs, Ca, Mg, PO2, ESR, CRP, Coag. screen
- AED levels – patients on Sodium Valproate/Phenytoin / Carbamazepine/Levetiracetam
- Toxicology

IV Access – if this cannot be immediately obtained consider:
- Intramuscular / Buccal Midazolam 10mg

Psychogenic non-epileptic attack (Pseudoseizure)

- Observe
- Monitor SaO2, pulse, resp rate
- Avoid parenteral drugs
- Review previous records

Still doubt?
- Consider urgent EEG

Epileptic seizure

- Lorazepam 4 mg iv / Midazolam 10mg buccal/IM

Continuing seizure at 5 minutes
- Repeat Lorazepam 4mg / Midazolam 10mg buccal/IM

Seizure activity stops

Further assessment
- History from family
- Neurological exam
- Review blood results
- If no previous h/o epilepsy, or abnormal exam
  - Urgent CT brain
- If febrile and no mass on CT-> LP
  - Aciclovir 10 mg/kg IV tds
  - Ceftriaxone 2g iv BD

Further management
- Disposition will be dictated by recovery of consciousness over 10-30 min
- If GCS <10, need urgent ICU review for airway management
- Obtain urgent EEG to exclude non-convulsive SE
- If phenytoin used, send levels 2hrs post loading
- Discuss with Neurology registrar on call re optimisation of AEDs

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- Seizure activity stops
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- Review previous records

Continuous seizure activity

Further assessment
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- Neurological exam
- Review blood results
- If no previous h/o epilepsy, or abnormal exam
  - Urgent CT brain
- If febrile and no mass on CT-> LP
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  - Ceftriaxone 2g iv BD

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Psychogenic non-epileptic attack
- Psychogenic non-epileptic attack (Pseudoseizure)

- Observe
- Monitor SaO2, pulse, resp rate
- Avoid parenteral drugs
- Review previous records

Still doubt?
- Consider urgent EEG
Suggested algorithm for management of refractory convulsive status epilepticus in adults

Convulsive seizure activity for 40 – 60 minutes, not terminated by IV lorazepam x 2 and second line agent (eg: IV valproate)

General anaesthesia with
- Propofol 1-2 mg/kg bolus, repeated as necessary and then continuous infusion titrated as appropriate or
  - Midazolam 0.1–0.2 mg/kg bolus, repeated as necessary then continuous infusion titrated as appropriate

- Intubate, ventilate, arterial line, central access
- Admit to ICU
- Observe for subtle convulsive activity
- If ongoing motor activity,
  - Thiopentone 3-5 mg/ kg bolus, and continuous infusion

- Obtain urgent EEG to ensure electrographic seizures abolished and burst suppression achieved

- Continuous EEG monitoring, or regular EEG recordings
- Correct any metabolic derangement
- Ensure on adequate antiepileptic medication
  - If on phenytoin, check level – consider further IV loading dose
- Neurology review re
  - Optimise pre-existing AEDs
  - Consider second line agents
  - Treatment of underlying cause

- Daily Bloods
  - FBC, U&E, LFT, CRP, CK, Coagulation screen, Phenytoin levels
  - Consider daily EEG (if continuous monitoring not available)

Further assessment
- History from family
- Neurological exam
- Review blood results
- Urgent CT brain (all patients)
- If febrile and no mass on CT- LP
  - Aciclovir 10 mg/kg IV tds
  - Ceftriaxone 2g iv BD

Maintain burst suppression with no breakthrough seizures (clinical or EEG) for 24 - 48 hours
Standards


   http://www.epilepsycurrents.org/doi/full/10.5698/1535-7597-16.1.48

Explanation of terms & Definitions

Terms explained in document

References and Supporting Documents

   http://brain.oxfordjournals.org/content/134/10/2802.long

   http://brain.oxfordjournals.org/content/135/8/2314.long

Appendices

Appendix 1: Administration of IV Phenytoin on ANU and medical wards

Although IV phenytoin will usually be administered in an emergency setting in the emergency department, neurosciences HDU or ICU, it is anticipated that the administration of IV phenytoin will occasionally be necessary on the Acute Neurology Unit, or other medical wards.

Circumstances where this may occur include, but are not limited to:

   a) Patients recovering from acute seizures or status epilepticus that may have been treated with benzodiazepines, but who are likely to have further seizures
   b) Patients at increased risk of seizures and who are nil by mouth
   c) Patients in status epilepticus awaiting transfer to ICU
   d) Patients with refractory seizures, but in whom there are other medical reasons for not being suitable for transfer to ICU

In such cases the treating physician may prescribe IV phenytoin to be administered on the ward. In all cases where the diagnosis is not status epilepticus, as defined by the protocol, the following criteria should be met, to reduce the risk of adverse events:

- Between 16 and 60 years of age
- No history of underlying cardiovascular problems
- No chronic or acute debilitating illness, emaciation, hyponatremia, peripheral vascular disease, hemodynamic instability, or sepsis
- Good intravenous access qualified by one of the following: size at least as large as antecubital fossa vein, catheter size 20 gauge or larger, pre-existing central venous catheter
- Pain assessment possible such that intolerance to phenytoin sodium may be recognized

Table 1 Adapted from reference 5
Once the decision to administer IV phenytoin is made the following points regarding drug administration need to be considered:

<table>
<thead>
<tr>
<th>Dose</th>
<th>15-20mg/kg IV</th>
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<tr>
<td>Rate</td>
<td>Max 50mg/min</td>
</tr>
<tr>
<td></td>
<td>Healthy adult – 30-40mg/min</td>
</tr>
<tr>
<td></td>
<td>Possible cardiovascular disease – 10-20mg/min</td>
</tr>
<tr>
<td>Monitoring</td>
<td>Continuous cardiac monitoring (rate, rhythm), blood pressure every 2 minutes</td>
</tr>
<tr>
<td></td>
<td>• If pulse &lt;55 SLOW infusion rate</td>
</tr>
<tr>
<td></td>
<td>• If pulse &lt;45 STOP infusion</td>
</tr>
<tr>
<td></td>
<td>• If pulse &lt;35 CALL doctor</td>
</tr>
<tr>
<td></td>
<td>• If systolic BP &lt; 110 SLOW infusion rate</td>
</tr>
<tr>
<td></td>
<td>• If systolic BP &lt; 100 STOP infusion</td>
</tr>
<tr>
<td></td>
<td>• If systolic BP &lt; 90 CALL Doctor</td>
</tr>
<tr>
<td></td>
<td>• If symptomatic with hypotension (clammy, lightheaded) CALL Doctor and commence IV Fluids (Gelofusin 500ml in 1 hr)</td>
</tr>
<tr>
<td></td>
<td>• If patient becomes unresponsive CRASH call, STOP infusion</td>
</tr>
<tr>
<td>Infusion</td>
<td>Begin and complete preparation and infusion within 1 hour</td>
</tr>
<tr>
<td></td>
<td>Infuse through free-flowing IV of 0.9% sodium chloride</td>
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<tr>
<td></td>
<td>Use 5 micrometre in-line particulate filter</td>
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Table 2. The above monitoring parameters may be altered by the attending physician in individual cases such as patients whose initial BP is very high (known hypertensives) or physiologically low (healthy young adults)
Appendix 2: Algorithm for IV phenytoin administration on ANU

Once the decision is made to administer IV phenytoin on ANU the following algorithm can be followed, particular attention must be paid to monitoring for infusion site reactions and cardiovascular instability:

IV Phenytoin

Criteria for administration met (see Table 1)

Give IV phenytoin (see Table 2)

Monitor injection site

Monitor cardiac rate rhythm and blood pressure

Extravasation?

Burning?

Bradycardia?

Hypotension?

Stop infusion

Slow infusion

Slow infusion, monitor

Restore volume, slow infusion, monitor

Persistent

Persistent

Persistent

Persistently stop infusion, elevate limb, apply heat

Persistently slow infusion

Persistently stop infusion

Persistently stop infusion