

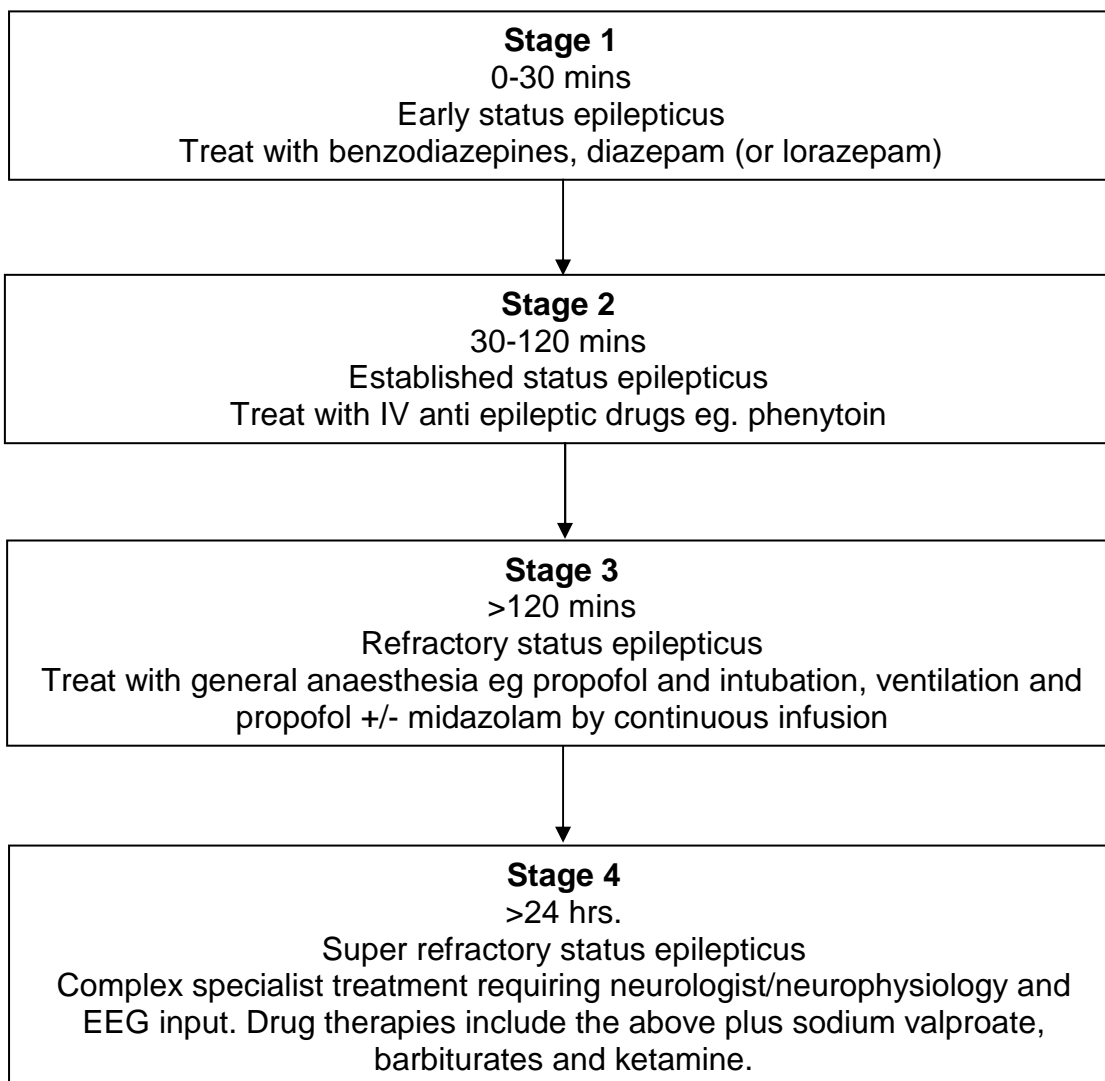
**Critical Care Guidelines  
FOR CRITICAL CARE USE ONLY**

## **Critical care guideline for the treatment of status epilepticus**

Status epilepticus is defined as more than 30 minutes of:

- Continuous seizure activity or;
- Two or more sequential seizures without full recovery of consciousness between seizures<sup>1</sup>

Management of status epilepticus is conveniently described by a stepwise approach. Critical Care is usually involved from stage 2 or 3 onwards or where intubation and ventilation are required.



<b>Title: Critical care guideline for the treatment of status epilepticus</b>	
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**Investigation**

History and examination.

Identify and treat the underlying causes of seizures.

Blood glucose: identify and treat hypoglycaemia.

Imaging: CT, MRI, EEG. CSF examination, metabolic screen, anti-NMDA receptor antibody assay.

**Drug Treatment Guidelines**

The general stepwise addition of drug treatment is outlined below. Preparation information for all drugs can be found in appendix 1.

**Stage 1.**

Early status epilepticus 0-30minutes.

Initial treatment is with **diazepam** emulsion (Diazemuls®).

- 2mg increments IV initially up to 10mg over 5 minutes.
- Alternative is IV lorazepam 4mg slow IV into a large vein.
- Repeat diazepam once 15 minutes later up to total 20mg if required.
- Repeat lorazepam once 15mins later up to a total of 8mg, if required.<sup>1</sup>

**Stage 2.**

30-120 mins

Established status epilepticus

- Load with **phenytoin** and commence maintenance dose.
- Loading dose 20mg/kg ( see appendix 2 for dosing in obesity).  
Caution in frail and elderly as may cause significant hypotension.  
Consider loading in two divided doses.
- Maintenance dose 100mg 8 hourly IV.
- Check level morning following loading to check adequate loaded. See appendix 2 for details of levels.<sup>2</sup>

**Stage 3**

>120 mins

Refractory status epilepticus

Induce general anaesthesia. Intubate and ventilate with general supportive ICU care. Use drugs as follows in a stepwise fashion.

**Propofol**

Initial bolus to induce anaesthesia

Maintenance infusion of up to 4mg/kg/hr<sup>4,5</sup>

**Midazolam**

Loading dose bolus: 0.1-0.2mg/kg

Maintenance infusion 0.05-0.4mg/kg/hr. If breakthrough SE give a further bolus and increase the infusion every 3-4hours by 0.05-0.1mg/kg/hr.<sup>4,5,6</sup>

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**Sodium valproate**

Loading dose of 30mg/kg i.e. 2100mg if 70kg. If obese use ideal body weight. Maintenance infusion of 2400mg over 24 hours. Ammonia levels should be performed for patients started on valproate approximately two days after starting valproate. See appendix 3. <sup>3,4,5</sup>

**Stage 4**

>24 hrs.

Super refractory status epilepticus. Status epilepticus that has continued despite general anaesthesia. This requires complex specialist treatment involving a collaborative approach with neurology and neurophysiology, EEG input and continuous EEG monitoring. By this stage the seizures are often non convulsive.

**Phenobarbitone**

Loading dose of 10mg/kg IV up to a maximum of 1000mg.

Maintenance dose of 120mg once daily IV. <sup>2,3</sup>

**Thiopentone**

Using a 25mg/ml solution for a 70kg adult infuse approximately:

40mls per hour for 1 hour

24mls per hour for 2 hours

12-20mls per hour thereafter <sup>14</sup>

**Ketamine**

There is evidence on the use of ketamine, it is mostly based on isolated case reports. From the information available:

Loading dose of 50mg

Maintenance infusion of 1-5mg/kg/hr. <sup>7,8,9,10,11,12</sup>

It is recommended that increased intracranial pressure should be excluded before ketamine is administered.<sup>9</sup> There are few published data on the theoretical risk of neurotoxic effects when the drug is used for prolonged periods and its safety in prolonged use is largely untested.

**Other treatments**

Inhalational anaesthetic agents

Magnesium infusion

Hypothermia

Ketogenic diet

For auto-immune encephalitis: high dose steroids, immunoglobulin and plasma exchange, in consultation with neurologist specialist/epileptologists.

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14. LUHD Critical Care monograph for administration of thiopentone.

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**Appendix 1**

<b>Drug</b>	<b>Preparation and administration details</b>
Diazemuls	Undiluted at max rate of 5mg per minute
lorazepam	Undiluted as slow IV into a large vein
phenytoin	<p>Undiluted if given centrally or up to 10mg/ml if diluted i.e up to 1g in 100ml sodium chloride 0.9%, &gt;1g &lt;2.5g in 250ml sodium chloride 0.9%. Incompatible in glucose 5%</p> <p>Phenytoin may be administered centrally without dilution at a maximum rate of 50mg/minute but it is preferable to administer more slowly to minimise the hypotensive effects e.g. 100mg over 3-5minutes, 1000mg over 60 minutes. If diluted as per the standard infusion the solution can be administered over 60 minutes (but no greater than 60 minutes due to physical incompatibility of the infusion). If there is concern over hypotensive effects of large doses the loading dose can be split into 2 infusions, each given over one hour.</p>
propofol	1g in 100ml NEAT
midazolam	<p>60mg in 60ml glucose 5%</p> <p>Boluses over 3-5 minutes, maintenance by continuous infusion</p>
sodium valproate	<p>Sodium valproate injection may be given undiluted by slow intravenous injection over 3-5 minutes, by an intermittent infusion or by a continuous infusion.</p> <p>Dilute the required dose of sodium valproate injection, whether for intermittent or continuous infusions, in 100ml glucose 5% infusion. Sodium valproate infusion is usually administered as an intravenous infusion over 60 minutes at a rate that does not exceed 20mg/minute i.e. maximum of 1200mg over 60 minutes.</p>
phenobarbitone	<p>loading dose and maintenance dose:</p> <p>One ml phenobarbitone injection should be diluted with 10ml water for injections and given at a max rate of 100mg/min.</p> <p>So for maintenance dose if using 60mg/ml injection, 2ml (120mg) should be diluted in 20ml water for injections (final volume 22ml) and given over at least two minutes.</p>
ketamine	<p>loading dose: if using 100mg/ml solution dilute with equal volume of sodium chloride 0.9%. 50mg/ml solution can be give undiluted. Give over at least one minute.</p> <p>maintenance infusion: 2000mg ketamine in 40mL UNDILUTED. i.e 50mg/ml . Reference for this is ketamine monograph in Renal Drug Handbook in administration section.</p> <p>Ketamine does not need to be administered in a locked syringe.</p>
thiopentone	1500mg in 60ml water for injections

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## **Appendix 2**

### **Phenytoin**

#### **Dosing in obesity**

The dose is calculated using an “adjusted body weight” (ABW) that is equal to the ideal body weight (IBW) plus the product of 1.33 times the excess over IBW.

IBW is calculated as follows:

IBW females= 45.5kg + (2.3kg per inch over 5 feet)

IBW males= 50kg + (2.3kg per inch over 5 feet)

ABW (obese) = IBW + (1.33 x (actual weight – IBW))

**Loading dose** = 20mg/kg (using ABW)

**Maintenance dose** = 4mg/kg (using ABW)

#### **Interpreting serum concentrations**

Aim for 15-20microgram/ml. Toxicity between 20-30 microgram/ml is ataxia

#### **Correcting for low albumin**

Factor=  $0.9 \times \frac{\text{albumin}}{40} + 0.1$

Actual level=  $\frac{\text{measured level}}{\text{Factor}}$

#### **Correcting for renal impairment**

Use this equation in patient's with a CrCl 10mls/min or if being haemofiltered. The free fraction of phenytoin increases in renal impairment.

Factor=  $0.48 \times \frac{\text{albumin}}{40} + 0.1$

Actual level=  $\frac{\text{measured level}}{\text{Factor}}$

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**Appendix 3**

**Ammonia blood concentrations**

Sodium valproate therapy can cause hyperammonaemia, especially in the early stages of therapy.

An ammonia concentration should be measured at approximately two days after starting sodium valproate. Consider rechecking while on sodium valproate particularly if the patient's conscious level does not improve despite control of the seizures or if the patient shows signs of encephalopathy.

Take samples of blood into Lithium Heparin tubes (avoiding any contamination with sweat).

Call the RHSC duty biochemist on 20403. Send by taxi during office hours.