MIL

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This Medicines Information Leaflet is produced locally to optimise the use of medicines by encouraging prescribing that is safe, clinically appropriate and cost-effective to the NHS.

Guidelines for the Management of Generalised Status Epilepticus in Adults

Status epilepticus is defined as seizure activity lasting 5 minutes or longer, or more than one seizure in 5 minutes without recovery between seizures[1]. Beyond 30 minutes, there is a risk of neurological injury[1]. Generalised tonic-clonic status epilepticus is a neurological emergency requiring urgent treatment.

Causes: Many cases occur in patients without a history of epilepsy. Possible causes include:[2]

▪ Encephalitis & meningitis	▪ Drug toxicity & alcohol abuse
▪ Trauma	▪ Cerebral tumours
▪ Acute metabolic disturbance e.g. hypoxia, hypoglycaemia, hyponatremia, hypocalcaemia.	

Mortality: The rate in adults has been estimated at 18% with 2% directly due to status epilepticus; the remainder are attributed to the underlying cause, e.g. tumour or encephalitis.[2]

Morbidity: Status epilepticus is a major risk factor for the development of:[2]

- Chronic Epilepsy
- Cerebral damage
- Focal deficits
- Intellectual deficits

Management

Seizure activity that continues for more than **5 minutes** should be managed with as a medical emergency with anti-seizure medication. This should be started as soon as possible to prevent neuronal damage.

General measures - Stabilisation Phase

(0-5 minutes of seizures activity)

Airway – Ensure the airway is patent. Focus on jaw thrust and nasopharyngeal / oropharyngeal adjuncts.

Breathing – Provide 15L/min oxygen via a non-rebreathe mask. Monitor for respiratory depression – use end tidal capnography placed under the oxygen mask if available. (Patients suffering from prolonged seizures are at risk of aspiration and therefore require early referral to Intensive Care Medicine for consideration of endotracheal intubation)

Circulation - Continuous monitoring oximetry, ECG and blood pressure every 5 minutes.

- Ensure the patient has intravenous (IV) access. Consider intraosseous (IO) access to the humeral head or tibia if unable to secure IV access. Remember that lorazepam can be given intramuscularly (onset of action will be slower).
- Check blood glucose. If hypoglycaemic give IV glucose 20% (75mL)
- Send samples for FBC, U&Es, Ca, Mg, LFTs and plasma anti-seizure medication concentrations if already taking carbamazepine, phenytoin, phenobarbital, or sodium valproate.
- For new onset seizures in A&E, do appropriate toxicology tests if an overdose or alcohol intoxication is suspected
- Check blood gases.
- Continue any anticonvulsant drugs for those already on medication (IV, PR or via nasogastric tube).
- Examine the patient to establish the cause of the seizures, obtain a history from any accompanying person, and check for MedicAlert jewellery.

Drugs – If seizure activity continues for more than two minutes then prepare benzodiazepine dose for administration as below

Early Status Epilepticus - (5-10 minutes of seizure activity)

Administer benzodiazepine **at 5 minutes** of ongoing seizure activity (see below)

- **Lorazepam** 4 mg given as a slow IV bolus over 2 minutes. This may be repeated once (5 minutes after the first dose) if seizures recur or fail to respond - Maximum cumulative dose of 8mg
  If IV access is not possible consider lorazepam via IM / IO route (onset of action will be slower).

Lorazepam is stored in a fridge. If lorazepam is not immediately available use diazepam emulsion injection instead (diazepam emulsion injection is not suitable for IM injection).

- **Diazepam** emulsion injection 5-10 mg given as a slow IV bolus over 2-4 minutes. This may be repeated after 5 minutes if seizures recur or fail to respond. Maximum cumulative dose of 20mg
- Ensure that full resuscitation facilities are readily available in case of respiratory compromise.

Established Status Epilepticus - (10-30 minutes of seizure activity)

If seizure activity continues for 10 minutes despite benzodiazepines, load with levetiracetam or phenytoin by IV infusion.

Levetiracetam dose and administration: Give IV levetiracetam 2g in 100ml sodium chloride 0.9% over 10 minutes (40mg/kg if body weight less than 40kg) followed up with 20ml sodium chloride 0.9% infusion line flush. For patients already on levetiracetam, or for patients already on both levetiracetam and phenytoin, levetiracetam 2g may still be administered (or levetiracetam 1g if existing renal impairment).

Phenytoin dose and administration: Loading dose in **phenytoin naïve patients**: 20mg / kg up to a maximum of 1.5g (Up to 2g has been used in exceptional circumstances)[3,4] . **For patients already taking phenytoin**: give half loading dose of 500 mg. **IV phenytoin** should be given undiluted into a large vein using a syringe pump at 1mg/kg /min (Max 50mg per minute). Slow or stop the infusion if evidence of cardiovascular compromise. After the end of the infusion, administer a slow flush (1mL/minute) of sodium chloride 0.9% through the giving set. Monitor ECG & BP continuously during phenytoin infusion.

If the status persists, call Neurology SpR on bleep 6243, inform ITU about a potential patient and consider giving IV levetiracetam / phenytoin if not already given. Alternatively following Neurology advice give sodium valproate or phenobarbital.

Intravenous sodium valproate 25-40 mg/kg bolus (up to 500mg/min, Max 3000mg) Avoid in pregnancy

Intravenous Phenobarbital must be administered only in the presence of an anaesthetist or intensivist, ideally in critical care as IV phenobarbital may cause respiratory depression and hypotension.

Phenobarbital loading dose: 15mg/kg to a maximum of 1000mg IV at a rate of 100mg/min. Use the 200mg/ml injection solution diluted with water for injection to a concentration of 20mg/ml
Phenobarbital maintenance dose: 1-4 mg/kg as a single daily dose, adjusted according to plasma concentration.

Consider a 3rd non-anaesthetic anticonvulsant before induction of coma (particularly if the patient is in non-convulsive status, where anaesthetic agents are preferably avoided) [4]

Refractory Status Epilepticus - (30-60 minutes of seizure activity)

If seizures continue despite benzodiazepines and levetiracetam, phenytoin +/- phenobarbital, the patient will require induction of anaesthesia, intubation and ventilation (if not already undertaken), transfer to Intensive Care for for treatment with IV anaesthetic agents (propofol ± midazolam ± thiopental) and discussion with a Neurologist.

Algorithm for the Management of Generalised Status Epilepticus

Time line	Interventions
0-5 minutes **Stabilisation**	**First aid**: Secure the airway & administer Oxygen **Access**: Aim to secure two IV lines (consider IO if unable to secure IV access) **Monitors**: Continuous oximetry, ECG and blood pressure **Assessment**: Cause and history of epilepsy **Blood Tests**: Blood glucose, blood gases, FBC, U&Es, (including Ca & Mg) LFTs, anti-seizure medications plasma concentrations if already taking carbamazepine, phenytoin, phenobarbital, or sodium valproate and toxicology tests as appropriate **Hypoglycaemia**: If blood glucose is below 4 mmol, commence glucose 20% (75ml) IV infusion over 10 minutes **Drugs:** If seizure activity continues for more than two minutes then prepare benzodiazepine dose for administration as below
5 – 10 minutes **Early status**	**Give Benzodiazepine, either lorazepam or diazepam at 5 minutes** **Lorazepam** 4mg given as a slow IV/IO bolus over 2 minutes or IM (lorazepam is stored the fridge. If lorazepam is not immediately available use diazepam emulsion injection instead **Diazepam** emulsion injection 5mg given as a slow IV/IO bolus over 2-3 minutes **Ensure full resuscitation facilities are readily available in case of respiratory compromise.** If IV access is not possible consider lorazepam via IM / IO route (onset of action will be slower).
10 – 30 minutes **Established**	**Yes** — **Seizures continue** — **NO** **Give IV** Levetiracetam or/and Phenytoin **Give Levetiracetam** IV infusion 2g in 100ml sodium chloride 0.9% over 10 minutes (40mg/kg if body weight less than 40kg) followed up with 20ml sodium chloride 0.9% infusion line flush. The **Phenytoin loading dose in phenytoin naïve** patients is 20mg / kg up to a maximum of 1.5g (Up to 2g has been used in exceptional circumstances). **For patients who are already taking Phenytoin,** whilst awaiting plasma phenytoin level results, give half loading dose of 500 mg Give Phenytoin undiluted into a large vein using a syringe pump at a rate of 1mg/kg/min (max 50mg/min) after the end of the infusion, administer a slow flush (1ml/min) of sodium chloride 0.9%. Monitor ECG and BP continuously during the infusion. **If the status continues a further dose of levetiracetam (1g if body weight 50-65kg or 2g if body weight above 65kg) may be administered after 10 minutes** **or following neurologist advice, sodium valproate or Phenobarbital** (refer to main document for dosing information) **Known history of epilepsy** Check for change in antiepileptic medicines, compliance, infection or progression of disease. Continue antiepileptic medicines IV, PR or NG if necessary Speak to a Neurologist **No history of seizures** Speak to a Neurologist
30 –60 minutes **Refractory status**	**Yes** — **Seizures continue** — **NO** **Transfer to Intensive Care and discuss with a Neurologist** **Maintenance Therapy** Discuss with a neurologist regarding future anti-epileptic therapy to prevent further seizures

- If alcohol abuse or malnutrition is suspected give intravenous Pabrinex. (refer to Alcohol withdrawal MIL)

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