Guideline for the in-hospital drug treatment of convulsive status epilepticus in adults

Generalised, convulsive status epilepticus refers to five or more minutes of continuous seizures, or two or more discrete seizures between which there is incomplete recovery of consciousness[1].

Evidence suggests that achieving seizure control quickly is a major determinant of good outcome[2]. **The priority in status epilepticus management is to achieve rapid termination of seizures, regardless of the agent used.**

Stage 1 - Early status epilepticus

Start high flow oxygen. Check glucose.
See full guideline for emergency management of seizures.

Administer benzodiazepine if seizure lasts ≥5 minutes.
If intravenous access is available:

- First choice: **lorazepam 4mg IV** over 2 minutes.
- OR **diazepam* 10mg IV** over 2 minutes.

If intravenous access is not available:

- First choice: **buccal midazolam 10mg.**
- OR **rectal diazepam 10mg**.

Benzodiazepine doses can be repeated once after 5-10 minutes if first administration does not terminate seizure. Beware respiratory depression.
*Diazepam is rapidly redistributed and may accumulate with repeated dosing.
Prepare Stage 2 drugs during Stage 1. Gain IV access.

Stage 2 - Established status epilepticus

If seizures persist, administer loading dose of antiepileptic drug intravenously. Notify intensive care.

First choice:

- **Levetiracetam 60mg/kg** (max dose 4500mg) over 10 minutes[3].

Second choice:

- **Phenytoin 20mg/kg** (max dose 2000mg) at max rate 50mg/minute[3].
  Infuse into a large vein with ECG and blood pressure monitoring due to risk of hypotension and bradycardia. Use with caution in elderly and patients with cardiac disease.

OR

- **Sodium valproate 40mg/kg** (max dose 3000mg) over 10 minutes[3]. First choice in severe renal failure. Use alternative where possible in **pregnancy**, acute liver failure or if there are concerns about mitochondrial disease.

Stage 3 – Refractory status epilepticus

If seizures persist 15 minutes after administration of stage 2 drug , proceed to general anaesthesia with intubation and ventilation.

Consider at any stage if haemodynamically unstable or respiratory support required. Drugs should be administered by experienced intensivist or anaesthetist in intensive care unit setting.

Consider addition of second anticonvulsant drug from Stage 2.

Loading dose administration

- Levetiracetam: administer in 100ml of 0.9% sodium chloride or 5% glucose over 10 minutes.
- Phenytoin: administer in 50-250ml of 0.9% sodium chloride (concentration not to exceed 10mg/ml) at a rate not exceeding 50mg/minute through an in-line filter (0.22-0.5 micron). Ensure working cannula in large vein prior to infusion due to risks associated with extravasation (see NHS Lothian IV guide).
- Sodium valproate: administer in 50ml of 0.9% sodium chloride or 5% glucose over 10 minutes.
  Note: levetiracetam and sodium valproate doses are based on the ESETT trial[3] and differ from those in NHS Lothian IV monographs.

Special circumstances

1. **Patient already prescribed levetiracetam:**
   Levetiracetam can be used as the first choice anticonvulsant drug during Stage 2 at full dose, even if the patient was already prescribed levetiracetam prior to admission. Levetiracetam levels are not available acutely, and supratherapeutic doses of levetiracetam are unlikely to be harmful. If there is concern about administering levetiracetam in this context, sodium valproate or phenytoin can be given instead.
2. **Pregnancy**
   Levetiracetam is the preferred Stage 2 drug in pregnancy. Avoid sodium valproate where possible (risk of teratogenicity).
3. **Known severe renal failure**
   Where eGFR is known to be less than 30 mL/min/1.73m^2, then sodium valproate should be used as first choice Stage 2 drug. No dose adjustment is required. Do not delay treatment to wait for blood results.
   Levetiracetam is an appropriate second-line option (no dose adjustment), but the maintenance dose should be reduced (see below).

Maintenance doses of anticonvulsant drugs:

- Levetiracetam: 1000-1500mg IV, oral or NG twice daily. Start 10-12 hours after loading dose. Aim for reasonable dosing times 12 hours apart.

  Maintenance doses of levetiracetam in renal impairment[4]:

Creatinine Clearance	Dose
50-79ml/min	1000mg twice daily
30-49ml/min	750mg twice daily
<30ml/min	500mg twice daily

  In CVVHD dialysis give 750mg twice daily. For other forms of dialysis consult renal physician.

- Phenytoin: 300mg IV once daily, or 100mg IV three times per day, or 300mg oral capsules once daily. Prescribe 270mg once daily if using oral liquid. Start 6-8 hours after loading dose. Check phenytoin trough level 24-48 hours after starting maintenance dose. If phenytoin is to be administered down a feeding tube contact pharmacy for advice.

- Sodium valproate: 1000-1200mg IV, oral or NG twice daily. Start at least 6 hours after loading dose. **Maintenance doses of sodium valproate must not be started in women of childbearing age unless a Pregnancy Prevention Programme is in place – contact neurology for advice**.

References

1. Trinka E, Cock H, Hesdorffer D, Rossetti AO, Scheffer IE, Shinnar S, et al. A definition and classification of status epilepticus--Report of the ILAE Task Force on Classification of Status Epilepticus. Epilepsia. 2015 Oct;56(10):1515–23.
2. Neligan A, Shorvon SD. Prognostic factors, morbidity and mortality in tonic–clonic status epilepticus: A review. Epilepsy Res. 2011 Jan 1;93(1):1–10.
3. Kapur J, Elm J, Chamberlain JM, Barsan W, Cloyd J, Lowenstein D, et al. Randomized Trial of Three Anticonvulsant Medications for Status Epilepticus. N Engl J Med. 2019 28;381(22):2103–13.
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