

In-Hospital **Emergency** Drug Management of Convulsive Status Epilepticus in Adults
See page 2 for essential parallel general measures

First choice:

Intravenous lorazepam; Usual dose bolus **2 to 4 mg** (maximum rate 2 mg/min). If necessary repeat up to a total maximum dose of 0.1 mg/kg.

OR Intravenous diazepam: Usual dose **5 to 10 mg** titrate for effect, up to 20 mg if necessary. Do not give too fast, to avoid respiratory depression (maximum rate 5 mg/min).

Diazepam is rapidly redistributed and may accumulate with repeated dosing.

OR Intravenous clonazepam: Usual dose 1 mg, if necessary repeat 1 mg dose after 5 minutes (maximum rate 0.5 mg/min).

If intravenous is difficult or not possible:

• **Buccal midazolam**: Usual dose **10 mg** (Caution: Give 5 mg in the elderly or patients less than 50 kg). Repeat dose once after 10 minutes if necessary.¹

If buccal preparation not available, use 10 mg/2 mL injection via buccal route.

OR Intramuscular midazolam: Usual dose 10 mg (Caution: Give 5 mg in the elderly or patients weighing less than 50 kg). Repeat dose once after 10 minutes if necessary.

If intravenous, buccal and intramuscular are not possible:

• **Rectal diazepam**: Usual dose **10 mg** (caution: give 5 mg in elderly patients or patients weighing less than 50 kg). Repeat dose once after 10 minutes if necessary.

STEP 1:
benzodiazepine
give if fitting for
> 5 min

If seizures stop, the recurrence rate is high; most patients need an intravenous stage 2 anti-epileptic drug (see below for doses) to prevent further seizures

Second stage antiepileptic drug given **intravenously and inform neurointensivist or experienced anaesthetist**

See loading dose proformas for administration guidance

If there is no specific contraindication or a clear preference for alternative:

Phenytoin; 18 mg/kg (range 15–20); **maximum rate 50 mg/min**. Infuse into large or central vein via filter with ECG and blood pressure monitoring (caution **hypotension, bradycardia**). Check concomitant drugs (phenytoin is an enzyme inducer—its effect on the half-life of affected drugs is not immediate). For patients already on phenytoin, see note on page 2* before administering.

OR

Levetiracetam; 30 mg/kg (range 20–70); **infuse over 10 minutes**; no interactions; good side effect profile in this setting but comparative efficacy remains to be established; renal excretion.^{2,3}

OR

Sodium Valproate; 30 mg/kg (range 15–30); **infuse over 5 minutes**

Contraindicated in mitochondrial disease. Avoid in status of unknown cause in young people.

Caution: in pregnancy or acute liver failure, where an alternative is preferable. Check concomitant drugs (valproate is an enzyme inhibitor, with immediate effect on half-life of affected drugs).^{4,5}

OR

Phenobarbital; 10 mg/kg (range 10–15); **maximum rate 100 mg/min**. Monitor blood pressure, ECG and respiratory function (Caution: **respiratory depression** may occur—only give if ventilatory support can be provided). Check concomitant drugs (phenobarbital is an enzyme inducer—the effect of enzyme induction on half-life of affected drugs is not immediate).

STEP 2:
If no response to
step 1 **WITHIN 10**
min, give stage 2
agent
and
**INFORM NEURO-
INTENSIVIST or
EXPERIENCED
ANAESTHETIST**

ENSURE NEUROINTENSIVIST/EXPERIENCED ANAESTHETIST IS AWARE OF THE PATIENT

If seizures recur in patients who are haemodynamically stable, optimise dose of initial second stage intravenous antiepileptic drug and then consider another second stage intravenous antiepileptic drug.

General anaesthesia with intubation and ventilation

Consider if haemodynamically unstable at any stage or if respiratory support is needed

- These drugs must be **administered by a neurointensivist/experienced anaesthetist in an intensive care unit (ICU) setting** as per local protocols to control clinical/EEG seizures
- **Induction** – usually propofol (1.5–3 mg/kg bolus) caution hypotension, bradycardia **OR**
 - thiopentone (usually 3–5 mg/kg bolus, additional boluses of 50 mg every 3 minutes until seizures terminated, may be given if blood pressure remains stable)
- **Maintenance** – Propofol 1–5 mg/kg/hour titrated to effect; prolonged use may lead to propofol infusion syndrome **OR**
 - midazolam if patient already ventilated, initial bolus 1 mg intravenously and titrate to effect then 0.05–0.20 mg/kg/hour titrated to effect **OR** consider propofol with midazolam **OR**
 - thiopentone 3–5 mg/kg/hour titrated to effect. Caution: hypotension, cardiac suppression, immunosuppression, hypokalaemia, pancreatitis and drug accumulation
- **EEG monitoring is indicated (continuous or minimum every 24 hours) to assess level of anaesthesia and abolition of ictal discharges.**

STEP 3:
If no response to
step 2 within 30
minutes of onset
anaesthesia and
ICU admission

Over next 24–48 hours, optimise doses and levels of non-anaesthetic anti-epileptic drugs and, if no electrical or clinical evidence of ongoing seizures, withdraw anaesthesia to assess response.

General Management - In Parallel to Drug Management

General Medical Measures

Secure airway and resuscitate

Administer oxygen

Assess cardiorespiratory function

Establish intravenous access (large veins if possible)

Measure capillary blood glucose and immediately correct hypoglycaemia.

Give 75 mL 20% glucose intravenously over 5 minutes

If no intravenous access 1 mg intramuscular glucagon

Re-check blood glucose after 15 minutes

Check temperature

Check blood gases

If poor nutrition/alcohol abuse suspected give:

Pabrinex[®] (thiamine, riboflavin, pyridoxine, ascorbic acid, nicotinamide) ONE PAIR intravenously
OR over 10 minutes

Thiamine 100 mg intravenously in 100 mL 0.9% sodium chloride over 30 minutes

If woman of child bearing age—consider pregnancy test

Take blood for:

electrolytes

glucose

calcium

magnesium

full blood count

liver function tests and INR

anti-epileptic drug levels

creatinine kinase

alcohol and toxicology screen

culture as appropriate

CAUTION: Not all seizures are epileptic

In psychogenic non-epileptic seizures 'pseudostatus' treatment with sedation or anti-epileptic drugs is not indicated

Consider urgent EEG and seek senior opinion

Mandatory Seizure Related Measures

- Investigate the cause of status and treat accordingly
- Consider reinstating any recently withdrawn anti-epileptic drug
- Continue existing anti-epileptic drugs
- Start maintenance anti-epileptic drug therapy promptly
- Refer to local specialist services

*For those on phenytoin, full loading is not appropriate but 'top-up' dose is given as per **clinical decision** or using the following formula:

$DOSE = (target\ level\ (mg/L) - actual\ level\ obtained\ urgently\ (mg/L)) \times 0.7 \times weight\ in\ kg$

Example: If desired level is 20 mg/L, actual level is 5 mg/L and weight is 70 kg, then
Dose = 20 - 5 = 15; 15 × 0.7 × 70 = 735 mg, rounded up to 750 mg

References:

1. Sibergleit R, Lowenstein D, Durbalski V, Conwit R and NETT investigations; RAMPART (Rapid Anticonvulsant Medication Prior to Arrival Trial); A double-blind randomized trial of the efficacy of intramuscular midazolam versus intravenous lorazepam in the prehospital treatment of status epilepticus by paramedics; *Epilepsia*; 2011; 52 (Suppl 8); 45-7.
2. Uges JW, Huizen MD, Engelsman J, Wilms EB, Touw DJ, Peeters E, Vecht CJ; Safety and pharmacokinetics of intravenous levetiracetam as add-on in status epilepticus; *Epilepsia*; 2009; Mar; 50 (3); 415-21.
3. Navarero V, Dagon C, De-meret S, An K, Baulac M, Carli P; Comparison of add-on levetiracetam versus placebo in a prehospital randomized trial in convulsive status epilepticus; Abstract at The 4th London-Innsbruck Colloquium on status epilepticus and acute seizures; Salzburg 4-6 April 2013.
4. Misra UK, Kalita J, Patel R; Sodium valproate vs phenytoin in status epilepticus: a pilot study; *Neurology*; 2006; Jul 25; 67 (2); 340-2.
5. Morton L, O'Hara KA, Coots BP, Pellock JM; Safety of Rapid Intravenous Valproate Infusion in Pediatric Patients; *Paediatr Neurol*; 2007; 36; 81-3.