STATUS EPILEPTICUS
Supporting information

This guideline has been prepared with reference to the following:

NICE. Epilepsies in children, young people and adults. 2025. London. NICE

https://www.nice.org.uk/guidance/ng217

Meierkord H, Boon P, Engelsen B et al. EFNS guideline on the management of status epilepticus in adults. Eur J Neurol. 2010;17:348-55

http://onlinelibrary.wiley.com/doi/10.1111/j.1468-1331.2009.02917.x/epdf

Oxygen at 10 L/min improves the clinical outcome?
Hypoxia is usually more severe than anticipated and thus oxygen administration is the first priority of emergency treatment in status epilepticus (SE) (Shorvon, 2001). In the opinion of others, however, "most patients breathe sufficiently well as long as the airway remains clear" (Marik, 2004). Animal studies have demonstrated that large increases in cerebral metabolic rate for both glucose and oxygen continue throughout SE and that brain damage occurs if these demands are not met (Wasterlain, 1993). A multivariate analysis of predictive indicators of mortality in 253 patients (Towne, 1994) found hypoxia was strongly associated with higher mortality.

Marik PE, Varon J. The management of status epilepticus. Chest 2004;126:582-91
http://journal.publications.chestnet.org/article.aspx?articleid=1082686

Shorvon S. The management of status epilepticus. J Neurol Neurosurg Psychiatry 2001;70(supp- II):ii22-ii27
http://jnnp.bmj.com/content/70/suppl_2/ii22.full

Towne AR, Pellock JM, Ko D, et al. Determinants of mortality in status epilepticus. Epilepsia 1994;35:27-34

Wasterlain CG, Fujikawa DG, Penix L, et al. Pathophysiological mechanisms of brain damage from status epilepticus. Epilepsia 1993;34(supp 1):S37-53

Evidence Level: IV

Intravenous benzodiazepines (Lorazepam/Diazepam) abort seizures?
A Cochrane systematic review (Prasad, 2014) identified 18 studies and concluded that intravenous diazepam was better than placebo in reducing the risk of non-cessation of seizures (risk ratio (RR) 0.73, 95% confidence interval (CI) 0.57 to 0.92), requirement for ventilatory support (RR 0.39, 95% CI 0.16 to 0.94), or continuation of status epilepticus requiring use of a different drug or general anaesthesia (RR 0.73, 95% CI 0.57 to 0.92). Intravenous lorazepam was better than placebo for risk of non-cessation of seizures (RR 0.52, 95% CI 0.38 to 0.71) and for risk of continuation of status epilepticus requiring a different drug or general anaesthesia (RR 0.52, 95% CI 0.38 to 0.71). Intravenous lorazepam was better than intravenous diazepam for reducing the risk of non-cessation of seizures (RR 0.64, 95% CI 0.45 to 0.90) and had a lower risk for continuation of status epilepticus requiring a different drug or general anaesthesia (RR 0.63, 95% CI 0.45 to 0.88).
Intravenous benzodiazepines are recommended as first-line treatment by European guidelines (Meierkord, 2010).

Meierkord H, Boon P, Engelsen B et al. EFNS guideline on the management of status epilepticus in adults. Eur J Neurol. 2010;17:348-55
http://onlinelibrary.wiley.com/doi/10.1111/j.1468-1331.2009.02917.x/epdf

Prasad K, Krishnan PR, Sequeira, R et al. Anticonvulsant therapy for status epilepticus. Cochrane Database of Systematic Reviews 2014. Art. No.: CD003723
http://onlinelibrary.wiley.com/doi/10.1002/14651858.CD003723.pub3/full

Evidence Level: I

Intravenous benzodiazepines carry a risk of respiratory depression?
A 2020 systematic review identified 2 RCTs comparing lorazepam and diazepam. Meta analysis showed no statistically significant difference was found for the risk of respiratory depression (RR, 1.07; 95% CI, 0.48 to 2.48) between the two benzodiazepines.

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All benzodiazepines cause sedation and respiratory depression and repeated doses have a cumulative effect (Chapman, 2001).

Chapman MG, Smith M, Hirsch NP. Status epilepticus. Anaesthesia 2001;56:648-59
http://onlinelibrary.wiley.com/doi/10.1046/j.1365-2044.2001.02115.x/full

Cruickshank M, Imamura M, Booth C et al. Pre-hospital and emergency department treatment of convulsive status epilepticus in adults: an evidence synthesis. Health Technol Assess. 2022;26:1-76
https://www.ncbi.nlm.nih.gov/pmc/articles/PMC8977974/

Evidence Level: I

Intravenous phenytoin aborts seizures but can cause hypotension, cardiac arrhythmia, impaired cardiac conduction, CNS depression or respiratory arrest?

Phenytoin aborts seizures in 30% of patients within 10 minutes of beginning intravenous administration, and when co-administered with diazepam, this rises to 60-80% (Delgado-Escueta, 1982). When administered at the maximal recommended rate of 50 mg/min, hypotension occurs in 28-50% of patients, and cardiac arrhythmia in 2% (Lowenstein, 2001). Fosphenytoin is a prodrug of phenytoin, recently licensed in the UK, that appears to be as effective as phenytoin whilst being tolerated at infusion rates up to three times as fast (Heafield, 2000). Infusion site reactions (phlebitis and soft-tissue damage) are less common with fosphenytoin, although hypotension and adverse cardiac effects are not significantly reduced (Lowenstein, 2001).

A randomised controlled trial comparing IV phenytoin with IV valproate in 100 patients (Agarwal, 2007) found the two drugs to be equally effective, but valproate was both easier to use and better tolerated.

Intravenous phenytoin is recommended as a first-line treatment in European guidelines (Meierkord, 2010).

Agarwal P, Kumar N, Chandra R, et al. Randomized study of intravenous valproate and phenytoin in status epilepticus. Seizure 2007;16:527-32
http://www.sciencedirect.com/science/article/pii/S105913110700088X

Delgado-Escueta AV, Wasterlain C, Treiman DM, et al. Management of status epilepticus. N Engl J Med 1982;306:1337-40

Heafield MT. Managing status epilepticus: new drug offers real advantages. BMJ 2000;320:953-4
http://www.bmj.com/content/320/7240/953.long

Lowenstein DH, Alldredge BK. Status epilepticus. N Engl J Med 2001;338:970-6

Meierkord H, Boon P, Engelsen B et al. EFNS guideline on the management of status epilepticus in adults. Eur J Neurol. 2010;17:348-55
http://onlinelibrary.wiley.com/doi/10.1111/j.1468-1331.2009.02917.x/epdf

Evidence Level: IV

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