

EPI2. In children with established status epilepticus, i.e. seizures persisting after the first-line agent (benzodiazepine-resistant status epilepticus), which antiseizure medicines are associated with better clinical outcomes (stopping seizures and with less adverse effects)?

Recommendation (update):	In children with established status epilepticus, i.e. seizures persisting after two doses of benzodiazepines, intravenous fosphenytoin, intravenous phenytoin, intravenous levetiracetam, intravenous phenobarbital or intravenous valproic acid (sodium valproate) should be considered with appropriate monitoring. The choice of these medicines depends on local resources, including availability and facilities for monitoring.
Strength of recommendation:	Conditional
Certainty of evidence:	Moderate

Justification

- A new systematic review and meta-analysis was conducted to study comparisons between the ASMs for status epilepticus in children: Sharma et al., 2023 (12 RCTs).¹³ There is moderate- to high-quality evidence that there is no clinically important difference in efficacy between intravenous phenytoin, fosphenytoin, levetiracetam or sodium valproate for the treatment of benzodiazepine-resistant status epilepticus in children. There is low-quality evidence that phenobarbital may be more effective than phenytoin or sodium valproate in the treatment of benzodiazepine-resistant status epilepticus in children.
- Another factor of concern is the speed of administration. Fosphenytoin, levetiracetam and sodium valproate can be administered within 10 minutes, whereas phenytoin and phenobarbital need to be infused over 20 minutes. Time is of the essence while treating status epilepticus.
- There is low- to moderate-quality evidence that the safety profile of levetiracetam was better than fosphenytoin, phenytoin or sodium valproate in terms of less requirement for intubation, and lesser overall adverse effects.
- There is insufficient evidence to recommend the use of lacosamide or diazepam infusion at this time.

Remarks

- Status epilepticus is a medical emergency which can lead to profound systemic and neurological damage and is associated with significant short-term and long-term mortality. Timely control of status epilepticus is of paramount importance to improve the outcomes.
- A staged treatment protocol for management of status epilepticus is recommended.
 - Approximately 30–40% of all individuals fail to respond to initial treatment with benzodiazepines (benzodiazepine-resistant or established status epilepticus) and need further treatment with other intravenous ASM, i.e. established status epilepticus. The treatment of established status epilepticus is the focus of this recommendation with the above medicines initiated when seizures persist after two doses of benzodiazepines.
- Both levetiracetam and sodium valproate are broad spectrum drugs active against all types of seizures, and hence may be a good agent for maintenance therapy after the acute control of seizures in children with genetic generalized epilepsy or when the type of seizure/epilepsy syndrome is not clear. If available, intravenous levetiracetam should be considered because of its superior safety profile.

¹³ Sharma S, Jain P, Aneja S. Antiseizure medicine treatment for established status epilepticus in adults. 2023 (in preparation).