

Lamotrigine versus levetiracetam or zonisamide for focal epilepsy and valproate versus levetiracetam for generalised and unclassified epilepsy: two SANAD II non-inferiority RCTs

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Plain English summary

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Background and methods

The SANAD II trial was a clinical trial designed to identify the most clinically effective and cost-effective treatment for adults and children aged > 5 years with newly diagnosed epilepsy.

There are two main epilepsy types: focal and generalised. In focal epilepsy, seizures start at a single place in the brain (a focus), whereas in generalised epilepsy seizures start in both sides of the brain at the same time.

Anti-seizure medications are the main treatment. For people with newly diagnosed epilepsy, the first anti-seizure medication should control the seizures as quickly as possible while avoiding side effects. The first-choice treatments are lamotrigine (Lamictal®, GlaxoSmithKline plc, Brentford, UK) for focal epilepsy and valproate (Epilim®, Sanofi SA, Paris, France) for generalised epilepsy (however, the latter should be avoided in women who could become pregnant).

A number of newer anti-seizure medications have been approved for NHS use, but it is unclear whether or not they should be used as first-line treatments. The SANAD II trial focused on the new medicines levetiracetam (Keppra®, UCB Pharma Ltd, Slough, UK) and zonisamide (Zonegran®, Eisai Co. Ltd, Tokyo, Japan).

We recruited 1510 people aged ≥ 5 years with newly diagnosed epilepsy: 990 with focal epilepsy and 520 with generalised or unclassified epilepsy.

Findings: focal epilepsy

People starting treatment with levetiracetam or zonisamide were significantly less likely to have a 12-month remission from seizures than people starting treatment with lamotrigine, unless they were changed to another anti-seizure medication. Side effects that were thought to be caused by anti-seizure medications were reported by 33% of participants starting lamotrigine, 44% of those starting levetiracetam and 45% of those starting zonisamide.

The cost-effectiveness analyses showed that neither levetiracetam nor zonisamide is value for money for the NHS when compared with lamotrigine.

The SANAD II findings do not support the use of levetiracetam or zonisamide as first-line treatments in focal epilepsy.

Findings: generalised and unclassifiable epilepsy

People starting treatment with levetiracetam were significantly less likely to have a 12-month remission from seizures than people starting valproate, unless they were changed to another anti-seizure medication. Side effects that were thought to be caused by anti-seizure medications were reported by 37% of participants starting valproate and 42% of participants starting levetiracetam.

The cost-effectiveness analyses showed that levetiracetam is not good value for money for the NHS when compared with valproate.

The SANAD II findings do not support the use of levetiracetam as a first-line treatment for newly diagnosed generalised epilepsy. Importantly, our results will inform treatment decisions for women, who may choose a less effective treatment that is safer in pregnancy.

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This report

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