



**PROPOSED REVIEW OF SIGN GUIDELINE
CONSULTATION FORM**

Title of guideline	SIGN 70: Epilepsy in Adults
Date of publication	2003
SIGN scoping search – sources	<p>MeSH headings for the condition specified and any common variations as free text, plus terms for the interventions and care processes discussed in the guideline</p> <p>Sources: Guidelines: NICE; National Library for Health guidelines finder; National Guidelines Clearinghouse; GIN Web site. Technology appraisals: NICE; UK HTA database (Southampton); INAHTA database. Cochrane reviews: Cochrane Library. Other good quality systematic reviews: UK HTA database (Southampton); DARE.</p>
SIGN scoping search - summary	<p>Guidelines – 10 HTAs – 6 Cochrane reviews – 18 Other good quality systematic reviews – 2</p>
Other guidelines/HTAs	<ul style="list-style-type: none"> ▪ NICE. The epilepsies: the diagnosis and management of the epilepsies in adults and children in primary and secondary care. October 2004. http://www.nice.org.uk/page.aspx?o=CG020 ▪ PRODIGY. Epilepsy. February 2006. http://www.prodigy.nhs.uk/epilepsy ▪ Faculty of Family Planning and Reproductive Health Care, RCOG. Faculty statement from the CEU on changes to prescribing information for lamotrigine. 24 August 2005. http://www.ffprhc.org.uk/admin/uploads/lamotrigine.pdf ▪ Emergency Care Specialist Library, Joint Royal Colleges Ambulance Liaison Committee. Fitting. 31 August 2004. http://www.library.nhs.uk/SpecialistLibraries/Download.aspx?resID=70855 ▪ Joint Epilepsy Council. National statement of good practice for the treatment and care of people who have epilepsy. 1 March 2002. http://www.jointepilepsycouncil.org.uk/nsgoodprac.asp ▪ Royal College of Ophthalmologists. The ocular side-effects of vigabatrin (sabril) information and guidelines for screening. 1 Apr 2000. http://www.rcophth.ac.uk/docs/publications/Vigabatrin.pdf ▪ Practice parameter: temporal lobe and localized neocortical resections for epilepsy: report of the Quality Standards Subcommittee of the American Academy of Neurology, in association with the American Epilepsy Society and the American Association of Neurological Surgeons. 2003. http://www.guideline.gov/summary/summary.aspx?doc_id=4108&nbr=003153 ▪ American College of Emergency Physicians. Clinical policy: critical issues in the evaluation and management of adult patients presenting to the emergency department with seizures. Ann Emerg Med 2004 May;43(5):605-25. http://www.guideline.gov/summary/summary.aspx?doc_id=5091&nbr=003558 ▪ Faculty of Family Planning and Reproductive Health Care Clinical Effectiveness Unit. FFPRHC Guidance (April 2005). Drug interactions with hormonal contraception. J Fam Plann Reprod Health Care 2005 Apr;31(2):139-51. http://www.guideline.gov/summary/summary.aspx?doc_id=7286&nbr=004

	<p>339</p> <ul style="list-style-type: none"> ▪ AHRQ (US) - Agency for Healthcare Research and Quality. Management of Treatment-Resistant Epilepsy [Evidence Report]. 1 January 2003. http://www.ahrq.gov/clinic/tp/epiltp.htm
<p>Main conclusions from new evidence</p>	<ul style="list-style-type: none"> ▪ A systematic review as part of an HTA found little good-quality evidence from clinical trials to support the use of newer monotherapy or adjunctive therapy AEDs over older drugs, or to support the use of one newer AED in preference to another. Newer AEDs, used as monotherapy, may be cost-effective for the treatment of patients who have experienced adverse events with older AEDs, who have failed to respond to the older drugs, or where such drugs are contraindicated. Newer AEDs used as adjunctive therapy may be cost-effective compared with the continuing current treatment alone. <i>The guideline recommends: Carbamazepine, sodium valproate, lamotrigine and oxcarbazepine can all be regarded as first-line treatments for partial and secondary generalised seizure (A) and sodium valproate and lamotrigine are drugs of choice for primary generalised seizures and should also be prescribed if there is any doubt about the seizure types and/or syndrome classification (A). No specific combinations of therapies are recommended for drug resistant epilepsy.</i> ▪ A systematic review found insufficient evidence regarding effectiveness and cost-effectiveness of imaging techniques in the work-up for epilepsy surgery. <i>Work-up for surgery is not detailed in the guideline.</i> ▪ Lamotrigine is significantly less likely to be withdrawn than carbamazepine but results for time to first seizure suggested that carbamazepine may be superior in terms of seizure control. <i>In general, the guideline does not recommend one drug over another in any circumstances, as this is dependent on what works for the individual patient – this applies to much of the evidence listed below.</i> ▪ Lorazepam is better than diazepam or phenytoin alone for cessation of seizures and carries a lower risk of continuation of status epilepticus requiring a different drug or general anaesthesia. Both lorazepam and diazepam are better than placebo for the same outcomes. In the treatment of premonitory seizures, diazepam 30 mg in an intrarectal gel is better than 20 mg for cessation of seizures without a statistically significant increase in adverse effects. <i>As above.</i> ▪ A Cochrane review did not find evidence that a significant difference exists between carbamazepine and phenytoin for some specific outcomes. Confidence intervals were wide and the possibility of important differences existing has not been excluded. <i>As above.</i> ▪ There is no overall difference between carbamazepine and phenobarbitone for time to 12-month remission or time to first seizure. Subgroup analyses for time to first seizure suggest an advantage with phenobarbitone for partial onset seizures and a clinical advantage with carbamazepine for generalized onset tonic-clonic seizures. Phenobarbitone is significantly more likely to be withdrawn. <i>As above.</i> ▪ There is no evidence on whether or not oxcarbazepine is equivalent, superior or inferior to phenytoin in terms of seizure control. For patients with partial onset seizures oxcarbazepine is significantly less likely to be withdrawn. <i>As above.</i> ▪ Topiramate has efficacy as an add-on treatment for drug-resistant partial epilepsy. <i>As above.</i> ▪ Zonisamide has efficacy as an add-on treatment in people with drug-resistant partial epilepsy. Minimum effective and maximum tolerated doses cannot be identified. <i>As above.</i> ▪ Tiagabine reduces seizures frequency but is associated with some adverse effects when used as an add-on for people with drug-resistant localization related seizures. <i>As above.</i> ▪ Remacemide has only a modest effect on seizure frequency and has a

	<p>significant withdrawal rate and it is unlikely that it will be further developed as an antiepileptic drug. <i>As above.</i></p> <ul style="list-style-type: none"> ▪ The current evidence does not support acupuncture as a treatment for epilepsy. <i>Mentioned in the guideline but no recommendations are made.</i> ▪ From the best current available evidence it would seem advisable for women to continue medication during pregnancy using monotherapy at the lowest dose required to achieve seizure control. Polytherapy would seem best avoided where possible. <i>The guideline recommends that if AEDs are to be used in pregnancy the relative risks of seizures and fetal malformation should be discussed with the woman (C) and that whenever possible, a woman should conceive on the lowest effective dose of one AED appropriate for her epilepsy syndrome. If she has good seizure control and presents already pregnant, there is probably little to be gained by altering her AEDs (C) The guideline states that polytherapy carries a much higher risk but doesn't make a specific recommendation about polytherapy versus monotherapy.</i> ▪ There is no evidence from which to derive any reliable conclusions regarding the optimal rate of tapering of AEDs. <i>The guideline has a good practice point that says the rate of withdrawal of AEDs should be slow, usually over a few months, and longer with barbiturates and benzodiazepines and that one drug should be withdrawn at a time</i> ▪ There is no reliable evidence from RCTs to support the use of ketogenic diets for people with epilepsy. Large observational studies, some prospective, suggest an effect on seizures. For those with a difficult epilepsy on multiple antiepileptic drugs, a ketogenic diet may be a possible option. <i>No related recommendations.</i> ▪ VNS for partial seizures appears to be an effective and well tolerated treatment. <i>No related recommendations.</i> ▪ A Cochrane review found no reliable evidence to support the routine use of vitamins in patients with epilepsy. <i>Vitamins only discussed in context of pregnancy.</i> ▪ No reliable conclusions can be drawn regarding the efficacy of yoga as a treatment for epilepsy. <i>Mentioned in the guideline but no recommendations are made</i> ▪ There was no evidence of improvement of seizure frequency or severity when comparing specialist clinics with generalist neurology out-patient clinics, but it cannot be concluded that there is no effect because the available evidence was sparse and of limited quality. <i>The guideline says that the relevant clinical studies have not yet been undertaken to establish the effectiveness of epilepsy clinics and makes some good practice points about service provision.</i> ▪ Specialist nurses: there was no evidence of improvement of seizure frequency or severity in comparison with usual care (GP or hospital), but there was some evidence of reduced rates of depression. No effect on generic QOL was shown. There was good evidence of improvements in patient satisfaction for the care process involving specialist nurses, but this was not reflected in the clinical outcomes. <i>The guideline has a good practice point saying that each epilepsy team should include epilepsy nurse specialists.</i>
New areas that could be added to the guideline	<ul style="list-style-type: none"> ▪ The role of VNS in treating partial seizures
Summary of the recommendations that could be updated	<ul style="list-style-type: none"> ▪ Recommendations on pharmacological management could be made more specific

Please answer the following questions as fully as possible:

Name, designation, organisation:	GP: 1 Other: 7 Academics: 1 Nurse: 1 Neurologist: 2 Pharmacy Advisor: 1
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1(a) Is there still a requirement for an evidence-based guideline on this topic?
<ul style="list-style-type: none"> ▪ Yes = 13 ▪ There is very much a need for evidence-based guideline on this topic. NICE guidelines are now out-of-date ▪ Epilepsy as a condition can be difficult to treat and clinicians require as many sources of help to be able to do this effectively. An updated SIGN guideline would help to support clinical practice. Much has changed since the publication of the original guideline. An update would allow for these developments to be recognised.
1(b) If no, should the guideline be withdrawn?
2(a) Do you agree with the assessment of the impact of the new evidence and its likely effect on recommendations?
<ul style="list-style-type: none"> ▪ Yes = 13 ▪ Largely I agree with the assessment. The data about effectiveness of specialist clinics and nurses is difficult due to many confounding factors. No changes in drug recommendations needed ▪ The SANA study has not been mentioned. ▪ Lamotigine evidence on pregnancy unclear ▪ Numbers of important pharmacological studies have been published since this report was published. ▪ Major review is required of therapeutic approach and drugs used to treat epilepsy. ▪ plus recently published SANAD study – see Lancet 2007 ▪ Yes, and as annotated there is new data that needs to be considered. ▪ Comments: <ol style="list-style-type: none"> 1) The recommendation for monotherapy treatment should be changed in the light of the SANAD studies reported in the Lancet. Sodium valproate (followed by lamotrigine) would appear to be drug of choice in primary generalised and Lamotrigine (followed by carbamazepine) in partial epilepsy with the caveat that therapy may need to be individualised. 2) The work-up for surgery should not be part of a guideline other than to say it should only be performed at specialist centres. What is the reference for the effectiveness of imaging techniques? 3) See point 1 4) Lorazepam should be recommended as first-line in status epilepticus. 5) Not sure about clinical relevance of phenytoin v carbamazepine 6) Ditto phenobarbitone v carbamazepine 7) Ditto oxcarbazepine v phenytoin 8) Topiramate, zonisamide, pregabalin and tiagabine should all be included as possible add-on drugs in partial epilepsy 9) Acupuncture should be removed from guideline other than to say that evidence for the efficacy of complimentary and alternative therapies is lacking. 10) For pregnancy, the pregnancy registers do suggest that valproate is associated with a higher risk of fetal malformations than carbamazepine 11) The rate of withdrawal recommendation should remain unchanged 12) VNS for partial epilepsy should be mentioned 13) Vitamins in pregnancy should remain 14) Yoga – see acupuncture above 15) Epilepsy clinic recommendation should remain 16) The specialist nurse study was I presume not a randomised study and should therefore be treated with caution. Perhaps a caveat to the specialist nurse recommendation should be included. ▪ Yes but with some additions. <p>There is now much more evidence on the effectiveness of the psychologist in supporting people with epilepsy. Key recent studies include:</p> <p>Hoie, Sommerfelt, Waaler, Alsaker, Skeidsvoll, Mykletun (2006)</p> <p>Schachter (2006)</p> <p>Chmelarová (2005)</p> <p>Engelberts, Klein, Kasteleijn-Nolst Trenite, Heimans, van der Ploeg (2002)</p>

Recent academic literature has covered the issue of SUDEP. This new evidence goes to show the importance of telling people with epilepsy about SUDEP. The original SIGN guideline established that this was an “essential” piece of information. Any new guideline should make this more explicit. Key studies include:

Morton, Richardson, Duncan (2006)

Monte et al. (2007)

The use of buccal midazolam as a rescue medication is not covered in the original guideline. This relatively new and now quite widely used medication needs to feature in any updated guideline.

There is also now much more evidence with regards to multidisciplinary working, the use of Managed Clinical Networks and the importance of specialist nurses and allied health professionals in improving patient care. This evidence needs to feature in any updated guideline. There are also now moves at a national level to support people with long term conditions to “self manage”. This fact needs to be recognised and included in an updated guideline.

2(b) Based on the information given above, and your own clinical judgement, does the guideline require revision in the light of new evidence? *Please give details.*

- Yes = 11
- No = 1
- N/A – not in clinical practice
- No major revision likely to be needed at present
- I feel revision of the lamotrigine question and epilepsy could be looked at. The effect, if any, of the female hormonal change (menstruation) on seizure frequency
- Yes, particularly pharmacotherapy, oral contraception and pregnancy.
- Yes, clear need to update drug management.
- Agree VNS should be in guideline (30,000 pts worldwide). Pharmacology could be updated to be more specific and include new drugs/evidence.
- The guideline should be revised. I agree that the role of VNS should be included and that with SANAD pharmacological management should perhaps be more specific.
- Yes the guideline requires to be revised. Epilepsy medication has developed substantially in the last few years. This needs to be recognised and evaluated in clinical guidelines. The use of VNS technology is an exciting prospect for people with poorly controlled epilepsy. Uptake, though, has been slow in Scotland. This is due, at least partly, to a lack of clinical guidelines and lack of awareness among clinicians. There is also new evidence on the importance of providing people with epilepsy information about SUDEP and there is now more evidence to support multi-disciplinary, team based working
- Yes, update treatment recommendations in light of new therapies & investigations that are available

3 Please list any additions to the remit of the guideline that you think would be beneficial

- Genetics
- Models of care need to be looked at in relation to specialised nurses.
- Recent (post 2003) trials on growing use of midazolam for stat. Ep. Could be included. Eg. McIntyre et al 2005 lancet
- Epilepsy surgery, Out of hospital treatment of seizures: buccal midazolam

4 Please tick your preferred option for reviewing this guideline

a. there is no new evidence that will affect existing recommendations and the guideline should not be reviewed at this time	1
b. some recommendations will change in the light of the new evidence and selected elements of the guideline should be reviewed	8
c. the entire guideline should be reviewed	5
d. the guideline should be withdrawn	

Thank you very much for taking part in this consultation.

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