## PROPOSED REVIEW OF SIGN GUIDELINE
### CONSULTATION FORM

<table>
<thead>
<tr>
<th>Title of guideline</th>
<th>SIGN 70: Epilepsy in Adults</th>
</tr>
</thead>
<tbody>
<tr>
<td>Date of publication</td>
<td>2003</td>
</tr>
<tr>
<td>SIGN scoping search – sources</td>
<td>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</td>
</tr>
<tr>
<td></td>
<td>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.</td>
</tr>
</tbody>
</table>
| SIGN scoping search - summary | Guidelines – 10  
HTAs – 6  
Cochrane reviews – 18  
Other good quality systematic reviews – 2 |
- 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  
Main conclusions from new evidence

- 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. 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.

- A systematic review found insufficient evidence regarding effectiveness and cost-effectiveness of imaging techniques in the work-up for epilepsy surgery. Work-up for surgery is not detailed in the guideline.

- 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. 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.

- 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. As above.

- 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. As above.

- There is no overall difference between carbamazepine and phenobarbitalone for time to 12-month remission or time to first seizure. Subgroup analyses for time to first seizure suggest an advantage with phenobarbitalone for partial onset seizures and a clinical advantage with carbamazepine for generalized onset tonic-clonic seizures. Phenobarbitalone is significantly more likely to be withdrawn. As above.

- 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. As above.

- Topiramate has efficacy as an add-on treatment for drug-resistant partial epilepsy. As above.

- Zonisamide has efficacy as an add-on treatment in people with drug-resistant partial epilepsy. Minimum effective and maximum tolerated doses cannot be identified. As above.

- 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. As above.

- Remacemide has only a modest effect on seizure frequency and has a
significant withdrawal rate and it is unlikely that it will be further
developed as an antiepileptic drug. As above.

- The current evidence does not support acupuncture as a treatment for
epilepsy. Mentioned in the guideline but no recommendations are made.
- 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. 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.
- There is no evidence from which to derive any reliable conclusions
regarding the optimal rate of tapering of AEDs. 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
- 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. No related recommendations.
- VNS for partial seizures appears to be an effective and well tolerated
treatment. No related recommendations.
- A Cochrane review found no reliable evidence to support the routine use
of vitamins in patients with epilepsy. Vitamins only discussed in context of
pregnancy.
- No reliable conclusions can be drawn regarding the efficacy of yoga as a
treatment for epilepsy. Mentioned in the guideline but no
recommendations are made
- 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. 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.
- 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. The guideline has a good
practice point saying that each epilepsy team should include epilepsy
nurse specialists.

New areas that could be added to the guideline

- The role of VNS in treating partial seizures

Summary of the recommendations that could be updated

- Recommendations on pharmacological management could be made more specific

Please answer the following questions as fully as possible:

<table>
<thead>
<tr>
<th>Name, designation, organisation:</th>
<th>GP: 1 Other: 7 Academics: 1 Nurse: 1 Neurologist: 2 Pharmacy Advisor: 1</th>
</tr>
</thead>
</table>

JFH / 22/11/2007
C:\Documents and Settings\duncans\Local Settings\Temporary Internet Files\OLK66\epilepsy in adults review report 2007 - ANON.doc
1(a)  Is there still a requirement for an evidence-based guideline on this topic?

- 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?

- 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:
  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 phenutoin
  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.

There is now much more evidence on the effectiveness of the psychologist in supporting people with epilepsy. Key recent studies include:

Schachtner (2006)
Chmelarová (2005)
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 bucal 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.
- Epilepsy surgery, Out of hospital treatment of seizures: bucal 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
- b. some recommendations will change in the light of the new evidence and selected elements of the guideline should be reviewed
- c. the entire guideline should be reviewed
- d. the guideline should be withdrawn

Thank you very much for taking part in this consultation.

Please return to: Safia Qureshi, SIGN Executive, 28 Thistle Street, Edinburgh EH2 1EN, safia.qureshi@nhs.net