

## **Appendices e-1 – e-6**

### **Appendix e-1: 2011–2013 AAN Guideline Development Subcommittee Members and**

#### **Mission Statement**

John D. England, MD, FAAN (Chair); Cynthia Harden, MD (Vice-Chair); Melissa Armstrong, MD; Eric Ashman, MD; Misha-Miroslav Backonja, MD; Richard L. Barbano, MD, PhD, FAAN; Diane Donley, MD; Terry Fife, MD, FAAN; David Gloss, MD; John J. Halperin, MD, FAAN; Cheryl Jaigobin, MD; Andres M. Kanner, MD; Jason Lazarou, MD; Steven R. Messé, MD, FAAN; David Michelson, MD; Pushpa Narayanaswami, MD, MBBS; Anne Louise Oaklander, MD, PhD, FAAN; Tamara Pringsheim, MD; Alexander Rae-Grant, MD; Michael Shevell, MD, FAAN; Theresa A. Zesiewicz, MD, FAAN; Jonathan P. Hosey, MD, FAAN (Ex-Officio); Stephen Ashwal, MD, FAAN (Ex-Officio); Deborah Hirtz, MD, FAAN (Ex-Officio).

The mission of the GDS is to prioritize, develop, and publish evidence-based guidelines related to the diagnosis, treatment, and prognosis of neurological disorders.

The GDS is committed to using the most rigorous methods available within our budget, in collaboration with other available AAN resources, to most efficiently accomplish this mission.

## **Appendix e-2: CNS Practice Committee Members**

Bruce Cohen, MD, FAAN (Chair); Deborah Hirtz, MD, FAAN (Co-Chair for Practice Parameters); Michael Goldstein, MD (Emeritus); Gary Clark, MD (Liaison); Terence Edgar, MD; Cesar Santos, MD; Walter Molofsky, MD; Diane Donley, MD.

### Appendix e-3: Search Strategy

Database: Ovid MEDLINE(R) <1950 to January Week 4 2010>

Search Strategy:

- 
- 1 Spasms, Infantile/ [MeSH Term] (2228)
  - 2 Infantile Spasm/ [EMTREE term] (2228)
  - 3 blitz nick saalam krampfe.mp. (0)
  - 4 (blitz adj1 nick ajd1 saalam adj1 krampfe).mp. (0)
  - 5 encephalopathy, infantile myoclonic/ (0)
  - 6 (flexion adj1 spasm\*).mp. (48)
  - 7 flexor spasm\*.mp. (60)
  - 8 hypsarrhythmi\*.mp. (458)
  - 9 infant\* spasm\*.mp. (1399)
  - 10 infant\* myoclonic encephalopath\*.mp. (23)
  - 11 (jackknife seiz\* or jack knife seiz\*).mp. (0)
  - 12 lightning attack\*.mp. (0)
  - 13 massive myoclon\* spasm\*.mp. (0)
  - 14 minor motor epilesp\*.mp. (0)
  - 15 nodding spasm\*.mp. (13)
  - 16 petit mal quadrette\*.mp. (0)
  - 17 propulsive petit mal.mp. (9)
  - 18 salaam attack\*.mp. (0)
  - 19 salaam seiz\*.mp. (14)
  - 20 spasmus nutans.mp. (82)
  - 21 spasms, infantile.mp. (2231)
  - 22 west syndrom\*.mp. (632)
  - 23 or/1-22 (3095)
  - 24 ((blitz adj1 nick adj1 saalam adj1 krampfe) or (spasm adj1 flexion) or blitz nick saalam krampfe or encephalopathy, infantile myoclonic or flexion spasm\* or flexor spasm\* or hypsarrhythmi\* or infant\* myoclonic encephalopath\* or infant\* spasm\* or jack knife seiz\* or jackknife seiz\* or lightning attack\* or massive myoclon\* spasm\* or minor motor epilesp\* or myoclonic infant\* encephalopath\* or nodding spasm\* or petit mal quadrette\* or propulsive petit mal or salaam attack\* or salaam seiz\* or spasm in flexion or spasms, infantile or spasmus nutans or west syndrom\*).mp. (3095)
  - 25 (2009\* or 2010\*).ed. (783706)
  - 26 24 and 25 (105)
  - 27 from 26 keep 1-105 (105) Database: Ovid MEDLINE(R) <1950 to January Week 4 2010>
- Search Strategy:

- 
- 1 Spasms, Infantile/ [MeSH Term] (2228)
  - 2 Infantile Spasm/ [EMTREE term] (2228)
  - 3 blitz nick saalam krampfe.mp. (0)
  - 4 (blitz adj1 nick ajd1 saalam adj1 krampfe).mp. (0)
  - 5 encephalopathy, infantile myoclonic/ (0)
  - 6 (flexion adj1 spasm\*).mp. (48)

7 flexor spasm\*.mp. (60)  
 8 hypsarrhythmi\*.mp. (458)  
 9 infant\* spasm\*.mp. (1399)  
 10 infant\* myoclonic encephalopath\*.mp. (23)  
 11 (jackknife seiz\* or jack knife seiz\*).mp. (0)  
 12 lightning attack\*.mp. (0)  
 13 massive myoclon\* spasm\*.mp. (0)  
 14 minor motor epileps\*.mp. (0)  
 15 nodding spasm\*.mp. (13)  
 16 petit mal quadrette\*.mp. (0)  
 17 propulsive petit mal.mp. (9)  
 18 salaam attack\*.mp. (0)  
 19 salaam seiz\*.mp. (14)  
 20 spasmus nutans.mp. (82)  
 21 spasms, infantile.mp. (2231)  
 22 west syndrom\*.mp. (632)  
 23 or/1-22 (3095)  
 24 ((blitz adj1 nick adj1 saalam adj1 krampfe) or (spasm adj1 flexion) or blitz nick saalam  
 krampfe or encephalopathy, infantile myoclonic or flexion spasm\* or flexor spasm\* or  
 hypsarrhythmi\* or infant\* myoclonic encephalopath\* or infant\* spasm\* or jack knife seiz\* or  
 jackknife seiz\* or lightning attack\* or massive myoclon\* spasm\* or minor motor epileps\* or  
 myoclonic infant\* encephalopath\* or nodding spasm\* or petit mal quadrette\* or propulsive petit  
 mal or salaam attack\* or salaam seiz\* or spasm in flexion or spasms, infantile or spasmus nutans  
 or west syndrom\*).mp. (3095)  
 25 (2009\* or 2010\*).ed. (783706)  
 26 24 and 25 (105)  
 27 from 26 keep 1-105 (105)  
 Database: EMBASE <1980 to 2010 Week 05>  
 Search Strategy:

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1 Spasms, Infantile/ [MeSH Term] (1583)  
 2 Infantile Spasm/ [EMTREE term] (1583)  
 3 blitz nick saalam krampfe.mp. (0)  
 4 (blitz adj1 nick adj1 saalam adj1 krampfe).mp. (0)  
 5 encephalopathy, infantile myoclonic/ (1583)  
 6 (flexion adj1 spasm\*).mp. (17)  
 7 flexor spasm\*.mp. (49)  
 8 hypsarrhythmi\*.mp. (497)  
 9 infant\* spasm\*.mp. (1915)  
 10 infant\* myoclonic encephalopath\*.mp. (6)  
 11 (jackknife seiz\* or jack knife seiz\*).mp. (0)  
 12 lightning attack\*.mp. (0)  
 13 massive myoclon\* spasm\*.mp. (0)  
 14 minor motor epileps\*.mp. (0)  
 15 nodding spasm\*.mp. (6)  
 16 petit mal quadrette\*.mp. (0)

17 propulsive petit mal.mp. (3)  
 18 salaam attack\*.mp. (0)  
 19 salaam seiz\*.mp. (8)  
 20 spasmus nutans.mp. (61)  
 21 spasms, infantile.mp. (5)  
 22 west syndrom\*.mp. (1048)  
 23 or/1-22 (2846)  
 24 ((blitz adj1 nick adj1 saalam adj1 krampfe) or (spasm adj1 flexion) or blitz nick saalam  
 krampfe or encephalopathy, infantile myoclonic or flexion spasm\* or flexor spasm\* or  
 hypsarrhythmi\* or infant\* myoclonic encephalopath\* or infant\* spasm\* or jack knife seiz\* or  
 jackknife seiz\* or lightning attack\* or massive myoclon\* spasm\* or minor motor epileps\* or  
 myoclonic infant\* encephalopath\* or nodding spasm\* or petit mal quadrette\* or propulsive petit  
 mal or salaam attack\* or salaam seiz\* or spasm in flexion or spasms, infantile or spasmus nutans  
 or west syndrom\*).mp. (2846)  
 25 (2009\* or 2010\*).em. (736766)  
 26 24 and 25 (171)  
 27 from 26 keep 1-171 (171)  
 Database: Ovid MEDLINE(R) <1948 to August Week 5 2011>, Embase <1980 to 2011 Week  
 35>  
 Search Strategy:

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1 Spasms, Infantile/ [MeSH Term] (5024)  
 2 Infantile Spasm/ [EMTREE term] (5024)  
 3 blitz nick saalam krampfe.mp. (0)  
 4 (blitz adj1 nick adj1 saalam adj1 krampfe).mp. (0)  
 5 encephalopathy, infantile myoclonic/ (2614)  
 6 (flexion adj1 spasm\*).mp. (104)  
 7 flexor spasm\*.mp. (129)  
 8 hypsarrhythmi\*.mp. (1270)  
 9 infant\* spasm\*.mp. (4623)  
 10 infant\* myoclonic encephalopath\*.mp. (48)  
 11 (jackknife seiz\* or jack knife seiz\*).mp. (0)  
 12 lightning attack\*.mp. (0)  
 13 massive myoclon\* spasm\*.mp. (0)  
 14 minor motor epileps\*.mp. (0)  
 15 nodding spasm\*.mp. (29)  
 16 petit mal quadrette\*.mp. (0)  
 17 propulsive petit mal.mp. (18)  
 18 salaam attack\*.mp. (0)  
 19 salaam seiz\*.mp. (37)  
 20 spasmus nutans.mp. (183)  
 21 spasms, infantile.mp. (2425)  
 22 west syndrom\*.mp. (2119)  
 23 or/1-22 (7678)  
 24 ((blitz adj1 nick adj1 saalam adj1 krampfe) or (spasm adj1 flexion) or blitz nick saalam  
 krampfe or encephalopathy, infantile myoclonic or flexion spasm\* or flexor spasm\* or

hypsarrhythmi\* or infant\* myoclonic encephalopath\* or infant\* spasm\* or jack knife seiz\* or jackknife seiz\* or lightning attack\* or massive myoclon\* spasm\* or minor motor epilep\* or myoclonic infant\* encephalopath\* or nodding spasm\* or petit mal quadrette\* or propulsive petit mal or salaam attack\* or salaam seiz\* or spasm in flexion or spasms, infantile or spasmus nutans or west syndrom\*).mp. (7677)

25 24 and (2010\* or 2011\*).em. (807)

26 remove duplicates from 25 (611)

Database: Ovid MEDLINE(R) <1948 to August Week 5 2011>, Embase <1980 to 2011 Week 35>

Search Strategy:

- 
- 1 Spasms, Infantile/ [MeSH Term] (5024)
  - 2 Infantile Spasm/ [EMTREE term] (5024)
  - 3 blitz nick saalam krampfe.mp. (0)
  - 4 (blitz adj1 nick adj1 saalam adj1 krampfe).mp. (0)
  - 5 encephalopathy, infantile myoclonic/ (2614)
  - 6 (flexion adj1 spasm\*).mp. (104)
  - 7 flexor spasm\*.mp. (129)
  - 8 hypsarrhythmi\*.mp. (1270)
  - 9 infant\* spasm\*.mp. (4623)
  - 10 infant\* myoclonic encephalopath\*.mp. (48)
  - 11 (jackknife seiz\* or jack knife seiz\*).mp. (0)
  - 12 lightning attack\*.mp. (0)
  - 13 massive myoclon\* spasm\*.mp. (0)
  - 14 minor motor epilep\*.mp. (0)
  - 15 nodding spasm\*.mp. (29)
  - 16 petit mal quadrette\*.mp. (0)
  - 17 propulsive petit mal.mp. (18)
  - 18 salaam attack\*.mp. (0)
  - 19 salaam seiz\*.mp. (37)
  - 20 spasmus nutans.mp. (183)
  - 21 spasms, infantile.mp. (2425)
  - 22 west syndrom\*.mp. (2119)
  - 23 or/1-22 (7678)
  - 24 ((blitz adj1 nick adj1 saalam adj1 krampfe) or (spasm adj1 flexion) or blitz nick saalam krampfe or encephalopathy, infantile myoclonic or flexion spasm\* or flexor spasm\* or hypsarrhythmi\* or infant\* myoclonic encephalopath\* or infant\* spasm\* or jack knife seiz\* or jackknife seiz\* or lightning attack\* or massive myoclon\* spasm\* or minor motor epilep\* or myoclonic infant\* encephalopath\* or nodding spasm\* or petit mal quadrette\* or propulsive petit mal or salaam attack\* or salaam seiz\* or spasm in flexion or spasms, infantile or spasmus nutans or west syndrom\*).mp. (7677)
  - 25 24 and (2010\* or 2011\*).em. (807)
  - 26 remove duplicates from 25 (611)

## **Appendix e-4: Classification of Evidence for Therapeutic Intervention**

**Class I:** A randomized, controlled clinical trial of the intervention of interest with masked or objective outcome assessment, in a representative population. Relevant baseline characteristics are presented and substantially equivalent among treatment groups or there is appropriate statistical adjustment for differences.

The following are also required:

- a. concealed allocation
- b. primary outcome(s) clearly defined
- c. exclusion/inclusion criteria clearly defined
- d. adequate accounting for dropouts (with at least 80% of enrolled subjects completing the study) and crossovers with numbers sufficiently low to have minimal potential for bias.
- e. For noninferiority or equivalence trials claiming to prove efficacy for one or both drugs, the following are also required\*:
  1. The authors explicitly state the clinically meaningful difference to be excluded by defining the threshold for equivalence or noninferiority.
  2. The standard treatment used in the study is substantially similar to that used in previous studies establishing efficacy of the standard treatment. (e.g., for a drug, the mode of administration, dose and dosage adjustments are similar to those previously shown to be effective).
  3. The inclusion and exclusion criteria for patient selection and the outcomes of patients on the standard treatment are comparable to those of previous studies establishing efficacy of the standard treatment.

4. The interpretation of the results of the study is based upon a per protocol analysis that takes into account dropouts or crossovers.

**Class II:** A randomized controlled clinical trial of the intervention of interest in a representative population with masked or objective outcome assessment that lacks one criteria a-e above or a prospective matched cohort study with masked or objective outcome assessment in a representative population that meets b-e above. Relevant baseline characteristics are presented and substantially equivalent among treatment groups or there is appropriate statistical adjustment for differences.

**Class III:** All other controlled trials (including well-defined natural history controls or patients serving as own controls) in a representative population, where outcome is independently assessed, or independently derived by objective outcome measurement.\*\*

**Class IV:** Studies not meeting Class I, II or III criteria including consensus or expert opinion.

\* Note that numbers 1–3 in Class Ie are required for Class II in equivalence trials. If any one of the three is missing, the class is automatically downgraded to Class III.

\*\*Objective outcome measurement: an outcome measure that is unlikely to be affected by an observer's (patient, treating physician, investigator) expectation or bias (e.g., blood tests, administrative outcome data).



## **Appendix e-5: Classification of Recommendations**

A = Established as effective, ineffective or harmful (or established as useful/predictive or not useful/predictive) for the given condition in the specified population. (Level A rating requires at least two consistent Class I studies.)\*

B = Probably effective, ineffective or harmful (or probably useful/predictive or not useful/predictive) for the given condition in the specified population. (Level B rating requires at least one Class I study or two consistent Class II studies.)

C = Possibly effective, ineffective or harmful (or possibly useful/predictive or not useful/predictive) for the given condition in the specified population. (Level C rating requires at least one Class II study or two consistent Class III studies.)

U = Data inadequate or conflicting; given current knowledge, treatment (test, predictor) is unproven.

\*In exceptional cases, one convincing Class I study may suffice for an “A” recommendation if 1) all criteria are met, 2) the magnitude of effect is large (relative rate improved outcome  $> 5$  and the lower limit of the confidence interval is  $> 2$ ).

**Appendix e-6: Online information resources for medical treatments for infantile spasms (United States only)**

<b>Drug class, name</b>	<b>Resource(s)</b>
Antiepileptic drugs	
Levetiracetam	<ul style="list-style-type: none"> <li>• <a href="#">PubMed Health</a></li> <li>• <a href="#">Keppra UCB</a></li> <li>• <a href="#">NIH MedLine drug information</a></li> </ul>
Nitrazepam	<ul style="list-style-type: none"> <li>• <a href="#">RxMed</a></li> </ul>
Topiramate	<ul style="list-style-type: none"> <li>• <a href="#">Topamax</a></li> <li>• <a href="#">MedlinePlus</a></li> <li>• <a href="#">RxList.com</a></li> </ul>
Sulthiame	<ul style="list-style-type: none"> <li>• <a href="#">PubMed.gov</a></li> </ul>
Valproic acid	<ul style="list-style-type: none"> <li>• <a href="#">RxList.com</a></li> </ul>
Vigabatrin	<ul style="list-style-type: none"> <li>• <a href="#">Drugs.com</a></li> </ul>
Zonisamide	<ul style="list-style-type: none"> <li>• <a href="#">Eisai</a></li> </ul>
Hormone therapies	
Adrenocorticotrophic hormone	<ul style="list-style-type: none"> <li>• <a href="#">Questcor Pharmaceuticals</a></li> </ul>
Dexamethasone	<ul style="list-style-type: none"> <li>• <a href="#">MedlinePlus</a></li> <li>• <a href="#">International Myeloma Foundation</a></li> </ul>
Hydrocortisone	<ul style="list-style-type: none"> <li>• <a href="#">MedlinePlus</a></li> </ul>
Methylprednisolone	<ul style="list-style-type: none"> <li>• <a href="#">Pfizer</a></li> <li>• <a href="#">MedlinePlus</a></li> </ul>
Prednisolone	<ul style="list-style-type: none"> <li>• <a href="#">Medicine.net</a></li> </ul>
Thyrotropin-releasing hormone	<ul style="list-style-type: none"> <li>• <a href="#">Sigma Aldrich</a></li> <li>• <a href="#">Uscn Life Science</a></li> <li>• <a href="#">Antibodies-online.com</a></li> </ul>
Plasma antibody therapies	
IV immunoglobulin	<ul style="list-style-type: none"> <li>• <a href="#">Medscape.com</a></li> </ul>
Vitamins	
Pyridoxine (vitamin B6)	<ul style="list-style-type: none"> <li>• <a href="#">National Institutes of Health</a></li> </ul>

Note: The internet links to these resources are the results of internet searches performed by AAN staff. The information provided in this table is not intended to be representative of a comprehensive internet search or an endorsement of any pharmaceutical/manufacturer website. For more information regarding these drugs, please consult with a physician or pharmacist.