Management of Partial Epilepsy: Focus on Sodium Valproate

Asia Pacific Epilepsy Meeting 2008

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Topics

- General consideration in partial epilepsy
- Clinical trial of monotherapy AEDs
- V. I. P.e study

Objectives

- How to manage partial epilepsy
- Review clinical trials of monotherapy AEDs
- V. I. P. e study

International Classification of Epileptic Seizures

Partial seizures

A. Simple partial seizures

B. Complex partial seizures

C. Partial seizures evolving to secondary generalized seizures

International Classification of Epileptic Seizures

- **Partial seizures**

A. Simple partial seizures

1. With motor signs
2. With somatosensory or special-sensory symptoms
3. With autonomic symptoms or signs
4. With psychic symptoms

ILAE 1981 Proposal for revised clinical and electroencephalographic classification of epileptic seizures. Epilepsia. 1981;22:249-260.

International Classification of Epileptic Seizures

B. Complex partial seizures

1. Simple partial seizures at onset, followed by impairment of consciousness
   a. With simple partial features
   b. With automatisms
2. With impairment of consciousness at onset
   a. With impairment of consciousness only
   b. With automatisms

ILAE 1981 Proposal for revised clinical and electroencephalographic classification of epileptic seizures. Epilepsia. 1981;22:249-260.

International Classification of Epileptic Seizures

C. Partial seizures evolving to secondary generalized seizures

1. Simple partial seizures evolving to generalized seizures
2. Complex partial seizures evolving to generalized seizures
3. Simple partial seizures evolving to complex partial seizures evolving to generalized seizures

ILAE 1981 Proposal for revised clinical and electroencephalographic classification of epileptic seizures. Epilepsia. 1981;22:249-260.

Diagnosis partial epilepsy: easy or not

Diagnosis partial epilepsy: easy or not

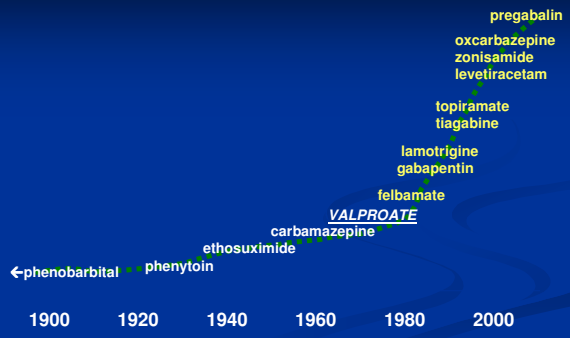
Home VDO by mobile phone

Management of Epilepsy

- Goals of therapy[1]
  - Control seizures
  - Minimize adverse events
  - Improve quality of life
- Important considerations
  - Comorbidities[2,3]
  - Psychosocial needs[4]

1. Dam M. In: Engel J Jr, Pedley TA, eds. *Epilepsy: A Comprehensive Textbook.* Vol 2. Philadelphia, Pa: Lippincott-Raven; 1997:1103-1105.
2. Boro A, Haut S. *Epilepsy Behav.* 2003;4:S2-S12.
3. Karceski S, et al. *Epilepsy Behav.* 2005;7:S1-S64.
4. Schachter SC. *Epilepsy Behav.* 2000;1:120-127.

Antiepileptic Drugs in the United States



Standard AEDs

- Phenobarbital
- Phenytoin
- Carbamazepine
- *Sodium valproate*

New AEDs

- Topiramate
- Gabapentin
- Lamotrigine
- Levetiracetam
- Oxcarbazepine
- Felbamate
- Pregabalin
- Others

TABLE : Variables that affect a specific AED's suitability for patients with newly diagnosed or untreated epilepsy

AED-specific variables	Patient-specific variables	Nation-specific variables
Seizure or epilepsy syndrome specific efficacy/ effectiveness	Genetic background	AED availability
Dose-dependent adverse effects	Gender	AED cost
Idiosyncratic reactions	Age	
Chronic toxicities	Comedications	
Teratogenicity	Comorbidities	
Carcinogenicity	Insurance coverage	
Pharmacokinetics	Relative wealth	
Interaction potential	Ability to swallow pills/tablets	
Formulations		

Journal of Neurology, Neurosurgery and Neuropsychiatry 1985;48:639-44

A prospective study between carbamazepine, phenytoin and sodium valproate as monotherapy in previously untreated and recently diagnosed patients with epilepsy

N CALLAGHAN, RA KENNY, BO'NEILL, M CROWLEY, T GOGGIN
From the Department of Neurology and Neurology Research Laboratory, Cork Regional Hospital, and Department of Statistics, University College, Cork, Eire

SUMMARY One hundred and eighty one patients with previously untreated epilepsy were randomised to sodium valproate, phenytoin or carbamazepine as monotherapy and followed up for a median period which ranged from 14 to 24 months. **All three drugs were highly effective** in the control of generalised seizures but less effective for partial seizures. Excellent or good control was achieved with therapeutic levels of sodium valproate and carbamazepine, but with sub-therapeutic levels of phenytoin.

Table : Overall response in patients with partial seizures with or without secondary generalised attacks

Drug	*Control*		
	Excellent	*Good*	*Poor*
Phenytoin	N 12 (PC 5 SP 7) (57.1%)	N 4 (PC 3 SP 1) (19.0%)	N 5 (PC 4 SP 1) (23.8%)
Carbamazepine	N 11 (PC 5 SP 6) (33.5%)	N 12 (PC 10 SP 2) (38.7%)	N 8 (PC 6 SP 2) (25.8%)
Valproate	N 12 (PC 6 SP 6) (44.4%)	N 9 (PC 7 SP 2) (33.3%)	N 6 (PC 4 SP 2) (22.2%)
Total	N 35 (44.3%)	N 25 (31.6%)	N 19 (24%)

PC = Partial Complex. SP = Simple Partial.

Vol. 327 No. 11 THE NEW ENGLAND JOURNAL OF MEDICINE 1992;327:765-71

A COMPARISON OF VALPROATE WITH CARBAMAZEPINE FOR THE TREATMEMT OF COMPLEX PARTIAL SEIZURES AND SECONDARILY GENERALIZED TONIC-CLONIC SEIZURES IN ADULTS

Richard H. Mattson, M.D., Joyce A. Cramer, B.S., Joseph F. Collines, Sc.D., And the Department of Veterans Affairs Epilepsy Cooperative Study No. 264 Group

Conclusion: VPA is as effective as carbamazepine for treatment of secondarily GTC

Journal of Neurology, Neurosurgery and Neuropsychiatry 1994;57:682-87.

A multicentre comparative trial of sodium valproate and carbamazepine in adult onset epilepsy

A Richens, D L W Davidson, N E F Cartlidge, D J Easter on behalf of the Adult EPITEG Collaborative Group

Figure 3 Remission analysis: percentage of patients free of seizures for 12 months: patients with partial seizures with or without generalisation.

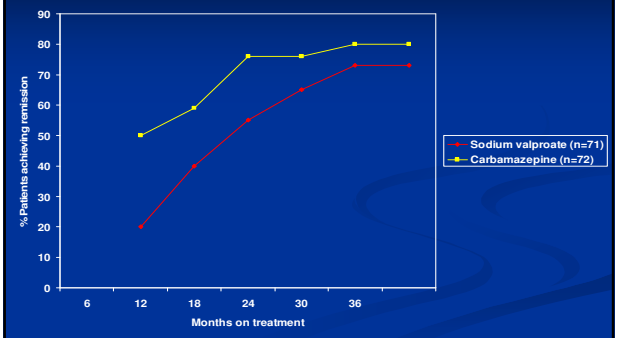


Table Adverse events reported by four or more patients at any time during treatment

Adverse event	*Number of patients reporting adverse event*	
	Sodium valproate	*Carbamazepine*
Fatigue	15	17
Somnolence	12	20
Nausea/vomiting/dyspepsia	13	15
Weight increase	**21****	**2**
Rash	**3**	**18****
Headache	6	11
Dizziness	**5**	**12***
Tremor	9	3
Amnesia	6	3
Depression	4	4
Pregnancy	1	6
Alopecia	5	1
Abnormal hepatic function	2	3
Ataxia	0	4
Appetite increase	4	0
Aphasia	1	3
Other events	43	14
Total no adverse events	151	163

*p = 0.05; **p = 0.01 between treatments, Fisher's exact test. Data from 174 patients on valproate (165 for at least three months) and 178 patients on carbamazepine (147 for at least three months)

Journal of Neurology, Neurosurgery and Neuropsychiatry 1995;58:44-50

Phenobarbitone, phenytoin, carbamazepine, or sodium valproate for newly diagnosed adult epilepsy: a randomised comparative monotherapy trial

A J Heller, P Chesterman, R D C Elwes, P Crawford, D Chadwick, A L Johnson, E H Reynolds

Figure1 Actuarial percentages of patients remaining seizure free in the four durg groups.

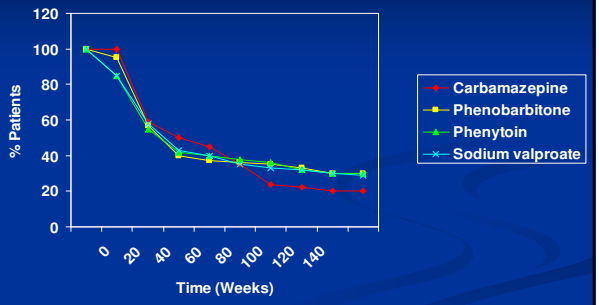
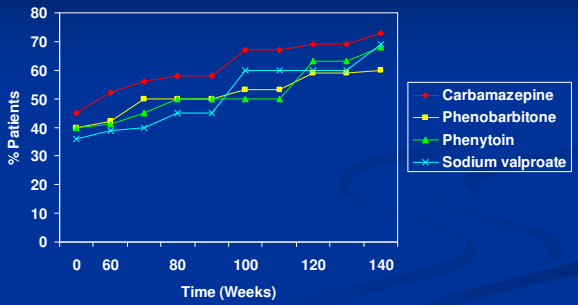
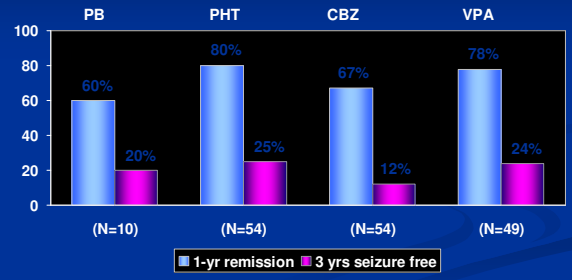


Figure 2 Actuarial percentages of patients achieving one year remission in the four drug groups.



Newly Diagnosed Epilepsy : Randomised Comparative Trial



de Silva M et al. Lancet 347:709, 1996

Randomized comparative monotherapy trial of phenobarbitone, phenytoin, carbamazepine or sodium valproate for newly diagnosed childhood epilepsy

THE LANCET, vol 347, March 16, 1997

Results: efficacy

Actuarial percentage seizure free by selected times from randomization

	Number of children			Actual % seizure free			
	randomised	With seizure recurrence	Seizure free	6 m.	12 m.	24 m.	36 m.
Treatment							
Phenobabitone	10*	8*	2*	40*	40*	20*	20*
Phenytoin	54	42	12	46	39	27	25
Carbamazepine	54	47	7	30	28	21	12
Sodium Valproate	49	39	10	37	30	24	24
Total	167	136	31	38	33	24	20

*Number at risk small

No significant different in efficacy between PHB, PHT, CBZ, VPA

ELSEVIER

EPILEPSY RESEARCH

Epilepsy Research 26 (1997) 451–460

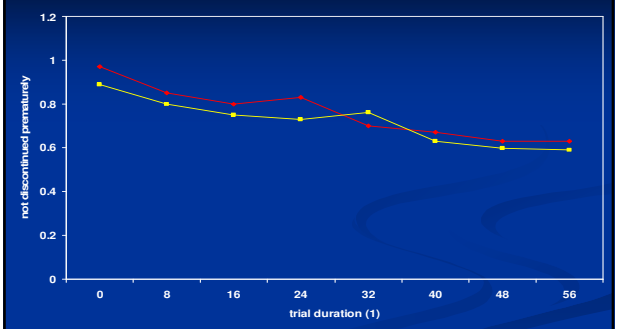
A double-blind controlled clinical trial: oxcarbazepine versus sodium valproate in adults with newly diagnosed epilepsy[1]

Walter Christe[a], Günter Krämer[2,b], Ulf Vigonius[c,*], Harald Pohlmann[c], Bernhard J. Steinhoff[3,d], Martin J. Brodie[e], Alan Moore[c]

[a]*Department of Neurology, University Hospital Rudolf-Virchow, Berlin, Germany*
[b]*Department of Neurology, University Hospital, Mainz, Germany*
[c]*Ciba-Geigy Ltd., Basel, Switzerland*
[d]*Department of Neurology, University Hospital Munich-Grosshadern, Munich, Germany*
[e]*Epilepsy Unit, Western Infirmary, Glasgow, UK*

Received 25 January 1996; revised 30 October 1996; accepted 5 November 1996

Fig.2 Patients remaining in the trial Kaplan-Meier curve



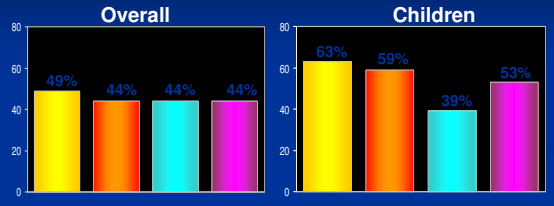
(1) Weeks between randomisation visit and last regularly visit

Monotherapy Comparison Trial

- Physician selects "best standard treatment" (CBZ or VPA) for individual patient
- Patient assigned to CBZ or VPA branch
- Patient randomised to physician's selected treatment or TPM (100 or 200 mg/day)

Privitera MD et al. Epilepsia 41(Suppl 7):93, 2000

Monotherapy Comparison Trial: Patients Seizure-Free ≥6 Months*



Privitera MD et al. Epilepsia 41(Suppl 7):93, 2000
Wheless JW et al. Neurology 56(Suppl 3):A234, 2001

Discontinuations Due to Adverse Events

TPM 100	19%
TPM 200	28%
CBZ 600	25%
VPA 1250	23%

Privitera MD et al. Epilepsia 41(Suppl 7):93, 2000
Wheless JW et al. Neurology 56(Suppl 3):A234, 2001

Cognitive Complaints

	TPM 100 (N=210)	CBZ 600 (N=126)	VPA 1250 (N=78)
Somnolence	12	14	15
Memory difficulty	8	5	6
Concentration/attention difficulty	4	4	1
Psychomotor slowing	4	4	1
Confusion	3	3	0
Language problems	3	6	4
Cognitive problems	3	1	1
Speech problems	2	2	0

Privitera MD et al. Epilepsia 41(Suppl 7):93, 2000

Neurology 1997;48:182-188

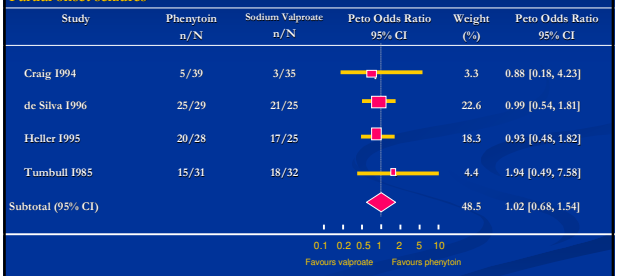
Safety and efficacy of divalproex sodium monotherapy in partial epilepsy:
A double-bind, concentration-response design clinical trial

A. Beydoun,MD; J.C. Sackellares, MD; V. Shu, PhD; and the Depakote Monotherapy for Partial Seizures Study Group

- Median reduction for secondarily GTC was 70%
- Efficacy of divalproex sodium as monotherapy for patient with partial epilepsy

Comparison Phenytoin versus Sodium valproate, Outcome : Time to I2 month remission

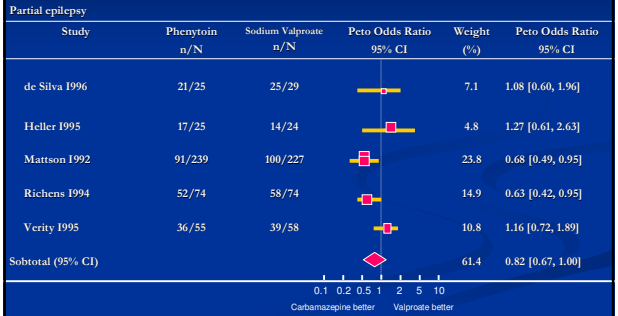
Partial onset seizures



Cochrane Database of Systematic Reviews 2001, Issue 4. Art. No.: CD001769.

Comparison Carbamazepine versus Sodium valproate, Outcome : Time to I2 - month remission from seizures

Partial epilepsy



Cochrane Database of Systematic Reviews 2000, Issue 3. Art. No.: CD001030.

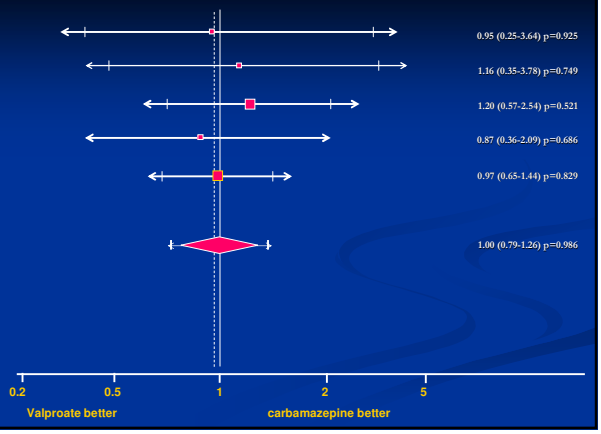
Epilepsia 43(5):505-513, 2002
Blackwell Publishing Inc.

Carbamazepine versus Valproate Monotherapy for Epilepsy: A Meta-analysis

Antohny G. Marson, Paula R. Williamson, Helen Clough, Jane L. Hutton, and David W. Chadwick, on behalf of the Epilepsy Monotherapy Trial Group

Department of Neurological Science, Faculty of Medicine, and Division of Statistics and Operational Research, University of Liverpool, Liverpool; and Department of Statistics, University of Warwick, England

Partial onset seizures: Hazard Ratio

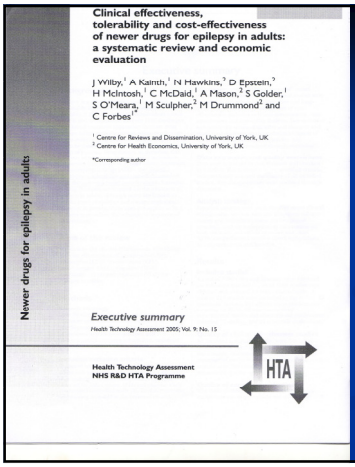


Recommendations Regard the Initial Medication Choice With Maintenance Dosing for Epilepsy in Adults

AEDs as Monotherapy of Partial Seizures	AAN	NICE	SIGN	Typical Dose (mg)/Day	Cost/Unit, U.S.$	Cost/Mth U.S.$ (30-Day Supply)
Phenobarbital	1 st	-	-	100	0.07 (97.2 mg)	2
Carbamazepine	1 st	1 st	1 st	1,000	0.18 (200 mg)	27
Phenytoin	1 st	1 st	-	300	0.31 (100 mg)	28
Valproic acid	1 st	1 st	1 st	1,000	0.29 (250 mg)	34
Gabapentin	1 st	-	-	1,200	0.85 (300 mg)	102

A Comparison of CPGs in the Initial Pharmacological Management of New-Onset Epilepsy in Adults.

Nalin P. Journal of Managed Care Pharmacy 2006;12:55-60.



Assessment of Cost-effectiveness: Monotherapy for Newly Diagnosed

- Integrated ***economic analysis*** showed similar health benefits for various AEDs and that new AEDs were more expensive than older AEDs.
- Consequently, the ***older AEDs were more likely to be cost-effective.***

Epilepsia 47(7):1094-1120, 2006
Blackwell Publishing Inc.

Original Research

ILAE Treatment Guidelines: Evidence-based Analysis of Antiepileptic Drug Efficacy and Effectiveness as Initial Monotherapy for Epileptic Seizures and Syndromes

Tracy Glauser, Elinor Ben-Menachem, Blaise Bourgeois, Avital Cnaan, David Chadwick, Carlos Guerreiro, Reetta Kalviainen, Richard Mattson, Emilio Perucca, And Torbjorn Tomson

TABLE : Adults with partial-onset seizures: number of relevant studies categorized by class of study and AED involved

Class	CBZ	PT	VPA	LTG	PB	OXC	TPM
I	2	1	0	0	1	0	0
II	1	0	1	0	0	0	0
III-DB	6	4	2	3	0	4	3
III-OL	1	6	8	2	4	0	0
Total	19	11	11	5	5	4	3

TABLE : Summary of studies and level of evidence for each seizure type and epilepsy syndrome

Seizure type or epilepsy syndrome	Class I studies	Class II studies	Class III studies	Level of efficacy and effectiveness evidence (in alphabetic order)
Adults with partial-onset seizures	2	1	30	Level A: CBZ, PHT Level B: VPA Level C: GBP, LTG, OXC, PB, TPM, VGB
Children with partial-onset seizures	1	0	17	Level A: OXC Level B: None Level C: CBZ, PB, PHT, TPM, VPA
Elderly adults partial-onset seizures	1	1	2	Level A: GBP, LTG Level B: None Level C: CBZ

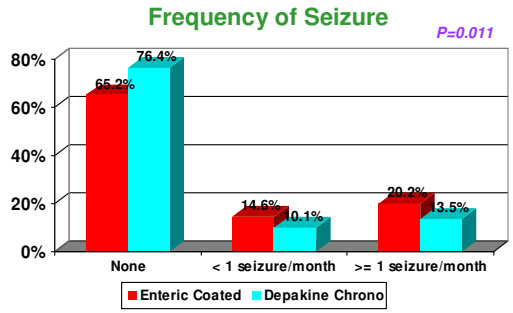
THADEC

THAILAND DEPAKINE CHRONO STUDY

OBJECTIVES

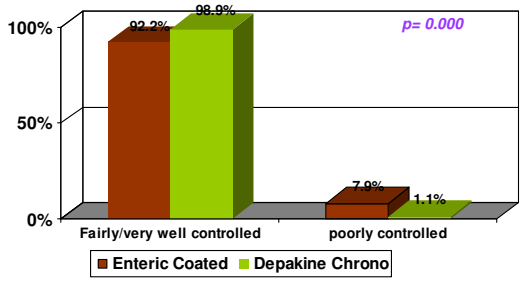
To assess the compliance and satisfaction consequences in epileptic patients switched from more than two times daily enteric coated tablet of Depakine® regimen to the same total daily dose of Depakine Chrono® given once or twice daily

RESULT of SECONDARY OUTCOME



Sig. Diff. in seizure frequency between Enteric Coated & Depakine Chrono, p<0.05

RESULTS of SECONDARY OUTCOME



Sig. Diff. in seizures control between Enteric Coated & Depakine Chrono, p<0.05

Table 2. Main outcome according to treatment groups

Anti-epileptic therapy	SVSR (%)	SVEC (%)	p value
Administration			0.000
Once daily	85.4	12.4	
Twice daily	14.6	34.8	
> 2 times/day	0.0	52.8	
Satisfaction			0.000
Very/fairly happy	94.4	56.2	
Neither happy/unhappy	3.4	21.3	
Fairly/very unhappy	2.2	22.5	
Experiencing problem			0.000
Never	67.4	38.2	
Sometimes/often	23.6	41.6	
Occasional	9.0	20.2	
Missing medication			0.000
Never	77.5	40.4	
Less1/month	19.1	31.5	
≥ 1 month but < 1/week	2.2	18.0	
≥ 1 week	1.1	10.1	
Over taking of drug dose			0.206
Never	96.6	91.0	
Sometimes/occasional	2.2	9.0	
Often	1.1	0.0	

SVSR: Sodium Valproate slow-release , SVEC: Sodium Valproate Enteric coated form

VIP

A MULTINATIONAL, OBSERVATIONAL STUDY OF THE EFFECTIVENESS AND TOLERABILITY OF FIRST-LINE MONOTHERAPY WITH SODIUM VALPROATE IN FOCAL EPILEPSY

Depakine

Jedrzejczak J et al. An observational study of first-line valproate monotherapy in focal epilepsy. Eur J Neurol 15(1):66-72, 2008.

V.I.P.e – Valproate In Partial epilepsy

- Study dates: 2001-2004
- Study period: 6 months (or 12 months*) for each patient

* Study period was chosen by participating countries

Depakine

Jedrzejczak J et al. An observational study of first-line valproate monotherapy in focal epilepsy. Eur J Neurol 15(1):66-72, 2008.

Study design

Participating countries

Croatia
Czech Republic
India
Korea
Lebanon
Malaysia
Poland
Portugal
Romania
Russia
Slovenia
South Africa
Taïwan
Thailand
Morocco
Tunisia

N=1989 patients

Depakine

Jedrzejczak J et al. An observational study of first-line valproate monotherapy in focal epilepsy. Eur J Neurol 15(1):66-72, 2008.

Study objective

- Observational, open-label, multinational prospective study
- To assess the safety and efficacy of sustained-released valproate (Depakine Chrono®) used as first monotherapy in a cohort of patients newly or recently diagnosed with partial epilepsy
- To assess efficacy according to the type, aetiology and topographic localisation of partial seizures

Depakine

Jedrzejczak J et al. An observational study of first-line valproate monotherapy in focal epilepsy. Eur J Neurol 15(1):66-72, 2008.

Inclusion criteria

- Adults and children over six years
- Male or female (in women of childbearing potential, the patients practicing efficient contraception)
- Patient newly or recently diagnosed with partial epilepsy with or without secondary generalized seizure and requiring a first anti-epileptic treatment
- Patients able to complete the patient's diary seizure card and to follow the study procedures

Depakine

Jedrzejczak J et al. An observational study of first-line valproate monotherapy in focal epilepsy. Eur J Neurol 15(1):66-72, 2008.

Inclusion criteria

- Patients requiring a first monotherapy treatment for partial epilepsy and who may benefit from the use of valproate
- Patients who reported at least 2 partial seizures with or without secondary generalisation during the previous 6 months
- Patients or his / her legal representative (for children) signed the informed consent form after the nature of the study has been fully explained (if required by local regulations)

Depakine

Jedrzejczak J et al. An observational study of first-line valproate monotherapy in focal epilepsy. Eur J Neurol 15(1):66-72, 2008.

Exclusion criteria – according to the local SmPC

- Patients with:
  - Acute or chronic hepatitis, personal or family history of hepatitis
  - Hypersensitivity to valproate
  - Hepatic porphyria
  - History of non epileptic seizures
  - Active CNS infection, demyelinating disease, any CNS disease deemed to be significantly progressive during the course of the study (low grade brain tumor can be included)
  - History of drug or alcohol abuse
- Patients who:
  - Are pregnant/ trying to become pregnant or who are lactating
  - Have taken investigational drug within 30 days prior to first visit

Depakine

Jedrzejczak J et al. An observational study of first-line valproate monotherapy in focal epilepsy. Eur J Neurol 15(1):66-72, 2008.

Evaluation criteria

Primary efficacy endpoint

- remission rate: proportion of seizure-free patients at 6 months

Safety

- spontaneous reporting of adverse events
- adverse events leading to drop out

Depakine

Jedrzejczak J et al. An observational study of first-line valproate monotherapy in focal epilepsy. Eur J Neurol 15(1):66-72, 2008.

Evaluation criteria

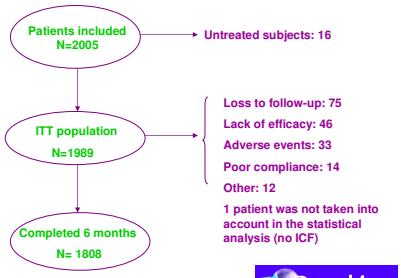
Secondary efficacy endpoints

- retention rate: proportion of patients who completed the 6-month study
- Clinical Global Impression
- dose to reach maximal efficacy according to the age range
- efficacy according to type, aetiology, topographic localisation and age of the patient

Depakine

Jedrzejczak J et al. An observational study of first-line valproate monotherapy in focal epilepsy. Eur J Neurol 15(1):66-72, 2008.

Patient flow diagram



Depakine

Jedrzejczak J et al. An observational study of first-line valproate monotherapy in focal epilepsy. Eur J Neurol 15(1):66-72, 2008.

Patient characteristics

Sex ratio (men/women/missing data)	54.5% / 45.2% / 0.3%
Mean age (years)	24.5 +/- 17.3
Mean duration of epilepsy (months)	7.6 +/- 29.5

40% of the patients were children ≤ 15 years

Depakine

Jedrzejczak J et al. An observational study of first-line valproate monotherapy in focal epilepsy. Eur J Neurol 15(1):66-72, 2008.

Clinical patient characteristics

Type of Seizure (n - %)		
Simple Partial (SP)	448	22,5%
Complex Partial (CP)	432	21,7%
Secondary Generalized Tonic-Clonic (SGTC)	527	26,5%
SP + CP	80	4,0%
SP + SGTC	240	12,0%
CP + SGTC	213	10,7%
SP + CP + SGTC	49	2,5%
Not determined	1	0,1%
Aetiology (n - %)		
Idiopathic	638	32,1%
Symptomatic	738	37,1%
Cryptogenic	418	21,0%
Not Determined	194	9,7%
Missing data	2	0,1%
Localisation (n - %)		
Temporal	758	38,1%
Extratemporal	732	36,8%
Temporal + extratemporal	24	1,2%
Not Determined	472	23,7%
Missing data	4	0,2%

Jedrzejczak J et al. An observational study of first-line valproate monotherapy in focal epilepsy. Eur J Neurol 15(1):66-72, 2008.

Mean daily dose of sustained-release valproate

Patients	n	Mean daily dose (mg/d)
Seizure Type		
SP seizures	448	779
CP seizures	432	878
SGTC seizures	527	841
SP + CP seizures	80	885
SP + SGTC seizures	240	899
CP + SGTC seizures	213	991
SP + CP + SGTC seizures	49	1065

SP – simple partial, CP – complex partial, SGTC – secondary generalised tonic clonic

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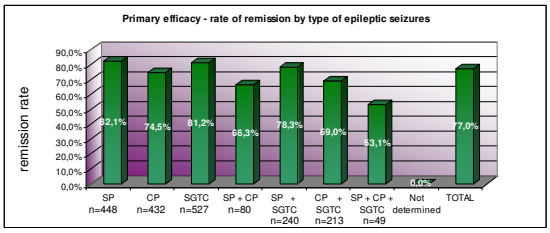
Jedrzejczak J et al. An observational study of first-line valproate monotherapy in focal epilepsy. Eur J Neurol 15(1):66-72, 2008.

High rates of remission at six months – by type of epileptic seizures



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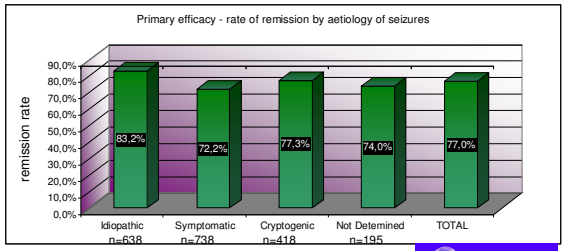
Jedrzejczak J et al. An observational study of first-line valproate monotherapy in focal epilepsy. Eur J Neurol 15(1):66-72, 2008.

High rates of remission at six months – by aetiology of seizures



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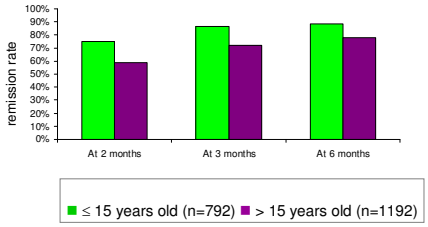
Jedrzejczak J et al. An observational study of first-line valproate monotherapy in focal epilepsy. Eur J Neurol 15(1):66-72, 2008.

Seizure free rate improved over the 6-month period



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High retention rates and marked improvement in CGI scale

	Age group		
	≤ 15 years (N = 792)	> 15 years (N = 1192)	Total (N = 1989)
SEIZURE OUTCOME			
Retention Rate (%)	92.0 [90.1 – 93.9]	88.7 [86.9 – 90.5]	90.0 [88.7 – 91.4]
Neurological exam	90.6% normal	85.4% normal	87.5% normal
CLINICAL GLOBAL IMPRESSION			
Improvement			
Marked	662 (89.0%)	908 (82.9%)	1572 (85.3%)
Unchanged or worsened	9 (1.2%)	7 (0.6%)	16 (0.9%)
Side effects			
None	674 (90.6%)	981 (89.6%)	1658 (90.0%)

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Overall good safety profile

	N° of subjects with AEs	N° of subjects with SAEs
All adverse events	245 (12.3%)	15 (0.8%)
Leading to treatment discontinuation	34 (1.7%)	3 (0.2%)
Severity		
Mild	136 (6.8%)	1 (<0.1%)
Moderate	107 (5.3%)	5 (0.3%)
Severe	16 (0.8%)	9 (0.5%)
Individual AEs		
Weight gain	51 (2.6%)	-
Alopecia	43 (2.2%)	-
Nausea	24 (1.2%)	-
Vomiting	21 (1.1%)	1 (<0.1%)
Tremor	20 (1.0%)	-
Somnolence	12 (0.6%)	-
Dizziness	11 (0.6%)	-
Headache	11 (0.6%)	1 (<0.1%)

AE – adverse event, SAE – serious adverse event

Jedrzejczak J et al. An observational study of first-line valproate monotherapy in focal epilepsy. Eur J Neurol 15(1):66-72, 2008.

Conclusion

- **Efficacy**
  - **Overall high remission rates at six months - 77% in patients with focal epilepsy**
  - **High 90% treatment retention**
- **Safety**
- **Overall good safety of the treatment**

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CGI – Clinical Global Impression

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SUSTAINED RELEASE SODIUM VALPROATE IS EFFECTIVE AND SHOWS OVERALL GOOD TOLERABILITY AS FIRST-LINE MONOTHERAPY IN FOCAL EPILEPSY

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