

Neurontin: Doctors need to be Warned - The ABCs

- A. Illegal Marketing for off label use was successful
- B. 8 million (at least) off label scripts – 2007
- C. Off label use means:
 - More suicide risk (depression, pain, anxiety)
 - NO benefits except \$\$\$

A. List of “ ‘Movers and Shakers’ in regards to the off label use of NEURONTIN”

Jul-09-96 06:01A Richard Grady 914-738-1620 P.02

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CC: Laura Johnson
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PARKE-DAVIS

TO: Medical Liaisons Phil Magistro DATE: July 9, 1996

CC: NEURONTIN Marketing Team

FROM: Richard Grady *RG*

Please find listed below pertinent information regarding the off label use of NEURONTIN. Note that if you have any additions/deletions please feel free to contact me.

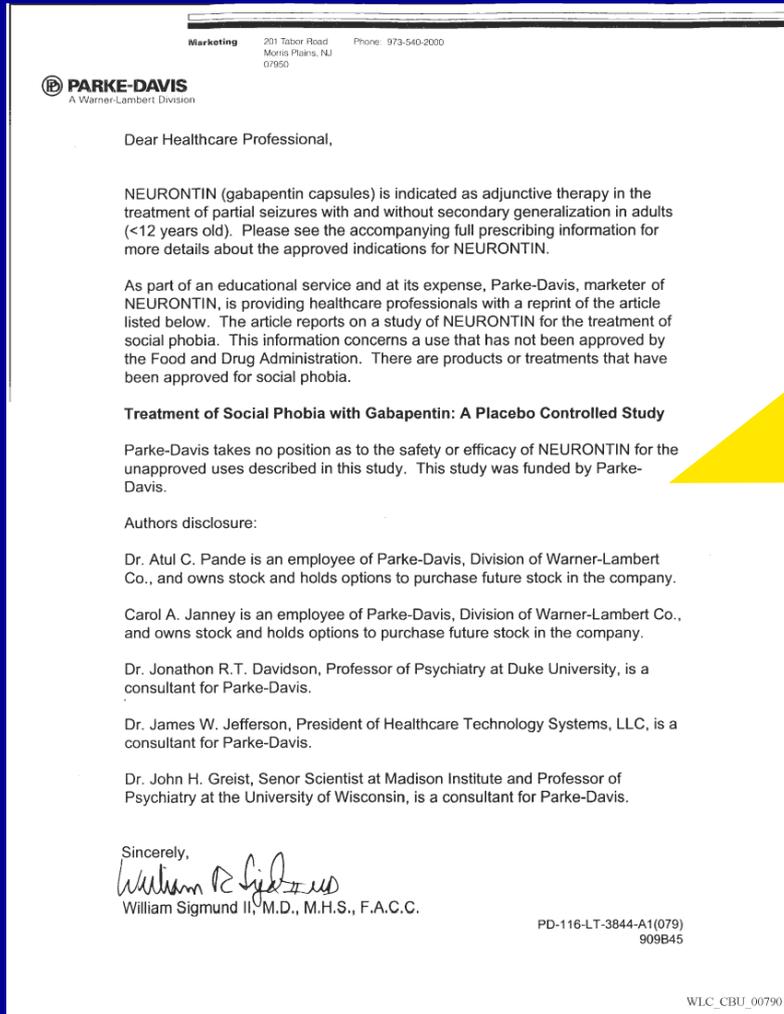
One important point first, there have been cases of pharmacists questioning Rx's for NEURONTIN if the patient does not have epilepsy. To avoid any problems, just tell the physician to write on the Rx pad, *For pain management*, when he/she is Rx'ing NEURONTIN.

BOSTON

1. Bruce Ehrenberg, M.D. New England Medical Center, Tufts Medical School
 - * Has over 100 patients with restless leg syndrome on NEURONTIN with 90% of those patients receiving some benefit. Dr. Ehrenberg is the investigator for a restless leg syndrome trial. Secretary- Lois Phone- (617) 636-7504
2. Ken Gorson, M.D. St. Elizabeth's Medical Center, Tufts Medical School
 - * Participating in a single site, placebo controlled NEURONTIN for painful diabetic neuropathy study.
3. Daniel Carr, M.D. New England Medical Center, Tufts Medical School Anesthesiologist/Pain Management
 - * Participating in multi-center, post-herpetic neuralgia study.
4. Steven Schachter, M.D. Beth Israel Medical Center, Harvard Medical School Director of Epilepsy Center
 - * Decile 10, over 20% nRx share for NEURONTIN, I think we all are aware of Dr. Schachter's background.

“ . . . there have been cases of pharmacists questioning Rx's for NEURONTIN if the patient does not have epilepsy. To avoid any problems, just tell the physician to write on the Rx pad, *For pain management*, when he is RX'ing NEURONTIN.”

A. Dear Doctor Letter Pushing Neurontin for Social Phobia



Dear Healthcare Professional:

“Treatment of
Social Phobia
with gabapentin”

A. CME used to promote off-label use

Neurontin cont'd

Strategies/Tactics

- Target high-potential physicians -- representatives are focusing their selling effort on decile 8-10 neurologists. Moving our high deciles will give us the greatest gains in our market share.
- Training -- renewed emphasis is being placed on preparing the sales force to aggressively sell Neurontin to the neurology audience. The sales force will be more effective with their time when calling on the neurologists.
- Shadowing/Preceptorships -- each representative will participate in a preceptorship with a high-decile no-see neurologist. They will also participate in Preceptorships on their own with influential called-on physicians to build relationships and spur more meaningful discussions.
- Expand the speaker base -- identify and train strong speakers to speak locally for Neurontin. Peer-to-peer speaking is one of the most effective ways to communicate our message.
- Medical Liaisons -- 90% percent of their time is dedicated to responding to inquiries face to face with our area neurologists. It is critical to take advantage of the momentum regarding Neurontin in other uses.
- Consultants Programs -- Continued interaction with our local thought-leaders. Programs will be held throughout the CBU on a local level. Hosted by a local thought-leader and presentations given by national speakers. Key topics for discussion include:
 - monotherapy -- especially use in the non-refractory pt.
 - special pt populations (children, women, elderly)
 - new uses for anticonvulsants
 - optimal use of Neurontin
- Psychiatry CME Program -- support for education regarding anticonvulsants in the treatment of bipolar disorders taking advantage of our high potential.
- Chronic Pain CME Study Groups -- Continue the series throughout the CBU.
- Funding for Local Studies and Published Findings -- Protocols placed at key institutions with the goal of publishing data.
- Strengthen Relationships with Thought-Leaders -- they are not convinced of Neurontin superiority, their support is critical.

• Special populations (children, women, elderly)

• Psychiatry CME Program

• Chronic Pain CME Study Groups

A. Methods of Marketing Neurontin for Psychiatric Disorders

Communication

General Suggestions:

- Deliver safety and efficacy message to Psychiatric community
- Establish a way for representatives to visit Psychiatrists' offices
- Parke-Davis should not look to promote Neurontin as a monotherapy agent for psychiatric disorders, but rather focus attention on promoting as a second line agent to Lithium.
- Efforts should be focused on taking some of the market from benzodiazepines for the treatment of panic disorder, general anxiety, acute stress and refractory bipolar disorders.

Educational Suggestions:

- CME Programs
- Blanket Psychiatric convention market with satellite symposia, posters and papers.
Psychiatric conventions discussed:
 - US Psych Congress
 - CINP
 - AC Posters
 - NCDEU
 - ACNP
 - ASCP
- Initiate quarterly advisory board meetings in order to stay abreast of current events within the psychiatric community. The first of which should commence immediately following the completion of new data.
- Create a slide kit which would entail new data from ongoing and future studies, Neurontin slides, and summary slides
- Generate mailings to the Psychiatric community on updated and relevant information on anticonvulsants and psychiatric disorders
- Following the completion of the ongoing and additional studies, write and publish papers in psychiatric journals.
- Develop journal supplements

Conclusion

With the increasing recognition of Lithium's inadequacy as an acute and prophylactic treatment for many patients with bipolar illness, the search for alternative agents has centered around anticonvulsants. Through discussions with the advisory board, it was determined that there is a definite need for further studies and additional information to be distributed within the psychiatric community on the usage of anticonvulsant therapy for psychiatric disorders. Recommendations for the appropriate resources and tools are mentioned above. Furthermore, there was a general consensus that Gabapentin has a positive anxiolytic effect profile, lack of drug-drug interactions, non-addicting hypnotic effects, and overall safety and efficacy, therefore it can move rapidly to the front of the anticonvulsant class in the treatment of psychiatric disorders. With this in mind, it is important to execute the studies and educational tactics mentioned above in order to bypass the other anticonvulsants within this market.

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CONFIDENTIAL

- Target psychiatrists
- Take some of the market from benzodiazepines
- Seed the literature

A. Seeding the Medical Literature

Emerging Applications in the Use of AEDs

Program #15: Review Article

Objective(s): Legitimize use of AEDs for emerging applications through journal publication

Audience: Neurologists and pain specialists

Description: Provide a complete "historical synopsis" of AED use in existing and emerging applications (10-15 pages)
☆safety and efficacy
☆QOL
☆monotherapy
☆first line therapy
☆dosing
☆old vs new

Timing: T9-May 1997

Publish in a respected, indexed journal
Reprints available through newsletter

V057677

- Target Pain Specialists
- Publish in respected pubmed journal
- Send Reprints

B. Off Label a continuing success



Do these drugs really belong to a single class?
Differences in mechanisms and clinical uses

Compound	Mechanism of Action	Total Rx (1000s)	% Epilepsy	% Non-epilepsy
Pregabalin	$\alpha_2\delta$ ligand	10,503	1.8	98.2
Gabapentin	$\alpha_2\delta$ ligand	12,784	7.2	92.8
Topiramate	Na ⁺ channel blocker; enhance GABA-A; inhibit AMPA/kainate	7,053	25.8	74.2
Valproate	Na ⁺ channel blocker; T Ca ²⁺ channel blocker; GABA-T inhibitor	7,428	28.6	71.4
Lamotrigine	Na ⁺ channel blocker; N/P Ca ²⁺ channel blocker	8,971	32.7	67.3
Oxcarbazepine	Na ⁺ channel blocker	3,929	50.8	49.2
Carbamazepine	Na ⁺ channel blocker	24,553	52.7	47.3
Tiagabine	GAT-1 blocker	147	60.7	39.3
Zonisamide	Na ⁺ channel blocker; T Ca ²⁺ channel blocker	4,123	78.6	21.4
Levetiracetam	SVA-2 ligand	2,645	85.7	14.3
Felbamate	Na ⁺ channel blocker; enhance GABA-A; inhibit NMDA receptors	29	97.0	3.0



WARNING
NEEDED



“Neurontin’s Labeling
lacked adequate
directions for such [off
label] use”

Doctors need to know

FDA SHOULD REQUIRE that Pfizer use all the methods it used to illegally market to get the truth out about risks and off label use

- 1.CME on Off Label uses
- 2.Publish Literature on the truth
- 3.Detailing on the truth
- 4.Conferences

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Not paid for work on this project.

Have served as a consultant to authors of
the citizens petition and suicide patients