

OFF-LABEL MARKETING & THE FALSE CLAIMS ACT

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FRANKLIN V. PFIZER

WHO IS DAVID FRANKLIN?

- Ph.D. in biology
- Hired by Warner-Lambert as a medical liaison 1996
- Witnessed off-label marketing and kickbacks
- Uncomfortable placing sales over science
- Worried that he would be made a scapegoat
- Left Warner-Lambert after 4 months
- Filed lawsuit under False Claims Act (FCA)

GLOBAL SETTLEMENT

- Warner-Lambert pled guilty to two counts of violating the Food Drug & Cosmetic Act
- Warner-Lambert paid \$430 million:
 - \$152 million to settle federal civil False Claims Act liabilities
 - \$38 million to settle its state civil liabilities to the fifty states and fund remediation program
 - \$240 million federal criminal fine
- Relator's share = \$26.6 million
- Corporate Integrity Agreement

WHAT DR. FRANKLIN HEARD

- Medical affairs supervisor: “When we get out there, we want to kick some ass on Neurontin, we want to sell Neurontin on pain. All right? And monotherapy and everything we can talk about, that’s what we want to do”
(Voicemail 1-2)

WHAT DR. FRANKLIN HEARD

- Director of sales: “I want you out there every day selling Neurontin...We all know that Neurontin’s not growing for adjunctive therapy, besides that’s not where the money is. Pain management, now that’s money. Monotherapy, that’s money...Neurontin for pain, Neurontin for monotherapy, Neurontin for bipolar, Neurontin for everything...I don’t want to see a single patient coming off Neurontin before they’ve been up to at least 4800 mg/day. I don’t want to hear that safety crap either” (Disclosure at 11)

WHAT DR. FRANKLIN HEARD

- Human resources director: “Make sure you sell yourself, remember this is a sales position, you’ve got to be aggressive” (Disclosure at 12)
- Director of sales: “If we are going to market Neurontin effectively, we have to do it for monotherapy...also for pain and bipolar and other psychiatric uses. And, now, you know, that is a labeling issue” (Voicemail at 1-23 – 1-24)

WHAT DR. FRANKLIN HEARD

- Medical liaison: “I just completed a neurology preceptorship with a physician in Yonkers...The structure, basically, was that the doctor would review the chart of each patient with me in a one-on-one fashion. Then we would go meet the patient. The patient would be examined, and then, while the patient was dressing, the doctor and I, one-on-one, would discuss the patient and therapeutic options...Two prescriptions were generated today...I felt that I influenced [the physician] to the need of titrating up...The second situation was a 65-year-old man who has neuralgia in all of his limbs...And the patient, you know, basically agreed to give the drug a try” (Voicemail at 1-155 – 1-159)

WHAT DR. FRANKLIN HEARD

- Director of sales: “But, gee, just think of how we could expand the market here with Neurontin and some of these other disorders. So, I guess the sky is the limit, right?” (Voicemail at 1-59 – 1-60)

WHAT IS THE FALSE CLAIMS ACT (FCA)?

- A primary tool of government to fight fraud
- Enacted in 1863 in response to unscrupulous profiteering during Civil War
- Broad remedial statute intended to reach all types of fraud
- Relator's share = 15% - 30%
- Original source
- Protection against retaliation

WHAT IS THE FALSE CLAIMS ACT (FCA)?

- Imposes liability for any person who –
 - (1) Knowingly presents, or causes to be presented, to the United States Government **a false or fraudulent claim for payment** or approval; or
 - (2) Knowingly makes, uses, or causes to be made or used, **a false record or statement** to get a false or fraudulent claim paid or approved by the Government
- In addition to federal FCA, 12 states now have state false claims laws

MEDICAID & FALSE CLAIMS

- Medicaid reimbursement:
 - Prescription → Pharmacy → Medicaid
 - Blend of federal and state funds
- With limited exceptions, off-label uses are not covered by Medicaid and are not eligible for reimbursement

OFF-LABEL PROMOTION

- In general, doctors may prescribe a drug for unapproved uses
- In general, manufacturers may not promote unapproved uses.
- Benefits: some off-label uses are scientifically valid and provide tremendous benefits to patients, especially in areas of life-saving drugs
- Risks: no guarantee of scientific validity; unknown health risks; waste of public resources; certain side effects not justified

OFF-LABEL PROMOTION

- Profit motive:
 - Clinical trials costly
 - Off-label sales can be significant
 - These factors can affect corporate judgment
- Off-label promotion relies on covert marketing techniques
- Before 1997, FDA allowed dissemination of information about off-label uses only when such information was solicited by the physician



NEURONTIN

NEURONTIN

- **APPROVED INDICATION (between 1994 – 2001)**

Neurontin® (gabapentin) is indicated as adjunctive therapy in the treatment of partial seizures with and without secondary generalization in adults with epilepsy, at doses ranging between 900 mg to 1800 mg per day

NEURONTIN

● UNAPPROVED INDICATIONS

Alcohol Detoxification
Amyotrophic Lateral Sclerosis
Antidepressant-Induced Bruxism
Anxiety Disorder; Panic Disorder; OCD
Behavior Problems - Dementia-Related
Bipolar Disorder; Mania
Borderline Personality Disorder
Brachioradial Pruritus
Central Nervous System Disorders
Charles Bonnet Syndrome
Ciguatera Poisoning
Cluster Headache
Cocaine Dependency
Dystonia
Essential Tremor
Failed Back Surgery Syndrome
Glossodynia
Sensory Deficits
Headache (SUNCT)
Migraine Prophylaxis
Multiple Sclerosis Complications
Myalgias - Taxane Induced
Neuropathic Cancer Pain
Neuropathic Pain Syndromes
Neuropathy - HIV-Related
Nicotine Withdrawal
Nystagmus
Orthostatic Tremor
Pain - Postpoliomyelitis Pain
Pain - Reflex Sympathetic Dystrophy
Partial Seizures - Monotherapy
Phantom Limb Syndrome
Restless Legs Syndrome
Dosages Exceeding 1800 Mg
Social Phobia
Spasticity



HOW DO YOU PROVE FALSE CLAIMS?

WHAT IS THE EVIDENCE?

- Voicemail recordings
- Internal documents
- Vendor documents
- Data (IMS, Scott-Levin, Verispan, Medicaid)
- Witnesses (Sales people, doctors)
- Patent applications

PARKE-DAVIS'S MARKETING STRATEGY

- Decision not to seek regulatory approval for off-label uses, but market the uses anyway
- Publication strategy—disseminate articles describing off-label use ‘to create a drum beat in the literature’
- Marketing Assessments

PARKE-DAVIS'S MARKETING STRATEGY

- Neuropathic pain & spasticity:
“results of [exploratory trials], if positive, will be publicized...but there is no intention to fully develop the indication”
- Psychiatric uses:
“due to lack of scientific rationale...it is recommended to implement only an exploratory trial...with the results highlighted through peer-reviewed publication”

PARKE-DAVIS'S MARKETING STRATEGY

- Migraine prophylaxis:
 - “The decision is to conduct only publication study(ies)”
 - “There is no established pre-clinical rationale that would support the use in migraine prophylaxis”
 - “A 12 week migraine prophylaxis study...revealed no statistically significant difference [between placebo and Neurontin]”

PARKE-DAVIS'S MARKETING STRATEGY

- Neurontin Indication Decision Analysis Group: positive return on investment for publication strategy
- Neurontin Development Team Meeting Minutes: coordinated marketing, regulatory, patent and clinical research activities
- Advertising and promotion budgets

PARKE-DAVIS'S MARKETING TACTICS

- Medical Liaisons
- Consultant and advisory board meetings
- CMEs
- Dinner meetings and teleconferences
- Preceptorships

PARKE-DAVIS'S MARKETING TACTICS

- Payments to physicians (~\$ 50 million to 3,000 physicians)
 - Grants
 - Speaker fees
 - Honoraria
 - Paid vacations
 - Olympics tickets
- Ghostwritten articles
- Suppress negative information

MARKETING MESSAGE

- False and misleading statements:
 - Pain
 - Psychiatric uses
 - Migraines
 - Monotherapy
 - Dosages above 1800 mg
 - Lack of side effects

MARKETING MESSAGE

- Examples:
 - “Now approved for monotherapy”
 - “Good for back pain”
 - “Effective treatment of bipolar”
 - Failure to disclose negative trials for migraine and bipolar
 - “Clinical usage requires [daily dosages of] 2200, 3200, 3600 [mg]”

PATENT APPLICATIONS

- US Patent 5,084,479: “neuro-degenerative diseases” (1990)
- US Patent 5,510,381: “mania and bipolar disorder” (1995)
- US Patent 5,792,796: “anxiety and panic” (1995)
- US Patent 6,242,488: “pain” (2000)
- US Patent 6,426,368: “alcoholism” (2001)

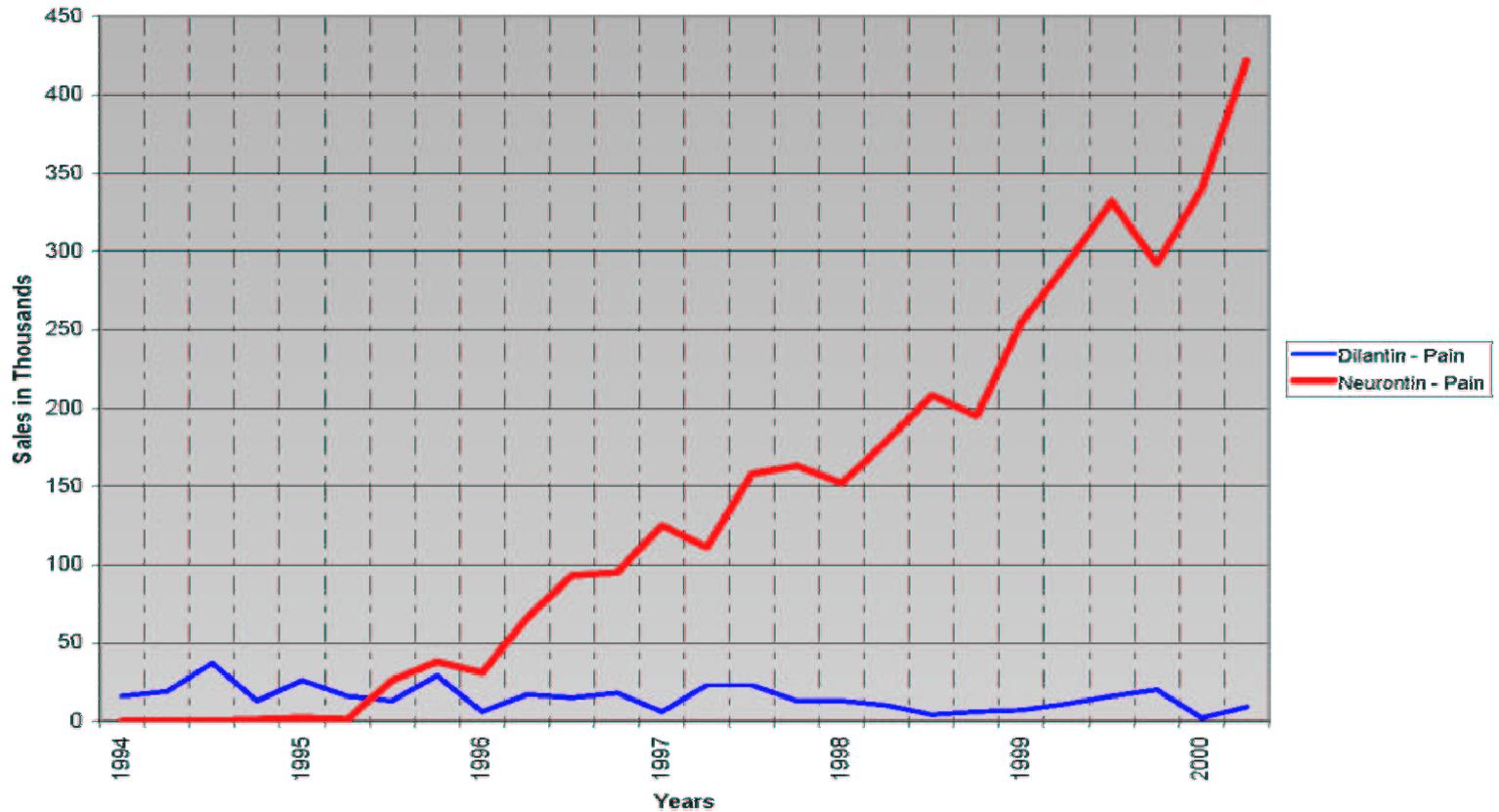
RESULTS

- Initial estimate for lifetime sales of Neurontin was \$500 million
- Off-label marketing was successful: in 2003 use of Neurontin for unapproved uses accounted for nearly 90% of its sales
- Sales of Neurontin now exceed \$2 billion annually

RESULTS

PAIN (NEURONTIN V. DILANTIN)

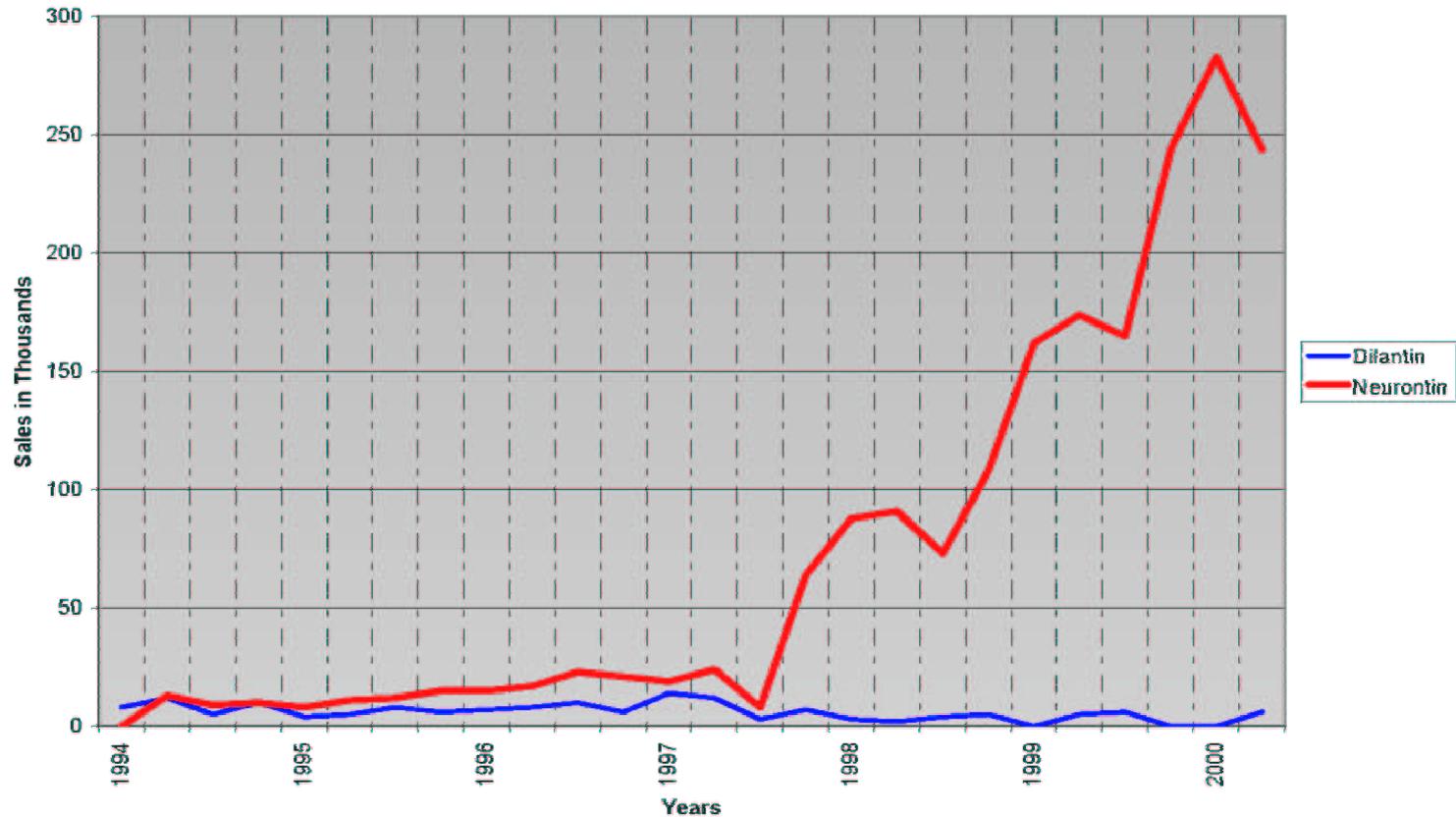
Neurontin - Dilantin Comparison (Pain)



RESULTS

PSYCHIATRIC (NEURONTIN V. DILANTIN)

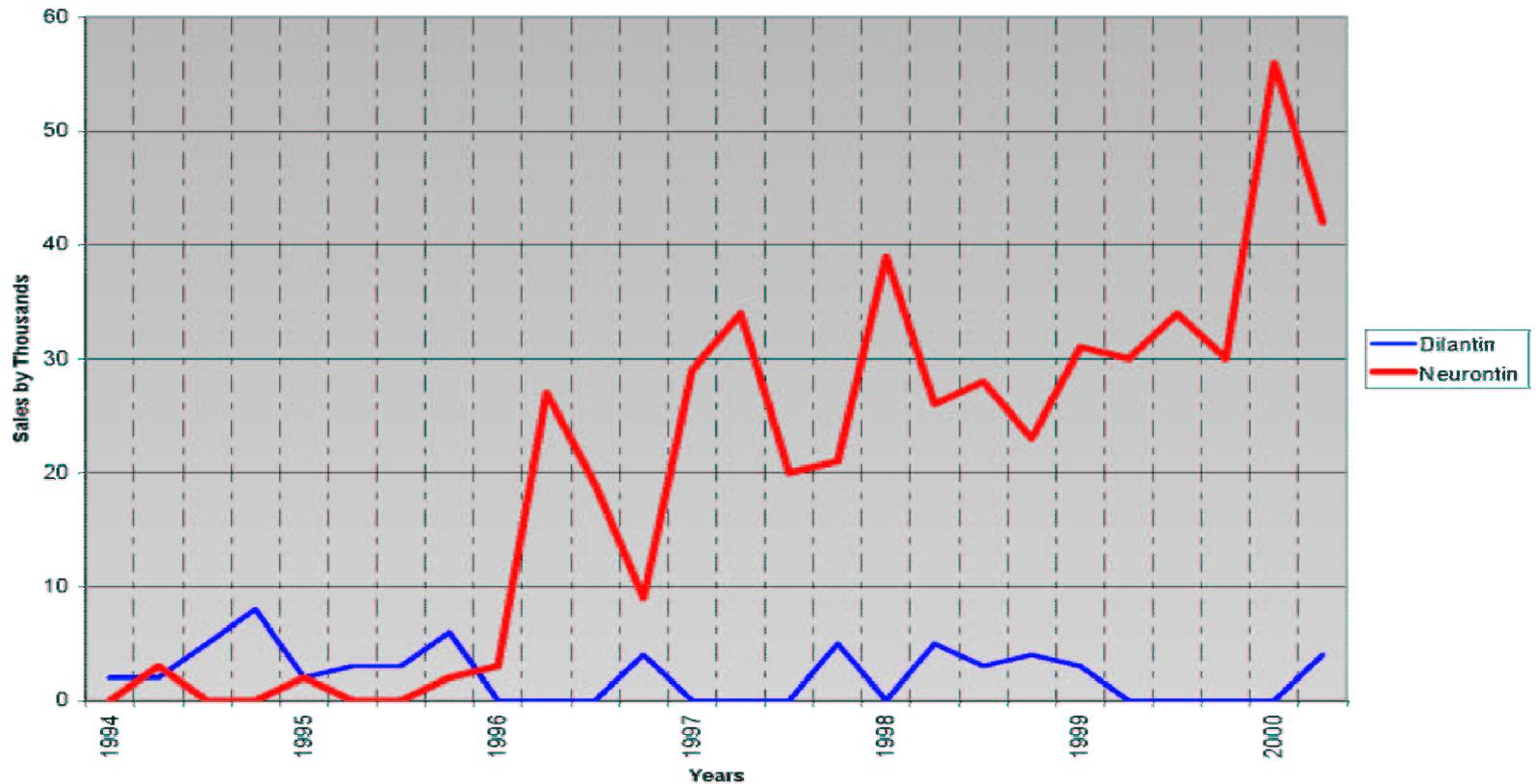
Neurontin - Dilantin Comparison (Psychiatric)



RESULTS

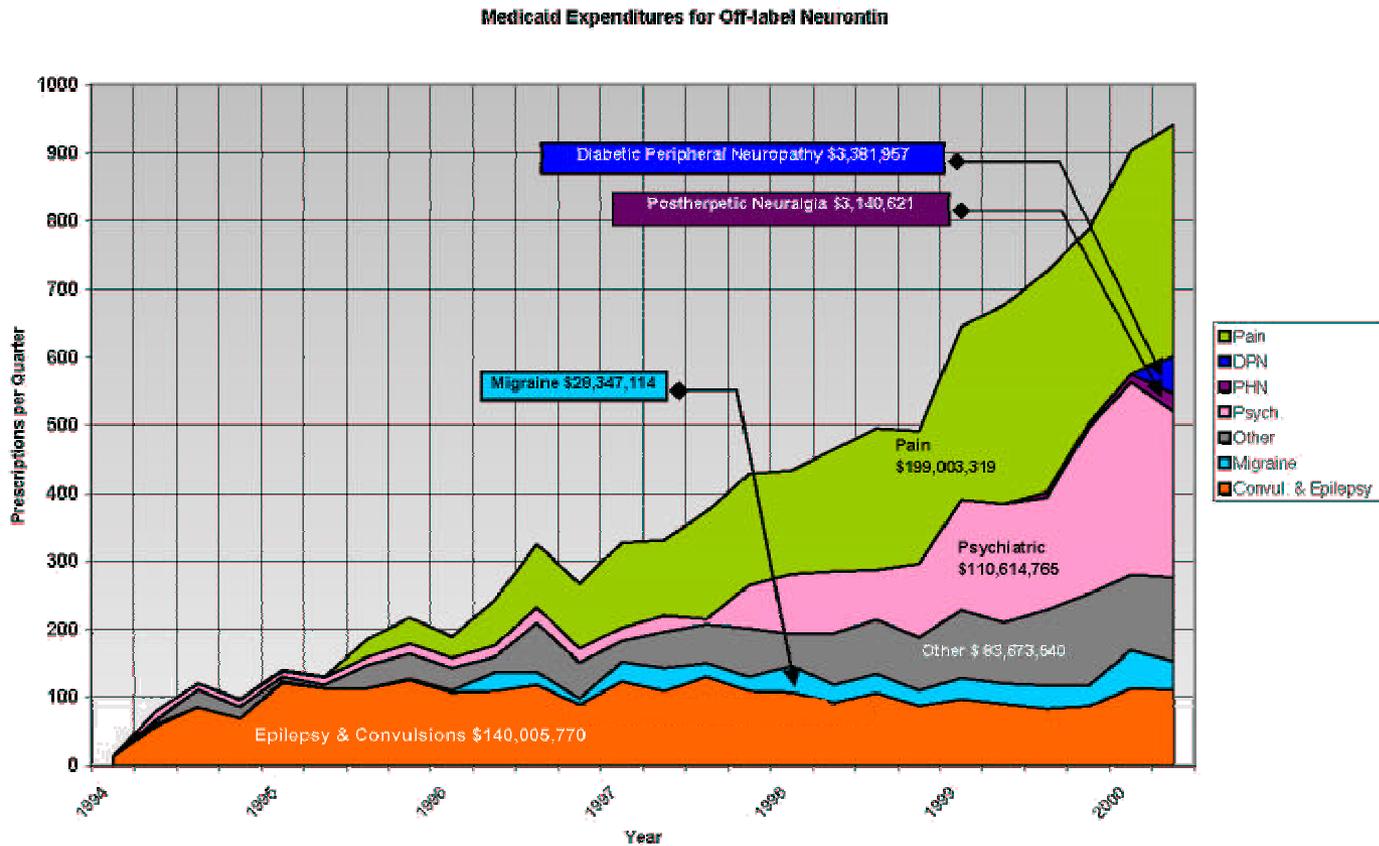
MIGRAINE (NEURONTIN V. DILANTIN)

Neurontin - Dilantin (Migraine)



RESULTS

MEDICAID EXPENDITURES FOR OFF-LABEL NEURONTIN





LEGAL DISCUSSION

MEDICAID & FALSE CLAIMS

- Motion to dismiss: *United States ex rel. Franklin v. Parke-Davis, Division of Warner-Lambert*, 147 F. Supp. 2d 39 (D. Mass. 2001)
- Motion for summary judgment: *United States ex rel. Franklin v. Pfizer et al.*, No. 96-11651-PBS, 2003 U.S. Dist. LEXIS 15754, (D. Mass. Aug. 22, 2003)

MEDICAID & FALSE CLAIMS

- Submission of ineligible claim is false claim
- “The only issue is whether Parke-Davis ‘caused to be presented’ a false claim, and § 3729 does not require that the ‘cause’ be fraudulent or otherwise independently unlawful”
(2003 U.S. Dist. LEXIS 15754, *6)

MEDICAID & FALSE CLAIMS

- “Court holds that Relator has presented evidence showing that it was foreseeable that Parke-Davis's conduct (including non-fraudulent promotion of off-label Neurontin uses) would ineluctably result in false Medicaid claims” (2003 U.S. Dist. LEXIS 15754, *15)

MEDICAID & FALSE CLAIMS

- Court also recognized that kickbacks could form independent cause of action (2003 U.S. Dist. LEXIS 15754, *19-20)

FUTURE OFF-LABEL CASES

- Even covert off-label marketing and kickbacks can be detected
- DOJ will prosecute for off-label promotion
- Whistleblower cases are a primary way that evidence of off-label promotion is brought to government attention

FOOD AND DRUG ADMINISTRATION MODERNIZATION ACT (FDAMA)

- In 1997, Congress passed FDAMA allowing manufacturers to disseminate information about off-label uses to health care providers under certain circumstances
- FDAMA purports to liberalize the dissemination of information regarding off-label use to health care professionals, but the requirements for legally disseminating such information are burdensome

FOOD AND DRUG ADMINISTRATION MODERNIZATION ACT (FDAMA)

- FDAMA requirements:
 - Submit an application to the FDA seeking approval of the off label use or certify that one will be filed
 - Submit a copy of the information to the FDA in advance prior to dissemination
 - Materials must be unabridged
 - Materials must prominently state that they pertain to unapproved uses, disclose whether authors received compensation from company and give bibliography of other scientific articles about the off-label use
 - Information must be peer-reviewed or scientifically sound
 - Information can't be false or misleading
 - Submit semiannually a list to FDA of the articles disseminated

WASHINGTON LEGAL FOUNDATION CHALLENGES FDA RESTRICTIONS

- Washington Legal Foundation (WLF) cases
- WLF I: WLF challenged FDA guidances that preceded FDAMA regarding enduring materials and CMEs arguing restrictions violate First Amendment free speech provisions. Court held that the guidances regarding enduring materials and CME guidances restricted speech more than necessary. (Court recognizes FDA could enforce rules and regulations regarding the dissemination of information that was “false or misleading” and require manufacturers to disclose their financial support or involvement in any of the disseminated materials)

WASHINGTON LEGAL FOUNDATION CHALLENGES FDA RESTRICTIONS

- WLF II: WLF challenged FDAMA provisions on same grounds as it challenged FDA guidances. Court held FDAMA provisions were unconstitutional and infringed on manufacturers' rights to disseminate information about off-label uses. District court enjoined FDA from enforcing FDAMA provisions

WASHINGTON LEGAL FOUNDATION CHALLENGES FDA RESTRICTIONS

- WLF III: Appeals court vacates injunction of lower court, because FDA argued that neither FDAMA nor the CME guidance authorize the FDA to prohibit or sanction speech but were merely FDA interpretations, thus eliminating the controversy about the constitutionality of FDAMA
- WLF IV: WLF seeks clarification of its position and status of court's order; court laments "after six years' worth of briefs, motions, opinions, Congressional acts, more opinions, issue remains 100% unresolved" leaving drug manufacturers "still without clear guidance as to their permissible conduct"

SUMMARY

- FDAMA and WLF rulings neither expand off-label marketing opportunities nor diminish the FDA's power to regulate and enforce the dissemination of any information that is false or misleading
- The conclusion that off-label promotion merits First Amendment protection is limited at best

SUMMARY

- While FDAMA offers “safe harbor” provisions for manufacturers seeking to disseminate truthful information, these provisions have burdensome compliance requirements
- Pharmaceutical manufacturers should be aware of the potential for off-label promotion to trigger claims under the False Claims Act

SUMMARY

- Even truthful off-label promotion could be grounds for a claim under the FCA, if the pharmaceutical manufacturer was aware that its actions would cause the submission of ineligible Medicaid claims
- The law and industry guidelines must prevent industry marketing efforts from interfering with the trustworthiness of the medical profession
- The FDA continues to play an important role in monitoring off-label promotion and the interaction between the industry and healthcare professionals

SUMMARY

- Physicians should have access to the most recent information in order to provide the best care possible to their patients. But doctors must be able to rely on the information they receive from manufacturers, without suspicion that marketing goals are more important than the delivery of safe and effective medicine



RELATED PRESS ARTICLES

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- Gardiner Harris, Pfizer to pay\$430 Million Over Promoting Drug to Doctors, *The New York Times*, 5/14/2004

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- Liz Kowalczyk, Pfizer Unit Agrees to \$430m in Fines, *The Boston Globe*, 5/14/2004



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