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False Claims Act Prosecution Did Not Deter Off-Label Drug Use In The Case Of Neurontin

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ABSTRACT Since 2004 the United States has collected approximately \$8 billion from fraud enforcement actions against pharmaceutical manufacturers accused under the federal False Claims Act of illegally promoting drugs for off-label uses. Using the case of gabapentin (Neurontin), a drug approved for epilepsy but prescribed for a variety of conditions, we sought to determine whether the enforcement action also influenced off-label prescribing rates. We conducted a segmented time-series analysis using key legal milestones: the initiation of a sealed investigation, public announcement of the investigation, and settlement of the case. Off-label use grew steadily until settlement, when gabapentin prescriptions declined for both off-label and on-label indications. Because enforcement actions targeting illegal off-label promotion might not have a substantial deterrent effect on prescription rates until after settlement, they should be combined with other efforts to combat off-label promotion. These could include additional resources for enforcement and a steep increase in penalties because settlements to this point have been dwarfed by the financial gains to pharmaceutical companies from engaging in improper off-label marketing.

In 2004 the drug manufacturer Warner-Lambert (which had been acquired by Pfizer in 2000) pleaded guilty and paid \$430 million to resolve criminal charges and civil liabilities in connection with its illegal and fraudulent off-label marketing of gabapentin (Neurontin).¹ Off-label marketing is the promotion of a drug for purposes or patient populations outside of those approved by the Food and Drug Administration (FDA).² Although physicians may prescribe drugs for any purpose, the FDA prevents drug companies from actively marketing drugs for unapproved uses.

The FDA had approved gabapentin in 1993 as an adjuvant treatment for partial seizures in adults with epilepsy. Its manufacturer actively promoted its use for conditions such as peripheral neuropathy, depression, low back pain, mi-

graine headaches, and fibromyalgia, despite the absence of both FDA authorization and clinical evidence supporting many of those uses.^{3–5} Annual sales revenue for gabapentin reached \$2.72 billion in 2004,⁶ most of it from off-label uses.

In recent years federal and state fraud prosecutions have been the primary means of making the public aware of the pharmaceutical industry's off-label marketing activities.^{7,8} The federal government's main weapon in this approach has been the False Claims Act, which imposes liability of up to triple damages on those who knowingly submit false claims to the government for payment. The False Claims Act dates back to the Civil War era, when it was passed to combat unscrupulous defense contractors employed by the Union army. The act grew in prominence after

amendments in 1986 permitted citizen whistleblowers to initiate fraud investigations and receive a share of any settlement or judgment.⁹

The goals of false claims investigations are to punish inappropriate behavior, return improperly obtained funds to the government, and deter ongoing (or future) fraudulent activities. Since the mid-1990s, annual returns from such investigations have been increasing, mostly because dozens of cases have been filed against pharmaceutical manufacturers accused of illegal off-label promotion.¹⁰ In 2010 alone, the US government recovered more than \$4 billion in financial recoveries from these cases.

With increasing government involvement in the health care market through Medicare Part D and other insurance programs, fraud investigations have been singled out as a way of reducing spending. For example, President Barack Obama has made an unprecedented commitment to fighting health care fraud,¹¹ noting that “by curbing waste, fraud, and abuse and...taking a host of other cost-saving steps, we can save billions of dollars, while delivering better care to the American people.”¹² To that end, the Affordable Care Act of 2010 provided \$300 million over the next decade in additional support for antifraud work and contained a number of provisions that promoted public reporting of potentially fraudulent behavior.

Little is known about how well prosecutions perform in achieving deterrence. In a model that considered Medicaid Fraud Control Unit spending in all fifty states, David Becker and colleagues assessed stepped-up enforcement against Medicaid billing fraud and changes in hospitals’ billing practices.¹³ They found, in part, that stiffer enforcement led for-profit hospitals to decrease their use of high-reimbursement billing codes implicated in overcharging. But this study stands alone: We could find no other empirical investigations of the extent to which fraud prosecutions of this type affect behavior.

We investigated the relationship between off-label prescribing and a major federal fraud prosecution targeting illegal off-label promotion: the gabapentin case against Warner-Lambert. We conducted a segmented time-series analysis to identify whether any of the milestones in the case’s timeline—the initiation of the False Claims Act investigation, public announcement of the investigation, and settlement of the case—affected trends in off-label prescribing or spending for this drug.

We hypothesized that the initiation of the investigation would be associated with a slower rise in off-label use as the manufacturer adjusted its marketing practices. We also hypothesized that the rise in off-label use would slow further

after the investigation was made public, as physicians and payers became aware of the company’s questionable practices. To isolate the changes in prescribing behavior plausibly attributable to the prosecution, we separated trends in use and spending for gabapentin’s off-label indications from trends for its approved indications.

Study Data And Methods

LEGAL AND REGULATORY TIME PERIODS We began by establishing a timeline for the FDA’s approval of gabapentin and key dates in the federal fraud prosecution. The approval data came from the FDA’s website. Gabapentin was first approved in December 1993 for use in adults with a certain type of epilepsy, although it was not sold on the US market until February 1994. Its approved use was extended to children in 2000. It received a supplemental indication in May 2002 for the treatment of postherpetic neuralgia—a painful type of neuropathic pain (that is, pain arising from damage to or pathology within the nervous system) resulting from reactivation of the varicella zoster virus—the causative agent of chickenpox and shingles. No other uses received FDA approval.

We searched the online archives of US federal court filings¹⁴ as well as Department of Justice press releases¹⁵ to identify key dates in the gabapentin case, and we confirmed those dates with lawyers involved in the litigation. The False Claims Act action began in August 1996, when a whistle-blower in Massachusetts filed a complaint in federal court. The claim was sealed to the public, although the manufacturer was served with some initial interrogatories and subpoenas related to promotional practices. At that point, the Department of Justice’s Civil Division evaluated the allegations in the complaint.

It is common during this phase of an investigation for a defendant company to receive general subpoenas and interrogatories, which alert it to the fact that it is under scrutiny. If the Justice Department finds strong evidence supporting the case, it may intervene in an enforcement action. The court might also unseal the original complaint, signaling that the investigation is reaching a more active phase, including grand jury testimony.

The precise sequence of these events differs from case to case. In the gabapentin investigation, a judge ordered the complaint unsealed at the start of January 2000, opening it to dissemination through the media and the company’s required filings and reports.¹⁶ The Justice Department did not officially intervene until quite late—shortly before settlement was reached in May 2004.

Our analysis focused on three points in the prosecution timeline: the date of first filing of the complaint, the date the complaint was unsealed, and the date the enforcement action was concluded. This analysis was approved by the Brigham and Women's Hospital Institutional Review Board.

STUDY POPULATION To track gabapentin use, we used claims data for Medicare-eligible subjects enrolled in two publicly financed pharmaceutical benefit programs: the Pennsylvania Pharmaceutical Assistance Contract for the Elderly and the New Jersey Pharmaceutical Assistance for the Aged and Disabled program. Both programs offer generous prescription drug benefits with nominal copayments to low-income residents of the programs' states who are age sixty-five or older. Virtually all prescription medications are covered, without restrictions.

These databases had two notable advantages. First, state programs as well as Medicare Part D are grappling with high medication costs for their elderly enrollees. Second, false claims investigations address overpayments from such government-funded programs. The Pennsylvania and New Jersey databases contain detailed paid pharmaceutical claims data for approximately 225,000 and 200,000 beneficiaries, respectively, per year.

We linked these databases to Medicare Parts A and B claims data, which include all recorded diagnosis codes associated with each prescription and dates for inpatient and outpatient care. Diagnoses were coded using the *International Classification of Diseases*, Ninth Revision, Clinical Modification (ICD-9-CM) system. Individual-level patient data included age, sex, self-identified race, adjusted net income, concurrent drug treatments, and the presence of specific comorbid conditions.

We tracked prescriptions from February 1994, the first time gabapentin was marketed, through the end of the fourth quarter of 2005, when the introduction of Medicare Part D altered the availability of prescription use data through these state-based insurance programs. We contacted the state program administrators to identify any restrictions on gabapentin prescriptions during the study period—such as preauthorization requirements, higher copayments, or changes in program eligibility—that could affect our results.

Neither of the state programs placed any restrictions on gabapentin during the course of the False Claims Act investigation (Dominic Magnolo, New Jersey Department of Human Services, personal communication, August 12, 2010), but the Pennsylvania program temporarily expanded overall program enrollment in

November 2003 (Theresa Brown, Pennsylvania Department of Aging, personal communication, August 12, 2010).

TIME-SERIES DEFINITIONS To describe temporal trends in gabapentin prescribing and associated spending, we analyzed a time series of monthly claims data submitted to the Pennsylvania and New Jersey programs, starting in February 1994. Monthly claims data were aggregated by calendar quarter.

We defined a *new prescription* as a prescription for any version of gabapentin filled by a patient who had not filled a prescription for that drug in the preceding 180 days. To ensure that our data set did not include as new users those patients who might have filled prescriptions for the drug elsewhere before enrolling in one of the programs, we excluded all new users who did not have at least one inpatient or outpatient claim and one filled prescription during the prior 180 days. We allowed subjects to contribute multiple episodes in the time series if they stopped using the drug and then started using it again more than 180 days later.

We first identified patients who filled new gabapentin prescriptions and had diagnoses of epilepsy—the drug's original on-label use—prior to their first prescription. A *diagnosis of epilepsy* was broadly defined as a diagnosis for any seizure disorder or the use of any anticonvulsant other than gabapentin in the previous 180 days (for ICD-9-CM codes and coprescriptions contributing to definitions of gabapentin use categories, see Appendix A).¹⁷ Next we determined whether the remaining patients had diagnoses for postherpetic neuralgia based on similarly broad classification criteria (Appendix A in the online Appendix).¹⁷

For the patients who were left, we identified those with one or both of the two common off-label conditions for which physicians prescribe gabapentin: neuropathic pain and psychiatric disorders.¹⁸ We did this by analyzing all recorded diagnoses and prescriptions filled in the 180 days before the initial gabapentin prescription (Appendix A).¹⁷ We counted patients with both conditions in both categories. All subjects without neuropathic pain or psychiatric disorders were categorized as "other."

TIME-SERIES ANALYSIS We plotted the frequency of gabapentin use in the two state programs against the three important points in the False Claims Act investigation: August 1996 (the complaint filing), January 2000 (the complaint unsealing), and May 2004 (the settlement). This yielded four distinct time segments of interest: after the introduction of gabapentin in the market but before the complaint was filed (February 1994 to August 1996); after the complaint was

filed but before the investigation was unsealed and thus made public (September 1996 to December 1999); after the investigation was unsealed but before the settlement was announced (January 2000 to May 2004); and after the settlement was announced to the end of the study period (June 2004 to December 2005).

The outcomes of interest were the quarterly incidence of new gabapentin prescriptions for each indication (expressed as new prescriptions per 10,000 active program enrollees) and the quarterly expenditures on gabapentin by indication, adjusted to 2005 prices (expressed as new prescription spending per 10,000 active program enrollees). Prescription use was age standardized to the fourth quarter of 2005.

For each indication, we employed a piecewise linear regression spline (a spline uses a slope correction factor to allow continuity at breakpoints) with defined breakpoints at each important date to estimate trends in each period. Because the complaint was unsealed in early January 2000, we placed the second breakpoint in the fourth quarter of 1999. The regression line for the postherpetic neuralgia category was fitted with an additional breakpoint in the second quarter of 2002 to represent the FDA approval of gabapentin for postherpetic neuralgia.

We estimated slopes and their 95 percent confidence intervals using analysis of variance. We compared prescribing trends in each segment, defined as an increase or decrease in the slope of

the segment compared with the prior segment. Models assumed piecewise linearity and included a constant term—time (quarterly)—and terms for change in slope and intercept for each additional segment. We used R software, version 2.12.2, to perform the statistical analysis.

Study Results

CHARACTERISTICS OF GABAPENTIN USERS Users of gabapentin in the Pennsylvania and New Jersey programs were predominantly white, female, and elderly and had relatively low comorbidity scores (Exhibit 1). The relatively low comorbidity index suggests that this was not an extremely sick population. There were more users identified in the Pennsylvania program than in the New Jersey program, reflecting the former's larger size. Gabapentin users in the two databases had comparable demographic characteristics, comorbidity scores, and health care use profiles. Given these findings, we pooled prescription and spending data from the two programs for the trend analyses.

TRENDS IN PRESCRIPTIONS FOR GABAPENTIN There were 33,158 qualifying initial prescriptions from the Pennsylvania program and 25,659 from the New Jersey program. The analysis was based on first prescription filled after six months of nonuse, and only a small number of such new users had filled a prescription for gabapentin before the six-month window

EXHIBIT 1

Demographic Characteristics Of New Gabapentin Users, 1994–2005

Characteristic	State plan	
	Pennsylvania Pharmaceutical Assistance Contract for the Elderly (n = 28,077)	New Jersey Pharmaceutical Assistance for the Aged and Disabled program (n = 21,214)
Age, mean years (SD) [range]	78.4 (7.2) [68–108]	77.7 (7.2) [65–105]
SEX, NUMBER (PERCENT)		
Male	5,082 (18.1)	4,889 (23.0)
Female	22,995 (81.9)	16,325 (77.0)
SELF-IDENTIFIED RACE, NUMBER (PERCENT)		
White	26,457 (94.2)	21,801 (85.0)
Black	1,381 (4.9)	2,307 (10.8)
Other	239 (0.9)	806 (3.8)
MEDICAL HISTORY		
Total prescriptions filled, median (IQR)	9.0 (6.0)	10.0 (8.0)
Charlson-Romano comorbidity index, median (IQR)	2.0 (3.0)	2.0 (3.0)
Total physician visits in prior 180 days, median (IQR)	5.0 (5.0)	6.0 (7.0)
Psychiatric diagnosis, number (percent)	2,047 (7.3)	1,275 (6.0)
Neurologic diagnosis, number (percent)	5,412 (19.3)	4,544 (21.4)

SOURCE Authors' analysis. **NOTES** Not all percentages sum to 100 because of rounding. IQR is interquartile range.

($n = 10,326$, 17.6 percent). Patients who contributed multiple episodes as new users to the prescription and spending trends did not differ in demographic characteristics from those who contributed a single episode. However, those who contributed multiple episodes are not included in the demographic data displayed in Exhibit 1.

We observed the first prescriptions for gabapentin in the third quarter of 1994. Between that time and the end of 2005, the number of patients filling new prescriptions for all indications of gabapentin increased and then declined, with a net increase over the eleven-year period (Exhibit 2). Overall, usage rates in patients with diagnoses of neuropathic pain and psychiatric disorders—off-label uses—were highest. Many patients qualified for both categories and thus were counted in both cohorts. On-label use for epilepsy was less common than off-label use, and on-label use for postherpetic neuralgia was least common of all. By the time of the settlement in 2004, roughly five times as many patients were starting gabapentin for neuropathic pain or psychiatric disorders as for epilepsy.

During the period before the federal investigation began, there was minimal growth in the use of gabapentin for all indication categories (Exhibit 2). In the second stage (sealed investigation), while the Justice Department was con-

ducting its investigation of off-label marketing, trends increased for all indications but especially for off-label ones. In the second stage, use for psychiatric disorders and neuropathic pain increased from the first stage by 10.6 ($p < 0.0001$; 95% confidence interval: 7.24, 14.0) and 9.72 ($p < 0.0001$; 95% confidence interval: 6.44, 13.0) new users per 10,000 enrollees per quarter, respectively.

The third stage of the time series (unsealed investigation) represents the first time that the public, including prescribing physicians, could have known about the ongoing investigation of the manufacturer for illegal off-label marketing practices. During that period, off-label use continued to increase robustly (Exhibit 2). Growth in off-label use rates for psychiatric disorders and neuropathic pain did not differ statistically from growth during the sealed investigation stage (slopes of 8.7 and 9.6 new users per 10,000 enrollees, respectively). Overall rates of off-label use continued to rise faster than those for other indications.

By contrast, on-label epilepsy use rates declined from 3.37 new users per 10,000 enrollees to 0.91 ($p < 0.0001$; slope decrease of 2.4; 95% confidence interval: $-2.9, -2.0$) (Exhibit 2). The use of gabapentin for postherpetic neuralgia continued to grow, with no significant change in the rate of growth—0.338 per 10,000 en-

EXHIBIT 2

Time-Series Analysis Of New Users Of Gabapentin, By Health Condition Prescribed For, March 1994–March 2005



SOURCE Authors' analysis. **NOTES** Patients were enrolled in the Pennsylvania Pharmaceutical Assistance Contract for the Elderly or the New Jersey Pharmaceutical Assistance for the Aged and Disabled program. Epilepsy and (after May 2002) postherpetic neuralgia were on-label uses. Neuropathic pain, psychiatric disorders, and other were off-label uses. The dotted orange rule represents the date at which postherpetic neuralgia was added as an indication.

rollees ($p = 0.14$; 95% confidence interval: 0.911, 0.135)—after the supplemental indication was approved in the second quarter of 2002. The total numbers of new users for all indications per 10,000 enrollees declined toward the end of the stage, around the time the Pennsylvania program expanded.

In the final stage (after settlement), rates of new gabapentin use declined for all indications, but most dramatically for off-label indications. New use for psychiatric, neuropathic, and other off-label indications changed by -14.9 ($p < 0.0001$; 95% confidence interval: -19.1 , -10.7), -14.2 ($p < 0.0001$; 95% confidence interval: -18.3 , -10.1), and -6.42 ($p < 0.0001$; 95% confidence interval: -8.04 , -4.79) new users per 10,000 enrollees per quarter, respectively, while the on-label uses, epilepsy and postherpetic neuralgia, changed by -2.88 ($p < 0.0001$; 95% confidence interval: -3.91 , -1.84) and -1.03 ($p = 0.0105$; 95% confidence interval: -1.81 , -0.255), respectively.

TRENDS IN SPENDING ON GABAPENTIN Spending on new prescriptions in the two state programs (Exhibit 3) showed trends similar to those seen in the analysis of new users (Exhibit 2), with negligible growth during the first stage, modest growth during the second, continued growth during the third, and a flattening or decline in growth in the final stage. Some of the most dramatic changes occurred in prescriptions for neuropathic and psychiatric indica-

tions between the third stage and the final stage.

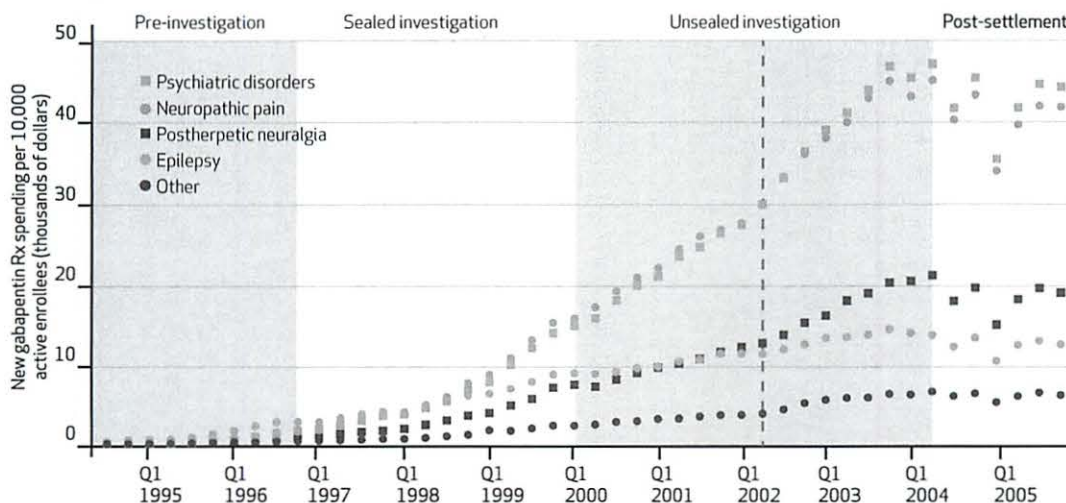
In the postsettlement period (after the second quarter of 2004), the change in spending for neuropathic pain use decreased. Spending in the previous stage had increased \$2,022 per 10,000 enrollees per quarter; in this stage, it declined \$1,056 per quarter ($p < 0.0001$; slope decrease of \$3,016; 95% confidence interval: $-\$3,764$, $-\$2,391$). The change in spending for psychiatric use also shifted, in this case from an increase of \$1,835 to a decline of \$1,181 per 10,000 enrollees per quarter ($p < 0.0001$; slope decrease of \$3,016; 95% confidence interval: $-\$3,677$, $-\$2,356$). Because the analysis included only the first prescription after six months of nonuse, the magnitude of spending indicated by Exhibit 3 is far less than the total spending from all uses.

Discussion

OFF-LABEL USE OF GABAPENTIN DURING THE INVESTIGATION In this time-series analysis of the fraud investigation's effects, we found that upward trends in the number of new prescriptions for gabapentin and spending on them continued unchecked during all phases of the Department of Justice's False Claims Act investigation and were greatest for off-label uses. Not until after the settlement did growth trends in gabapentin use become negative, but this occurred for both on- and off-label uses. Our initial hypothesis was

EXHIBIT 3

Time-Series Analysis Of Spending On New Prescriptions Of Gabapentin, By Health Condition Prescribed For, March 1994–March 2005



SOURCE Authors' analysis. **NOTES** Patients were enrolled in the Pennsylvania Pharmaceutical Assistance Contract for the Elderly or the New Jersey Pharmaceutical Assistance for the Aged and Disabled program. Epilepsy and (after May 2002) postherpetic neuralgia were on-label uses. Neuropathic pain, psychiatric disorders, and other were off-label uses. The dotted orange rule represents the date at which postherpetic neuralgia was added as an indication.

that we could detect a deterrent effect evidenced by a decline in off-label use during the sealed investigation period and a further decline after it was unsealed. However, this proved incorrect.

There are several possible explanations for the continued rapid growth in off-label use of gabapentin throughout the fraud prosecution. One is that the manufacturer made a business decision to continue its aggressive off-label marketing despite initiation of the litigation. If that is true, it would be difficult to call the decision irrational: The \$430 million settlement was dwarfed by revenue from off-label sales of gabapentin, which were approximately \$2 billion in 2004.¹⁹

Another possibility is that the manufacturer curbed its marketing practices in response to the initiation of the case but that prior off-label marketing had durable effects, creating a culture of persistent use among physicians. For example, manufacturer-funded articles encouraging off-label use of gabapentin⁴ remain available in the literature, and physicians could access them even now. In a study of one group of physicians, Catherine Fullerton and colleagues found that growth in the use of gabapentin for bipolar disease in Florida was not affected by a cessation of promotional activities.²⁰ In that study, gabapentin prescriptions did not decrease until the insurance provider instituted prior authorization requirements.

A third possibility is that off-label promotion did not have any substantial effects on physician prescribing practices, so whether it ceased, persisted, or became the subject of public scrutiny was irrelevant. Physicians are free to prescribe drugs for any indication, whether on or off label. Because of the difficulty in treating certain types of neuropathic pain syndromes or psychiatric disorders, prescribers may have decided to use gabapentin for patients with these conditions despite the absence of clearly demonstrated efficacy (apart from postherpetic neuralgia) in the peer-reviewed literature. This explanation is plausible in theory. However, it is contradicted by findings in numerous studies that marketing strategies do affect physicians' prescribing.²¹

USE OF GABAPENTIN AFTER SETTLEMENT There were major reductions in off-label use only after settlement. On-label uses declined as well at that point, which makes it less likely that the final step in the case had a deterrent effect. Widespread media coverage of the gabapentin settlement may have captured the attention of prescribers and patients and chilled interest in the drug across the board—in other words, there was a crude or undifferentiated behavioral response. Such a response would not be a desired public health outcome, particularly if it led to decreased use among patients who needed the

The Affordable Care Act has provided some support for fraud enforcement, but additional resources are needed.

drug as adjunctive therapy in epilepsy, a use that is FDA approved and evidence based.

However, the postsettlement trend changes were not the same across all uses of gabapentin. New prescriptions declined most steeply for psychiatric indications, the off-label use with the least evidence to support it.²² In sum, we interpret our findings as providing weak evidence that the settlement stage of the gabapentin prosecution produced a deterrent effect, but no evidence that any other stage did.

THE DETERRENT IMPACT OF THE FALSE CLAIMS ACT Our finding that sales of a drug that was the subject of a federal fraud prosecution remained robust, both overall and in connection with the specific target area of the prosecution, raises fundamental questions about the deterrent role of the False Claims Act. One of its limitations may relate to the slow pace of its enforcement actions. These actions often take many years to conclude because of limited resources at the Department of Justice and the complexity of the investigations.²³ There is currently a large backlog of cases awaiting investigation at the federal level.²⁴

Further government funding of fraud enforcement that would help speed prosecutions might increase the deterrent effect. The Affordable Care Act has provided some support for fraud enforcement, but more resources are needed because the capacity of the Justice Department to conduct investigations is still far outweighed by the pharmaceutical industry's legal and marketing resources. Further resources may come from individual states that have passed local false claims statutes mirroring the federal law and that have begun initiating a growing number of investigations themselves.²⁵ Enhancing enforcement resources as we have suggested would also provide a substantial return on investment. For example, one report calculated that the government receives \$15 in recoveries for every \$1 invested in investigation and litigation.²⁶

A second limitation of the False Claims Act is

that although some settlements—particularly those against pharmaceutical manufacturers—have led to billions of dollars in recoveries, the deterrent effect may be muted because the size of these settlements are dwarfed by the potential financial gains from thwarting the law. The only solutions for this problem would be to increase the financial penalties even further or to pursue individual penalties—such as imprisonment for executives found guilty of criminal conduct—with greater vigor than has been applied to date.²⁷

LIMITATIONS OF THE STUDY There are several limitations to this study. First, we identified on- and off-label uses of gabapentin based on diagnoses recorded in claims data rather than on a primary medical record review. However, we employed broad (and therefore conservative) definitions of indications, such as epilepsy, to bias our sample against finding off-label use.

Second, external factors not considered in our model could have affected off-label use of gabapentin. These include spending on direct-to-consumer advertising,²⁸ the publication of certain high-impact research articles, and clinical practice reviews such as those favoring use of gabapentin for neuropathic pain.^{29,30}

The introduction of alternative therapies and generic competition could have had similar effects. For example, the FDA in December 2004 approved pregabalin (Lyrica)—made by the same manufacturer as gabapentin—for neuropathic pain associated with diabetic peripheral neuropathy, although the drug was not launched in the United States until September 2005. The selective serotonin reuptake inhibitor duloxetine (Cymbalta), made by a different company, was also approved in late 2004 for treatment of diabetic peripheral neuropathy. The decrease in new use of gabapentin near the end of our study period, therefore, could reflect physicians' shift to on-label use of products such as these.

Third, it is conceivable that a patient might have had an on-label indication even though the physician recorded an off-label one. Although a review of the primary medical record would be needed to determine this, we do not think that it is a major limitation of the data source we used. This is because the overall use of gabapentin far exceeded predicted rates of epilepsy and postherpetic neuralgia.

Fourth, we focused on a particular prosecution for a particular drug and its use in two large patient populations. The state programs we studied were large and covered diverse populations of nonaffluent elderly, similar to those in the current Medicare D programs. However, the generalizability of our findings to other populations, drugs, investigations, and outcomes, is uncertain and will need to be evaluated in subsequent studies.

Conclusion

Fraud in pharmaceutical marketing, leading to non-evidence-based drug use and unnecessary spending, is an ongoing public health problem. With the recent government expansion of drug insurance coverage in Medicare Part D, the goals of ensuring appropriate use and containing unnecessary spending have taken on paramount importance.³¹ Effectively combating fraud and abuse represents an important means of achieving these difficult goals.^{12,32-34}

Although False Claims Act prosecutions of off-label promotion of pharmaceuticals have recovered some improper payments for the government,⁸ the case of gabapentin suggests that such legal approaches may have little or no impact on commercial behavior by the manufacturer under investigation. This points to the need to reexamine the goals of enforcement and to consider additional administrative responses to off-label promotion. ■

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In this month's *Health Affairs*, Aaron Kesselheim and coauthors report on their study of the results of a federal enforcement action against a leading pharmaceutical manufacturer, Warner-Lambert, for promoting of off-label uses of the drug gabapentin. Gabapentin is approved for use in epilepsy but has been prescribed for other conditions, including depression, low back pain, migraine headaches, and fibromyalgia.

The study determined that federal investigation and prosecution did not deter off-label marketing until after a legal settlement in the case was reached. The authors suggest that additional resources for enforcement and steep increases in penalties will be necessary to pressure drug companies to stop off-label marketing.

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