

WHAT PHYSICIANS CAN SAY ABOUT OFF-LABEL THERAPIES – LAWSUITS COULD SET NEW PRECEDENTS

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ARTICLE IN BRIEF:

✓ Lawsuits against a neurologist and psychiatrist, alleging they engaged in unlawful promotion of off-label therapies, could be a sign of things to come for other physicians as the government steps up its efforts to curtail the promotion of therapies for indications not approved by the Food and Drug Administration.

Neurologist David Longmire, MD, thought that gabapentin (Neurontin) was an effective pain therapy for patients in his Alabama practice. And he said so during continuing medical education (CME) seminars sponsored by drug companies. At CME events, Peter Gleason, MD, a Maryland-based psychiatrist, actively promoted gamma-hydroxybutyrate (GHB), or Xyrem, for chronic pain, weight loss, and depression.

Both physicians were named in separate lawsuits against the companies that make the drugs they discussed for off-label use. [The Food and Drug Administration (FDA) approved gabapentin in 1993 as an add-on therapy for partial seizures, and for post-herpetic neuralgia in 2002. The FDA approved GHB in 2005 for cataplexy associated with narcolepsy.]

The allegations and circumstances of the lawsuits involving Dr. Longmire and Dr. Gleason are different. But both scenarios reflect new efforts by the gov-

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ernment to prosecute individual physicians in efforts to stop pharmaceutical companies from promoting drugs for off-label uses.

In fact, according to one Washing-

ton, DC, law firm, Batton Boggs LLP, which specializes in defending health care fraud cases, "The government has confirmed that it has over 150 investigations of pharmaceutical companies in the pipeline, involving 500 or more products." An in-depth analysis of the



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Dr. Gleason's case is posted on the firm's Web site: www.pattonboggs.com/news/detail.aspx?news=276.

Dr. Longmire was not available to discuss his case. But *Neurology Today* interviewed his defense co-counsel Paul W. Shaw of Brown Rudnick Berlack Israels LLP, and Robert A. Griffith of

Gargiulo/Rudnick LLP. "This is the first lawsuit brought against a physician for participating in educational programs," said Shaw. "If these plaintiffs win, we are going to be seeing many more down the road," he warned.

AAN General Counsel Murray G. Sagsveen agreed that such cases could be a sign of things to come. "I would not be surprised if, during lawsuits against drug companies, prosecutors who come across information about money paid to physicians might investigate," he said. "If it looks that there's been collusion, they could take action against physicians, which could have a chilling effect."

THE CASES IN ATLANTA

Dr. Longmire is now subject to two lawsuits filed in Alabama state court by Blue Cross Blue Shield of Alabama and a consortium of union and employee health plans including Alabama Associated General Contractors – in an action against Warner-Lambert, the Pfizer subsidiary. The second suit by the Alabama Associated General Contractors is scheduled to go to court some time this

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month.

The complaints allege that Warner-Lambert engaged in a marketing scheme using Dr. Longmire and other physicians to get around the restrictions against off-label marketing placed on manufacturers.

After Warner-Lambert admitted guilt to charges that it violated federal regulations prohibiting off-label promotion and marketing of gabapentin, and agreed to a \$430 million settlement in 2004, a number of third-party payers filed lawsuits, which were consolidated in the District Court of Massachusetts. Several insurers, however, decided to sue in their own state courts. But in order to defeat the diversity jurisdiction



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that would have moved the cases to federal court in Boston, a resident defendant was needed, Dr. Longmire's co-counsel Griffith explained.

Shaw added: "They simply chose from speakers referenced in litigation, and if they are successful in Alabama, anytime they need a defendant, they will simply pluck a name off a list," he predicted.

Dr. Longmire was originally named in one of the lawsuits decided in 2004, but he countersued Pfizer, claiming that the drug company misled him by inviting him to speak at events that actually were thinly disguised marketing efforts. Dr. Longmire settled his suit against Pfizer in July, and his lawyers have submitted a motion to dismiss the lawsuits against him based on the statute of limitations. (He hasn't participated in events sponsored by the drug company

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since 1998.)

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DR. GLEASON: ALLEGATIONS OF FRAUD

Perhaps even more ominous are the ramifications of the case involving Dr. Gleason. The government charged that Dr. Gleason engaged in a scheme along with Orphan Pharmaceutical to defraud public and private insurance plans. The FBI arrested him in March in New York City after he had finished giving a talk in a neurologist's office in Long Island, NY. He is now out and free on bail.

"Any physician who speaks at any

Dr. Gleason was approached by Orphan Medical, the original makers of GHB, after the company noticed he was prescribing the drug frequently. (Jazz Pharmaceuticals acquired Orphan in June, 2005.) From 2003 to 2006, Dr. Gleason lectured at numerous CME events. He started getting so many requests to speak about the drug that the speaking fees became his primary source of income.

The indictment states that in 2004 alone, Dr. Gleason spoke at more than 100 events and was paid more than \$70,000. Dr. Gleason has acknowledged receiving more than \$100,000 in 2005, according to the New York Times.

"Dr. Gleason was in high demand by Orphan sales representatives because of his proven ability to generate 'off-label' sales of Xyrem in their respective sales territories," the indictment states. "In the course of promoting Xyrem ... (Gleason) engaged in deceptive and misleading behavior."

The FDA Office of Criminal Investigations had also been investigating the drug company. A "cooperating witness" inside the company – a physician who pleaded guilty in 2003 to health care fraud – recorded one of Dr. Gleason's lectures during which he claimed GHB was less dangerous than table salt. The witness also recorded conversations between Gleason and Orphan sales reps.

That behavior, according to the indictment, included making false claims that GHB was not a "date-rape" drug and was never banned by the FDA, and that the FDA regarded GHB as a "miracle treatment" for narcolepsy. He also falsely stated that the drug was safe for children, and posed no overdose danger. (Because GHB suppresses breathing, overdose can cause coma or death.)

At these events, Dr. Gleason promoted GHB for chronic pain, weight loss, depression, bipolar disorder, fibromyalgia, insomnia, movement disorders such as Parkinson disease, and fatigue, as well as for excessive daytime sleepiness, the only condition for which the drug is approved. In addition, it is alleged that Dr. Gleason coached physicians on ways to get reimbursed by insurance companies for off-label uses of GHB by using alternative diagnosis codes, or even no codes at all. The indictment against him states that he provided physicians with model prescription forms that contained suggested diagnosis codes.

The Gleason prosecution may have been regarded by the government as more urgent since GHB is regarded as a "date-rape" drug, and classified as a Schedule III Controlled Substance for medical use, like the painkiller hydrocodone (Vicodin). The drug carries a "black box" warning about its potential

for abuse, and is dispensed through a centralized source – a pharmacy in Missouri – with each prescription tracked.

Dr. Gleason faces five charges, including conspiracy to introduce a misbranded drug into interstate commerce and health care fraud conspiracy. The indictment seeks forfeiture of all property derived from proceeds traced to the money he received from the drug company. If convicted, he faces a maximum sentence of three to ten years in prison for each count, and a maximum fine of \$250,000 on each count.

Such harsh penalties could induce Gleason to cooperate. "Only the individual, not the company, has been in-

and their reputation.

The three Patton Boggs attorneys who analyzed the Gleason case emphasize that drug companies – and by association, physicians who accept payments from them – should expect further investigations. The FDA used to handle alleged misconduct by issuing a warning letter. These cases, however, reflect the government's willingness to use undercover operatives to pursue criminal prosecution of off-label violations, even when the drug company is small and the sales of the drug are limited.

That's why they warn drug companies and physicians to be more careful. "In general, if it sounds too good to be

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dicted," said Laura Laemmle-Weidenfeld, of the law firm Batton Boggs LLP. The former trial attorney at the Department of Justice who focused on off-label promotion by pharmaceutical companies added: "He may be getting pressured to testify."

CONFLICTING PRESSURES

Aside from the legal implications of these cases, many doctors question the overarching issues concerning relationships with pharmaceutical companies. Neurologist Gary L. Cohen, MD, author of the *Neurology* 2002 Nisus story 'Off-Label' believes that physicians have made a mistake in accepting too much drug company sponsored research, and that they have suffered damaging consequences as a result. He said, "Doctors are too willing to do what drug companies want. In essence, some have sold out." Dr. Cohen advises, "When you are asked to speak about off-label uses, just say 'no.'"

Cases brought against individual physicians bring into stark relief the conflicting pressures they face. Physicians are entitled to discuss among themselves new uses for drugs – a practice that has potential benefits for patients. Dr. Longmire, for example, began touting the pain-relieving ability of gabapentin after he noticed that epilepsy patients who also suffered from neuropathic pain reported relief when they started taking the drug.

However, physicians who receive large sums from drug companies for promoting off-label uses of drugs justly arouse skepticism that they are promoting marketing messages rather than engaging in the free exchange of information.

Drug companies certainly possess freedom of speech to talk about their products. They may, for example, pay independent doctors to talk to other physicians about drugs, including off-label uses. However, doctors such as Dr. Gleason who accept such largesse run the risk of compromising their integrity

true, it probably is," Laemmle-Weidenfeld said of the lucrative speaking fees drug companies offer to physicians. "If physicians enter into contracts with a pharmaceutical company or a hospital for significant amounts of time and money, they should have legal counsel to make sure the arrangement doesn't send up red flags." *

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venue on behalf of a drug or device company, needs to be aware of this indictment and to be alert to its implications," said Wayne L. Pines, a former FDA Associate Commissioner for Public Affairs who is now a consultant on advertising and promotion issues to pharmaceutical and device companies.

WHAT PHYSICIANS CAN OR CAN'T DO: OFF-LABEL PROMOTION

Former FDA Association Commissioner of Public Affairs Wayne L. Pines advises physicians that there is a fine line between education and promotion, offering these guidelines for steering clear of problems:

- If a pharmaceutical company wants to promote a drug, it can sponsor a dinner meeting, but all talks and discussions must be 100 percent on-label, although the speaker can respond to unsolicited questions involving off-label use.
- If a physician is hired by a drug or device company to promote a product, the physician must give up the freedom to speak freely about his or her own experience in off-label usage, except in response to an unsolicited request for such information.
- Promotions must include a fair balance of risks and benefits and not be false or misleading.
- Physicians attending CME programs or courses should be alert to these issues and try to distinguish between information that is educational or purely promotional.

OFF-LABEL THERAPIES, LAWSUITS

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IF SUED IN OFF-LABEL CASES: WHAT PHYSICIANS SHOULD KNOW

Physicians facing lawsuits – such as those being brought against Drs. Longmire and Gleason – can find themselves suddenly subject to large legal fees, as medical liability insurance plans do not cover these matters. Dr. Longmire's legal co-counsel Robert A. Griffith of Gargiulo/Rudnick LLP said, "I would expect that most malpractice and business owner's policy insurers would deny the claim as being outside the terms of coverage, and any physician should anticipate a fight on this issue."

Even in the event that coverage is ultimately provided, he suspects that it may be limited to the cost of defense only, with a reservation of rights on the liability portion. Griffith explained that if a physician was held liable in a case where the damages exceed the policy limits, the physician would be left with no coverage for that portion beyond the policy limits. Furthermore, according to Griffith, some business owner liability policies are reduced by any amounts spent on investigation and defense. "This is one reason why it is important for physicians to seek advice about asset protection early on in their careers," he advised.

Wayne L. Pines, who serves as a consultant on advertising and promotion issues to pharmaceutical and de-

vice companies, said, "By law, drug and device companies cannot *promote* a drug off-label, but a doctor may *prescribe* a drug off-label."

The former FDA Associate Commissioner for Public Affairs added, "A few years ago, the Office of Inspector General (OIG) came up with a new twist – they began to apply the False Claims Act signed into law in 1863 to the drug and device industries. If a drug company promotes a drug or device off-label, and if on the basis of off-label promotion, a doctor prescribes it, and if the government reimbursed for the product (for example, under Medicare or Medicaid), it could constitute an act of fraud." Pines explained that the government went after Warner-Lambert under this law, and is continuing to go after others in the same manner.

Under the whistleblower's provision, the False Claims Act, said Pines, anyone can bring a case to the government and claim that a drug or device company is committing fraud. "There is a strong incentive for employees to report mispromotion or other acts that might be regarded as a false claim – whistleblowers get 15 to 30 percent of what the government collects," he points out.

A whistleblower – David P. Franklin, PhD, a microbiologist and former fellow at Harvard Medical School – triggered the case against Warner-Lambert (Parke-Davis) by testifying how he and others were pressured to circumvent laws that prohibit the marketing of drugs for off-label uses. At the trial, the prosecution presented documents obtained from Parke-Davis revealing the company's extensive efforts to boost sales of gabapentin by persuading doctors to prescribe it off label. Dr. Franklin received about \$24.6 million of the \$430 million ultimately paid by Pfizer after it acquired Parke-Davis, she said.

Dr. Franklin's success here will undoubtedly encourage others to follow suit, said Laura Laemmle-Weidenfeld of Patton Boggs. "If a case like this is resolved in the whistleblower's favor, more cases will be brought. That's why the government suddenly has a flood of new cases."

Pines warned: "Any time a physician accepts money from a drug or device company for any service – speaking engagement, dinner meetings, Grand Rounds, etc. – they become an agent of the company and they have to abide by the same rules regarding off-label promotion to which the company is held."