# Drug firms paid 'independent' experts

## Practice led to AG-whistleblower lawsuit



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AUSTIN (KXAN) - When Cliff Gay was told to switch medications to treat his bipolar disorder, he never dreamed a significant gain in weight and then to twice-daily injections of insulin would follow.

In 1999, Gay's doctor recommended he begin taking Zyprexa, which then was a new antipsychotic medication. At the time, Gay says it seemed like a good idea.

"The side effects were going to be less," he said.

Gay says he immediately noticed a profound change -- not so much in his symptoms, but in his appetite. Within a few months, he put on about 60 pounds, and that was followed by diabetes.

Records maintained by the U.S. Food and Drug Administration show that such stories are not uncommon among patients across Texas who, who beginning in the middle to late 1990s, were switched to medications called "atypical antipsychotics."

Many who have been put on the new class of drug reported similar gains in weight over time.

Doctors working in state hospitals and community mental health centers began switching patients to the atypical antipsychotics because they were deemed the best treatment by an expert panel convened by the Texas Department of Mental Health and Mental Retardation.

But a detailed examination of public records documents on file in a whistleblower lawsuit that has been joined by the Texas Attorney General's Office allege that the experts hired to evaluate the drugs and make recommendations for their usage were also accepting hundreds of thousands of dollars in payments from the companies developing and marketing the medications.

It started in the middle 1990s when MHMR contracted with University of Texas and some of its professors to evaluate the medications and develop a set of treatment guidelines.

The program was named the Texas Medication Algorithm Project, or TMAP. The result was step-by-step guidelines for treating major depression, bipolar disorder, schizophrenia, attention-deficit hyperactivity disorder.

TMAP was supposed to be based on the latest science, evaluated by an independent group of experts in the field.

But a 2004 lawsuit filed by whistleblower Allen Jones and the Texas Attorney General's Medicaid Fraud Division against Janssen Pharmaceuticals, a division of Johnson & Johnson, suggests that the project was actually a vehicle for boosting sales of expensive new drugs that government funded studies found were not more effective, but cost far more than conventional medications.

According to records compiled from company documents, Janssen was making substantial payments over several years to the decision makers, many of whom were University of Texas professors.

While the professors were under contract with the state of Texas to provide their expert opinions on medications,

records show many were also being paid by the companies whose drugs were being evaluated.

The suit alleges that Janssen improperly influenced the development of TMAP and compromised the objectivity of the decision makers by paying consulting fees, funding research and providing extravagant meals and lavish travel.

Such relationships were not always disclosed in TMAP manuals distributed to state hospitals and community mental health centers.

The depth of the financial relationship between the drug companies and the Texas Department of Mental Health weren't always disclosed, either.

**Extent of funding not fully disclosed**

Steven Shon, who then was medical director for Texas MHMR, publicly reported in media interviews pharmaceutical company funding for TMAP was only $285,000.

However, documents obtained through the Texas Public Information Act show far more funding from the companies whose drugs were recommended as a first-line treatment in the TMAP guidelines.

Donations to the Texas Department of Mental Health/Mental Retardation from pharmaceutical giants Eli Lilly, Pfizer, GlaxoSmithKline, Abbott, Bristol-Myers Squibb, Forest, AstraZeneca, Novartis, Janssen and Forest and Wyeth-Ayerst totaled more than $1.2 million.

An additional $2.8 million was donated by the Robert Woods Johnson Foundation, which stock portfolio benefits from sales of Janssen's medication.

Shon claimed he never personally received any money from the drug companies. A claim that was disputed in financial records turned to the court over by Janssen.

According to court records, Janssen paid Shon nearly $30,600 in honoraria and travel expenses. An additional $17,000 was directed to Association of Korean Americans at Shon's direction.

In June, 2002, Janssen hosted a meeting and paid the travel expenses for seven TMAP decision makers. The meeting was held at the lavish Mansion on Turtle Creek Resort in Dallas with the purpose of advising Janssen on its newest antipsychotic.

Attendees included Steve Shon MD, Madhukar Trivedi MD, Tricia Suppes MD, John Rush MD, Larry Ereshefsky MD, Lynn Crismon, John Chiles MD and Alexander Miller MD.

Trivedi, Suppes, Rush and Ereshefsky were employees of University of Texas Southwestern Medical Center in Dallas.

Crismon was a professor

at the University of Texas School of Pharmacy in Austin.

Chiles and Miller were professors at University of Texas Health Science Center in San Antonio.

According to an expert report filed in the Janssen lawsuit, the meeting cost the company $114,000. The report says that the investment paid off. Shortly after, emails between some of the TMAP decision makers and Janssen discuss where the company wanted to place its newest antipsychotic on the guidelines.

The expert report, notes that other similar meetings were held at resorts in Scottsdale, Ariz., and the Ritz Carlton in Amelia Island, Fla. In most cases, participants were paid an honorarium.

Court records show Janssen paid Crismon, now the dean of the UT College of Pharmacy, more than $61,200 for various consulting fees and speaking engagements, including some that took place in state hospitals and community MHMR clinics.

Janssen reported paying Alexander Miller, professor at UT Health Science Center in San Antonio, $82,485.42. John Chiles, a UT professor at the time, was paid $151,254.73. Crismon, Miller and Chiles served on the TMAP panel at the time they received the payments.

**Huge boosts in sales**

The pharmaceutical companies funded trips for certain members of the TMAP team for travel to other states to expand TMAP to other states. More than a dozen states adopted the guidelines.

It meant huge sales for the drug companies because TMAP not only recommended their drugs for disorders in which the FDA had granted approval.

But for some illnesses that were not approved. Doctors are allowed to prescribe a drug with FDA approval for any reason, but manufacturers are only allowed to promote drugs for disorders that have been approved by the FDA.

While TMAP was touted as evidence-based or based on science and actual experience, the medications chosen to be included in the guidelines raised questions to exactly what evidence was considered by decision makers.

For example, several of the participants were involved in one of the largest independently funded studies to determine which medications provide the best treatment for schizophrenia.

The Clinical Antipsychotic Trials of Intervention Effectiveness Study, known as CATIE compared several of the new antipsychotics, risperidone (Risperdal), olanzapine (Zyprexa), quetiapine (Seroquel) and ziprasidone (Geodon) with an older, cheaper drug, perphenaxine (Trilafon).

The results, announced in 2005, found the new drugs, which cost roughly 10 times as much, had no substantial advantage over the older medication.

Despite the scientific findings, the TMAP team continued to recommend the more expensive drugs as a first-line treatment.

In 2008, the TMAP guideline for major depression was revised. The first non-medication treatment was added. The Vagal Nerve Stimulator, or VNS, manufactured by Cyberonics, is a medical device that is surgically implanted and sends electrical impulses to the brain.

The studies provided to the FDA during the approval process were conducted by several of the members of the TMAP team, including John Rush of the University of Texas Southwestern Medical Center in Dallas.

Reviewers with the FDA found the evidence submitted to the FDA to be lacking.

They recommended against approval. However, their decision was overruled and the device was approved.

**Alarm bells sounded**

The reviewers sounded an alarm, and the U.S. Senate Finance Committee launched an investigation into the approval process. Its findings raised questions about how the device could be approved by the FDA absent the scientific data showing the product was safe and effective.

In a speech on the floor of the Senate about the investigative report, U.S. Senator Charles Grassley said the conclusions of the person overruling the decision raise serious questions.

He read from the override memo, “I think it needs to be stated clearly and unambiguously that [certain VNS data]failed to reach, or even come close to reaching, statistical significance with respect from its primary endpoint. I think that one has to conclude that, based on [that] data, either the device has no effect, or, if it does have an effect, that in order to measure that effect a longer period of follow-up is required.”

The FDA approved the VNS with the condition that the company would conduct further studies and report the results to the FDA.

The Centers for Medicare/Medicaid refused to pay the estimated $25,000 bill for VNS treatment for depression. Most insurance companies wouldn’t pay, either.

But that didn’t deter the TMAP team from including the VNS on the revised guideline for treating depression. Such decisions were made behind closed doors and records revealing which members approved the inclusion are not

available.

Rush's relationship with Cyberonics was not fully disclosed to the University of Texas in his annual Statement of Financial Interest filing. His filing dated Aug. 7, 2006, lists his role as a member Cyberonics Speakers Bureau with an annual income equal or

less than $10,000.

But in records submitted to the office of U.S. Sen. Charles Grassley, R-Iowa, by Cyberonics, Rush was paid $100,000 in 2006 by the maker of the VNS. Cyberonics also reported paying Rush more than $75,000 in 2003 and 2004, and $62,000 in 2005.

Of the 10 decision makers who worked on the revision to the TMAP guideline for depression, six reported they owned stock or had a financial relationship with Cyberonics, including the project director, Crismon. Such disclosures were made to their employers or though industry publications.

The UT School of Pharmacy reported Cyberonics was the source of funding for a $54,938 research project in which Crismon was the principal investigator.

In a news release by Cyberonics, the company said the purpose of funding the research was to use the data to convince Medicaid and insurance companies to pay for VNS.

"By demonstrating the cost-effectiveness of VNS Therapy for treatment resistant depression (TRD) through this standardized, extensive and thorough analytical approach," the release said, "it is our expectation that many more payers will come to recognize and understand the unique safety, effectiveness and cost effectiveness of VNS Therapy and grant psychiatrists and Americans with TRD access to VNS Therapy through national and regional coverage policies."

Several TMAP panel members wrote letters urging the Centers for Medicaid to reconsider and pay for VNS treatment for depression.

Cyberonics cited it's inclusion in the revised TMAP guideline for depression as reason for the government to pay.

It didn't work.

CMS ruled the evidence did not show the treatment was effective for treating depression. A year after the ruling, the revised TMAP guideline was published recommending VNS, although many patients in the states hospitals and community centers would have had to pay out-of-pocket for the treatment.

Travel and out-of-state lobbying

Some of the TMAP team members were instrumental in expanding its usage across the nation. Largely funded by the drug companies, UT professors and state employees traveled to other states to lobby state legislatures and conduct training sessions.

But not all doctors in Texas centers and state hospitals were on board with the program. Emails between the TMAP team blamed a reluctance to change.

Texas MHMR paid two University of Texas at Dallas professors $100,000 to design a change management program.

Doctors were still reluctant, so the state made complying with the TMAP program a condition of its contract with community centers. The centers were required to show they were in compliance or would lose a percentage of their medication funding.

TMAP was at one time heralded. It was included in recommendation by the White House New Freedom Commission Report.

Psychiatrist Daniel Fisher, who was appointed to the commission said, members were encouraged to include TMAP in the recommendations, but never told of the pharmaceutical company involvement or that members of the consensus panel that developed the guidelines received money from the drug companies.

Fisher said he was stunned to learn the depth of involvement of the drug companies.

“This is the story of the century,” he said.

The pharmaceutical involvement came as a surprise to Cliff Gay. He was asked to participate in TMAP activities early on in the development. His role was as a patient and family advocate.

“I am totally blown away by the amount of money that was put into this thing,” said Gay. “I didn’t find out about the extent of the payments until I went to work for NAMI Texas.”

According to expert reports filed in the lawsuit against Janssen, NAMI, the National Alliance on Mental Illness in Texas, played a big role in helping TMAP and the pharmaceutical companies.

The expert report quotes from internal Janssen memos and depositions, efforts to utilize advocacy groups to their advantage, particularly NAMI Texas executive director Joe Lovelace.

The expert report filed in court reads “Lovelace received funding from J&J not only for the organization but personally, noting in his deposition that he deposited the monies in his wife’s law firm account because “she needed the money…there was a loss there.”

One of Janssen’s employees explained that “Lovelace desired to partner with Janssen as a consultant.”

Lovelace became a frequent speaker for J&J between 2000 and 2003. The report details the value of Lovelace when company officials asked if he would have NAMI members “come up to testify and relate their personal stories”, he responded by noting the when he had a chairman of a legislative insurance committee from Amarillo, he “made sure that a person in his church sat down in front of him.”

Lovelace no longer works for NAMI Texas. He is now the Associate Director of Behavioral Health for Texas Council of Community Centers.

TMAP’s rapid expansion began to crumble in 2004, when the first whistleblower lawsuit was filed against one of the drug companies involved. The State of Texas

Attorney General’s office joined in the lawsuit and filed suits against the other companies. Attorney Generals in other states filed suits, too.

**Big-dollar settlements**

To date, all but one of the suits has settled.

Bristol-Myers Squibb paid $15.7 million to Texas under a national settlement for allegations relating to its anti-depression drug, Serzone.

According to the press release issued by the Attorney General, the investigation also revealed BMS unlawfully marketing and promoting, Abilify, an atypical antipsychotic drug. It’s marketing partner, Otsuka paid $220,OOO to settle that claim.

Eli Lilly paid more than $30 million to Texas in a state and federal lawsuit over the marketing of its drug Zyprexa. In total, Eli Lilly paid $1.6 billion in criminal fines and reimbursing the government for charges to Medicaid.

The Texas Attorney General and 42 other states reached a $33 million agreement with Pfizer to settle claims of its marketing of Geoden to health care providers.

In a separate action, Pfizer also settled another case involving Geoden and another medication by paying $55 million to Texas as part of a $1 billion multi-state agreement.

Texas and 38 states reach a $68.5 million settlement with AstraZeneca stemming from a federal suit charging the company with unlawfully marketing Seroquel.

Texas share of the settlement was $3.8 million.

Janssen settled multiple Medicaid fraud and deceptive drug marketing cases related to its drug, Topamax, by agreeing to pay $50.7 million to several states.

Texas share is $2.86 million.

The Texas case against Janssen is pending and scheduled to go to trial in November.

Shon was fired as medical director for the state of Texas on Oct. 9, 2006. However, he was allowed to stay on the payroll in an unpaid capacity until he qualified to retire with full benefits.

He is now living in Las Vegas.

Crismon was promoted from professor to Dean of the UT School of Pharmacy. His work on TMAP was cited in the press release announcing his promotion. He continues to consult on guidelines for mental health treatment through a contract with the Reach Institute.

Rush left the University of Texas Southwestern Medical Center and is now working for Duke University in Singapore.

The other TMAP professors are still employed at various University of Texas System campuses.

Crismon declined to grant an interview for the report. KXAN's request for an interview with Chancellor Francisco Cigarroa was denied, but UT System Vice Chancellor Barry Burgdorf said outside employment arrangements decisions are made by the individual campuses within the system.

"Supervisors are charged with evaluating requests to approve outside employment by assessing whether the potential outside employment constitutes a conflict of commitment – whether the time required to fulfill the outside employment would interfere with UT job duties -- or a conflict of interest," said Burgdorf, also the system's general counsel.

"With regard to conflicts of interest in some cases the employee requesting approval of outside employment is required to enter into a conflict of interest management plan designed to prevent potential conflicts from maturing to an actual conflict," he added. "Many times approved outside employment is synergistic with UT employment such as when a faculty member works for a start -up company spun out from UT using technology invented by the faculty member."

In 2010, The Texas Department of State Health Services approved recommendations by a committee tasked to review the TMAP to stop using the guidelines.

Cliff Gay said he feels betrayed. He is among those who they were supposed to be helping.

“I don’t think any of them could look me in the eye and tell me they were doing it for me,” said Gay. “They did it for the money. It’s all about the money.”