

BUSINESS DAY

Paid to Promote Eye Drug, and Prescribing It Widely

By **KATIE THOMAS** and **RACHEL ABRAMS** DEC. 7, 2014

When the drug maker Genentech introduced a major product in 2006, it found itself in an awkward position: persuading eye doctors to start using its new more expensive drug instead of a popular cheaper version that the company already sold.

Ophthalmologists had been enthusiastically using the company's cancer drug Avastin, which cost about \$50 a dose, to treat a common eye disease in the elderly, wet macular degeneration. Then Genentech introduced Lucentis, a nearly equivalent drug that cost \$2,000 a dose and was approved specifically to treat the disease.

Use of Lucentis took off, and it has become one of Medicare's most expensive treatments — costing the federal government about \$1 billion a year — even though several studies have concluded Lucentis has no significant advantage over its cheaper alternative.

Now, a new federal database shows that many of the doctors who were the top billers for Lucentis were also among the highest-paid consultants for Genentech, earning thousands of dollars to help promote the drug. The data raises questions about whether financial relationships between doctors and drug companies influence treatment decisions, even though physicians maintain they cannot be swayed.

Half of the 20 doctors who received the most money from Genentech to promote Lucentis in 2013 were among the highest users of the drug in 2012, billing for higher amounts of Lucentis than 75 percent of their peers. The figures were compiled from two federal databases that covered different periods, and it is not known whether or how much Genentech paid the doctors in 2012.

The 20 doctors earned \$8,500 to \$37,000 over five months in 2013, payments that included consulting and speaking fees as well as travel expenses and meals. Genentech says it has an annual cap of \$50,000 a doctor for speaking fees.

Specialists who study conflicts of interest between physicians and the drug industry say even modest payments have been shown to influence behavior.

“That’s why a sandwich is so effective — no one wants to feel like they were being bought off for \$5,” said Dr. Adriane Fugh-Berman, an associate professor at Georgetown University Medical Center in Washington and director of **PharmedOut**, a project that educates doctors about drug marketing claims. “That’s why they convince themselves that the drug is better.”

Doctors who speak on behalf of Lucentis say they do so because they believe in it and because they want to educate colleagues on its use. Some said that while they continued to use Avastin, it carried risks that should not be ignored.

“There are certain instances where you would prefer one over the other,” said Alan Ruby, an ophthalmologist based in Livonia, Mich., who received nearly \$12,000 from Genentech in the second half of 2013 for conducting what he described as workshops to educate other medical professionals about Lucentis. Dr. Ruby said that Lucentis was a better choice for some patients because of some evidence showing that Avastin carries a slightly higher chance of strokes in patients who are already at risk of developing them.

Dr. Ruby said he used Avastin on roughly a quarter of his macular degeneration patients, and used Lucentis more frequently. A federal database of Medicare billing showed that he billed for a higher amount of Lucentis than 75 percent of his peers. “I think to suggest that physicians are in any way influenced by their interactions with drug companies is very shortsighted,” he said.

Edward Lang Jr., a spokesman for Genentech, which is owned by the Swiss drug maker Roche, said the company chose to work with doctors based on their clinical expertise. “We’re looking to work with doctors who are in the top of their field, and who can provide us an honest perspective on what patients need and don’t need,” he said.

While Genentech says Lucentis is a better option, it supports a doctor’s choice about what is best for a patient, Mr. Lang said, adding, “That comes before us and anything else.”

Lucentis and Avastin, as well as Regeneron’s drug Eylea, are prescribed for the eye disease, which, if left untreated, can lead to blindness. Use of Avastin became popular after clinical trials for Lucentis showed that it worked well for macular degeneration. Doctors speculated that Avastin, which works in the same way as Lucentis, could also be used to treat the disease.

Since Lucentis was approved in 2006, several studies have shown that the drugs are nearly equivalent, including a large government-sponsored clinical trial involving 1,200 patients that was completed in 2011. Avastin is still the most popular choice of doctors: About half of patients who were treated for wet macular degeneration received Avastin, with Lucentis and Eylea sharing the rest of the market.

Genentech has aggressively promoted Lucentis to doctors to encourage them to switch, even paying rebates to those who use large amounts of Lucentis, a practice that critics have described as improper but the company says is legal. For Genentech, the stakes are high. Lucentis is one of its top

products, generating \$1.3 billion in sales in the first nine months of this year, an increase of 5 percent over that period last year.

Even with widespread Avastin use, injecting Lucentis remains one of Medicare's costliest procedures. In 2010, Medicare paid \$1 billion to treat macular degeneration patients with Lucentis, while it spent \$27 million for such patients treated with Avastin, according to a 2012 study from the Office of the Inspector General for the Department of Health and Human Services.

In 2011, the office determined that if all patients being treated with Lucentis were instead given Avastin, the federal government would have saved about \$1.4 billion.

A review released this year of nine clinical trials showed that Avastin and Lucentis had similar safety profiles and that Avastin did not appear to increase deaths or serious side effects. The review was conducted by the nonprofit Cochrane Collaboration.

Still, several doctors, including those who speak on behalf of Lucentis and those who do not, said the choice between Avastin and Lucentis was not simply a matter of cost.

For example, Lucentis is specially prepared to be injected into the eye, but Avastin must be divided into smaller doses by outside compounding pharmacies, which can lead to contamination in rare cases. In 2011, more than a dozen people developed severe eye infections, and some were blinded, after they received injections of contaminated Avastin.

Some doctors say there is no good reason to use Lucentis more frequently than Avastin.

"They keep talking about evidence-based medicine, and they keep pretending the corporate-sponsored research is nonbiased," said J. Gregory Rosenthal, a retina specialist in Toledo who has become an outspoken critic of

Lucentis and Eylea. “The evidence says that Avastin has at least the clinical efficacy of Lucentis and is perhaps safer.”

Some doctors who were paid to promote Lucentis said they also used Avastin. “I usually start with Avastin,” said Dr. Mathew MacCumber, a retina specialist in Illinois who received about \$8,500 from Genentech from August through December 2013, mostly to advise the company on topics that included how to promote the drug to doctors.

He received even more, about \$16,000, from Regeneron in connection with Eylea, which was approved in 2011. Dr. MacCumber says he switches patients to Lucentis or Eylea if they do not do well on Avastin. He said some patients asked for those two drugs because they are F.D.A.-approved to treat macular degeneration. The federal Medicare database showed that the amount he billed for Lucentis was more than 50 percent of his peers. Dr. MacCumber, who noted he is a retina specialist who treats a high number of patients with macular degeneration, said he also used Lucentis to treat other eye conditions.

Dr. MacCumber said he worked for the companies because it was the best way to learn about the drugs. He says he is not influenced by the money he receives in compensation for his time. “People come to me and ask my advice, so I have to know the real story about things, and the only way to really do that is to know the people in the company who do the research, who know the drug the best,” he said.

Eric Campbell, a professor of health care policy at Harvard Medical School, said doctors frequently denied that relationships with drug companies could change their behavior, despite many studies to the contrary. “They are suggesting that the drug companies that are spending this money, that these companies are dumb enough to be wasting their money,” he said.

Not every top Lucentis biller was paid to promote the drug. In fact, several of the highest billers in 2012 got no such payments.

Mr. Campbell said that was because drug companies selected doctors based on their sway in their community. “You don’t have to influence every doctor, you just have to influence the right doctors,” he said.

Agustin Armendariz contributed reporting.

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