The New York Times https://www.nytimes.com/2023/02/28/business/jazz-narcolepsy-avadel-patents.html

A Drug Company Exploited a Safety Requirement to Make Money

With a history as a date rape drug, a medication needed strict distribution controls. Its maker, Jazz Pharmaceuticals, used that to delay competition.

By Rebecca Robbins

Feb. 28, 2023 6 MIN READ

The pharmaceutical industry is rife with tales of companies dreaming up ways to prolong their monopolies on lucrative drugs. They tinker with chemicals. They tweak dosing. They swap out capsules for tablets.

By piling up patents, drug companies delay the day when competitors can introduce similar, cheaper products.

Jazz Pharmaceuticals has figured out a way to push the boundaries even further — a feat that demonstrates the lengths to which drug makers go to eke out extra profits and that two federal courts have now ruled was improper.

Jazz's most important product is a medication for the sleep disorder narcolepsy. The company patented the drug's formulation. But Jazz also went further, arming itself with a new weapon to block competition.

Because of the drug's serious side effects and its history of being abused for date rape, federal regulators required Jazz to come up with a plan to ensure that the drug was safely distributed to patients without falling into unintended hands. Jazz's program included having a single pharmacy nationwide send the medication directly to patients.

Jazz took the unusual step of patenting that safety program and then listing those patents in a federal registry known as the Orange Book. Under an obscure federal rule, if a rival contested one of the patents in certain circumstances, federal regulators would be barred for more than two years from approving that competitor's product.

That was precisely the strategy that Jazz deployed when a rival was poised to introduce an improved version of the drug.

Jazz's narcolepsy drug, which is used by thousands of patients, is enormously lucrative, generating more than $13 billion in revenue since Jazz acquired it in 2005. Medicare now spends hundreds of millions of dollars annually for it. The drug accounted for 58 percent of Jazz's revenue in 2021.

In other words, for every month that Jazz could delay the arrival of competition, the company and its shareholders stood to benefit financially.

But the tactics deprived narcolepsy patients of access to a new drug that was much easier to take.

Patent law experts say Jazz's strategy of enforcing the patent on how the drug is distributed has strayed far from the ostensible purpose of the U.S. intellectual property regime, which is meant to reward drug makers for taking risks to develop and improve innovative products. The case, they say, is an egregious example of how drug companies exploit the patent system to shield their products from competition for as long as possible.

"It has very little to do with all of the reasons why we allow the patenting of drugs," said Michael Carrier, a drug patent expert at Rutgers Law School in Camden, N.J. "A lot of this stuff is just a computer program."

Jazz Pharmaceuticals' headquarters in Dublin. Its narcolepsy drug accounted for most of its revenue in 2021. Paulo Nunes dos Santos for The New York Times

Xyrem is now 19 times as expensive as it was in 2007, when SSR began tracking it.

Jazz's medication is a pharmaceutical-grade derivative of gamma-hydroxybutyric acid, or GHB, which is tightly regulated because of its history of abuse as a date rape drug after health food stores sold it as a dietary supplement in the late 1980s.

GHB was first synthesized and tested in the 1960s. Jazz, which is legally domiciled in Ireland but has many top executives based in California, did not do the original development work on the prescription version of the drug; the company acquired it nearly three years after its first approval.

Both versions of Jazz's medication come as a bottled liquid. Patients mix it with water and drink it. Patients must take two doses daily: the first at bedtime and the second up to four hours later.

Brian Mahn, a 53-year-old consultant in Cypress, Texas, said he had to stop taking Xyrem several years ago because the dosing schedule was too difficult. He would sleep through the multiple alarms he set between 2:30 and 3 a.m., disrupting his family. Mr. Mahn would often take the second dose too late, leaving him with such severe brain fog in the morning that he was unable to drive to work.

Avadel's product, Lumryz, shares the same drug substance as Xyrem but comes as a powder and, crucially, has an easier dosing schedule. Avadel's powder is taken only once daily at bedtime, so patients don't have to wake up in the middle of the night.

Because of that advantage, many patients are expected to switch to the Avadel drug once it becomes available.

Jazz decided to take action to defend its golden goose. Its strategy hinged on the federally mandated safety program, known as Risk Evaluation and Mitigation Strategies, or REMS, that it had patented and listed in the Orange Book.

Brian Mahn said he had to stop taking Xyrem because it was too difficult to wake up in the middle of the night for the second dose. Michael Stravato for The New York Times

Jazz's REMS program consisted of a computerized system for tracking which physicians can prescribe a drug and having a single pharmacy ship the drug to patients nationwide.

About a decade ago, Jazz received seven patents related to its REMS program, and it listed them in the Food and Drug Administration's Orange Book, according to an analysis by Mr. Carrier.

One of those patents, granted and listed in 2014, is at the center of Jazz's dispute with Avadel.

Listing a patent in the Orange Book had important implications. Under a 1984 federal law, if a drug company accuses a rival of infringing on a patent in the Orange Book in certain circumstances, the F.D.A. cannot approve the competitor's drug for at least 30 months.

The catch is that only certain types of drug patents — such as those protecting a medication itself or a method of using it — are allowed to be listed in the Orange Book. It is unclear how a REMS program, which is a system for getting the drug from a pharmacy to patients, fits either definition.

Because of those limitations, it is unusual but not unprecedented for a drug company to patent a REMS program and list it in the Orange Book.

Jazz has taken this strategy to a new level, with its chief executive even bragging to investors about how its REMS patents would make it hard for a manufacturer of generic drugs to set up its own REMS program.

Before the Avadel case, Jazz had sued nine companies that sought authorization for a generic version of Xyrem, accusing them of infringing on Jazz's REMS patents. The strategy worked: Those manufacturers reached settlements with Jazz agreeing to delay the introduction of their products.

Experts in drug patents said such tactics were an abuse of the patent system.

REMS programs are “supposed to promote drug safety,” said Dr. Aaron Kesselheim, a professor of medicine at Brigham and Women’s Hospital and Harvard Medical School. “That’s not supposed to be a mechanism for extending revenue streams.”

In 2020, Avadel asked the F.D.A. to approve its powdered narcolepsy drug. Over the next two years, Jazz filed a barrage of lawsuits claiming that Avadel was infringing on various patents. Included in those was a suit last summer that accused Avadel of violating the 2014 REMS patent in the Orange Book.

Because of the 1984 federal law, the lawsuit automatically meant that for 30 months, the F.D.A. couldn’t approve Avadel’s drug, even though, days after the suit was filed, the agency determined that the product was safe and effective.

In this case, the automatic delay was to last only about 12 months, not 30, because Jazz’s REMS patent was set to expire on June 17.

Jazz’s lawyers, at the firms Sidley Austin and Quinn Emanuel Urquhart & Sullivan, argued that Jazz’s REMS program represented “a method of using” the drug for the purposes of being included in the Orange Book.

But both federal courts rejected that argument, ruling that Jazz’s patent was inappropriately listed in the Orange Book because the REMS program was not related to the drug itself or to a method of using it. As a result, Jazz should not have been able to delay the F.D.A.’s approval of the rival drug.

“We have considered Jazz’s remaining arguments and find them unpersuasive,” judges on the U.S. Court of Appeals for the Federal Circuit wrote in their ruling on Friday.