Doctors decry lack of Wyeth vaccine
Health policy officials urge rationing of Prevnar, which prevents meningitis

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When Barry Prystowsky heard last November about a sudden shortage of the Prevnar vaccine for meningitis, he was frustrated and alarmed.

"It was very aggravating. The explanation was never clear," said the Nutley pediatrician. "But I had to tell parents that I couldn't protect their babies against this horrible bacteria."

He was even more upset during February, when Wyeth, the only company to make the vaccine, said supplies were still hampered by unspecified production problems. Today, the medicine is being rationed, and many doctors say Wyeth should have disclosed the full extent of a series of manufacturing problems that caused the shortage.

Wyeth experienced numerous manufacturing issues for several years before the shortage was announced, according to the Food and Drug Administration. The two plants that make Prevnar were annually cited for extensive shortcomings -- most recently last September and October. And one plant avoided taking steps to improve quality control, according to a whistleblower lawsuit filed by a former employee.

A number of doctors say they were upset by the lack of timely information, because it forced them to grapple with both an unexpected shortage and an inability to plan. Doctors are rationing the widely praised vaccine, which is supposed to be administered to children four times by the age of 15 months. Instead, children are given just two shots.

"Being kept in the dark for a protracted period of time really does wreak havoc," said Tom Saari, a University of Wisconsin pediatrics professor and member of the infectious diseases committee at the American Academy of Pediatrics. "My concern is if they're going to shut down, they should've had a pretty good idea how long it would take to get up and running."

WIDER IMPLICATIONS

Beyond the immediate shortage, the episode may have wider implications for Wyeth. Prevnar is one of the Madison-based drug maker's biggest-selling products, generating nearly $1 billion in revenue last year.

Wyeth officials acknowledged manufacturing problems, but maintain they took steps to fix them. And they stressed the plant problems didn't pose a safety issue. "We're as frustrated as anybody else," said Peter Paradiso, Wyeth's vice president of scientific affairs. "We want to make sure we maximize coverage of this vaccine."

The Centers for Disease Control and Prevention, which establishes national health policy, had to issue two different advisories about Prevnar rationing during less than four months. This caused confusion and anxiety among doctors and patients, according to the federal agency.

"Had we known that the shortage was going to get much worse, we wouldn't have done things the way we did," said Lance Rodewald, director of the immunization division at the CDC, which recommended the reduction in the number of shots.

At issue is whether Wyeth should have disclosed more information sooner about manufacturing problems that may cause shortages. Although disclosure wasn't required, Wyeth didn't reveal that a team of FDA inspectors last October found numerous quality-control failings at its Pearl River, N.Y., plant. Prevnar is made at a Sanford, N.C., facility, but is packaged in Pearl River. A production shutdown occurred at the Pearl River site late last year.

BAD REPORT

The FDA inspection report, which was obtained by The Star- Ledger, detailed sloppy operating procedures, dirty work areas, instances of contamination, improper environmental monitoring and insects in a hallway outside a room where the vaccine was filled in vials. Wyeth's own internal investigations also took longer than expected and were incomplete, the report said. "Manufacturing investigation reports are not always completed in a timely manner," the FDA inspectors wrote in reviewing Wyeth's follow-up to problems noted previously by the agency. "Further, there is a lack of evidence that product impact is addressed in a timely manner and that all batches/processes are fully investigated."

Bruce Burlington, a Wyeth executive vice president in charge of quality, regulatory and safety matters, said FDA inspectors found significant shortcomings during the inspection at the Pearl River plant last October,

Detailed inspections are routine in the pharmaceutical industry, which must adhere to strict manufacturing practices. But lengthy inspection reports aren't the norm. In this case, FDA inspectors chronicled 59 problems in their 15-page account. But FDA spokeswoman Lenore Gelb said any serious problems would be conveyed to the medical community.

In a brief interview last month, Bernard Poussot, a Wyeth executive vice president, said the stoppage at the Pearl River plant late last year took place because "the FDA shut us down." Such a step would indicate the company had no choice but to interrupt production. However, the FDA spokeswoman said the agency never took such action. A Wyeth spokesman didn't make Poussot available for further comment.

SECOND INSPECTION

This was the second time the FDA inspected the facility since October 2000, when Wyeth signed a consent decree with the federal government. As part of the decree, Wyeth agreed to correct manufacturing problems and relinquish $30 million in profit. The company still faces as much as $5 million in fines for failing to improve operations.

A consent decree results when a company repeatedly fails to comply with FDA standards. Repeated citations by FDA inspectors reflect an ongoing inability to satisfy the decree requirements, according to Suggy Chrai, a drug-industry manufacturing consultant.

Wyeth officials have repeatedly said the safety or effectiveness of the vaccine was never compromised. They said deficiencies were willingly disclosed to FDA inspectors and that last year's Pearl River shutdown was part of a scheduled maintenance procedure. The stoppage ran longer than expected due to ongoing manufacturing problems, they said.

"We shut it down to do a routine maintenance and because of the issues that arose, we had a pronounced shutdown," said Wyeth's Paradiso. He added the CDC and doctor groups were alerted to an impending shortage very quickly last fall, but the extent of the plant problems weren't disclosed.

In addition, Wyeth's Burlington defended the company's efforts and also noted Prevnar is a difficult product to make.

"At this point, we're where we want to be," he said. "We sent a remediation plan to the FDA and the response we received indicates our action appears to be adequate. And we'll be on a full production schedule, hopefully, later this year."

SHARED PRODUCTION

To do so, Wyeth has enlisted two companies, Cardinal Health and Baxter Healthcare, to assume part of the production process that was previously handled at Pearl River.

Normal production would cheer Wall Street. Despite the difficulties, which include a previous shortage, Prevnar has been a shot in the arm for Wyeth. Approved by the FDA during 2000, Prevnar quickly filled a medical void. Until then, pneumococcal infection each year killed 200 children under the age of 5 and caused more than 700 meningitis cases.

Last year, the vaccine generated $946 million in sales. That was much-needed revenue for a drug maker plagued by a pair of serious setbacks -- costly diet-pill litigation and plunging sales of hormone replacement treatments.

To capitalize, Wyeth has wanted to produce as much vaccine as possible, even while grappling with the consent decree. But Chrai, the manufacturing consultant, said drug makers that don't quickly fix mistakes run the risk of a financial hit and losing investor confidence.

"Prevnar is an important product for Wyeth. It's an earnings driver," said David Moskowitz, an industry analyst at Friedman Billings Ramsey. "At this point, it's a show-me story. It's very unfortunate they haven't been able to supply the product. They really need to show the marketplace they can supply it in sufficient quantities by the end of the year."

One former Wyeth employee maintains shareholders have already suffered.

In a whistleblower lawsuit filed last December in U.S. District Court in Greensboro, N.C., Mark Livingston, a quality-control expert, charged Wyeth managers at the Sanford, N.C., plant cut corners to boost Prevnar production. He also charged that his suggestions for meeting FDA standards were deliberately ignored and that he was wrongly fired during 2002.

The company's practices, according to the lawsuit, amounted to fraud and violated the Sarbanes- Oxley Act, which was designed to improve corporate governance and financial disclosure to shareholders. For instance, filings with the Securities and Exchange Commission didn't mention a negative FDA inspection report at the Sanford plant during September 2003.

MISREPRESENTATIONS

"They misrepresented the real state of manufacturing," said Joanne Royce, an attorney with the Government Accountability Project, which represents Livingston. "And so there was misrepresentation of Wyeth's financial condition. When noncompliance goes on so long, shareholders have a right to know. It's bound to reflect on the bottom line at some point."

A Wyeth spokesman, Doug Petkus, said the lawsuit was filed by a disgruntled employee and was without merit. He also said Prevnar remains safe and effective.

Despite the ongoing shortage, Margaret Rennels, a University of Maryland pediatrics professor and chair of the American Academy of Pediatrics infectious diseases committee, praised Wyeth for providing weekly inventory updates, creating an effective rationing system and opening a hot line for doctors.

"They're trying to ensure that every doctor has enough vaccine to administer, and in an equitable way," she said.

Yet she and other doctors say the episode is worrisome, and are concerned another shortage may occur unless Wyeth improves its manufacturing procedures.

"With Wyeth, there's a pattern here, and it concerns me," said Saari of the University of Wisconsin. "The fact that these issues are still going on is disturbing, because of the impact on kids who can't get the vaccine. There are some real risks in terms of disease prevention."

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