

Rezulin

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Press Accounts

Drugmaker Hires NIH Researcher

December 7, 1998

Los Angeles Times

By David Willman

Rezulin: Doctor, superior deny any conflict of interest. Questions are raised about claims Warner-Lambert made in promoting the pill.

WASHINGTON- On June 11, 1996, the Warner-Lambert Co. announced that its new drug Rezulin had been selected for use in the federal government's largest study of diabetes.

In the company news release, Dr. Richard C. Eastman, the National Institute of Health's top diabetes researcher who is overseeing the study, praised Rezulin as a drug that "corrects the underlying cause of diabetes."

The release was remarkable for two reasons:

First, Eastman's quoted claim that Rezulin corrects the cause of diabetes was--and remains--unproven. Eastman now denies making the remark.

Second, the news release did not disclose a potential conflict of interest. At the exact moment that he had overall responsibility for the \$ 150-million government study, Eastman also was on Warner-Lambert's payroll as a consultant.

Eastman said he has acted properly and with the consent of his National Institutes of Health superiors. He said that he has "overall global responsibility" for the study but that he abstained from one or more votes backing Rezulin's selection.

These disclosures raise questions about conflict of interest, according to legal experts. Federal law makes it a crime for a high-ranking public official to have a financial arrangement with a company while participating "personally and substantially" in government matters that affect the company.

The revelations also raise questions about claims Warner-Lambert made in promoting Rezulin during its brief, troubled history: The drug has been linked to at least 33 deaths, additional liver-related injuries and three urgent warnings to doctors since it became available in the U.S. in March 1997. The drug remains on the market.

So far, Rezulin has paid off for Warner-Lambert with sales approaching \$ 1 billion. The company reports that more than 1 million people with adult-onset diabetes have used the drug.

Warner-Lambert officials have achieved this while making a series of dubious statements about the drug, records and interviews show.

Last year, for example, the Food and Drug Administration accused the company of making "false and misleading" statements in a 1997 news release announcing the launch of the drug.

Company executives said that they have sought only to truthfully describe the drug.

"The medication is something that really does add value to patients," said Dr. Robert L. Zerbe, the company's senior vice president for worldwide clinical research and development. "We've tried to be very highly responsible in everything that we've done."

The dual government and private-sector roles played by Eastman also shed light on how the NIH--long considered a temple of objective scientific inquiry--has in recent years developed closer relationships with pharmaceutical and biotechnology companies. These firms stand to earn fortunes by developing breakthrough drug therapies jointly with NIH.

Such a blend of public and business interests also threatens to erode the trust that doctors and patients place in the government's top health officials. The FDA, which regulates the sale of prescription drugs, prohibits its employees from entering such consulting arrangements.

Eastman expressed concern that disclosure of his role with Warner-Lambert--not reported publicly until now--will undermine confidence in the government's diabetes study, which has dropped Rezulin.

Warner-Lambert's recruitment of Eastman to help promote Rezulin was only part of a marketing campaign that vaulted the drug from an obscure laboratory compound to one of the world's hottest-selling prescription pills.

The company said the arrangement with Eastman is entirely proper.

"Dick is a man of great integrity," said Dr. Randall W. Whitcomb, vice president of diabetes research for Warner-Lambert.

Warner-Lambert officials and Eastman declined to specify the amount of money he has been paid by the company.

Company spokesman Stephen J. Mock said the drug firm has paid Eastman "fair-market" value for his consulting services.

Asked the specific total amount of money he has received from Warner-Lambert, Eastman said, "I can't tell you exactly, but it's in the thousands of dollars." His federal salary is about \$ 122,000.

Prohibition in NIH Policy

NIH policy explicitly prohibits officials from engaging in consulting that "will interfere in any way" with their government responsibilities.

"They are not supposed to be consultants to drug companies," said Dr. George J. Galasso, a recently retired NIH official who helped draft the institute's ethics rules.

Eastman was hired in late 1995 to help Warner-Lambert in its efforts to launch Rezulin, company officials said.

Records show that Eastman's duties for the company have included serving on the "faculty" of the "Rezulin National Speakers Bureau," a group that urged doctors to prescribe the drug for their patients.

Eastman said he served in an "advisory capacity" for Warner-Lambert at the company's request.

As director of the division of diabetes, endocrinology and metabolic diseases at NIH's National Institute of Diabetes and Digestive and Kidney Diseases, Eastman acknowledged he had responsibility for the government's largest diabetes study.

According to Eastman, Rezulin was selected for the government study "with the greatest care" after a "tedious and lengthy" evaluation. This, he said, made it "impossible for any one individual to influence the process very much, including myself."

The ties between Warner-Lambert and Eastman took form as Rezulin was developing into one of the world's hottest-selling prescription drugs.

Along the way, the company has made these claims:

Warner-Lambert hailed Rezulin in a 1997 news release as "the first anti-diabetes drug designed to target insulin resistance." This and two other statements about Rezulin in the release were determined to be "false and misleading" by federal regulators. The company boasted in glossy magazine ads that Rezulin was virtually free of side effects, or "comparable to placebo." Warner-Lambert's own research had indicated that Rezulin users were nearly four times more likely to experience some degree of liver injury than patients taking the placebos. This claim disappeared from advertisements in January after the first deaths due to sudden liver failure were acknowledged.

Warner-Lambert sought to absolve Rezulin in May when a 55-year-old high school teacher taking the drug in the NIH study died

after sudden liver failure. The company announced that the woman died, "apparently due to complications unrelated to Rezulin ." NIH physicians decided the most likely cause of the liver failure was Rezulin, and they withdrew the drug from the study. The death was viewed by some doctors as especially significant because the woman suffered liver failure despite taking strict precautionary tests recommended by the company and health authorities. Warner-Lambert and the FDA then recommended additional monitoring steps to help prevent more deaths.

The disavowal of Rezulin's role in causing the death--conveyed by both Warner Lambert and its Parke-Davis drug unit--troubled some physicians.

Warner-Lambert and the FDA continue to maintain that further tragedies will be largely prevented by submitting Rezulin users to such tests.

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"Parke-Davis had put a real spin on a high-profile death," said Dr. David S.H. Bell, a diabetes specialist at the University of Alabama at Birmingham School of Medicine who has been a paid consultant for Parke-Davis. "It was absolute garbage."

At Warner-Lambert, representatives said that the company has acted in good faith and that each of the disputed representations was well supported at the time they were made.

"This company's in the business for the long haul," said Zerbe, senior vice president for worldwide clinical research and development.

"It is of no value whatsoever to mislead. . . . To not deal honestly and candidly is a recipe for disaster."

Eastman's immediate superior at NIH's Institute for Diabetes Research, Deputy Director L. Earl Laurence, said he sees no conflict of interest in Eastman's ties to the company. Laurence said that on one occasion, he granted Eastman's request to consult for Warner-Lambert. He added that Eastman's outside employment activities also have been approved by Dr. Phillip Gorden, director of NIH's diabetes institute. Gorden declined to be interviewed.

"It was not part of his official duties," Laurence said. " . . . He has a right to have outside employment activities other than his position here."

Laurence says NIH has financial-disclosure records that detail Eastman's arrangement with Warner-Lambert. But he declined to make them available.

Drug Profits Had Suffered

Just three years ago, Warner-Lambert was a \$ 7 billion-a-year company performing well, but not spectacularly, for its shareholders.

The self-proclaimed "superpower" of consumer health products continued to profit from its stable of solid brands, including Halls cough drops and Listerine mouthwash.

But sales were not so sweet for Warner-Lambert's \$ 2-billion pharmaceutical business.

Revenue from the company's most popular drug, a cholesterol pill called Lopid, had been plunging since 1993. Due to the expiration of its patent on Lopid, Warner-Lambert estimated that it lost \$200 million in sales in 1994 alone to competing generic medications.

The company's once-touted Alzheimer's drug, Cognex, was foundering. The drug, according to Warner-Lambert's annual report to shareholders in spring 1995, had "yet to deliver" on expectations.

And, in November 1995, the company pleaded guilty to a felony in connection with concealing deficiencies from the FDA in its manufacture of several drugs.

Warner-Lambert agreed to pay a \$ 10-million fine--one of the largest ever imposed on a drug manufacturer. The prosecution

resulted from a joint inquiry by the FDA and the Justice Department.

Company officials vowed to put the episode in the past and to recommit to developing a new, big-selling drug.

"We have placed our pharmaceutical research dollars squarely behind compounds we firmly believe capable of producing a large health care dividend," the company told shareholders.

First on Warner-Lambert's list of stars in waiting: Rezulin.

Company Didn't Want Long Wait

Development of a new drug typically is costly--up to \$ 300 million by one industry estimate--and fraught with uncertainties. After a compound is first tested on animals, it can take six or more years to get a drug to the point of FDA approval, provided it is deemed safe and effective.

Six years would be too long for Rezulin. As a 1996 mission statement of the company summed up:"Every day a new product fails to reach a market means missed opportunity."

Warner-Lambert, in its annual report issued in March 1996, showcased Rezulin as "A Breakthrough Drug" that "may delay the onset of diabetes."

And, although Rezulin had yet to be approved for sale by the FDA, Warner-Lambert already was forecasting its blockbuster potential.

"The company believes this breakthrough therapy, once approved, could become one of the largest-selling pharmaceuticals it has ever marketed," said the annual report.

For drug companies, adult-onset, or Type 2, diabetes holds tremendous profit potential. About 15 million Americans--or about 6% of the population--have the disease. Type 2 diabetics have difficulty controlling their blood sugar, and a minority of them take insulin.

By contrast, juvenile-onset, Type 1, diabetics, of whom there are 800,000 in the United States, would die without daily injections of insulin.

On July 31, 1996, the company submitted a formal new-drug application for Rezulin. The agency committed itself to an evaluation and decision within a "fast track" of six months.

Warner-Lambert was about to become the envy of its competitors.

*

"Beyond treating diabetes, we are asking the bold question: Can Rezulin actually prevent the disease?"

--Ronald M. Cresswell, research chairman of Warner-Lambert's drug division, in remarks to shareholders.

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Even as the FDA began evaluating Rezulin, it was already part of the \$ 150-million NIH study of two diabetes prevention drugs.

That clinical trial began as one of the government's premier experiments--designed to run until 2002 and involve the testing of up to 4,000 volunteers at 27 research sites across the country, including two in Los Angeles.

With an additional 21 million Americans considered at risk for developing the disease, a bonanza loomed for the pair of winning companies if the study proved that their particular drug could prevent Type 2 diabetes.

"It was clear to anybody who had thought about it that what we were doing in this study was potentially defining a new area for drug therapy," said Dr. David M. Nathan, a Harvard medical professor who serves as chairman of the ongoing NIH experiment.

With so much at stake, one of the competing firms--Warner-Lambert--and the top NIH official overseeing the government study--Dr. Eastman--had entered into a financial arrangement.

Why did Warner-Lambert want to hire Eastman?

"My expertise in pharmaco-economic modeling and my leadership in the diabetes community," Eastman said. (The modeling allows the company to demonstrate to health care providers and consumers that a costly drug is worth its price.)

In addition, Eastman is the only government official listed on the company's Rezulin National Speakers Bureau roster. He also has served prominently for two years with the "National Diabetes Education Initiative," an organization partly financed by Warner-Lambert. In 1997 lecture materials, the group named Rezulin as a recommended drug in five of seven diabetes-treatment scenarios.

The education group's Web site, which has informed physicians about Rezulin's emergence as a Type 2 diabetes therapy, lists Eastman on its editorial advisory board and features a photograph of him.

Eastman said the group has been "pretty balanced" and has not, in his view, favored Rezulin. He said he has received "in excess" of \$ 150 per hour for consulting provided to the company-funded diabetes education initiative.

Yet at the same time, Eastman maintained "overall" responsibility for the NIH study, he told The Times in July. Last month, Eastman said that, at some point in 1996, he filed a "recusal" with NIH and did not participate in one or more final votes that selected Rezulin for the government study.

However, Eastman acknowledged participating in a series of deliberations concerning the drug's status before Rezulin was selected in 1996 until it was withdrawn from the study six months ago.

For instance, Eastman indicated that he was among officials who met with Warner-Lambert's Whitcomb to discuss Rezulin's side effects before the drug was chosen. Whitcomb said he made full disclosure to NIH of everything that was known about Rezulin's potential liver toxicity.

In his defense, Eastman said that over the last six years, he has consulted for five other drug companies, in addition to Warner-Lambert. Eastman and other NIH officials also pointed out that the decisions concerning which drugs to select were made by more than 20 researchers. They said no one person controlled or unduly influenced the decisions.

Still, Eastman's senior rank and participation in deliberations and decisions other than just the final votes to select Warner-Lambert's drug calls into question why the arrangement was approved, according to legal experts.

The June 11, 1996, Warner-Lambert news release announcing the government's selection of Rezulin for the study included this statement:

"According to Dr. Richard C. Eastman, director, division of diabetes at NIH, 'The group of investigators conducting the study unanimously chose to use Rezulin after considering all other potential agents because they felt it had a favorable safety profile, few side effects and it corrects the underlying cause of diabetes--insulin resistance.' "

Eastman disavowed this statement in a recent interview. He explained that insulin resistance, or the body's improper use of insulin to absorb blood sugar, is "not the only factor" that causes Type 2 diabetes:

"I don't think I would ever say . . . that insulin resistance is the underlying cause," he added.

Mock, said he is certain that the disputed quote was submitted to the publicity staff of NIH for Eastman's review.

Another company representative, Zerbe, said he was unfamiliar with an NIH ethics guideline that prohibits an outside employer from referring to a consultant such as Eastman "in anything distributed for publicity or promotion."

Asked if he was aware, as the NIH study got underway, of the company's own research showing that about 2% of patients who took Rezulin experienced some degree of liver injury, Eastman said he was uncertain.

"I couldn't tell you for sure," Eastman said. "We knew there were liver-function abnormalities from the drug. But no one was

concerned about it."

"Rezulin has the potential to virtually redefine the diabetes market and the therapeutic options open to millions of patients around the world."

--Lodewijk J.R. de Vink, Warner-Lambert president and chief operating officer, in a 1995 address.

The selection of Rezulin--over several competing pills--conferred an immediate cachet that Warner-Lambert leveraged to promote the drug. This helped to create a buzz on Wall Street and momentum to get the drug on pharmacy shelves throughout the country.

From the company's headquarters in Morris Plains, N.J., to its 1,000 or more sales representatives, or "detailers," throughout America, the message was unmistakable: Rezulin's cutting-edge importance must be conveyed to doctors responsible for the care of the nation's 15 million Type 2 diabetics.

But first, Warner-Lambert needed to secure FDA approval. The company assured investors in spring 1996 that it was "working aggressively to accelerate" this approval.

U.S. law requires the FDA to first ensure that these drugs are safe and effective. And, at the FDA's offices in Rockville, Md., a potential obstacle to Rezulin remained.

One of the agency's veteran experts, Dr. John L. Gueriguian, began questioning the safety and effectiveness of the drug.

In an October 1996 medical review, Gueriguian recommended that the agency reject Rezulin.

Gueriguian also raised what he termed "the propensity of the company to dismiss a possible association between Rezulin and adverse events" among research patients who took the drug. He questioned whether the company had "gone into a denial mode."

For their part, Warner-Lambert executives said they behaved responsibly.

Senior FDA officials removed Gueriguian from the review of Rezulin on Nov. 4, 1996, after complaints from Warner-Lambert. The FDA declined to discuss the basis for removal; Gueriguian retired in September.

Mock, the Warner-Lambert spokesman, said the company had objected to what he termed Gueriguian's "inappropriate behavior" during a meeting to discuss the drug. The company was confident that it would be able to satisfy any concerns raised in Gueriguian's medical review, Mock added.

With Gueriguian gone, the drug began receiving upbeat reviews at the FDA.

On Dec. 11, 1996, the panel unanimously recommended that Rezulin be approved as a prescription drug. That day, Warner-Lambert's shares soared to a then-all-time high on the New York Stock Exchange.

The FDA granted final approval on Jan. 29, 1997.

Back at company headquarters, Warner-Lambert officials issued a news release announcing the FDA action and touting Rezulin's benefits. The statement boasted that Rezulin "is the first anti-diabetes drug designed to target insulin resistance."

The company also stated: "Rezulin is the first anti-diabetes drug to work at the cellular level to improve insulin resistance directly enhancing the effects of circulating insulin. . . . Until now other therapies lowered blood glucose by increasing insulin production or decreasing liver glucose output."

These claims drew a quick rebuke. After reviewing the release, the FDA's drug-marketing and advertising division accused Warner-Lambert of making three "false and misleading" claims. An agency regulatory officer, Mark W. Askine, recommended that the company "immediately discontinue" circulating the news release "and any other pieces containing the same or similar claims."

Mock, the Warner-Lambert spokesman, said the company had a scientific basis to make the statements.

"We discussed it the letter with the FDA," Mock said. "We still believe our point was well taken, and basically we came to a compromise."

The company, he noted, continued to make a similar claim, with more carefully qualified wording.

Perhaps the boldest of the company's claims came in full-page, color magazine advertisements, including one that ran in the May 1, 1997, New England Journal of Medicine. In the ad, Warner-Lambert described Rezulin as a drug with breakthrough effectiveness and "Side Effects Comparable to Placebo."

Again, the company's own clinical studies indicated that Rezulin users were 3.6 times more likely to suffer liver injury than patients taking placebo.

The claim that the side effects were comparable to placebo, "is technically true," said Zerbe, a Warner-Lambert executive. He explained that, while it is true that clinical tests found that the drug showed signs of injuring the liver of people taking it, most of the patients did not report symptoms to their doctors.

Zerbe also said the FDA reviewed and approved the claim made in the advertisement. Warner-Lambert stopped making this statement in its advertising in January, the company said.

As for the liver problems that occurred once the drug went on the market, Zerbe said: "I think to a man everybody in this organization has taken the issue very seriously . . ."

Scarcely two months after the drug had hit the market, Warner-Lambert's chairman and chief executive officer, Melvin R. Goodes, praised Rezulin and a cholesterol pill, Lipitor, as the company's new profit engines.

"We plan to double our profits as we enter the next millennium," Goodes told a group of investors on May 5, 1997, adding: "We believe that both Lipitor and Rezulin have the potential to be billion-dollar blockbusters."

"The patient subsequently died, apparently due to complications unrelated to the study or the medication."

--June 5, 1998 Warner-Lambert news release

With that statement, Warner-Lambert sought to absolve Rezulin in the May 17 death of the woman in the government's diabetes-prevention study.

The victim, a 55-year-old high school teacher from East St. Louis, Ill., named Audrey LaRue Jones, had been in good health, according to her family. She was taking no other drugs. She did not have diabetes. She volunteered for the NIH study because she wanted to help find a way to prevent the disease.

But, after taking Rezulin for about seven months, she developed sudden liver failure that required an organ transplant. Eighteen hours after the transplant surgery, she died.

Ominously for the future of Rezulin, this happened even though Jones had submitted to regular precautionary monitoring.

A panel of specialists hired by NIH concluded that Jones' liver failure was "probably" caused by Rezulin.

A statement issued at the time by NIH officials did not identify a certain cause of death.

And, according to Jones' death certificate, sudden liver failure also was the "underlying cause." A copy of the document was obtained by The Times; the newspaper identified Jones as the victim through records and interviews independent of federal officials.

The death posed a delicate question for the National Institutes of Health: After five years of work and tens of millions of dollars of public funds, should Rezulin be removed from the government's largest-ever study of diabetes?

The decision fell in part to Eastman--the Warner-Lambert consultant and the government's overseer of the NIH study--and the other officials leading the project.

The NIH officials agonized, but announced on June 4 that, to protect the 580 or more trial participants taking the drug, Rezulin was out.

"In the face of the case of liver failure--and the inability to prevent that, even in the context of a very carefully controlled clinical trial--the feeling was that it was not viable to continue," Eastman told The Times.

". . . This was a tragedy for this person. And for the drug. And the trial."

The question for Warner-Lambert:

What, if anything, to tell doctors and the general public about the death of Audrey Jones?

Warner-Lambert denied that Rezulin killed her.

The company issued a June 5 news release suggesting that Jones died for another reason--perhaps a "bowel lesion" found during the liver transplant.

"The patient subsequently died," Warner-Lambert announced, "apparently due to complications unrelated to the study or the medication."

The company news release did not report that the specialists retained by NIH found that Rezulin "probably" caused Jones' sudden liver failure.

The death certificate on file at the Missouri Department of Health, dated May 19, 1998, states that the underlying cause of Jones' death was sudden liver failure, which "initiated . . . multiple organ system failure" and "mesenteric thrombosis," or abnormal blood clotting in the intestines.

'It Was Due to Another Complication'

Asked Warner-Lambert's basis for the June 5 news release, Zerbe, the senior vice president, said:

"No one, I don't believe, is saying the drug could have played no role in the liver failure. . . . That's serious enough in itself and worthy of concern. But ultimately, my assessment would be, the death was not due to that, it was due to another complication, perhaps related to the transplant surgery."

Warner-Lambert's position puzzled some doctors who were prescribing Rezulin. They wondered whether the NIH death was an indication that precautionary liver monitoring was not enough to prevent the possibility of liver damage in Rezulin users.

Warner-Lambert representatives note that other adult-onset, Type 2, diabetes drugs also carry harmful potential side effects and, indeed, all prescription drugs pose risks.

Now, although Rezulin is out of the NIH study, Eastman said he is pleased that it remains for sale.

"I'm glad to see that the drug continues to be on the market and available for people to use it," Eastman said.

Eastman also indicated that he hopes the latest monitoring recommendations by Warner-Lambert would help eliminate any more deaths or serious liver injuries.

"It may not," he said. "I'm sure they're watching it very carefully."

Times librarian Janet Lundblad provided research for this article. Also contributing were Times staff writers Alissa J. Rubin and Jeff Leeds. The Times retained Thomas J. Moore, fellow in health policy at George Washington University Medical Center, as a consultant.

SIDEBAR 1: A Conflict of Interest?

The U.S. government's top diabetes researcher helped guide a \$ 150-million federal study involving the diabetes pill Rezulin while serving as a paid consultant for the drug's manufacturer, Warner-Lambert Co. The tie raises questions of whether his

outside consulting was in conflict with his official duties.

Age: 52

Government position: Director of the division of diabetes, endocrinology and metabolic diseases at the National Institutes of Health

Government salary: \$ 122,000 annually

Government role: Oversaw selection of Rezulin for the government's study of whether adult-onset diabetes can be prevented
Company position: Consultant to Warner-Lambert and faculty member of the "Rezulin National Speakers Bureau," which urged doctors to use Rezulin

Company income: Thousands of dollars

Company role: Praised Rezulin in a Warner-Lambert press release, prepared research, gave lectures and helped with drug promotion

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Researched by JANET LUNDBLAD / Los Angeles Times

Sources: National Institutes of Health, Warner-Lambert Co., U.S. and European patent records, Photo: www.ndei.org/newslet2b.htm

SIDEBAR 2: Disputed Claims

Warner-Lambert Co. has made these claims regarding the benefits or effects of its diabetes drug Rezulin:

CLAIM: The company denies that its drug Rezulin caused the death of a 55-year-old high schoolteacher who participated in a government diabetes-prevention experiment. "The patient subsequently died, apparently because of complications unrelated to the study or the medication. "

FACT: The victim's death certificate reports the "underlying cause" of the May 17, 1998, death was "fulminant hepatic failure," or sudden liver failure. Her liver failure was most likely caused by Rezulin, doctors found.

CLAIM: A Rezulin ad makes a strong claim that the drug is safe, stating: "Side effects comparable to placebo."

FACT: Warner-Lambert's own research found that patients taking Rezulin developed liver injury at nearly four times the rate of those given placebo pills. The company stopped making this claim after the first reported deaths of patients.

CLAIM: The company announces the government has approved Rezulin as a prescription drug: "Rezulin is the first anti-diabetes drug designed to target insulin resistance. . ." and "Rezulin is the first drug to work at the cellular level to improve insulin resistance. . . . "

FACT: The government terms these Warner-Lambert promotional claims "false and misleading." The FDA recommends that Warner-Lambert "immediately discontinue" publishing "the same or similar claims."

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SIDEBAR 3: Inside the Liver

The liver serves as the body's main chemical factory.

Among its many vital functions, the liver filters a wide range of harmful substances from the blood. These include drugs, insecticides, food additives and industrial chemicals.

Liver damage or disease can be life-threatening because the liver performs so many crucial jobs. However, most liver diseases--including drug-induced injury--are painless in their earliest stages and difficult to detect.

One of the most severe consequences of such drug-related injury is hepatitis, or inflammation, of the liver.

Some patients taking Rezulin, the adult-onset diabetes drug, have developed sudden, "idiosyncratic" liver failure. In these cases, the liver swells and may cease functioning--leaving the body no way to purify its own blood.

Death occurs if the liver stops functioning, unless the patient is able to obtain and survive an organ transplant.

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SIDEBAR 4: Liver Testing

The Warner-Lambert Co. and the Food and Drug Administration now recommend that users of Rezulin undergo regular liver testing in hopes of detecting early signs of injury before they may become life-threatening. The company and the FDA say that Rezulin, which has been tied to 33 deaths since it was introduced last year, is safe when used with liver-function monitoring. This testing of the liver entails taking regular blood samples.

* How Rezulin Works: Rezulin is used primarily in combination with other drugs to treat adult-onset, or Type 2 diabetes. In this disorder, individuals experience higher than normal blood-sugar levels, which over time can lead to higher risk of heart disease and other complications. Rezulin is thought to work primarily by helping insulin stimulate the body's fat and muscle cells so they will absorb more sugar. Rezulin is not used for juvenile-onset, Type 1 diabetes, in which the body can not produce insulin.

* Rezulin's Side Effects: The drug causes some injury to the liver detectable with laboratory tests in about 2% of patients. When liver injury is detected, Rezulin treatment should be stopped to prevent the danger of severe injury or death.

Researched by: JANET LUNDBLAD / Los Angeles Times
Sources: Handbook of Anatomy and Physiology; American Medical Assn. encyclopedia of medicine

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Where to Get Help

For more information about diabetes drugs, contact these sources:

Food and Drug Administration

Web site: <http://www.fda.gov/cder>

Los Angeles District Office: (949) 978-7714

By mail: Food and Drug Administration

19900 MacArthur Blvd., Suite 300

Irvine, CA 92612

* * *

National Institute of Diabetes and Digestive and Kidney Diseases

Web site: <http://www.ep.niddk.nih.gov/divisions/dem/demhome.htm>

Office of Public Affairs: (301) 496-3583

By mail:

National Institute of Diabetes and Digestive and Kidney Diseases

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