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THE UNCERTAIN HOUR

Purdue Pharma statement on The Uncertain Hour's OxyContin episode

By Marketplace staff
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Purdue Pharma spokesman Robert Josephson provided Marketplace with this statement in response to questions from The Uncertain Hour about OxyContin, the company, and its relationship with the FDA. The company's responses are published in full below.

Purdue Pharma L.P. Response
December 12, 2017

1. Why did Purdue not do any clinical studies to back up the "delayed absorption" sentence?

RESPONSE: The "delayed absorption" sentence was added to the label at FDA's suggestion, not Purdue Pharma's, and FDA did not require Purdue to do any clinical studies to back up the delayed absorption statement.

As shown in the excerpt of the deposition that you quoted, Dr. Robert Reder, who was the Purdue employee responsible at the time for discussing the label with FDA, testified:

Q: Were you surprised to see it in the label?

A: Surprised? No. There are a lot of changes. *To me, it was FDA's representation of their ideas of how the label should read.*

Q: Had you discussed with the FDA about a desire to add the hypothesis we talked about earlier about delayed absorption?

A: No.

Q: They did it on their own?

A: As best I can recall, yes.

Q: And you never asked them why you [sic] added this?

A: No. It seemed obvious.

Q: It seemed obvious to change from "we have not done any studies about the controlled release oral dosage form as regards to abuse liability" to change it to "delayed absorption is believed to reduce the abuse liability?"

A: Well, what it says is, if I can find it, "delayed absorption as provided by OxyContin tablets is believed to reduce the abuse liability of a drug." So it's a more general statement underpinned by the rate hypothesis. It's believed to. It doesn't say it definitely does. So it made sense in the context of that time and the information that was available.

Q: Don't you have to have-- are you aware of-- in terms of making sense, you had provided no studies to the FDA that said this dosage form appears to have a reduced liability

A: Yes.

Q: Yet somebody at the FDA on their own initiative decided to add that phrase?

A: I believe that's what happened. Yes.

Dr. Reder's testimony is consistent with the recollection of Dr. Curtis Wright, who at the time was one of the FDA officials who approved OxyContin's labeling.

FDA believed the delayed absorption statement to be true based in part on the experience with MS Contin, another controlled-release opioid pain medication, that had been marketed without significant reports of abuse and misuse. As Dr. John Jenkins, FDA's Director, Office of New Drugs, Center for Drug Evaluation and Research testified before the Senate in 2002:

In fact, at the time of its approval, FDA believed that the controlled-release characteristics of the OxyContin formulation would result in less abuse potential since, when taken properly, the drug would be absorbed slowly and there would not be an immediate ``rush" or high that would promote abuse. In part, FDA based its judgment of the abuse potential for OxyContin on the prior marketing history of MS-Contin, a controlled-release formulation of morphine that had been marketed in the U.S. by Purdue Pharma without significant reports of abuse and misuse for many years (https://www.gpo.gov/fdsys/pkg/CHRG-107shrg77770/html/CHRG-107shrg77770.htm).

FDA's view of the correctness of that statement was also supported by other scientific research. At the time, studies that showed that abusers preferred faster acting drugs included:

- Brookoff, D., Abuse Potential of Various Opioid Medications, J Gen Intern Med. 8:688-690 (1993) ("These results suggest that controlled-release narcotic formulations may have a lower potential for abuse than do other narcotic medications....In some emergency departments, controlled-release formulations have become the analgesics of choice due to physicians' perceptions that they are rarely abused.").
- Mumford, G., et al., Alprazolam Absorption Kinetics Affects Abuse Liability, Clinical Pharmacol Ther. 57:356-65 (1995)("ratings of positive subjective effects and indirect and direct measures of drug reinforcement indicate that the XR formulation of alprazolam has less abuse liability than the IR formulation.").
- Oldendorf, W., Some Relationship Between Addiction and Drug Delivery to the Brain, NIDA Monograph 120, Bioavailability of Drugs to the Brain and the Blood-Brain Barrier, 13-25 (1992) ("The rapidity and abruptness of drug delivery to the brain using various routes of administration are factors in drug addiction. The shorter the interval between intake and perceived effect of a drug, the greater the propensity toward a more severe addiction. . . .The more immediate the effect after intake, the more addicting the substance is likely to be.").
- de Wit, et al., Rate of Increase of Plasma Drug Level Influences Subjective Response in Humans, Psychopharmacology 352-358 (1991)("The data provide empirical support for a commonly held notion regarding the effects of rate of onset, and they have implications for the development of drugs that may have some liability for abuse: for example, pharmacological agents and drug formulations with relatively slower onset would clearly have a lower potential for abuse than those with faster onset.).
- Griffiths, R., et al., Comparison of Diazepam and Oxazepam: Preference, Liking and Extent of Abuse, J. of Pharmacol. and Exper. Ther. 229(2):501-508 (1984).
- Griffiths, R., et al., Relative Abuse Liability of Diazepam and Oxazepam: Behavioral and Subjective Effects, Psychopharmacology 84:147-154 (1973).

2. Did the focus group report influence the writing of the sentence?

RESPONSE: No, the March 1995 focus group report did not influence the writing of the sentence. The sentence was added to the label at FDA's suggestion, not Purdue Pharma's.

As FDA's Dr. John Jenkins testified, FDA believed that sentence to be true at the time of approval based in part on the experience with MS Contin and scientific literature.

3. How do you respond to the fact that a draft label from December 1994, before the focus group report, does not contain the "delayed absorption" sentence? And the label after the focus report, from August of 1995, contained the delayed absorption sentence?

RESPONSE: As explained above, the delayed absorption sentence was added to the label at FDA's suggestion, not Purdue's, and was supported by other scientific research. The delayed absorption sentence was added to the label without regard to the focus group report.

4. How do you respond to the argument that the marketing department influenced the sentence, not Purdue's own abuse studies?

RESPONSE: For the reasons explained above, that argument is not accurate. It was the FDA, and not Purdue or Purdue's marketing department, that requested that the sentence be added.

5. In documents, Purdue claimed that by approving OxyContin, the FDA said the drug was safe and effective. What is your response to that now given the label change the FDA required in 2001 and the multiple changes since then?

RESPONSE: Purdue has always sold OxyContin with approval from FDA that the medicine is safe and effective. It is wrong to believe that because FDA approved changes to the label for OxyContin subsequent to its original approval in 1995, including the 2001 label changes, the medication was not previously safe and effective. Labels for drugs are routinely changed over the years as additional information is collected.

Indeed, as FDA's Dr. John Jenkins testified after the 2001 label changes, "FDA believes that OxyContin is a valuable product for the treatment of moderate to severe pain when it is used according to the approved labeling."

6. Why did it take you until 2001 to address the issue of OxyContin abuse?

RESPONSE: OxyContin was not expected to be abused beyond that anticipated for other Schedule II opioid pain medications. As FDA's Dr. Jenkins testified:

> "At the time of approval, the abuse potential for OxyContin was considered by FDA to be no greater than for other Schedule II opioid analgesics that were already marketed in the U.S. Based on the information available to FDA at the time of its approval, including the record of other modified release Schedule II opioids, the widespread abuse and misuse of OxyContin that has been reported over the past few years was not predicted."

Purdue learned that OxyContin was being abused to the extent beyond what was expected was in February 2000. Jay McCloskey, then U.S. Attorney for Maine, reported that OxyContin was being widely abused in that state. Similarly, FDA first received reports of widespread abuse of OxyContin in 2000. As FDA's Dr. Jenkins testified:

> "Senator, first of all, the abuse of OxyContin really started almost 5 years after the approval of the product. It was approved in 1995 and the first reports started coming in in about the year 2000 and the reports that we have been receiving at the FDA really started increasing in the year 2001. So it took several years after that product was approved before we started seeing widespread reports."

Purdue then met with Mr. McCloskey, and other members of law enforcement, to understand the problem and seek ways to work together to deal with it. In May 2001, Purdue enacted its 10-point plan designed to address the abuse problem. That plan included the following elements:

- A mailing of educational brochures on ways to prevent drug diversion

- Distribution of tamper-resistant prescription pads
- Sponsorship of over 300 continuing medical education programs for healthcare professionals
- Changing the indicia on all products shipped into Mexico and Canada
- Production and sponsorship of a series of Public Service Radio Announcements targeted to teens in six states
- Sponsorship of a series of education programs for law enforcement officials
- Refinement of a predictive model to identify the 100 counties in the country where the demographics suggest the problem of OxyContin abuse and diversion could spread
- Development of the curriculum, including DEA faculty, for retraining of 180 sales professionals so that their primary task will be to work with health care professionals to prevent the spread of drug diversion and abuse into these 100 counties.
- The provision of placebos to law enforcement officials to be used in 'buy and bust' operations in areas of heavy drug abuse.
- Underwriting of a study of best practices in state prescription monitoring programs, to develop a national model program which would prevent 'doctor shopping' by drug abusers..."

In July 2001, FDA, working in cooperation with Purdue, approved changes to the OxyContin labeling that significantly strengthened the warnings and precautions, including adding a black box warning and deleting the delayed absorption statement.

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