

HHS NEWS

U.S. DEPARTMENT OF HEALTH AND HUMAN SERVICES

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P86-21
FOR IMMEDIATE RELEASE
May 1, 1986

Food and Drug Administration
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The Food and Drug Administration said today that it has received 16 reports of an unexpected and puzzling adverse reaction developing in patients shortly after their initial dose of McNeil Pharmaceutical Laboratories' new analgesic drug Suprol: flank and back pain accompanied by evidence of decreased kidney function.,

All patients had full recovery, generally within five to 10 days after they stopped taking the drug, but the decreased kidney function is a serious concern. McNeil, in a letter to physicians, and FDA are therefore asking physicians to prescribe Suprol only with caution and to consider alternative analgesics while the cause, frequency and severity of the reaction are being assessed.

McNeil's letter also asked that similar reactions be reported immediately. The company received and then promptly reported to FDA the initial complaints.

The next FDA Drug Bulletin, which is mailed to every physician in the United States, will contain a description of the reports and request that physicians look for and report such reactions in patients taking Suprol or related drugs. The reports may help determine whether Suprol is the only drug of its class capable of causing the flank pain-kidney failure reaction or just

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the first in which it has been recognized.

A puzzling aspect of these reports is that there has been reasonably extensive use of Suprol in several European countries for up to two and a half years with only three similar reports.

About 300,000 patients have received the drug since marketing began early this year. It is one of about a dozen drugs belonging to the class of products known as non-steroidal anti-inflammatory drugs, some of which are used for pain and some for arthritis.

McNeil, which is located in Spring House, Pa., is voluntarily revising the physician labeling of the drug to include a warning about the reactions. /

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FDA TALK PAPER

FOOD AND DRUG ADMINISTRATION
U.S. Department of Health and Human Services
Public Health Service 5600 Fishers Lane Rockville, Maryland 208

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T86-56
July 24, 1986

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SUPROFEN UP DATE

On April 25, McNeil Pharmaceutical of Springhouse, Pa., notified doctors of sixteen reports of patients who had experienced the abrupt onset of flank and back pain accompanied by evidence of decreased kidney function after one or two doses of suprofen (Suprol), a new nonsteroidal anti-inflammatory drug. At that time, McNeil and FDA solicited from physicians additional reports of this puzzling and unexpected adverse reaction. (See press release P86-21.)

McNeil recently wrote to physicians saying reports now total about 100. The letter says that "the rate at which this reaction is reported is approximately one per 5,000 patients, although because the reporting of adverse events for all drugs postmarket is never complete, the true rate is higher... All patients have recovered on discontinuing Suprol and increased fluid intake...

"Of the approximately 100 cases, over three quarters occurred in males, and the mean age is in the mid-thirties. About one quarter of the patients were hospitalized for evaluation. The pain is most commonly described as severe bilateral flank pain; its onset usually occurs in one-half to five hours after the dose and usually last 12-43 hours, although the pain has lasted rarely as long as two weeks. It is frequently accompanied by nausea and sometimes vomiting."

The letter said that approximately half of the patients did not have laboratory tests. In the patients who did, about 75 percent had abnormal kidney function tests. The abnormalities usually resolved within four or

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five days, although some took two weeks, according to the letter. McNeil went on to say, "It is also of note that some patients with flank pain after Suprol have taken the drug on other occasions without incident.

"We are investigating possible mechanisms for the reaction and ways to avoid it. Thus far, we have completed three studies which show Suprol has uricosuric activity (promotes excretion of uric acid in the urine). We are evaluating the possibility that this finding is related to the syndrome.

"Please continue to report all reactions to us. We are particularly interested in the results of appropriate diagnostic studies during the acute episode. Therefore, we ask you to promptly call our medical department at (215) 628-3000 if a patient presents with this reaction...."

McNeil and FDA continue to monitor Suprol adverse reaction reports in order to determine the cause of the reaction and ways in which it can be avoided, if possible.

A few patients experiencing this reaction to Suprol report that they have had similar reactions to other drugs of its class in the past. FDA is interested in such reports in order to determine if the reaction is actually common to all drugs in this class but occurs at a higher rate in patients taking Suprol. The June FDA Drug Bulletin, which is sent to all physicians, contained a reporting form.

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10TH ITEM of Level 1 printed in FULL format.

Congressional Record -- House

Monday, August 3, 1992

102nd Cong. 1st Sess.

138 Cong Rec H 7201

REFERENCE: Vol. 138 No. 112

TITLE: PROVIDING POLICIES WITH RESPECT TO APPROVAL OF BILLS PROVIDING FOR PATENT TERM EXTENSIONS

SPEAKER: MR. COBLE; MR. FAWELL; MR. FISH; MR. HUGHES; MR. MOORHEAD; MR. STARK; MR. WOLPE; MR. WYLIE

TEXT:

Text that appears in UPPER CASE identifies statements or insertions which are not spoken by a Member of the House on the floor.

[*H7201] Mr. HUGHES. Mr. Speaker, I move to suspend the rules and pass the bill (H.R. 5475) providing policies with respect to approval of bills providing for patent term extensions, and to extend certain patents, as amended.

The Clerk read as follows:

H.R. 5475

BE IT ENACTED BY THE SENATE AND HOUSE OF REPRESENTATIVES OF THE UNITED STATES OF AMERICA IN CONGRESS ASSEMBLED,

SECTION 1. STATUTORY EXTENSION OF PATENT TERMS.

(a) In General. -- The Congress finds that, in the future, any bill providing for the extension of the term of a patent should not be approved by the Congress unless the requirements set forth in subsection (b) or (c) are met.

(b) Requests based on Delay in Premarket Approval. -- When the basis for a bill providing for a patent extension is delay in premarket regulatory approval of a patented invention, the following requirements should be met before the bill is approved by the Congress:

(1) Governmental misconduct. -- (A) Delay in the approval process must have been beyond the control of the patent holder and directly caused by governmental misconduct.

(B) For purposes of this paragraph, governmental misconduct is established by presentation of adequate proof of --

(i) dishonest or deceitful conduct,

(ii) vindictive or retaliatory action,

(iii) arbitrary, capricious, or grossly negligent performance of governmental duties, or

138 Long Rec H 7201, *H7207

n50 ID. at 296.

n51 SEE ID. at 327-333, 509-532.

n52 SEE ID. at 533-555.

On December 2, 1983, the House Committee on Government Operations issued a report concerning "FDA's Regulation of Zomax." n53 Among other things, the Committee recommended that "FDA establish procedures for prompt processing, review, and analysis of all adverse reaction reports for marketed drugs." n54 The controversial nature of the entire Zomax episode and of certain of the Committee's findings is reflected in the numerous dissenting and additional views accompanying the report. n55

n53 "FDA'S REGULATION OF ZOMAX," Thirty-First Report by the (House Comm. on Gov't Operations, H. Rept. No. 584, 98th Cong., 1st Sess. (1983)).

n54 ID. at 27.

n55 SEE ID. at 28-36.

D. Suprol

After a virtual moratorium on NSAID approvals, FDA finally approved a new NSAID, Suprol (suprofen), on December 24, 1985. A few months later, however, the drug's manufacturer began receiving reports of unusual adverse kidney effects, frequently combined with flank pain, associated with Suprol. Sales of the drug ultimately were halted on May 18, 1987, in the face of mounting criticism. n56

n56 SEE FDA'S REGULATION OF THE NEW DRUG SUPROL, Hearing Before a Subcomm. of the House Comm. on Gov't Operations, 100th Cong., 1st Sess. 417-418 (1987).

Reports of the flank pain syndrome associated with Suprol had begun to appear almost immediately after the drug was approved for marketing. n57 Subsequently, numerous reports were made to FDA, and the Agency became occupied with reviewing new and revised labeling for the drug. An article also appeared in the June 1986 edition of the FDA Drug Bulletin. n58 In addition to the Agency itself, Advisory Commission reviewed Suprol in light

n57 SEE ID. at 35-36.

n58 SEE ID. at 36-41 of the new adverse events reports. n59 FDA resources were also devoted to responding to a petition filed in September 1986 seeking removal of Suprol from the market. n60

n59 SEE ID. at 42.

n60 SEE ID. at 364.

Once again, FDA officials testified at a House oversight hearing devoted to examining the Agency's NSAID regulatory processes. Among the issues raised by the House Subcommittee at the hearing were whether FDA adequately investigated the drug sponsor's reporting of adverse drug events and whether the Agency had properly weighed the risks and benefits of the drug. n61 The overall goal of the hearing was to use the case of Suprol to evaluate "whether or not our current