



DEPARTMENT OF HEALTH & HUMAN SERVICES

Public Health Service

Food and Drug Administration
Rockville MD 20857

MAY 13 1997

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Jill A. Cashen
Cancer Prevention Coalition
520 North Michigan Avenue, Suite 410
Chicago, IL 60611

Re: Docket No. 95P-0018/CP

Dear Ms. Cashen:

This responds to your citizen petition, submitted January 17, 1995, requesting that the Food and Drug Administration (FDA) (1) ban the use of lindane as a treatment for lice and scabies, and (2) conduct a hearing under 21 CFR 10.30(h)(2) so that you can present your scientific evidence.

Based on the agency's review and analysis of your requests, and, for the reasons stated below, we must deny your petition.

Lindane is safe and effective if used as directed

In 1947, the FDA approved lindane, in a concentration of one percent, for the treatment of pediculosis and scabies. Reed & Carnrick, the manufacturers of the referenced lindane products (trade name "Kwell"), recently informed the agency that they are no longer manufacturing or distributing the 1% lindane-containing products (shampoo, lotion, and cream). However, generic lindane-containing products are still marketed.

As you are aware, issues concerning lindane have been presented to FDA's Dermatologic Drugs Advisory Committee (the committee) numerous times. The committee is composed of experts from the fields of dermatology and epidemiology, and includes a consumer-nominated representative. The committee is consulted on drug product issues of importance to the dermatologic community. In 1975, 1976, 1977, 1983, 1984, 1985, and 1993, the committee conducted in-depth reviews of lindane.

In 1977, the committee concluded that lindane was safe and effective in the treatment of both pediculosis and scabies, if used as directed. The committee found that most, if not all of the adverse reactions reported were associated with misuse of the drug. The committee recommended that the FDA continue to allow marketing of lindane for scabies and pediculosis, confirming an earlier (1972) agency conclusion of safety and effectiveness, and published this

95P-0018

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Jill A. Cashen

conclusion in the *Federal Register* (42 FR 5123, January 28, 1977). The *Federal Register* announcement noted that the agency would conduct a hearing regarding lindane if sufficient interest was expressed. Sufficient interest was not expressed, and no hearing was held.

The committee also recommended that sponsors update lindane's labeling to increase the margin of safety. At a September 30, 1977, meeting, the committee and the manufacturers agreed that the "Warning" section of the label should include the following statement: "KWELL CREAM SHOULD BE USED WITH CAUTION, ESPECIALLY ON INFANTS, CHILDREN AND PREGNANT WOMEN. LINDANE PENETRATES HUMAN SKIN AND HAS A POTENTIAL FOR CNS TOXICITY. STUDIES INDICATE THAT POTENTIAL TOXIC EFFECTS OF TOPICALLY APPLIED LINDANE ARE GREATER IN THE YOUNG." The labeling also included instructions that the product be left in place 8 to 12 hours rather than 12 to 24 hours, which would allow less chance for absorption of the product, and that one application is usually sufficient. The professional labeling for Kwell was updated to include these changes.

In addition to requesting the advisory committee to review lindane, the agency highlighted some adverse experiences associated with the use of lindane in the June-July, 1976, issue of the *FDA Drug Bulletin*. This article described the signs and symptoms due to CNS toxicity related to the absorption of the drug through the skin. The agency published this article to increase physicians' awareness of the potential hazards of overuse of the drug.

The National Cancer Institute (NCI) has also examined lindane for possible carcinogenicity. On November 11, 1977, the NCI published the results of a study indicating lindane is not carcinogenic in topical use (42 FR 58791).

In 1983, 1984, and 1985, the committee met again to review lindane's labeling, and to discuss the role of prescription topical antibiotics in skin infections. The committee recommended that Kwell and other similar drugs not be removed from the market place. The committee also suggested changes in the physicians' labeling and a package insert for lindane products to prevent product misuse. The committee endorsed FDA's position that gloves be worn by pregnant women and any person applying lindane on more than one person. The labeling for lindane products was revised in 1984, 1985, 1989, and 1992. The "Warning" section of the labeling for lindane shampoo, cream, and lotion was revised to include the following statements:

LINDANE PENETRATES HUMAN SKIN AND HAS THE POTENTIAL FOR CNS TOXICITY. * * * KWELL [SHAMPOO/CREAM/LOTION] SHOULD BE USED ACCORDING TO RECOMMENDED DOSAGE (SEE DIRECTIONS FOR USE)

Jill A. Cashen

ESPECIALLY ON INFANTS, PREGNANT WOMEN AND NURSING MOTHERS. ANIMAL STUDIES INDICATE THAT POTENTIAL TOXIC EFFECTS OF TOPICALLY APPLIED LINDANE ARE GREATER IN THE YOUNG. SEIZURES AND, IN RARE INSTANCES, DEATHS HAVE BEEN REPORTED AFTER EXCESS DOSAGE, OVER-EXPOSURE, FREQUENT REAPPLICATIONS, AND ACCIDENTAL AND INTENTIONAL INGESTION OF LINDANE. THESE INSTANCES OF PATIENT MISUSE HAVE BEEN ASSOCIATED WITH LACK OF PATIENT UNDERSTANDING OF DIRECTIONS OF USE, PRESCRIBING OR DISPENSING EXCESSIVE QUANTITIES, AND IMPROPER REAPPLICATIONS.

At the committee meeting held May 6-7, 1993, the committee found that most, if not all, of the adverse reactions reported were associated with misuse of lindane. The committee unanimously concluded that based on the data presented at the meeting and subsequent committee discussions on the topic, lindane 1% shampoo should remain approved for marketing in the United States because lindane is safe and effective in the treatment of both pediculosis and scabies, if used as directed. The committee also unanimously concluded that because the current Kwell label addresses potential carcinogenicity, the product was appropriately labeled.

On March 17, 1996, the agency again reviewed the label for lindane lotion, cream, and shampoo, and again concluded that lindane is safe and effective when used as directed. The agency found, however, that post-treatment pruritus (or uncontrolled itching) is a common occurrence, caused by hypersensitivity to remaining dead mites and mite products, that may cause patients to misuse lindane. Because post-treatment pruritus is common and may lead to misuse, the agency revised the "INDICATIONS AND USAGE" section of the labeling to include the following language:

Because post-treatment pruritus is common and may lead to misuse, [trade name] lindane shampoo is indicated only for the treatment of patients with pediculosis capitis (head lice) and pediculosis pubis (crab lice) who have either failed to respond to adequate doses, or are intolerant of, other approved therapies. Reinfestation should be considered carefully before attributing the post-treatment presence of ectoparasites to a failure of response to adequate doses of other approved therapies.

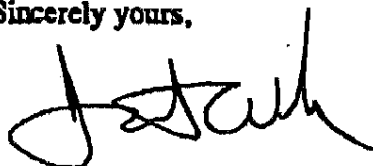
As discussed above, effective alternatives to lindane are available. These alternatives, however, do not work in all cases. The agency has considered all of the available data and has determined that lindane should remain on the market because a reliable alternative medication should be available to those patients who have been unsuccessfully treated with other products.

Jill A. Cashen

Conclusion

Therefore, because lindane is safe and effective if used as directed, the agency denies your request (1) to ban the use of lindane as a treatment for lice and scabies, and (2) to conduct a hearing under 21 CFR 10.30(h)(2) so that you can present your scientific evidence.

Sincerely yours,



Janet Woodcock, M.D.

Director

Center for Drug Evaluation and Research