

20. OTHER
20.D. CIU EXPERT PANEL REVIEW



SCHERING-PLOUGH RESEARCH INSTITUTE

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**CONSENSUS STATEMENT OF EXPERT PANEL
ON THE APPROPRIATENESS OF CHRONIC IDIOPATHIC URTICARIA
AS AN OTC INDICATION FOR LORATADINE**

Introduction

On January 14, 2002, Schering-Plough Corporation (Schering-Plough) convened a panel of outside experts to consider whether chronic idiopathic urticaria (CIU) is an appropriate over-the-counter (OTC) indication for loratadine. This consensus statement summarizes the conclusions reached by the expert panel, and has been specifically approved by each of the participating experts.

The Expert Panel

The expert panel consisted of a moderator, and the following four physicians:

- Randy P. Juhl, PhD. (Moderator) – Dean and Professor, Pharmaceutical Sciences, University of Pittsburgh School of Pharmacy
- Richard Ahrens, M.D. – Associate Professor, Pediatric Allergy and Pulmonary Division, Department of Pediatrics, University of Iowa College of Medicine
- Philip L. Lieberman, M.D. – Clinical Professor of Medicine and Pediatrics, Departments of Internal Medicine and Pediatrics, Divisions of Allergy and Immunology, University of Tennessee College of Medicine
- Eugene W. Monroe, M.D. – Advanced Healthcare/Milwaukee Medical Clinic
- Ronald A. Simon, M.D. – Head; Division of Allergy, Asthma and Immunology, Scripps Clinic; Assistant Clinical Professor, Medicine & Pediatrics, University of California School of Medicine, San Diego

Two specific questions were put to the panel, as follows:

Question 1: Can patients self-recognize and safely self-treat a recurring episode of chronic idiopathic urticaria with OTC loratadine after initial diagnosis by a physician?

Question 2: Are there serious medical consequences from a patient self-treating "hives" with OTC loratadine without prior consultation with a physician? If so, can these consequences be mitigated with labeling?

Background

In connection with FDA's 1992 promulgation of the final monograph for OTC antihistamine drug products, FDA considered whether the symptomatic treatment of allergic itching was an appropriate indication for OTC antihistamines.¹ FDA concluded that the data available at that time were insufficient to support recognition of an allergic itching indication in the OTC antihistamine monograph. FDA stated in particular that there were not data to demonstrate that a patient could distinguish between a mild allergic reaction and a life-threatening anaphylactic reaction, and that a patient suffering an anaphylactic reaction might use an antihistamine and delay more appropriate treatment.

At the expert panel meeting, Schering presented data to the panel on the safety of loratadine and the management of CIU. Based upon the worldwide marketing experience with loratadine (consisting of over 13.7 billion patient days of exposure) and experience in countries where loratadine is approved and marketed for use without a prescription, company representatives informed the panel that loratadine has an excellent safety profile, with a low incidence of adverse events, low toxicity, and an absence of significant risks from drug

interactions. Schering reported that it has seen no meaningful difference in the adverse event profile in those countries where loratadine is marketed for CIU, with or without a prescription. Schering also presented data to the panel from two recent studies it conducted on current patient and physician practices with respect to CIU, and from a third study on the ability of consumers to self-recognize episodes of CIU. [Note: The complete and final reports of these studies are included in their entirety in the New Drug Applications requesting the switch from Rx to OTC for the CIU indication.]

Panel Conclusions

The panel believes that CIU is a condition that patients can safely self-manage after an initial physician diagnosis. In fact, the clinician members of the panel currently rely on patients to self-manage most aspects of their CIU after initial evaluation and diagnosis. The initial physician diagnosis serves to distinguish CIU from acute urticaria and from other skin conditions, and permits the physician to address any co-morbid conditions or other complications that may exist. Once the physician has confirmed a diagnosis, patients are able to recognize a recurrence of CIU symptoms and initiate antihistamine therapy. This is what typically takes place in current practice. Patients easily recognize the signs and symptoms of a recurrence of CIU (itching, erythema, wheals, etc.), and if symptoms persist or become more serious patients understand the need to seek further medical attention or see their physician.

¹ 57 Fed. Reg. 58356, 58371-72 (Dec. 9, 1992).

The panel considers CIU and anaphylaxis to be qualitatively distinct diseases, with different etiologies. CIU and anaphylaxis patients are different patients, and CIU sufferers are not at increased risk for anaphylaxis. CIU patients may therefore be left to self-manage their CIU without an increased concern for anaphylaxis. Illustrative of this point, none of the clinician panel members provide epinephrine pens to their CIU patients.

Recurring acute urticaria is different than CIU. Recurring acute urticaria is distinguished from CIU based on the duration and continuity/persistence of symptoms over time. While oral antihistamines are properly used to treat acute urticaria, any OTC indication should not expand beyond CIU at this time. Limiting the OTC indication to CIU is appropriate because those patients with recurring acute urticaria should be seen by a physician who will attempt to find the cause of the urticaria. Furthermore, the broader indication is not currently in the prescription labeling and data are not now available on use for a broader urticaria indication. There may also be a small group of patients for whom acute urticaria symptoms are a precursor to a later anaphylactic episode. It would be prudent to have these patients to remain under a physician's management.

The OTC labeling for loratadine should instruct patients to immediately seek medical care if signs of an acute reaction exist (e.g., difficulty breathing, faintness, swelling of the tongue or in the throat, or gastro-intestinal distress). Labeling should also state that patients should see their physicians if symptoms do not improve in a specified number of days.

Making loratadine available OTC for the treatment of CIU will not present an increased risk to the public health relative to current practice, particularly with labeling that includes appropriate warnings/precautions. Currently, many CIU patients self-treat their

symptoms with first-generation OTC antihistamines. The labels for these products contain no directions for use in CIU or other skin allergy/allergic reactions. The availability of an OTC loratadine, with a CIU label and educational insert, may even improve public health to the extent that patients now using unlabeled, sedating first-generation antihistamines to self-treat CIU switch to an appropriately labeled, non-sedating product.

In 1992 the FDA concluded that there was insufficient data to support OTC antihistamines being labeled for use in the broadly defined category of allergic itching. The panel agrees that it has not seen sufficient data to support such a broad OTC use. However, the panel concludes that the more narrowly more narrowly defined proposal of an OTC antihistamine labeled for use in CIU after an initial physician diagnosis is a relatively easy proposition to support. In addition to the reasoning stated above, the new data provided by Schering describing consumer behavior and understanding of CIU, corroborated by their own clinical experience, were important in making this judgment. Further support for the OTC use of loratadine for CIU may be found in the currently available safety data available for the compound. Data on experience in countries where loratadine is marketed for use without a prescription would be particularly informative.