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ADMIN PROCEEDINGS STAFF
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May 15, 1985

Dockets Management Branch [HFA-305]
Food and Drug Administration
Room 4-62
5600 Fishers Lane
Rockville, Maryland 20857

Re: [Docket No. 76N-052H; Cold, Cough, Allergy, Bronchodilator, and Anti-asthmatic Drug Products for Over-the-Counter Human Use: Tentative Final Monograph for OTC Decongestant Drug Products]

Dear Madam:

Pursuant to 21 CFR Part 341, the Food and Drug Administration issued two notices of proposed rulemaking in the form of tentative final monographs that would establish conditions under which over the counter (OTC) nasal decongestant and antihistamine drug products are generally recognized as safe and effective. Interested parties have been invited to submit comments by May 15, 1985. These following comments are filed on behalf of Schering Corporation which is engaged in the discovery, development, manufacture and distribution of a broad line of drug products, including a number of well-known OTC cough cold and allergy products. Clearly, we are interested in and affected by the proposal.

I. Use of the Terms Warnings and Cautions

We believe the Agency should differentiate between "Warnings", "Cautions" and "Precautions" in OTC labeling. A "Warning" is the strongest of the terms and should be taken the most seriously. A "Caution" should be used to convey important information related to the safe and effective use of the product but which allows for judgement on the part of the user, e.g., "This product may cause drowziness". We believe it undermines the importance of a "Warning" Section if it contains too much information or if it includes less than serious language.

With respect to specific ingredients, we recommend the following language:

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1. Products containing pseudoephedrine:

Warnings: Do not take this product for more than seven days. Do not take this product if you have heart disease, high blood pressure, thyroid disease, diabetes or difficulty in urination due to enlargement of the prostate gland unless directed by a doctor.

Cautions: If symptoms do not improve or are accompanied by fever, consult a doctor.

2. Products containing oxymetazoline:

Warnings: Do not use this product for more than three days. If symptoms persist, consult a doctor.

Cautions: The use of the dispenser by more than one person my spread infection. Keep these and all medicines out of reach of children.

II. Use of Oxymetazoline Hydrochloride in Children

The Agency is proposing that labeling for the use of oxymetazoline hydrochloride in children under age 6 be restricted to professional labeling and be excluded from general consumer labeling. We believe this recommendation is unnecessary and may be based on a misinterpretation of the existing information.

Studies in dogs which compared the doses of oxymetazoline given intranasally and intravenously required to elicit a cardiovascular effect (i.e.,increase in blood pressure) showed substantial differences. The amount of oxymetazoline required to elicit any systemic effect by the intranasal route would be virtually unachievable with marketed products. Thus, it is extremely unlikely that a child could receive a dose of oxymetazoline that would have systemic effects.

In addition, a review of our adverse experience files indicates that we have never had a cardiovascular side effect from oxymetazoline which was not associated with significant over use, either in frequency of use, quantity of use or both.

Lastly, the Agency has expressed concern that it is difficult to measure the correct dose in a small child and that the child may receive an excessive dose by swallowing the administered medication. (50 FR 2230, 1/15/85) To the best of our knowledge, however, all pediatric formulations (0.25%) of oxymetazoline are drops, not sprays. It is our belief that drops are the easiest administered formulation and sufficiently accurate to assure safe use in children. Specifically, with respect to Afrin[R], Schering's brand of oxymetazoline pediatric nasal drops, the orifice of the dropper is controlled so that it

consistantly delivers an average drop volume of .028 ± .008 ml. This additional safety feature further assures the accuracy of the dose. In addition, as described above, it is extremely unlikely that a child could receive a dose of oxymetazoline that would have a systemic effect, even if the child inadvertently swallowed some of the drops.

For the reasons stated above, we would urge the Agency to accept the Panel's recommendation to permit consumer labeling for oxymetazoline for children, age 2-6. We believe this is a sound recommendation and one which is clearly supported by scientific evidence.

III. Additional Warning for Topical Nasal Decongestants

The Agency is proposing an additional warning for certain topical nasal decongestants: "Do not use this product if you have heart disease, high blood pressure, thyroid disease, diabetes, or difficulty in urination due to enlargement of the prostate gland unless directed by a doctor." For the reasons described above we do not believe such a warning is warranted for topical products containing oxymetazoline. Based on the amount of the drug which is required to cause a systemic effect, there is no reason to believe that patients with cardiac problems, diabetes or hyperthyroidism would be at any greater risk than the general population. We believe that the admonition not to overuse the product deals with this issue adequately and that the additional warning is not necessary.

IV. Timed Release Formulations

In the Notice the Agency has reiterated its position that timed release formulations are new drugs within the meaning of Section 201(p) of the Federal Food Drug and Cosmetic Act. We support the Agency's position on this question and agree that such products are not appropriately included in the applicable monographs and require an approved NDA for marketing.

Schering appreciates the opportunity to express its views in connection with the above referenced Federal Register notice.

Very truly yours,

Maureen Chelius

Maureen Chelius
Legal Director

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