Food and Drug Administration

[Docket No. 78N-301H]

RIN 0905-AA06

Hydrocortisone; Marketing Status as an External Analgesic Drug Product for Over-the-Counter Human Use; Notice of Enforcement Policy

AGENCY: Food and Drug Administration, HHS.

ACTION: Notice.

SUMMARY: The Food and Drug Administration (FDA) is announcing an enforcement policy allowing over-the-counter (OTC) marketing of external analgesic drug products containing above 0.5 percent up to 1 percent hydrocortisone or its hydrocortisone acetate equivalent. The OTC marketing of such drug products is being permitted pending establishment under the OTC drug review of a final monograph covering external analgesic drug products. FDA anticipates that external analgesic drug products containing above 0.5 up to 1 percent hydrocortisone or its hydrocortisone acetate equivalent will be determined to be generally recognized as safe and effective and not misbranded.

EFFECTIVE DATE: The enforcement policy is effective August 30, 1991.

ADDRESSES: Written comments to the Dockets Management Branch (HFA-305), Food and Drug Administration, rm. 1-23, 12420 Parklawn Dr., Rockville, MD 20857.

FOR FURTHER INFORMATION CONTACT: William E. Gilbertson, Center for Drug Evaluation and Research (HFD-210), Food and Drug Administration, 5600 Fishers Lane, Rockville, MD 20857, 301-295-8000.

SUPPLEMENTARY INFORMATION: In an amendment of the tentative final monograph for OTC external analgesic drug products, published in the **Federal Register** of February 27, 1990 (55 FR 6932), FDA proposed conditions under which products containing hydrocortisone or its hydrocortisone acetate equivalent above 0.5 percent up to 1 percent could be marketed OTC. This proposal was based on an evaluation of available data and submitted studies supporting general recognition of the safety and effectiveness of topical hydrocortisone for such use. The studies have been placed in the Dockets Management Branch (address above) and may be seen there by interested persons.

The agency also invited public comment on the proposed change in marketing status that would switch hydrocortisone above 0.5 percent up to 1 percent from its current status as a prescription drug to OTC status. The agency proposal did not allow OTC marketing to begin at the time of publication of the amendment of the tentative final monograph. The agency referred to the **Federal Register** of June 3, 1983 (48 FR 24925), in which FDA explained the enforcement policy for drugs that were originally on prescription status but which were being proposed for OTC marketing under the OTC drug review. As noted there, 21 CFR 330.13 permits OTC marketing of a drug previously limited to prescription use prior to publication of a final monograph provided that certain conditions are met. To qualify for such treatment, the drug must at a minimum have been considered by an OTC drug advisory review panel and either been recommended for OTC marketing by the panel or subsequently determined by FDA to be suitable for OTC marketing. Hydrocortisone was evaluated by the Advisory Review Panel on OTC Topical Analgesic, Antirheumatic, Otic, Burn, and Sunburn Prevention and Treatment Drug Products (the Panel) in its consideration of the prescription-to-OTC switch of hydrocortisone preparations, but the Panel recommended limiting the concentration for OTC use to 0.25 to 0.5 percent (December 4, 1979, 44 FR 69768 at 69813 through 69824).

In response to the proposal to switch above 0.5 up to 1 percent hydrocortisone from prescription to OTC status, eight drug manufacturers, numerous health professionals, one manufacturer's association, one law firm, and three health professional associations submitted comments. There was one request for an oral hearing from the American Academy of Dermatology (Ref. 1). In a subsequent letter, the Academy withdrew its request for a hearing, stating that its Board of Directors had taken definitive action not to oppose the switch (Ref. 2). Copies of the comments are on public display in the Dockets Management Branch.

After carefully reviewing all of the comments received, the agency is issuing a notice of enforcement policy permitting OTC marketing of above 0.5 up to 1 percent hydrocortisone or its hydrocortisone acetate equivalent for topical use prior to publication of the final monograph for OTC external analgesic drug products. This decision is based on extensive supportive safety and effectiveness data, and the following facts: (1) The majority of the comments, both for and against the proposal, were of a testimonial nature without substantive data; (2) many of the comments opposed to the proposal misunderstood that the proposed indication for OTC use was limited to temporary use to relieve the itching associated with minor skin irritation and rashes due to specific limited causes listed in the proposed monograph and the drug was not to be labeled for the treatment or cure of any skin disease with symptoms of itching; (3) no information not previously known by the agency was provided by the comments; and (4) the objections and concerns regarding the current proposal are the same or similar to those raised when 0.25 to 0.5 percent hydrocortisone was originally proposed for OTC use. Those objections and concerns have been disproven by the available scientific and medical evidence and a history of safe marketing of 0.25 to 0.5 percent hydrocortisone during 9 years of OTC use as well as years of safe use experience of 1 percent hydrocortisone as a prescription drug.

The agency addressed the safety, effectiveness, and labeling concerns expressed by the comments in the amendment of the external analgesic tentative final monograph proposing OTC status for above 0.5 up to 1 percent hydrocortisone (55 FR 6932). Based on the comments received in response to the proposal, the agency is revising the proposed label warning on the 7-day use limitation from "Do not use this or any other * * *" to read, "* * * stop use of this product and do not begin use * * *" (see below). With this revision, the agency believes there are no unresolved safety or effectiveness issues relating to the OTC use of above 0.5 up to 1 percent hydrocortisone as an antipruritic (anti-itch) external analgesic. Accordingly, the agency has determined that it would be inappropriate to continue to bar the interim marketing of such products. The agency's enforcement policy, which is set out in § 330.13, relating to OTC marketing of drug products containing certain ingredients that are under consideration in FDA's review of OTC drugs makes it clear that FDA may by notice in the **Federal Register** permit interim marketing of products such as hydrocortisone above 0.5 up to 1 percent. The agency advises that any drug product intended for OTC use as an antipruritic external analgesic that contains above 0.5 up to 1 percent hydrocortisone or its hydrocortisone acetate equivalent may be marketed pending issuance of the final monograph, subject to the risk that the agency may, in the final monograph, adopt a different position that could require relabeling, recall, or other regulatory action. Marketing of such products with labeling not in accord

with the labeling proposed in the amended tentative final monograph and this notice also may result in regulatory action against the product, the marketer, or both.

The labeling for OTC hydrocortisone products proposed in the amended tentative final monograph, as revised, is stated below. This labeling is required for marketing any OTC drug product containing above 0.5 up to 1 percent hydrocortisone or its hydrocortisone acetate equivalent. Also, as indicated in the amendment (55 FR 6932 at 6945 and 6946), the same labeling should apply to all OTC concentrations of hydrocortisone, ranging from 0.25 to 1.0 percent. The agency encourages manufacturers to revise the labeling of the currently marketed lower concentrations (0.25 to 0.5 percent) as soon as possible. The following labeling is to be used for all OTC drug products containing hydrocortisone or its hydrocortisone acetate equivalent:

Statement of Identity: "Antipruritic (anti-itch)," "anti-itch," "antipruritic (anti-itch) (insert dosage form, e.g., cream, lotion, ointment, or spray,)" or "anti-itch (insert dosage form, e.g. cream, lotion, or spray)."

Indications: One of the following should be used: (1) "For the temporary relief of itching associated with minor skin irritations and rashes" [which may be followed by "due to" (select one or more of the following: "eczema," "insect bites," "poison ivy, poison oak, or poison sumac," "soaps," "detergents," "cosmetics," "jewelry," "seborrheic dermatitis," "psoriasis,") and/or ("and for external" (select one or more of the following: "genital," "feminine," and "anal") "itching"); or (2) "For the temporary relief of itching associated with minor skin irritations, inflammation, and rashes due to" (select one or more of the following: "eczema," "insect bites," "poison ivy, poison oak, or poison sumac," "soaps," "detergents," "cosmetics," "jewelry," "seborrheic dermatitis," "psoriasis,") and/or ("and for external" (select one or more of the following: "gential," "feminine," and "anal") "itching").

In addition, the indications section must include the following statement: "Other uses of this product should be only under the advice and supervision of a" (select one of the following: "physician" or "doctor").

Warnings: "For external use only. Avoid contact with the eyes. If condition worsens, or if symptoms persist for more than 7 days or clear up and occur again within a few days, stop use of this product and do not begin use of any other hydrocortisone product unless you have consulted a" (select one of the following: "physician" or "doctor"). "Do not use for the treatment of diaper rash. Consult a" (select one of the following: "physician" or "doctor").

If the product is labeled with the indications "for external genital itching" or "for external feminine itching," the warnings must include the statement "Do not use if you have a vaginal discharge. Consult a" (select one of the following: "physician" or "doctor"). If the product is labeled with the indication "for external anal itching," the warnings must include the following statements: "Do not exceed the recommended daily dosage unless directed by a doctor. In case of bleeding, consult a doctor promptly. Do not put this product into the rectum by using fingers or any mechanical device or applicator." (The word "physician" may be substituted for the word "doctor" in these statements.)

Directions: Adults and children 2 years of age and older: Apply to affected area not more than 3 to 4 times daily. Children under 2 years of age: Do not use, consult a (select one of the following: physician or doctor).

If the product is labeled with the indication "for external anal itching," the directions must include the following statements: "Adults: When practical, cleanse the affected area" (selected one or both of the following: "with mild soap and warm water and rinse thoroughly" or "by patting or blotting with an appropriate cleansing pad"). "Gently dry by patting or blotting with toilet tissue or a soft cloth before application of this product." (Other appropriate directions in this section may be inserted here.) "Children under 12 years of age: consult a" (select one of the following: "physician" or "doctor").

The final monograph for OTC external analgesic drug products, when published, will establish the final labeling that will be required for all OTC drug products that contain hydrocortisone.

References

(1) Comment No. HER1, Docket No. 76N-301H, Dockets Management Branch.

(2) Comment No. WDL1, Docket No. 78N-301H, Dockets Management Branch.

Interested persons may submit written comments to the Dockets Management Branch (address above). Such comments will be considered in determining whether further amendments to or revisions of this policy are warranted. Three copies of all comments shall be submitted, except that individuals may submit single copies. Comments are to be identified with the docket number found in brackets in the heading of this document. Received comments may be seen in the Dockets Management Brai between 9 a.m. and 4 p.m., Monday through Friday.

Dated: August 14, 1991.

Michael R. Taylor,

Deputy Commissioner for Policy.

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[Docket No. 91N-0318]

Human Organ and Tissue Transplantation; Public Hearing

AGENCY: Food and Drug Administration, HHS.

ACTION: Notice of public hearing; requests for comments.

SUMMARY: The Food and Drug Administration(FDA), with the concurrence of the Health Resources and Services Administration (HRSA), the National Institutes of Health (NIH), the Centers for Disease Control (CDC), and the Health Care Financing Administration (HCFA), is announcing a public hearing to solicit information and views of interested persons on the need to expand the Federal regulation of organ and tissue transplantation. The information from this public hearing will be used to evaluate whether and how the Federal government should develop a new regulatory program to address aspects of this industry.

DATES: Written notices of participation should be filed by September 30, 1991. The hearing will begin at 9 a.m. on October 16, 1991. The record will remain open for 15 days following the hearing, by which time any additional written material must be submitted.

ADDRESSES: The public hearing will be held at the Jack Masur Auditorium, Warren Grant Magnusun Clinical Center, Bldg. 10, National Institutes of Health, 9000 Rockville Pike, Bethesda, MD 20892. Written notices of participation and any comments are to be sent to the Dockets Management Branch (HFA-305), Food and Drug Administration, rm. 1-23, 12420 Parklawn Dr., Rockville, MD 20857. Transcripts of the hearing, copies of data and information submitted during the hearing, and any written comments will be available for review at the Dockets Management Branch (address above).

FOR FURTHER INFORMATION CONTACT: Nicholas P. Reuter, Office of the Associate Commissioner for Health Affairs (HFY-20), Food and Drug Administration, 5600 Fishers Lane, Rockville, MD 20857, 301-443-1362.