DEPARTMENT OF HEALTH AND HUMAN SERVICES

Food and Drug Administration

21 CFR Part 348

[Docket No. 78N-0301]

RIN 0905-AA06

Male Genital Desensitizing Drug Products for Over-the-Counter Human Use; Final Monograph

AGENCY: Food and Drug Administration, HHS.

ACTION: Final rule.

SUMMARY: The Food and Drug Administration (FDA) is issuing a final rule in the form of a final monograph establishing conditions under which over-the-counter (OTC) male genital desensitizing drug products (premature ejaculation remedies) are generally recognized as safe and effective and not misbranded. FDA is issuing this final rule after considering public comments on the agency's proposed regulation, which was issued in the form of a tentative final monograph, and all new data and information on OTC male genital desensitizing drug products that have come to the agency's attention. This final monograph is part of the ongoing review of OTC drug products conducted by FDA.

EFFECTIVE DATE: June 19, 1993.

FOR FURTHER INFORMATION CONTACT: William E. Gilbertson, Center for Drug Evaluation and Research (HFD-810), Food and Drug Administration, 5600 Fishers Lane, Rockville, MD 20857, 301-295-8000.

SUPPLEMENTARY INFORMATION: In the **Federal Register** of September 7, 1982 (47 FR 39412), FDA published, under § 330.10(a)(6) (21 CFR 330.10(a)(6)), as part of the rulemaking for OTC external analgesic drug products, an advance notice of proposed rulemaking to establish a monograph for OTC male genital desensitizing drug products. The agency also published the recommendations on OTC male genital desensitizing drug products that were made by the Advisory Review Panel on OTC Miscellaneous External Drug Products (the Panel), which was the advisory review panel responsible for evaluating data on the active ingredients in these drug products. Interested persons were invited to submit comments by December 6, 1982. Reply comments in response to comments filed in the initial comment period could be submitted by January 5, 1983.

In accordance with § 330.10(a)(10), the data and information considered by the Panel, after deletion of a small amount of trade secret information, were placed on public display in the Dockets Management Branch (HFA-305), Food and Drug Administration, Rm. 1-23, 12420 Parklawn Dr., Rockville, MD 20857.

The agency's proposed regulation, in the form of a tentative final monograph, for OTC male genital desensitizing drug products was published in the **Federal Register** of October 2, 1985 (50 FR 40260). Interested persons were invited to file by December 2, 1985, written comments, objections, or requests for oral hearing before the Commissioner of Food and Drugs regarding the proposal. Interested persons were invited to file comments on the agency's economic impact determination by January 30, 1986. New data could have been submitted until October 2, 1986, and comments on the new data until December 2, 1986.

The OTC drug procedural regulations (§ 330.10) provide that any testing necessary to resolve the safety or effectiveness issues that formerly resulted in a Category III classification, and submission to FDA of the results of that testing or any other data, must be done during the OTC drug rulemaking process before the establishment of a final monograph. Accordingly, FDA is no longer using the terms "Category I" (generally recognized as safe and effective and not misbranded), "Category II" (not generally recognized as safe and effective or misbranded), and "Category III" (available data are insufficient to classify as safe and effective, and further testing is required) at the final monograph stage, but is using instead the terms "monograph conditions" (old Category I) and "nonmonograph conditions" (old Categories II and III).

In the proposed regulation for OTC male genital desensitizing drug products (50 FR 40260), the agency advised that the conditions under which the drug products that are subject to this monograph will be generally recognized as safe and effective and not misbranded (monograph conditions) will be effective 12 months after the date of publication in the **Federal Register**. Therefore, on or after June 19, 1993, no OTC drug product that is subject to the monograph and that contains a nonmonograph condition, i.e., a condition that would cause the drug to be not generally recognized as safe and effective or to be misbranded, may be initially introduced or initially delivered for introduction into interstate commerce unless it is the subject of an approved application. Further, any OTC drug product subject to this monograph that is repackaged or relabeled after the effective date of the monograph must be in compliance with the monograph regardless of the date the product was initially introduced or initially delivered for introduction into interstate commerce. Manufacturers are encouraged to comply voluntarily with the monograph at the earliest possible date.

In response to the proposed rule on OTC male genital desensitizing drug products, one distributor of these products submitted a comment. A copy of the comment received is on public display in the Dockets Management Branch (address above). Additional information that has come to the agency's attention since publication of the proposed rule is also on public display in the Dockets Management Branch.

All "OTC Volumes" cited throughout this document refer to the submissions made by interested persons pursuant to the call-for-data notices published in the **Federal Register** of November 16, 1973 (38 FR 31697), and August 27, 1975 (40 FR 36179), or to additional information that has come to the agency's attention since publication of the notice of proposed rulemaking. The volumes are on public display in the Dockets Management Branch.

I. The Agency's Conclusions on the Comment

One comment suggested that the word "aids" in the indications statements in proposed § 348.50(b)(4) (50 FR 40260 at 40265) be changed to "helps" because of the undesirable association of the word "aids" with the disease acquired immunodeficiency syndrome (AIDS). The comment was concerned with this negative association because male genital desensitizing drug products are used in connection with sexual activity, which is also a suspected manner in which the disease AIDS is transmitted. The comment concluded that its proposed substitution of words in no way changes the meaning of the indications statements because the word "help(s)" is a recognized synonym for the word "aid(s)." The agency agrees that the change suggested by the comment can be made. The word "help(s)" is a recognized synonym for the word "aid(s)" (Ref. 1). In view of the possible negative association of the word "aids" with the disease AIDS, the substitution of words can be done without impairing the intent of the labeling of male genital desensitizing drug products. Accordingly, the agency is amending the indications statements in proposed § 348.50(b)(4)(i) and

(b)(4)(ii) to change the word "aids" to "helps."

Reference

1. "Webster's New World Dictionary," 3rd College Ed., Simon & Schuster, Inc., New York, 1988, s.v. "aid," "help."

II. Agency Initiated Changes

1. In the proposed rule for OTC male genital desensitizing drug products (50 FR 40260 at 40265), the agency recommended the following indications statement for these drug products: "Aids in the prevention of premature ejaculation." The agency also proposed five other allowable indications that could be used in addition to the above indication, which are as follows: (1) "For temporary male genital desensitization, helping to slow the onset of ejaculation." (2) "Aids in temporarily retarding the onset of ejaculation." (3) "Aids in temporarily slowing the onset of ejaculation." (4) "Aids in temporarily prolonging time until ejaculation." (5) "For reducing oversensitivity in the male in advance of intercourse." Except for the use of the word "aids" in these statements, the agency did not receive any comments regarding the content of these statements. The agency has determined that several of the indications statements can be combined to allow for a choice of words to be used, and that any one or more of the statements would be acceptable as indications statements for these OTC drug products. Therefore, the agency is providing in § 348.50(b)(1) of this final monograph that the labeling of OTC male genital desensitizing drug products may contain any one or more of the following indications statements: (1) "Helps in the prevention of premature ejaculation." (2) "For temporary male genital desensitization, helping to slow the onset of ejaculation." (3) "Helps in temporarily" (select one of the following: "retarding the onset of," "slowing the onset of," or "prolonging the time until") followed by "ejaculation." (4) "For reducing oversensitivity in the male in advance of intercourse."

2. The agency is revising the format of the directions statements. In the tentative final monograph, the agency stated that the directions should be followed by the words "or as directed by a doctor." The agency has incorporated these words into the individual statements for each active ingredient so that placement occurs in the correct place. As worded in the tentative final monograph, this might not have occurred.

3. The agency is redesignating portions of the monograph for OTC external analgesic drug products that were proposed in the tentative final monograph for OTC male genital desensitizing drug products because the segment of the monograph covering these products is being finalized prior to other proposed segments of the monograph. For the convenience of the reader, the following chart is included to show these redesignations.

REDESIGNATED SECTION NUMBERS

Old Section Number	Provision	New Section Number
348.3(f)	Definitions	348.3(a)
348.10(e)	Active ingredients	348.10(a)
348.50(a)(3)	Statement of identity.	348.50(a)(1)
348.50(b)(4)	Indications	348.50(b)(1)
348.50(c)(8)	Warnings	348.50(c)(1)
348.50(d)(2)	Directions	348.50(d)(1)

III. Summary of Changes from the Proposed Rule

1. The agency is revising the indications statements in proposed § 348.50(b)(4) to replace the word "aids" with the word "helps." (See section I.)

2. The agency is combining several of the proposed indications statements and providing that any one or more of these statements may be used for these products. (See section II.)

IV. The Agency's Final Conclusions on OTC Male Genital Desensitizing Drug Products

Based on available evidence, the agency is issuing a final monograph establishing conditions under which OTC male genital desensitizing drug products are generally recognized as safe and effective and not misbranded. Specifically, the agency has determined that the only ingredients that meet monograph conditions are benzocaine and lidocaine. All other ingredients considered in this rulemaking have been determined to be nonmonograph conditions for use in an OTC male genital desensitizing drug product. These ingredients include, but are not limited to, benzyl alcohol, camphorated metacresol, and ephedrine hydrochloride. In the **Federal Register** of November 7, 1990 (55 FR 46914), the agency published a final rule in 21 CFR Part 310 establishing that certain active ingredients that had been under consideration in a number of OTC drug rulemaking proceedings were not generally recognized as safe and effective. That final rule included in § 310.545(a)(10)(iii) the three nonmonograph OTC male genital desensitizing drug product ingredients mentioned above and was effective May 7, 1991. This current final rule does not result in the addition of any other ingredients to those already listed in § 310.545(a)(10)(iii). Accordingly, any drug product labeled, represented, or promoted for use as an OTC male genital desensitizing drug product that contains any of the ingredients listed in § 310.545(a)(10)(iii) or that is not in conformance with the monograph (21 CFR Part 348), may be considered a new drug within the meaning of section 201(p) of the Federal Food, Drug, and Cosmetic Act (the act) (21 U.S.C. 321(p)) and misbranded under section 502 of the act (21 U.S.C. 352) and may not be marketed for this use unless it is the subject of an approved application under section 505 of the act (21 U.S.C. 355) and Part 314 of the regulations (21 CFR Part 314). An appropriate citizen petition to amend the monograph may also be submitted under 21 CFR 10.30 in lieu of an application. Any OTC male genital desensitizing drug product initially introduced or initially delivered for introduction into interstate commerce after the effective date of the final rule mentioned above or this final rule that is not in compliance with the regulations is subject to regulatory action.

No comments were received in response to the agency's request for specific comment on the economic impact of this rulemaking (50 FR 40260 at 40264). The agency has examined the economic consequences of this final rule in conjunction with other rules resulting from the OTC drug review. In a notice published in the **Federal Register** of February 8, 1983 (48 FR 5806), the agency announced the availability of an assessment of these economic impacts. The assessment determined that the combined impacts of all the rules resulting from the OTC drug review do not constitute a major rule according to the criteria established by Executive Order 12291. The agency therefore concludes that no one of these rules, including this final rule for OTC male genital desensitizing drug products, is a major rule.

The economic assessment also concluded that the overall OTC drug review was not likely to have a significant economic impact on a substantial number of small entities as defined in the Regulatory Flexibility Act (Pub. L. 96-354). That assessment included a discretionary regulatory flexibility analysis in the event that an individual rule might impose an unusual or disproportionate impact on small entities. However, this particular rulemaking for OTC male gential desensitizing drug products is not

expected to pose such an impact on small businesses. This final rule will require some relabeling for products containing monograph ingredients. Manufacturers will have 1 year to implement this relabeling. No reformulations should be necessary, and there are no additional nonmonograph ingredients. Therefore, the agency certifies that this final rule will not have a significant economic impact on a substantial number of small entities.

The agency has determined under 21 CFR 25.24(c)(6) that this action is of a type that does not individually or cumulatively have a significant effect on the human environment. Therefore, neither an environmental assessment nor an environmental impact statement is required.

List of Subjects in 21 CFR Part 348

External analgesic drug products, Labeling, Over-the-counter drugs.

Therefore, under the Federal Food, Drug, and Cosmetic Act and under authority delegated to the Commissioner of Food and Drugs, 21 CFR Part 348 is added to read as follows:

PART 348—EXTERNAL ANALGESIC DRUG PRODUCTS FOR OVER-THE-COUNTER HUMAN USE

Subpart A—General Provisions

Sec.
348.1 Scope.
348.3 Definitions.

Subpart B—Active Ingredients

348.10 Analgesic, anesthetic, and antipruritic active ingredients.

Subpart C—Labeling

348.50 Labeling of external analgesic drug products.

Authority: Secs. 201, 501, 502, 503, 505, 510, 701 of the Federal Food, Drug, and Cosmetic Act (21 U.S.C. 321, 351, 352, 353, 355, 360, 371).

Subpart A—General Provisions

§ 348.1 Scope.

(a) An over-the-counter external analgesic drug product in a form suitable for topical administration is generally recognized as safe and effective and is not misbranded if it meets each condition in this part and each general condition established in § 330.1 of this chapter.

(b) References in this part to regulatory sections of the Code of Federal Regulations are to Chapter I of Title 21 unless otherwise noted.

§ 348.3 Definitions.

As used in this part:

(a) *Male genital desensitizing drug product.* A drug product applied to the penis to help in temporarily slowing the onset of ejaculation.

(b) [Reserved]

Subpart B—Active Ingredients

§ 348.10 Analgesic, anesthetic, and antipruritic active ingredients.

The active ingredient of the product consists of any of the following within the specified concentration established for each ingredient:

(a) *Male genital desensitizers.* (1) Benzocaine, 3 to 7.5 percent in a water-soluble base.

(2) Lidocaine in a metered spray with approximately 10 milligrams per spray.

(b) [Reserved]

Subpart C—Labeling

§ 348.50 Labeling of external analgesic drug products.

(a) *Statement of identity.* The labeling of the product contains the established name of the drug, if any, and identifies the product as follows:

(1) *For products containing any ingredient identified in § 348.10(a).* "Male genital desensitizer."

(2) [Reserved]

(b) *Indications.* The labeling of the product states, under the heading "Indications," any of the phrases listed in paragraph (b) of this section. Other truthful and nonmisleading statements, describing only the indications for use that have been established and listed in paragraph (b) of this section, may also be used, as provided in § 330.1(c)(2) of this chapter, subject to the provisions of section 502 of the Federal Food, Drug, and Cosmetic Act (the act) relating to misbranding and the prohibition in section 301(d) of the act against the introduction or delivery for introduction into interstate commerce of unapproved new drugs in violation of section 505(a) of the act.

(1) *For products containing any ingredient identified in § 348.10(a).* (i) "Helps in the prevention of premature ejaculation."

(ii) "For temporary male genital desensitization, helping to slow the onset of ejaculation."

(iii) "Helps in temporarily" (select one of the following: "retarding the onset of," "slowing the onset of," or "prolonging the time until") followed by "ejaculation."

(iv) "For reducing oversensitivity in the male in advance of intercourse."

(2) [Reserved]

(c) *Warnings.* The labeling of the product contains the following warnings under the heading "Warnings":

(1) *For products containing any ingredient identified in § 348.10(a).* (i) "Premature ejaculation may be due to a condition requiring medical supervision. If this product, used as directed, does not provide relief, discontinue use and consult a doctor."

(ii) "Avoid contact with the eyes."

(iii) "If you or your partner develop a rash or irritation, such as burning or itching, discontinue use. If symptoms persist, consult a doctor."

(2) [Reserved]

(d) *Directions.* The labeling of the product contains the following information under the heading "Directions":

(1) *For products containing any ingredient identified in § 348.10(a)*—(i) *For products containing benzocaine identified in § 348.10(a)(1).* "Apply a small amount to head and shaft of penis before intercourse, or use as directed by a doctor. Wash product off after intercourse."

(ii) *For products containing lidocaine identified in § 348.10(a)(2).* "Apply 3 or more sprays, not to exceed 10, to head and shaft of penis before intercourse, or use as directed by a doctor. Wash product off after intercourse."

(2) [Reserved]

(e) The word "physician" may be substituted for the word "doctor" in any of the labeling statements in this section.

Dated: March 18, 1992.

Michael R. Taylor,

Deputy Commissioner for Policy.

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