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DEPARTMENT OF HEALTH AND HUMAN SERVICES

Food and Drug Administration

[Docket Nos. 98N-0718 and 76N-0377; DESI 7661]

Eli Lilly & Co. and Bristol-Myers Squibb Co.; Withdrawal of Approval of Three New Drug Applications for Estrogen-Androgen Combination Drugs

AGENCY: Food and Drug Administration, HHS.

ACTION: Notice.

SUMMARY: The Food and Drug Administration (FDA) is withdrawing approval of three new drug applications (NDA's) for estrogen-androgen combination drugs. The NDA's are held by Eli Lilly & Co. and Bristol-Myers Squibb Co. The products are no longer marketed. Both companies requested that the NDA's be withdrawn and waived their opportunity for a hearing. The products will be removed from the list of drug products with effective approvals.

EFFECTIVE DATE: *(Insert date of publication in the Federal Register.)*

FOR FURTHER INFORMATION CONTACT: David T. Read, Center for Drug Evaluation and Research (HFD-7), Food and Drug Administration, 5600 Fishers Lane, Rockville, MD 20857, 301-594-2041.

SUPPLEMENTARY INFORMATION: Previous **Federal Register** notices regarding the regulatory status of the three applications named below, as well as two others (NDA's 10-597 and 11-267), were published on September 8, 1972 (37 FR 18225), and September 29, 1976 (41 FR 43112). (The approvals of NDA 10-597 (Tace with Androgen Capsules containing chlorotrianisone and methyltestosterone) and NDA 11-267 (Halodrin Tablets containing fluoxymesterone and ethinyl estradiol) were withdrawn in **Federal Register** notices of June 25, 1993 (58 FR 34466), and March 2, 1994 (59 FR 9989), respectively; see also 43 FR 49564 (October 24, 1978), which was a proposal

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to withdraw approval of estrogen-containing drug products labeled for use in postpartum breast engorgement.)

By letter dated June 5, 1998, Bristol-Myers Squibb Co., P.O. Box 4000, Princeton, NJ 08543, requested that FDA withdraw approval of NDA 9-545 (Deladumone OB Injection and Deladumone Injection, each containing testosterone enanthate and estradiol valerate), stating that the marketing of Deladumone OB Injection was discontinued in 1989 when the indication for postpartum breast engorgement was withdrawn (noting that this was the only indication for Deladumone OB Injection), and that the marketing of Deladumone Injection was discontinued in 1991 because there was no longer a significant patient population requiring the concurrent therapy of an estrogen and an androgen in a fixed dose.

By letters dated July 15, 1998, and July 30, 1998, Eli Lilly & Co., Lilly Corporate Center, Indianapolis, IN 46285, requested that FDA withdraw approval of NDA 7-661 (Tylosterone Tablets) and NDA 8-099 (Tylosterone Injection), both containing diethylstilbestrol and methyltestosterone, stating that the marketing of both products was discontinued in 1988 because there was no longer a significant patient population requiring the concurrent therapy of an estrogen and an androgen in a fixed dose.

Both applicants waived their opportunity for a hearing. The agency concurs in the applicants' finding that there is not a significant patient population requiring the concurrent therapy of an estrogen and an androgen in a fixed dose.

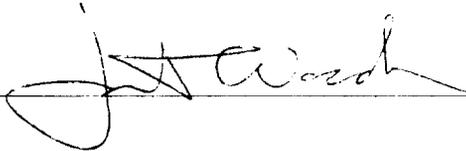
Approval of a new drug application will be withdrawn if there is a lack of substantial evidence that the drug product covered by the application has the clinical effect that it purports or is represented to have under the conditions of use prescribed, recommended, or suggested in its labeling (21 U.S.C. 355(e)). For fixed combination prescription drugs, such substantial evidence exists only if each component makes a contribution to the claimed effects and the dosage of each component (amount, frequency, duration) is such that the combination is safe and effective for a significant patient population requiring such concurrent therapy, as defined in the labeling for

the drug (21 CFR 300.50). Estrogen and androgen fixed-dose combination products, therefore, lack substantial evidence of effectiveness due to the fact that there is not a significant patient population requiring the concurrent therapy of an estrogen and an androgen in a fixed dose.

Therefore, under section 505(e) of the Federal Food, Drug, and Cosmetic Act (21 U.S.C. 355(e)) and under authority delegated to the Director, Center for Drug Evaluation and Research (21 CFR 5.70 and 5.82), approval of NDA's 7-661, 8-099, and 9-545 and all amendments and supplements thereto, is hereby withdrawn for the reasons stated above, effective (*insert date of publication in the **Federal Register***). Under 21 CFR 314.161 and 314.162(a)(1), four of the estrogen and androgen fixed-dose combination products named above (NDA's 7-661, 8-099,

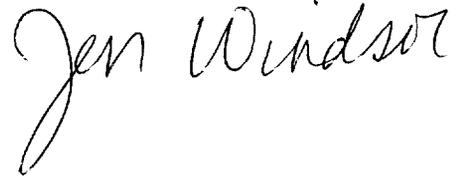
9-545, and 11-267) will be removed from the list of drug products with effective approvals published in FDA's publication, "Approved Drug Products with Therapeutic Equivalence Evaluations." FDA will not approve or accept ANDA's that refer to these drug products.

Dated: 10/22/98
October 22, 1998



Janet Woodcock
Director
Center for Drug Evaluation and Research

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[FR Doc. 98-???? Filed ??-??-98; 8:45 am]

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