DEPARTMENT OF HEALTH & HUMAN SERVICES

F.O.I

Food and Drug Administration
Rockville MD 20857

TRANSMITTED VIA FACSIMILE

JAN 4 1998

Donald E. Baker, J.D.
Director, Regulatory Affairs
Fujisawa USA, Inc.
Parkway North Center
Three Parkway North
Deerfield, Ill 60015-2548

RE: NDA 50-708
Prograf (Tacrolimus) Capsules
NDA 50-709
Prograf (Tacrolimus) Injection
MACMIS # 6885

Dear Mr. Baker:

This letter addresses Fujisawa's dissemination of a journal advertisement for Prograf (Tacrolimus) Capsules and Prograf (Tacrolimus) Injection (collectively referred to as "Prograf"). This advertisement was published in the September 1998 edition, volume 9, of the Journal of the American Society of Nephrology and in the June 27, 1998, edition, volume 65, number 12, of Transplantation (Official Journal of the Transplantation Society). The Division of Drug Marketing, Advertising, and Communications (DDMAC) has reviewed this advertisement as part of its monitoring and surveillance program. DDMAC has concluded that Fujisawa's advertisement is false or misleading and lacking in fair balance in violation of the Federal Food, Drug, and Cosmetic Act (the Act), 21 U.S.C. §§ 331(a)(b) & 352(n), and applicable regulations.

Brief Summary

Under 21 U.S.C. § 352(n), all prescription drug advertisements must contain a statement in brief summary relating to side effects, contraindications, and effectiveness, as shall be required in FDA regulations. (This is referred to as the "brief summary"

requirement.) The prescription drug advertisement regulations at 21 C.F.R. § 202.1(e)(1) state that the terms side effects and contraindications include side effects, warnings, precautions, and contraindications. DDMAC concludes from its review of Fujisawa's advertisement that Fujisawa failed to utilize the U.S. approved drug labeling as the basis for its Prograf "brief summary." For example, the brief summary omits critically important safety information that appears in the approved labeling. We note the absence of the boxed warning on the increased susceptibility to infection and the possible development of lymphoma that can result from immunosuppression. Additionally, the advertisement fails to disclose the bolded warning that Prograf should not be used simultaneously with cyclosporin. These violations do not constitute an exhaustive list, but are merely examples. Therefore, Fujisawa should review its brief summary for Prograf and revise it accordingly, so that it is consistent with the U.S. approved labeling.

Advertisement

The prescription drug advertising regulations also provide that an advertisement is false, lacking in fair balance, or otherwise misleading if: it contains a representation or suggestion, not approved in the labeling, that a drug is more effective or safer than has been demonstrated by substantial evidence or substantial clinical experience; or, it contains a drug comparison that represents or suggests that a drug is safer or more effective than another drug in some particular when it has not been demonstrated by substantial evidence or substantial clinical experience. (See 21 C.F.R. § 202.1(e)(6)) In this instance, Fujisawa appears to have not utilized the U.S. approved drug labeling as the basis for its advertisement for Prograf. For example, the following statement is used in the body of the advertisement: "compared with patients receiving "ciclosporin-based therapy." Ciclosporin is not the nomenclature adopted in the U.S. for the comparator product -- cyclosporin. Furthermore, the name "ciclosporin" has a barely noticeable asterisk that refers to an unidentified "old formulation." Fujisawa then proceeds to make comparative claims that Prograf has a "significantly lower incidence of . . ." and that Prograf patients have "less need for. . . ." Any comparisons made by Fujisawa are misleading in violation of the Act and applicable regulations. Additionally, this advertisement lacks fair balance since there is NO risk information presented in the body of the advertisement. This recitation of violations do not constitute an exhaustive list, but are merely examples.

In order to address these objections, DDMAC suggests that Fujisawa take the following actions:

(1) Immediately discontinue the dissemination of this advertisement upon receipt of this letter.

(2) Provide to DDMAC, in writing, Fujisawa's commitment to comply with number one above.

Fujisawa's response should be received no later than January 18, 1999. If Fujisawa has any questions or comments, please contact the undersigned or Sherrie Shade R.Ph., J.D., by facsimile at 301-594-6771, or in writing at the Division of Drug, Marketing, advertising, and Communications, HFD-40, Room 17B-20, 5600 Fishers Lane, Rockville, MD 20857.

In all correspondence related to this matter, please refer to MACMIS #6885, in addition to the NDA numbers.

Sincerely,

Lesley R. Frank, Ph.D., J.D.
Regulatory Counsel,
Division of Drug Marketing, Advertising,
and Communications