DEPARTMENT OF HEALTH & HUMAN SERVICES

Food and Drug Administration
Rockville MD 20857

August 27, 1998

TRANSMITTED VIA FACSIMILE

John Vandewalle, M.D.
CEO
Teva Marion Partners
10236 Marion Park Drive
Kansas City, MO 64134-0627

RE: NDA #20-622
Copaxone (glatiramer acetate) Injection
MACMIS #6462

WARNING LETTER

Dear Dr. Vandewalle:

This Warning Letter concerns Teva Marion Partners' (TMP) advertising and labeling materials for the promotion of Copaxone (glatiramer acetate) Injection.[1] The Division of Drug Marketing, Advertising and Communications (DDMAC) has reviewed these promotional materials as part of its routine monitoring and surveillance program. From its review, DDMAC has concluded that TMP is disseminating promotional materials that promote Copaxone for unapproved uses, and that contain statements or suggestions that are false, lacking in fair balance, or otherwise misleading, in violation of the Federal Food, Drug, and Cosmetic Act, 21 U.S.C. §§ 331(a), 502(a), 502(n), and 321(a) and applicable regulations.

1 These materials include: journal ad (ID 044201/8078E8); brochures and booklets (ID 50016903/080701/8009A8, 50017342/041001/8079C8, 50016554/034301/8022B8, 6922/031501/8034B8, and 50016877/044401/8033B8); slide kit (ID 043801/8051C8); letter (ID 043101/8014A8); press releases (021802/8040B8 and 022001/8112E8); Internet web pages (http://www.tevamarionpartners.com); reprint carrier (ID 50016757/040502/8026B8); and leaflets (50017604/040901/8103E8 and 50016878/43301/8036B8). These materials also include posters and advertising messages presented by TMP sales representatives at the American Academy of Neurology 50th Annual Meeting in Minneapolis, Minnesota.

Background

The approved product labeling (PI) for Copaxone (glatiramer acetate) Injection states that it "is indicated for the reduction of the frequency of relapses in patients with Relapsing-Remitting Multiple Sclerosis." TMP has not demonstrated, by substantial evidence, that Copaxone is safe and effective for other uses associated with multiple sclerosis (MS) such as having an effect on the progression or degree of disability.

Disability Claims

TMP has disseminated promotional materials containing misleading claims that Copaxone is safe and effective in slowing, preventing, or reversing the long term neurological deterioration or disability that is associated with the progression of MS. To support these disability claims in its promotional materials, TMP presents data from a multicenter study that it previously submitted to the agency during the application review process. At that time, the agency determined that these data were inadequate to support such claims.

Comparative or Superiority Claims

TMP's promotional materials also state or suggest that physicians, who are using other therapies for MS, should switch to Copaxone because it is safer, more tolerable, or more effective.[2] Claims that Copaxone is safer, more tolerable, or more effective than other therapies for MS, are false or misleading in the absence of adequate and well-controlled comparative trials demonstrating the claimed superiority or comparability.

TMP's claims state or suggest that more than half of the patients on other therapies discontinued those treatments within a year, and TMP suggests that the reason for such discontinuation was because of safety or effectiveness. For example, in a brochure entitled "Why are neurologists switching their MS patients to Copaxone?," TMP presented safety and effectiveness data regarding Copaxone. Thereafter, TMP claimed that 56% of Avonex patients and 69% of Betaseron patients quit therapy within a year, but that there were high levels of compliance with Copaxone.[3] TMP bases its statements about Copaxone on different compliance data sources. However, TMP's claims are based on data from a retail pharmacy database that measured nothing more than the fact that a prescription had been originally filled at a retail pharmacy and whether or not that prescription had been refilled. Data describing whether or not

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2 See, for example, Brochure 50017342/041001/8079C8 (1998).
3 TMP cites Walsh America/Source Informatics/PMSI data to support these claims.

patients refilled specific prescriptions at a particular retail pharmacy are clearly inadequate to substantiate claims that patients actually continued or discontinued therapy.

Requested Actions

TMP has disseminated promotional materials containing false or misleading information about the safety, tolerability, and effectiveness of Copaxone. Accordingly, TMP should propose an action plan, including the mailing and publication of a "Dear Healthcare Professional" letter to disseminate corrective messages about the issues discussed in this letter to all healthcare providers, institutions, and organizations who have received the violative messages.

TMP's action plan should also include:

A. The immediate cessation of dissemination of the advertisements, brochures and other promotional materials identified in this letter.

B. A written statement of TMP's intent to comply with "A" above.

C. The provision of (1) a complete list of all promotional materials for Copaxone that TMP will discontinue as a result of this Warning Letter, and (2) a complete list and a copy of all materials that TMP intends to continue to disseminate subsequent to this letter.

D. The dissemination, within 15 days of the date of this letter, of a message to all sales representatives and marketing personnel involved in the sale and marketing of Copaxone, instructing them to immediately cease dissemination of the promotional materials identified in this letter.

The "Dear Healthcare Professional" letter and TMP's action plan should be submitted to DDMAC for approval. After such approval, the letter should be disseminated by both direct mail and through a paid advertisement in all journals that contained advertisements for Copaxone during the 12 months prior to the date of this letter.

The violations discussed in this letter do not necessarily constitute an exhaustive list. We are continuing to evaluate other aspects of TMP's promotion of Copaxone and we may determine that additional remedial measures will be necessary to fully correct the false or misleading messages resulting from TMP's violative conduct.

TMP's response should be received on or before September 9, 1998. If TMP has any questions or comments, please contact Dr. Lisa Stockbridge, Dr. Lesley R. Frank, or

Norman A. Drezin, Esq. at (301) 827-2831, by fax at (301) 594-6771, or at the Food and Drug Administration, Division of Drug Marketing, Advertising and Communications, HFD-40, rm. 17B-20, 5600 Fishers Lane, Rockville, MD 20857. DDMAC reminds TMP that only written communications are considered official.

In all future correspondence regarding this particular matter, please refer to MACMIS ID # 6462 in addition to the NDA number.

Sincerely,

/S/

Minnie Baylor-Henry, R.Ph., J.D.
Director
Division of Drug Marketing,
Advertising and Communications