DEPARTMENT OF HEALTH & HUMAN SERVICES

Public Health Service

Food and Drug Administration
Rockville MD 20857

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TRANSMITTED BY FACSIMILE

Daryl DeKarske, M.P.H.
Associate
Regulatory Affairs
G.D. Searle & Co.
4901 Searle Parkway
Skokie, IL 60077

Re: NDA 18-841
Daypro (oxaprozin) Tablets
MACMIS ID #6682

Dear Mr. DeKarske:

This letter is in reference to G.D. Searle Co.'s (Searle) submission of promotional materials under cover of Form FDA 2253 for Daypro (oxaprozin) Tablets. These materials included promotional posters identified as A98DA15057W-3, A98DA15057W-4, a promotional brochure identified as A98DA14990Q, and promotional website banners. The Division of Drug Marketing, Advertising, and Communications (DDMAC) regards these promotional materials to be false or misleading and dissemination of them to be in violation of the Federal Food, Drug, and Cosmetic Act and regulations promulgated thereunder. Specific issues are discussed below.

1. Misleading Comparisons to Relafen (nabumetone)

In its promotional brochure (A98DA14990Q), Searle states that Daypro is "[s]uperior to Relafen 1000 mg" and "[c]omparable to Relafen 1500 mg." To substantiate these claims, Searle cites two references, an article by Weaver et al.[1] and an article by Makarowski et al.[2] Pursuant to DDMAC's telephone request of June 12, 1998, Searle submitted reprints of these articles. Both the Weaver et al. and Makarowski et al. articles contain summaries of studies comparing the efficacy and tolerability of Daypro, Relafen, and placebo in the treatment of osteoarthritis of the knee. The results of these two studies are presented in bar charts in the promotional brochure cited.

1 Weaver et al., *Comparison of the Efficacy and Safety of Oxaprozin and Nabumetone in the Treatment of Patients with Osteoarthritis of the Knee*, Clinical Therapeutics, 735, 742 (1995).
2 Makarowski, The Efficacy, Tolerability, and Safety of 1200 mg/d of Oxaprozin and 1500 mg/d of Nabumetone in the Treatment of Patients with Osteoarthritis of the Knee, Clinical Therapeutics, 114,124 (1996).

However, based upon these data, Searle cannot support a claim that Daypro is comparable or superior to Relafen. Comparative efficacy or safety advertising and promotional labeling must be based on substantial evidence. The data from Weaver et al. study only confirm that Daypro is superior to placebo in the treatment of osteoarthritis. These data are insufficient to serve as the substantial evidence necessary for claims of superiority of Daypro 1200 mg/day versus Relafen 1000 mg/day. Thus, claims of superiority for Daypro based upon the Weaver et al. data are false or misleading.

Similarly, after a review of the data derived from the Makarowski et al. study, DDMAC has concluded that it is insufficient to support claims of comparability of Daypro 1200 mg/day versus Relafen 1500 mg/day. Therefore, claims of comparability of Daypro 1200 mg/day versus Relafen 1500 mg/day based upon the Makarowski et al. data are false or misleading.

2. Misleading Implication of Improving Physical Function

In its promotional brochure, Searle suggests that the use of Daypro improves physical function. Through its use of the headline, "[r]elieve arthritis pain and inflammation to improve function," Searle implies that the use of Daypro results in improved joint function. Treatment with Daypro is symptomatic and the data submitted to date involves short-term studies in patients with knee or hip osteoarthritis (OA). Searle has not submitted data that demonstrate the use of Daypro improves the function of joints afflicted with osteoarthritis. Data from a validated knee or hip OA function measurement would need to be submitted for support of promotional claims concerning improved function in OA. Without such support, Searle's claims are false or misleading.

Additionally, on its poster (A98DA15057W-4), Searle states that the use of Daypro results in improvement in physician global assessments over time. This presentation suggests that the use of Daypro improves physical function over time. However, as noted above, Searle has not submitted data to support this claim. Thus, in the absence of such data, this claim is also false or misleading.

3. Misleading Health Related Quality of Life Claims

On its promotional poster (A98DA15057W-3), Searle presents data in bar chart form comparing the results after six weeks of therapy of Daypro 1200 mg/day, Relafen 1500 mg/day, and placebo based on changes in Quality of Life SF-36 scores. These data were derived from the Weaver et al. and Makarowski et al. studies discussed above. As noted previously, these studies are insufficient for comparative claims of efficacy between Daypro and Relafen. Moreover, Searle's presentation of these results misrepresent the findings from these two studies because Searle has

combined the results for Daypro from these two studies to suggest greater efficacy than was demonstrated. Searle has selectively presented only those quality-of-life parameters that suggest that Daypro is more effective than Relafen in the treatment of osteoarthritis, omitting those parameters where the results for the two drugs were similar. This presentation is false or misleading.

4. Lack of Fair Balance

In its advertisement in the professional website banners on the "Doctor's Guide Personal Edition," Searle makes representations concerning the efficacy of Daypro in the treatment of arthritis pain. DDMAC has reviewed these advertisements and regards them as lacking in fair balance or otherwise misleading under the Federal Food, Drug, and Cosmetic Act and regulations promulgated thereunder. These advertisements fail to present any information relating to side effects and contraindications or other risk information. This balancing risk information should be presented in a manner comparable in prominence and readability as the presentation of information relating to the effectiveness of the drug.

Searle should immediately suspend all promotional activities and materials that convey or contain the allegedly violative claims or information identified in this letter. Searle should submit a written response to DDMAC on or before August 14, 1998, describing the steps taken to ensure that the use of these materials, and all materials with the same or similar message, have been discontinued.

If Searle has any questions or comments, please contact the undersigned by facsimile at (301) 594-6771, or at the Division of Drug Marketing, Advertising and Communications, HFD-40, Rm 17B-20, 5600 Fishers Lane, Rockville, Maryland 20857. DDMAC reminds Searle that only written communications are considered official.

In all future correspondence regarding this matter, please refer to both the NDA number and the MACMIS ID #6682.

Sincerely,

Stephen W. Sherman, JD, MBA
Regulatory Review Officer
Division of Drug Marketing,
Advertising & Communications