



NOV 20 1996

**TRANSMITTED VIA FACSIMILE**

Raymond R. Sackler, M.D.  
President  
The Purdue Frederick Company  
100 Connecticut Avenue  
Norwalk, CT 06850-3590

**RE: NDA# 19-516**  
MS Contin (morphine sulfate controlled release) Tablets  
MACMIS ID #4247

**WARNING LETTER**

Dear Dr. Sackler:

This Warning Letter concerns The Purdue Frederick Company's (Purdue) promotional materials for the marketing of MS Contin (morphine sulfate controlled release) Tablets. The Division of Drug Marketing, Advertising, and Communications (DDMAC) has reviewed these materials as part of its monitoring and surveillance program. We have concluded that Purdue is disseminating promotional materials for MS Contin that contain statements, suggestions, or implications that are false or misleading in violation of the Federal Food, Drug, and Cosmetic Act (Act), 21 U.S.C. §§ 352(a) and 331(a) and applicable regulations. This violation is occurring despite repeated notification to Purdue by DDMAC that claims of product superiority were unsupported and were false and/or misleading and in violation of the Act.

The promotional materials disseminated by Purdue that are the subject of this letter are represented to be "reprints" of an article by Michael H. Levy entitled *Pharmacologic Management of Cancer Pain* that appeared in *Seminars in Oncology* (Vol. 21, No. 6, pages 718-739), December 1994.<sup>1</sup> These materials were

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<sup>1</sup> The materials Purdue represents to be reprints of the Levy article are identified as # OORM64 and # B4715. The OORM64 document appears to be a reprint of the original article that was published in *Seminars in Oncology*. Although portions of the article were deleted, these deletions are not relevant to the issues in this letter.

submitted to FDA by Purdue pursuant to the post-marketing reporting requirements for promotional labeling and advertising, 21 CFR 314.81(b)(3).

This Warning Letter does not concern Dr. Levy's published article. It does concern the use of reprints and promotional materials derived from the article that were disseminated by Purdue in its promotion of MS Contin.

## **VIOLATIONS**

These promotional materials contain false and/or misleading statements and suggestions that MS Contin is superior to other analgesics, either in effectiveness, safety, or other parameters, in the management of cancer pain. Specifically, the article states or suggests that controlled-release morphine (MS Contin) is superior to other opioid analgesics for chronic cancer pain. According to the modified reprint of the Levy article,<sup>2</sup>

- "Controlled-release morphine (MS Contin) is the best opioid analgesic for pain prevention in patients with chronic cancer pain." (See page 724).
- "MS Contin is recommended over Oramorph based on the smaller size and the color-coding of its tablets and the availability of its 15-mg and 200-mg dosage forms." (See page 724).
- "Because of its 12-hour dosing interval, MS Contin is the preferred opioid analgesic for these patients along with PRN supplements of MSIR for breakthrough pain." (See page 727).

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The promotional material identified as B4715 is a booklet entitled *Pharmacologic Management of Cancer Pain* by Michael H. Levy states that it was "reprinted with permission" citing to the original Levy article and was disseminated by Purdue. However, the content of the booklet is substantially different than the Levy article.

<sup>2</sup> The page numbers cited above refer to the modified reprint of the *Seminars in Oncology* article identified as # OORM64. The booklet, # B4715, does not have the identical content, but also contains suggestions that MS Contin is superior to other analgesics.

As you know, there are a variety of analgesic products, including other opioid products, other morphine products and other analgesic products for chronic cancer pain. Purdue has not demonstrated that MS Contin is superior in safety or effectiveness to either other morphine products, other opioid products, or other products used for pain control in cancer patients.

### **REPETITIVE CONDUCT**

The dissemination of these materials represents a repetitive course of violative conduct by Purdue in the promotion of MS Contin. Purdue has repeatedly disseminated materials that contain unsupported claims that MS Contin is superior to other analgesics including Oramorph. Such unsupported superiority claims have also appeared in brochures that targeted patients with cancer pain. DDMAC determined that these claims were false and/or misleading on several occasions and communicated this to Purdue in letters dated October 15, 1993, March 25, 1994, June 7, 1994, July 7, 1994, and October 3, 1994, and at a meeting between FDA and Purdue on March 24, 1994. Each of these instances involved Purdue's dissemination of promotional materials containing unsupported claims that MS Contin is, in some way, superior to its competitors' products.

### **CONCLUSION AND REQUESTED ACTIONS**

The materials and promotional messages Purdue disseminated contain false and/or misleading information about the safety and effectiveness of MS Contin. Accordingly, Purdue should propose a corrective 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, administrators at institutions, and organizations who received the violative messages.

This corrective action plan should also include:

- A. Immediately ceasing the dissemination of all materials that contain false, misleading, or unbalanced claims that state, suggest, or imply that MS Contin is better than other opioid analgesics, including other controlled release morphine products, for the control and management of cancer pain.
- B. A complete listing of all advertising and promotional materials that will remain in use and those that will be discontinued. Also, provide two copies of all promotional materials for MS Contin that Purdue intends to continue to distribute.

- C. Within 15 days of the date of this letter, disseminating a message to all Purdue sales representatives and marketing personnel involved in the marketing and sales of MS Contin, instructing them to immediately cease dissemination of all promotional materials and messages discussed in this letter and providing each person a copy of this letter.

The Dear Healthcare Professional letter and Purdue's corrective 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 MS Contin 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 Purdue's campaign for MS Contin and we may determine that additional remedial measures will be necessary to fully correct the false and/or misleading messages resulting from Purdue's violative conduct.

Purdue should respond to this letter no later than December 6, 1996. If Purdue has any questions or comments, please contact Thomas Abrams or Norman A. Drezin, Esq. by facsimile at (301) 827-2831, 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 Purdue that only written communications are considered official.

Failure to respond to this letter may result in regulatory action, including seizure and/or injunction, without further notice.

In all future correspondence regarding this particular matter, please refer to MACMIS ID #4247 in addition to the NDA number.

Sincerely,



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