DEPARTMENT OF HEALTH & HUMAN SERVICES

Public Health Service

Food and Drug Administration
Rockville MD 20857

NOV - 9 1999

TRANSMITTED VIA FACSIMILE

Edward Brann
Assistant Director, Regulatory Affairs
Janssen Pharmaceutica, Inc.
Janssen at Washington Crossing
1125 Trenton-Harbourton Road
P.O. Box 200
Titusville, New Jersey 08560-0200

Re: NDA #20-083
Sporanox (itraconazole) Capsules
MACMIS# 8281

Dear Mr. Brann:

As part of our routine monitoring program, the Division of Drug Marketing, Advertising, and Communications (DDMAC) has become aware of promotional materials for Sporanox (itraconazole) capsules by Janssen Pharmaceutica, Inc. (JPI) that violate the Federal Food, Drug and Cosmetic Act (Act) and its implementing regulations. Reference is made to visual aid (SP405), podiatry convention panel (SP394), pharmacy sell sheet (SP412), consumer file card (SP406), professional direct mail (SP407-1, 2 and 3), waiting room brochure (SP386), sample bins (SP416 and 416P), file card (SP392), managed care flash cards (MAN 053, 054, 055, 042 and 023R), and consumer compliance mailer (SP387E).

Unapproved Use

We note that you have previously received an untitled letter for making representations or suggestions in promotional materials not approved or permitted for use in the labeling (see letter dated March 27, 1997). In that letter, we objected to your promotion of the pulse dosing regimen of Sporanox in toenail onychomycosis because it is an unapproved dosing regimen. You responded that every effort was being made to prevent similar occurrences. However, you have continued to promote Sporanox pulse dosing in a manner

that suggests and represents that it is approved for toenail onychomycosis. Your promotional materials almost exclusively promote pulse dosing juxtaposed to promotion of all onychomycosis indications including toes and fingernails. Statements and presentations include, but are not limited to,

- Why did cowboys die with their boots on? ...[1]
- Why was Cinderella the only one at the ball wearing glass slippers? ...[2]
- Sporanox Pulse Pak; The Easy Way to *Kick* onychomycosis
- Pulse that *Kicks*
- Graphic of a foot on the cover of materials promoting pulse dosing
- Offering two options for Nail Fungus dosing (pulse and continuous) where the promotional material depicts a graphic of a foot and emphasizes the words "Pulse Dosing" and "Nail Fungus", but does not prominently disclose that the pulse dosing regimen is not approved for toenail fungus.[3]

Lack of Fair Balance

Prominence of Warnings in consumer promotional material

Generally, promotional materials are lacking in fair balance, or otherwise misleading if they fail to present the information relating to the contraindications, warnings, precautions and side effects with a prominence and readability reasonably comparable with the presentation of information relating to the effectiveness of the drug. The use of Sporanox is associated with risks which include a boxed warning concerning serious events including death when coadministered with certain drugs metabolized by the cytochrome P450 3A system. In contrast to the prominent presentations regarding the efficacy of Sporanox in consumer directed promotional materials using colorful bolded headings and white space, the presentations regarding risk information in these materials are minimized. For example, the risk information is presented in paragraph form with condensed text and no white space or other techniques to achieve emphasis to the information. Further, you have presented the

---

[1] Direct mail JPI SP-407-3
[2] Direct mail JPI SP-407-2
[3] For example, Consumer file card JPI SP-386

statement informing of potential serious cardiovascular events with the use of Sporanox, in a footnote with small print.[4]

Overstatement of Efficacy

An advertisement is false and/or misleading if it contains a representation or suggestion that the drug is more effective than has been demonstrated by substantial evidence. Phrases presented in the promotional materials such as "It's *Easy* to Kick Onychomycosis" and "*Easy* Way to Clear, Healthy Nails" suggests that by taking Sporanox, onychomycosis will be cured and nails will become clear. These statements are misleading because they overstate the efficacy of Sporanox. In fact, according to approved labeling, only 14% of patients with toenail onychomycosis are completely cured (mycological cure plus clinical cure- cleared of all signs, with or without residual nail deformity), and the overall success rate is 35% (mycological cure plus clear or minimal nail involvement with significantly decreased signs). Further, 21% of those who achieved overall success ultimately relapsed.

Unsubstantiated Claims

In the Managed Care Organization flash card materials,[5] you make the claims, "physician and patient preferred- 67% of people surveyed preferred the pulse therapy regimen" and "patient-preferred dosing". However, your reference does not represent substantial evidence to support these claims.

Action Requested

You should immediately cease distribution of these promotional materials. DDMAC is very concerned with the reoccurrence of promotion of the unapproved use described in this letter. In addition, you should conduct a review of all Sporanox materials and discontinue all other promotional materials for Sporanox[6] that contain the same or similar claims or presentations. You should submit a written response to us, on or before November 23, 1999 describing your intent and plans to comply with the above. In your letter to us, you should include a list of all promotional materials that were discontinued, and the discontinuation dates.

---

[4] For example, Consumer file card JPI SP-406
[5] Managed care flash cards JPI-MAN-023R, JPI-MAN-052, JPI-MAN-053
[6] Including, but not limited to, materials cited in this letter.

You should direct your response to me by facsimile at (301) 594-6771, or at the Food and Drug Administration, Division of Drug Marketing, Advertising, and Communications, HFD-42, Rm. 17B-20, 5600 Fishers Lane, Rockville, MD 20857. We remind you that only written communications are considered official. In all correspondence regarding this particular submission, please refer to MACMIS ID# 8281 in addition to the NDA number.

Sincerely,
/S/

Cheryl Y. Roberts
Regulatory Review Officer
Division of Drug Marketing,
Advertising and Communications