DEPARTMENT OF HEALTH & HUMAN SERVICES

Public Health Service

Food and Drug Administration
Rockville MD 20857

TRANSMITTED VIA FACSIMILE

FEB 19 1998

Carol D. Karp
Vice President, Regulatory Affairs
Vivus, Inc.
605 East Fairchild Drive
Mountain View, CA 94043

RE: NDA# 20-700
MUSE (alprostadil) urethral suppository
MACMIS ID #6115

Dear Ms. Karp:

As part of its routine monitoring and surveillance program, the Division of Drug Marketing, Advertising and Communications (DDMAC) has become aware of the following promotional materials for MUSE (alprostadil) urethral suppository that are in violation of the Federal Food, Drug, and Cosmetic Act (the Act) and applicable regulations.

Broadcast Advertisements

The broadcast advertisements (VIHL8303, VIHL 8304, VIHL 8305) for MUSE are misleading because the required information relating to the major side effects and contraindications is insufficiently communicated to the targeted consumer audience. The information is also not presented in a manner that is comparable to the presentation of information about effectiveness. Specifically, the voiceover that conveys the risk information regarding MUSE is read at a pace that is too rapid to effectively communicate this important information, especially given the complexity of information containing ratios, percentages, and unfamiliar terms. In addition, the statement "[t]hree percent of patients reported symptoms from lowering of blood pressure" does not adequately communicate to a consumer audience the potential severity of possible hypotensive related treatment emergent events associated with the drug. The risk disclosure should indicate the actual symptoms related to orthostasis that were observed in clinical trials for MUSE, including fainting, dizziness, and light-headedness.

Direct-To-Consumer (DTC) Journal Advertisement

The journal advertisement for MUSE that appears in the February 9, 1998, issues of *Newsweek* and *Time* magazines is misleading for the following reasons:

1. The ad fails to present information on side effects and contraindications with a prominence and readability comparable to information on effectiveness, taking into account all implementing factors, such as layout, typeography, white space, and any other techniques apt to achieve emphasis.

2. The prominent headline "IMPOTENCE IS OPTIONAL" implies that MUSE is more effective than has been demonstrated because it lacks adequate context. In our December 19, 1997, meeting, we discussed possible ways to provide information necessary to qualify this claim. One possible method that was discussed involved Vivus including a prominent "eyebrow" or sub-head, in direct conjunction with the headline, such as "For many men there may be a solution." However, the statement on page two lacks the prominence necessary to provide the context needed for the headline. Thus, the headline is misleading.

Press Release

The January 26, 1998, press release announcing the launch of Vivus' direct-to-consumer advertising campaign is misleading because it does not provide any information regarding contraindications, side effects, and other important risk information regarding MUSE.

In addition, DDMAC has no record that Vivus, Inc. (Vivus) submitted this promotional piece at the time of initial dissemination under Form FDA 2253, as required by 21 C.F.R. 314.81 (b) (3) (i).

Form FDA 2253 Submissions

Reference is also made to Vivus' November 24, 1997, and January 8, 1998, Form FDA 2253 submissions to DDMAC. DDMAC has determined that all of the promotional materials (listed below), contained in the submissions are in violation of the Act and regulations promulgated thereunder.

- Journal Ad (Material ID# VM00010297)
- Brochure (VM10010297)
- Brochure (VM50070197)
- Letter to Healthcare Providers (No Material ID#)
- Brochure (VM10720197)

The materials specified above are lacking in fair balance because the risk information is not presented with a prominence and readability reasonably comparable to claims of effectiveness, taking into account all implementing factors such as typography, layout, white space, etc.

In order to address these objections, DDMAC recommends that Vivus take the following actions:

1. Immediately discontinue the use of these, and all other promotional materials for MUSE that contain the same or similar violations.

2. Provide to DDMAC, in writing, a letter stating Vivus' intent to comply with #1 above. Your response should be received by March 5, 1998.

3. Provide a list of all promotional materials that have been discontinued.

If Vivus has any questions or comments, please contact the undersigned by facsimile at (301) 594-6771, or at the Food and Drug Administration, Division of Drug Marketing, Advertising and Communications, HFD-240, Rm 17B-20, 5600 Fishers Lane, Rockville, MD 20857. DDMAC reminds Vivus that only written communications are considered official.

In all future correspondence regarding this particular matter, please refer to MACMIS ID #6115 in addition to the NDA number.

Sincerely,

Mark W. Askine, R.Ph.
Regulatory Review officer
Division of Drug Marketing,
Advertising, and Communications