DEPARTMENT OF HEALTH & HUMAN SERVICES

Public Health Service

Food and Drug Administration
Rockville MD 20857

JAN 26 1998

TRANSMITTED VIA FACSIMILE

Jerry Klimek
Associate Director
Drug Regulatory Affairs
Associate General Counsel
Novartis Pharmaceuticals Corporation
59 Route 10
East Hanover, New Jersey 07936-1080

Re: NDA 20-261
Lescol (fluvastatin sodium)
MACMIS ID #5813

Dear Mr. Klimek:

Reference is made to Novartis Pharmaceuticals Corporation's (Novartis) July 21, 1997, form FDA 2253 submission for Lescol of a detail piece titled "Lescol Patients...You'll Know Them by Their Numbers" (LES-1043). Reference is also made to the journal advertisement "They're Lescol Patients.. You'll Know Them by Their Numbers" (LES-0197) appearing in the September 4, 1997, issue of The New England Journal of Medicine.

The Division of Drug Marketing, Advertising and Communications (DDMAC) has reviewed these materials and has determined that they are in violation of the Federal Food Drug and Cosmetic Act and applicable regulations for the following reasons:

Risk Information

The detail aid and the journal ad lack fair balance because they do not include important risk information for Lescol. The detail aid and journal ad fail to present the bolded warnings regarding monitoring liver function tests. The detail aid also fails to present the need to discontinue Lescol if markedly elevated CPK levels occur or myopathy is diagnosed or suspected. The journal ad fails to present the bolded warnings related to myopathy and rhabdomyolysis associated with the use of Lescol and the need to discontinue Lescol if markedly elevated CPK levels occur or myopathy is diagnosed or suspected.

In addition, the detail aid and the journal ad fail to present the most common adverse reactions for Lescol. Further, the statement in the detail aid, "Adverse reactions have usually been mild and similar in incidence to placebo," is misleading because it minimizes the side effect information by not including contextual information regarding the incidence rates. For example, the incidence of gastrointestinal (GI) side effects is greater for Lescol compared to placebo; i.e. dyspepsia 7.9% (Lescol) vs. 3.2% (placebo,) diarrhea 4.9% vs. 4.2%, abdominal pain 4.9% vs. 3.8%, and nausea 3.2% vs. 2.0%.

The journal ad and detail piece are also misleading because the risk information is presented in a manner that is not reasonably comparable to the presentation of efficacy information in terms of prominence and readability. The contraindications in the journal ad are presented in a nonprominent location as a footnote that overlays the graphic presentation of people jogging. The contraindications in the detail piece are presented in a nonprominent location as a footnote on the back cover. Other risk information in the detail aid is minimized by placement after a prominent presentation of the "TickerTape" Patient support program. The risk information is also difficult to read because it is presented in small type size and in block style with minimal white space.

DDMAC has previously objected to the lack of fair balance in promotional pieces for Lescol in our June 20, 1997, and August 13, 1996, letters. In the June 20, 1997 letter, DDMAC stated that a Lescol brochure lacked fair balance because it failed to provide the warning related to myopathy and rhabdomyolysis that may occur with Lescol. In the August 13, 1996 letter, DDMAC stated that a Lescol brochure was misleading because it failed to present adequate information regarding contraindications and warnings for Lescol.

Other Violative Issues

The journal ad is misleading because the indication is presented in a nonprominent location as a footnote overlaying the graphic presentation of people jogging. Lescol is indicated as an adjunct to diet in patients whose response to dietary restrictions has not been adequate. Without presenting this information prominently, Novartis suggests that Lescol may be used in a broader population than indicated. Further, the price disclaimer (price comparisons are not intended to imply similar levels of effectiveness and that retail pricing may vary) is presented as a small footnote that is difficult to read. This

footnoted information is not presented in a manner that would be sufficient to qualify the bold header "Unprecedented Value." DDMAC has previously objected to this similar issue in its August 13, 1996 letter to Novartis.

The journal advertisement has not been submitted to FDA by Novartis pursuant to the post-marketing reporting requirements for promotional labeling and advertising, 21 CFR §314.81(b)(3).

In order to address these violations, DDMAC requests that Novartis immediately discontinue the dissemination and use of the violative pieces noted in this letter and any other promotional materials that contain similar themes or presentations. DDMAC requests that Novartis submit a written response to this letter no later than February 9, 1998. This response should include:

- A list of all materials that have been discontinued; and
- Novartis' plan to comply with DDMAC's request.

If Novartis 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-40, Rm 17B-20, 5600 Fishers Lane, Rockville, MD 20857.

In all future correspondence regarding the materials discussed in this letter, please refer to MACMIS ID #5813 in addition to the NDA number.

Sincerely,

Anne M. Reb, NP
Regulatory Review Officer
Division of Drug Marketing,
Advertising and Communications