DEPARTMENT OF HEALTH & HUMAN SERVICES

Food and Drug Administration
Rockville MD 20857

FOI

TRANSMITTED VIA FACSIMILE

SEP 2 2 1999

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

Re: **Lescol (fluvastatin sodium) Capsules**
NDA 20-261
MACMIS ID # 8305

Dear Mr. Klimek:

As part of its routine monitoring program, the Division of Drug Marketing, Advertising, and Communications (DDMAC) has become aware of promotional materials for Lescol (fluvastatin sodium) that are lacking in fair balance or otherwise misleading. Reference is made to a flashcard (LES-1078), submitted under cover of Form FDA 2253 on July 19, 1999, and a single page leaflet (LES-F-1510), submitted on August 12, 1999. The dissemination of these materials by Novartis Pharmaceuticals (Novartis) violates the Federal Food, Drug, and Cosmetic Act (Act) and its implementing regulations. DDMAC requests that the use of the above referenced materials and those containing the same or similar violations cease immediately.

Lack of Fair Balance

Promotional materials may be lacking in fair balance, or otherwise misleading if they fail to present information relating to side effects and contraindications, with a prominence and readability reasonably comparable to the presentation of efficacy information. The aforementioned materials present efficacy or safety information in bold type with large print and utilize various color patterns and designs for emphasis. However, the risk information in both pieces is presented as a footnote in very small font at the bottom of

these materials.

Misleading cytochrome P450 3A4 interaction presentation

Promotional materials are false, lacking in fair balance, or otherwise misleading if they use statements or presentations that suggest that a drug is safer than another drug in some particular when it has not been demonstrated to be safer in such particular by substantial evidence or substantial clinical experience. Novartis makes statements and presentations about the hepatic metabolism of the HMG CoA Reductase Inhibitors ("HMGs") to imply that Lescol is safer than other HMGs (Lipitor, Baycol, Mevacor, and Zocor) without substantial evidence.

The presentation under the headers, "Lescol is not predominantly metabolized by cytochrome P450 3A4" and "Drugs that are metabolized by or inhibit cytochrome P450 3A4" is misleading because it makes an implied claim of superior safety that is not supported by substantial evidence. Specifically, the chart listing the hepatic metabolism of the HMGs (Lipitor, Baycol, Mevacor, and Zocor) among the listing of forty-three other drugs that are metabolized by or inhibit cytochrome P450 3A4 implies that Lescol will not interact with the listed drugs and that the other HMGs will. This implied claim of superior safety is not supported because not all the drugs listed have been shown to interact significantly with the other HMGs. Therefore, this presentation is misleading because it implies an unqualified risk (drug-interactions with all of the listed agents) associated with the use of other HMGs (and thus an advantage of Lescol) that is not supported by clinical data.

Importantly, there is also a clinically relevant distinction among the other forty-three drugs listed by Novartis. Specifically, this important distinction concerns substrates metabolized by cytochrome P450 3A4 and those drugs which inhibit cytochrome P450 3A4. In this regard, Novartis has not demonstrated to any clinically significant extent that the enzymatic metabolism of all of the substrates (listed in this chart) will have an effect, whether it is competitive or otherwise, on the metabolism of HMGs. The presentation by Novartis fails to make this distinction and thereby implies a clinically significant advantage for Lescol when compared to other HMGs. The statement, "Not a comprehensive list. Not all agents have been documented to have clinically significant drug interactions" buried in a footnote, in very small font, does not correct the prominent misleading implication.

Novartis should immediately cease using these, and all other promotional materials for Lescol that contain the same or similar violations. Novartis should submit a written response to DDMAC, on or before October 7, 1999, describing its intent and plans to comply with the above. In its letter to DDMAC, Novartis should include a list of all

promotional materials that were discontinued, and the discontinuation date.

Novartis should direct its response to the undersigned by facsimile at (301) 594-6771, or by written communication at the Division of Drug Marketing, Advertising, and Communications, HFD-40; Room 17B-20; 5600 Fishers Lane; Rockville, MD 20857. DDMAC reminds Novartis that only written communications are considered official.

In all correspondence related to this matter, please refer to MACMIS ID #8305 in addition to the NDA number.

Sincerely,

Michael A. Misocky R.Ph., J.D.
Regulatory Review Officer
Division of Drug Marketing,
Advertising, and Communications