



NDA 20-199/S-015

Hoffman-La Roche, Inc
Attention: Lynn DeVenezia-Tobias
Program Manager
Drug Regulatory Affairs
340 Kingsland Street
Nutley, NJ 017110-1199

Dear Ms. DeVenezia-Tobias:

Please refer to your New Drug Application (NDA) 20-199 for HIVID[®] (zalcitabine) tablets approved June 19, 1992 for use in combination with antiretroviral agents for the treatment of HIV infection. Also, please refer to your supplemental new drug application, SLR-015, dated August 27, 2001, received August 28, 2001, submitted under section 505(b) of the Federal Food, Drug, and Cosmetic Act.

This supplemental new drug application was submitted in response to requests from the Division to include information about fat redistribution in the package insert by adding the following language:

"PRECAUTIONS

- 3. *Fat Redistribution:*** Redistribution/accumulation of body fat including central obesity, dorsocervical fat enlargement (buffalo hump), peripheral wasting, facial wasting, breast enlargement, and "cushingoid appearance" have been observed in patients receiving antiretroviral therapy. The mechanism and long-term consequences of these events are currently unknown. A causal relationship has not been established.

Information for Patients: Patients should be informed that redistribution or accumulation of body fat may occur in patients receiving antiretroviral therapy and that the cause and long-term health effects of these conditions are not known at this time."

"ADVERSE REACTIONS

Body as a Whole: ...redistribution/accumulation of body fat (see PRECAUTIONS: *Fat Redistribution*)."

This supplemental new drug application also contains the following two minor spelling corrections:

WARNINGS

1. Peripheral Neuropathy: corrects the spelling of *occur* in the last paragraph of the section.

ADVERSE REACTIONS

Drug Interactions: Zidovudine: corrects the spelling of *stavudine*.

We have completed the review of this supplemental application, as amended, and have concluded that adequate information has been presented to demonstrate that the drug product is safe and effective for use as recommended in the agreed upon enclosed labeling text. Accordingly, the supplemental application is approved effective on the date of this letter.

The final printed labeling (FPL) must be identical to the enclosed labeling (text for the package insert).

Please submit the copies of final printed labeling (FPL) electronically according to the guidance for industry titled *Providing Regulatory Submissions in Electronic Format - NDA* (January 1999). Alternatively, you may submit 20 paper copies of the FPL as soon as it is available but no more than 30 days after it is printed. Please individually mount ten of the copies on heavy-weight paper or similar material. For administrative purposes, this submission should be designated "FPL for approved supplement NDA 20-199/SLR-015." Approval of this submission by FDA is not required before the labeling is used.

If a letter communicating important information about this drug product (*i.e.*, a "Dear Health Care Professional" letter) is issued to physicians and others responsible for patient care, we request that you submit a copy of the letter to this NDA and a copy to the following address:

MEDWATCH, HF-2
FDA
5600 Fishers Lane
Rockville, MD 20857

We remind you that you must comply with the requirements for an approved NDA set forth under 21 CFR 314.80 and 314.81.

If you have any questions, call Marsha S. Holloman, BS Pharm, JD, Regulatory Health Project Manager, at (301) 827-2335.

Sincerely,

{See appended electronic signature page}

Debra Birnkrant, MD
Director, Division of Antiviral Drug Products
Office of Drug Evaluation IV
Center for Drug Evaluation and Research

Enclosure: HIVID[®] Package Insert

**This is a representation of an electronic record that was signed electronically and
this page is the manifestation of the electronic signature.**

/s/

Debra Birnkrant
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NDA 20-199 SLR 015