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APPLICATION NUMBER:

17-430/S-026, S-027

APPROVAL LETTER

NDA 14-214/S-050, S-051
NDA 17-430/S-026, S-027

Sanofi-Synthelabo Inc.
Attention: Gary M. Lewis
Manager, Drug Regulatory Affairs
90 Park Avenue
New York, NY 10016

Dear Mr. Lewis:

Please refer to your supplemental new drug applications dated December 4, 1998 and April 27, 1999, received December 7, 1998 and April 30, 1999, submitted under section 505(b) of the Federal Food, Drug, and Cosmetic Act for NegGram® (nalidixic acid caplets) Caplets, 250 mg, 500 mg, 1 g (NDA 14-214/S-050 and S-051 respectively).

Please refer to your supplemental new drug applications dated December 4, 1998 and April 27, 1999, received December 7, 1998 and April 30, 1999, submitted under section 505(b) of the Federal Food, Drug, and Cosmetic Act for NegGram® (nalidixic acid suspension) Suspension, 250 mg/5 mL (NDA 17-430/S-026 and S-027 respectively).

We acknowledge receipt of your submissions to both NDA 14-214 and NDA 17-430 dated May 21, 1999 and October 26, 1999, received May 24, 1999 and November 1, 1999.

These supplemental new drug applications provide for the following changes to the label:

1. PRECAUTIONS

- In the **Information for Patients** subsection, another paragraph was added as follows:

> "Patients should be advised that convulsions have been reported in patients taking quinolones, including Nalidixic acid, and to notify their physician before taking this drug if there is a history of this condition. Patients should be advised that mineral supplements, vitamins with iron or minerals, calcium-, aluminum-, magnesium-based antacids, sucralfate or Videx®, (Didanosine), chewable/buffered tablets of the pediatric power for oral solution should not be taken within the two-hour period before or within the two-hour period after taking nalidixic acid (see **Drug Interactions**)."

- In the **Drug Interactions** subsection, the "antacids" statement was revised to read:

"Antacids containing magnesium, aluminum, or calcium; sucralfate or divalent or trivalent cations such as iron; multivitamins containing zinc; and Videx®, (Didanosine), chewable/buffered tablets or the pediatric power for oral solution may substantially interfere with the absorption of quinolones, resulting in systemic levels considerably lower than desired. These agents should not be taken within the two hour period before or within the two-hour period after nalidixic acid administration."

- A **Geriatric Use** subsection was added as follows:

"Clinical studies of NegGram® did not include sufficient numbers of subjects aged 65 and over to determine whether they respond differently from younger subjects. Other reported clinical experience has not identified differences in responses between the elderly and younger patients. Caution should therefore be observed in using nalidixic acid in elderly patients. This drug is known to be substantially excreted by the kidney, and the risk of toxic reactions to this drug may be greater in patients with impaired renal function. Because elderly patients are more likely to have decreased renal function, care should be taken in dose selection, and it may be useful to monitor renal function. (See PRECAUTIONS, General.)"

2. DOSAGE AND ADMINISTRATION

- An antacid statement was added to this section as follows:

"Antacids containing calcium, magnesium, or aluminum; sucralfate; divalent or trivalent cations such as iron; multivitamins containing zinc; or Videx® (didanosine), chewable/buffered tablets of the pediatric powder for oral solution should not be taken within the two-hour period before or within the two-hour period after taking nalidixic acid."

We have completed the review of these supplemental applications, 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 labeling text. Accordingly, these supplemental applications are approved effective on the date of this letter.

The final printed labeling (FPL) must be identical to the submitted draft labeling (package insert submitted October 26, 1999).

Please submit 20 copies of the FPL as soon as it is available, in no case more than 30 days after it is printed to each application. Please individually mount ten of the copies on heavy-weight paper or similar material. For administrative purposes, these submissions should be designated "FPL for approved supplements NDA 14-214/S-050, S-051 and NDA 17-430/S-026, S-027." Approval of these submissions by FDA is not required before the labeling is used.

NDA 14-214/S-050, S-051
NDA 17-430/S-026, S-027

If a letter communicating important information about this drug product (i.e., a "Dear Health Care Practitioner" 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, contact Robin Anderson, Regulatory Review Officer, at (301) 827-2127.

Sincerely,

Mark J. Goldberger, M.D., M.P.H.
Director
Division of Special Pathogen and Immunologic Drug Products
Office of Drug Evaluation IV
Center for Drug Evaluation and Research

APPEARS THIS WAY
ON ORIGINAL