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APPLICATION NUMBER:

21-087 / S-008
21-246 / S-003

ADMINISTRATIVE DOCUMENTS AND CORRESPONDENCE

DEPARTMENT OF HEALTH & HUMAN SERVICES Public Health Service

Food and Drug Administration
Rockville MD 20857

Memorandum of Project Manager's Labeling Review of Labeling Supplement Division of Antiviral Drug Products

NDA Number:	21-087/S-008 21-246/S-003
Date of Submission: Date Completed:	May 21, 2001 June 26, 2001
Applicant:	Hoffmann-La Roche Inc. 340 Kingsland Street Nutley, New Jersey 07110-1199
Product Name:	Tamiflu® (oseltamivir phosphate) Capsule and Oral Suspension
Materials Reviewed:	Final Printed Labeling submitted May 21, 2001

Background:

Labeling Supplements-Changes Being Effected (S-008 and S-008), submitted on May 21, 2001, provide for the following changes to the package and patient inserts:

- Information regarding treatment of influenza in geriatric patients
- Information regarding dosing of renally impaired patients with suspension formulation for prophylaxis of influenza.
- Clarification on age for pediatric indication.

The changes regarding dosing in geriatric patients are the result of a request from DAVDP.

The changes regarding dosing renally impaired patients are the result of extensive discussion between DAVDP and applicant during the reviews of both NDA 21-087/S-002 and NDA 21-246. These changes were dependent on the approval of the oral suspension (NDA 21-246), hence, delaying its implementation.

For further details please see the Medical Officer reviews. For minor editorial changes, please see the attached document compare.

REVIEW:

Labeling Revisions to the Patient Package Insert:

ADD: the following revised statment in the **INDICATIONS AND USAGE:** ***Treatment of Influenza*** section of the labeling.

Treatment of Influenza: TAMIFLU is indicated for the treatment of uncomplicated acute illness due to influenza infection in patients 1 year and older who have been symptomatic for no more than 2 days.

ADD: the following text in the ***Description of Clinical Studies: Studies in Naturally Occurring Influenza*** section of the labeling.

Geriatric Patients: Three double-blind placebo-controlled treatment trials were conducted in patients ≥65 years of age in three consecutive seasons. The enrollment criteria were similar to that of adult trials with the exception of fever being defined as >97.5°F. Of 741 patients enrolled, 476 (65%) patients were influenza-infected. Of the 476 influenza-infected patients, 95% were infected with influenza type A and 5% with influenza type B.

In the pooled analysis, at the recommended dose of TAMIFLU 75 mg twice daily for 5 days, there was a 1 day reduction in the median time to improvement in influenza-infected subjects receiving TAMIFLU compared to those receiving placebo (p=NS). However, the magnitude of treatment effect varied between studies.

DELETE: all text under the **PRECAUTIONS:** ***Geriatric Use*** section of the labeling and **REPLACE** with the following.

Geriatric Use: The safety of TAMIFLU has been established in clinical studies which enrolled 741 subjects (374 received placebo and 362 received TAMIFLU). Some seasonal variability was noted in the clinical efficacy outcomes (see *Description of Clinical Studies: Studies in Naturally Occurring Influenza:* Treatment of Influenza: Geriatric Patients).

ADD: the following revised statement in the **DOSAGE AND ADMINISTRATION:** ***Prophylaxis of Influenza*** section of the labeling.

Revisions to Patient Package Insert

There are NO changes to the Patient Package insert.

CONCLUSIONS/RECOMMENDATIONS:

It should be conveyed to the applicant that the proposed changes in the May 21, 2000 submission are acceptable.

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Grace N. Carmouze
Regulatory Project Manager
Division of Antiviral Drug Products

Supervisory Comment/Concurrence:

_____
Anthony W. DeCicco, R.Ph.
Chief, Project Management Staff
Division of Antiviral Drug Products

Attachments:
Document comparison between December 21, 2000 labeling and May 21, 2001 labeling
Clean copy of May 21, 2001 Final Printed Labeling.

WITHHOLD 32 PAGE(S)

Draft Labeling

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

/s/

Grace Carmouze
7/18/01 10:46:48 AM
CSO

Tony DeCicco
7/25/01 04:45:14 PM
CSO