CENTER FOR DRUG EVALUATION AND RESEARCH

APPLICATION NUMBER:

21-087 / S-009
21-246 / S-004

ADMINISTRATIVE DOCUMENTS AND CORRESPONDENCE

Division of Antiviral Drug Products

CONSUMER SAFETY OFFICER REVIEW

Application Number: NDA 21-087/S-009
NDA 21-246/S-004

Name of Drug: Tamiflu® (oseltamivir phosphate) Capsules and Oral Suspension

Sponsor: Hoffmann-La Roche

Material Reviewed:

Submission Date(s): July 9, 2001

Receipt Date(s): July 10, 2001

Background and Summary

Labeling Supplements-Changes Being Effected (S-009 and S-004), submitted on July 9, 2001, provide for additional wording under the Adverse Reactions, Observed During Clinical Practice for Treatment section of the label:

General: Rash, swelling of the face or tongue, toxic epidermal necrolysis
Digestive: Hepatitis, liver function tests abnormal.

These changes were requested by DAVDP as a result of hepatic dysfunction reports submitted to the FDA. It is noted that a causal relationship between Tamiflu and the hepatic dysfunction events has not been established.

For minor editorial changes, please see the attached document compare.

Review

In the **CLINICAL PHARMACOLOGY:** ***PHARMACOKINETICS*****: Table 2** section of the label, **DELETE** and **REPLACE** with **ADD** "AUC normalized to 48 hours" below Table 2.

In the **ADVERSE REACTIONS:** ***Observed During Clinical Practice for Treatment*** section of

the label, the following wording has been **REVISED**:

General: Rash, swelling of the face or tongue, toxic epidermal necrolysis
Digestive: Hepatitis, liver function tests abnormal

Conclusions

It should be conveyed to the applicant that the submission with proposed changes dated July 9, 2001 are acceptable.

{See appended electronic signature page}

Grace N. Carmouze
Regulatory Project Manager

Supervisory Comment/Concurrence:

{See appended electronic signature page}

Anthony W. DeCicco, R.Ph.
Chief, Project Management Staff

Drafted: GNC/September 28, 2001
Revised/Initialed:
Finalized:
Filename:
CSO LABELING REVIEW

Attachments:

- **Strikethrough version of Patient Insert and Patient Package Insert dated July 9, 2001**
- **Clean version of Patient Insert and Patient Package Insert dated July 9, 2001**

WITHHOLD 34 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
10/31/01 06:06:06 PM
CSO
CSO Review for NDA 21-087/S-009 and NDA 21-246/S-004
CSO Review

Tony DeCicco
11/2/01 03:23:39 PM
CSO

DEPARTMENT OF HEALTH & HUMAN SERVICES

Public Health Service

Food and Drug Administration
Rockville, MD 20857

NDA 21-246/S-004

CBE-0 SUPPLEMENT

Hoffmann-La Roche Inc.
Attention: Joanna Waugh
Program Director
340 Kingsland Street
Nutley, New Jersey 07110

Dear Ms. Waugh,

We have received your supplemental drug application submitted under section 505(b) of the Federal Food, Drug, and Cosmetic Act for the following:

Name of Drug Product: Tamiflu® (oseltamivir phosphate) for Oral Suspension

NDA Number: 21-246

Supplement number: S-004

Date of supplement: July 9, 2001

Date of receipt: July 10, 2001

This supplemental application was submitted as a "Supplement - Changes Being Effected." The appropriateness of reporting the proposed change(s) as changes being effected is under review.

Unless we notify you within 60 days of the receipt date that the application is not sufficiently complete to permit a substantive review, this application will be filed under section 505(b) of the Act on September 8, 2001 in accordance with 21 CFR 314.101(a).

All communications concerning this supplement should be addressed as follows:

Courier/Overnight Mail:
Food and Drug Administration
Center for Drug Evaluation and Research
Division of Antiviral Drug Products, HFD-530
Attention: Document Room
9201 Corporate Boulevard
Rockville, Maryland 20850

If you have any question, call Grace Carmouze, Regulatory Project Manager, at (301) 827-2335.

Sincerely yours,

Anthony W. DeCicco, R.Ph.
Chief, Project Management Staff
Division of Antiviral Drug Products
Office of Drug Evaluation IV
Center for Drug Evaluation and Research

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/s/

Tony DeCicco
7/25/01 04:52:10 PM