

NDA 021087/S-071
NDA 021246/S-054

**SUPPLEMENT APPROVAL
FULFILLMENT OF POSTMARKETING REQUIREMENT**

Hoffmann-La Roche, Inc.
c/o Genentech, Inc.
Attention: Peggy Omoruan
Program Manager, Regulatory Affairs
1 DNA Way
South San Francisco, CA 94080

Dear Ms. Omoruan:

Please refer to your supplemental new drug applications (sNDAs) dated and received on October 3, 2018, and your amendments, submitted under section 505(b) of the Federal Food, Drug, and Cosmetic Act (FDCA) for TAMIFLU® (oseltamivir phosphate) capsules, 30 mg, 45 mg, and 75 mg, and TAMIFLU® (oseltamivir phosphate) for oral suspension, 6 mg/ml.

These Prior Approval supplemental new drug applications provide for updates to the US prescribing information (USPI) based upon the data from clinical trial NV20234 which assessed the safety, tolerability and resistance profile of oseltamivir as a treatment for influenza in immunocompromised patients.

Specific updates to the USPI are as follows:

- **USE IN SPECIFIC POPULATIONS, *Immunocompromised Patients* subsection:** Editorial clarification to establish that the safety of TAMIFLU treatment for *prophylaxis* of influenza was obtained from a clinical trial in immunocompromised patients.
- **CLINICAL PHARMACOLOGY, *Microbiology* subsection:** updated with oseltamivir resistance information in the immunocompromised patient population obtained from clinical trial NV20234.
- **PATIENT INFORMATION:** The patient information (PPI) was revised to clarify that TAMIFLU for oral suspension should not be frozen to align with the information from the PI in the section entitled **HOW SUPPLIED/STORAGE AND HANDLING**.

In addition to the above, the container label for TAMIFLU® for oral suspension was updated to include the statement “Do not freeze” to align with the storage statements in the PI and PPI.

APPROVAL & LABELING

We have completed our review of these applications, as amended. They are approved, effective on the date of this letter, for use as recommended in the enclosed agreed-upon labeling.

WAIVER OF ½ PAGE LENGTH REQUIREMENT FOR HIGHLIGHTS

Please note that we have previously granted a waiver of the requirements of 21 CFR 201.57(d)(8) regarding the length of Highlights of Prescribing Information.

CONTENT OF LABELING

As soon as possible, but no later than 14 days from the date of this letter, submit the content of labeling [21 CFR 314.50(l)] in structured product labeling (SPL) format using the FDA automated drug registration and listing system (eLIST), as described at FDA.gov.¹ Content of labeling must be identical to the enclosed labeling (text for the Prescribing Information, Patient Package Insert and Instructions for Use), with the addition of any labeling changes in pending “Changes Being Effectuated” (CBE) supplements, as well as annual reportable changes not included in the enclosed labeling.

Information on submitting SPL files using eList may be found in the guidance for industry *SPL Standard for Content of Labeling Technical Qs and As*.²

The SPL will be accessible from publicly available labeling repositories.

Also within 14 days, amend all pending supplemental applications that include labeling changes for these NDAs, including CBE supplements for which FDA has not yet issued an action letter, with the content of labeling [21 CFR 314.50(l)(1)(i)] in Microsoft Word format, that includes the changes approved in this supplemental application, as well as annual reportable changes. To facilitate review of your submission(s), provide a highlighted or marked-up copy that shows all changes, as well as a clean Microsoft Word version. The marked-up copy should provide appropriate annotations, including supplement number(s) and annual report date(s).

¹ <http://www.fda.gov/ForIndustry/DataStandards/StructuredProductLabeling/default.htm>

² We update guidances periodically. For the most recent version of a guidance, check the FDA Guidance Documents Database <https://www.fda.gov/RegulatoryInformation/Guidances/default.htm>.

CARTON AND CONTAINER LABELING

Submit final printed container labeling that is identical to the enclosed container labeling, as soon as available, but no more than 30 days after they are printed. Please submit this labeling electronically according to the guidance for industry *Providing Regulatory Submissions in Electronic Format — Certain Human Pharmaceutical Product Applications and Related Submissions Using the eCTD Specifications*. For administrative purposes, designate this submission “**Final Printed Carton and Container Labeling for approved NDA 021087/S-054.**” Approval of this submission by FDA is not required before the labeling is used.

REQUIRED PEDIATRIC ASSESSMENTS

Under the Pediatric Research Equity Act (PREA) (21 U.S.C. 355c), all applications for new active ingredients (which includes new salts and new fixed combinations), new indications, new dosage forms, new dosing regimens, or new routes of administration are required to contain an assessment of the safety and effectiveness of the product for the claimed indication in pediatric patients unless this requirement is waived, deferred, or inapplicable.

Because none of these criteria apply to your applications, you are exempt from this requirement.

FULFILLMENT OF POSTMARKETING REQUIREMENT

We have received your submissions dated October 3, 2018, containing the final report for the following postmarketing requirement listed in the March 7, 2011, postapproval postmarketing commitment requirement letter under NDA 21087:

- 1734-1 Perform phenotypic resistance testing of neuraminidase activity and direct genotypic resistance testing of neuraminidase and hemagglutinin in a study to assess the safety and tolerability of oseltamivir when administered as treatment for influenza in immunocompromised patients.

We have reviewed your submission and conclude that the above requirement was fulfilled.

PROMOTIONAL MATERIALS

You may request advisory comments on proposed introductory advertising and promotional labeling. To do so, submit the following, in triplicate, (1) a cover letter requesting advisory comments, (2) the proposed materials in draft or mock-up form with annotated references, and (3) the Prescribing Information to:

OPDP Regulatory Project Manager
Food and Drug Administration
Center for Drug Evaluation and Research
Office of Prescription Drug Promotion (OPDP)
5901-B Ammendale Road
Beltsville, MD 20705-1266

Alternatively, you may submit a request for advisory comments electronically in eCTD format. For more information about submitting promotional materials in eCTD format, see the draft guidance for industry *Providing Regulatory Submissions in Electronic and Non-Electronic Format-Promotional Labeling and Advertising Materials for Human Prescription Drugs*.³

You must submit final promotional materials and Prescribing Information, accompanied by a Form FDA 2253, at the time of initial dissemination or publication [21 CFR 314.81(b)(3)(i)]. Form FDA 2253 is available at FDA.gov.⁴ Information and Instructions for completing the form can be found at FDA.gov.⁵ For more information about submission of promotional materials to the Office of Prescription Drug Promotion (OPDP), see FDA.gov.⁶

REPORTING REQUIREMENTS

We remind you that you must comply with reporting requirements for an approved NDA (21 CFR 314.80 and 314.81).

³ When final, this guidance will represent the FDA's current thinking on this topic. For the most recent version of a guidance, check the FDA guidance web page at <https://www.fda.gov/RegulatoryInformation/Guidances/default.htm>.

⁴ <http://www.fda.gov/downloads/AboutFDA/ReportsManualsForms/Forms/UCM083570.pdf>

⁵ <http://www.fda.gov/downloads/AboutFDA/ReportsManualsForms/Forms/UCM375154.pdf>

⁶ <http://www.fda.gov/AboutFDA/CentersOffices/CDER/ucm090142.htm>

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If you have any questions, call Suzanne Strayhorn, Sr. Regulatory Project Manager, at (240) 402-4247.

Sincerely,

{See appended electronic signature page}

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

ENCLOSURES:

- Content of Labeling
 - Prescribing Information
 - Patient Package Insert
 - Instructions for Use
- Container Labeling (TAMIFLU® for oral suspension)

This is a representation of an electronic record that was signed electronically. Following this are manifestations of any and all electronic signatures for this electronic record.

/s/

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