DEPARTMENT OF HEALTH AND HUMAN SERVICES

Food and Drug Administration
Silver Spring MD 20993

July 14, 2009

Thomas R. Frieden, MD, MPH
Director
Centers for Disease Control and Prevention
1600 Clifton Rd, MS D-14
Atlanta, GA 30333

Dear Dr. Frieden:

On April 27, 2009, a letter was issued authorizing the emergency use of certain oseltamivir phosphate capsules and oral suspension for treatment and prophylaxis of influenza subject to the terms of that letter. On the same day, an amendment to the letter was also issued.[1] I am issuing this letter in response to your July 7, 2009, request to address, among other things, issues that have arisen relating to certain oseltamivir phosphate oral suspension product for which the expiry has been extended under the federal government's Shelf Life Extension Program (SLEP). The letter of authorization, as amended, appears below in its entirety:

This letter is in response to your request that the Food and Drug Administration (FDA) issue an Emergency Use Authorization (EUA) for the emergency use of certain oseltamivir phosphate capsules and oral suspension for treatment and prophylaxis of influenza, pursuant to section 564 of the Federal Food, Drug, and Cosmetic Act (the Act) (21 U.S.C. § 360bbb-3).

On April 26, 2009, pursuant to section 564(b)(1)(C) of the Act (21 U.S.C. § 360bbb-3(b)(1)(C)), the Secretary of the Department of Health and Human Services (HHS) determined that a public health emergency exists involving Swine Influenza A that affects or has significant potential to affect national security. Pursuant to section 564(b) of the Act (21 U.S.C. § 360bbb-3(b)), and on the basis of such determination, the Secretary of HHS then declared an emergency justifying the authorization of the emergency use of certain oseltamivir phosphate products subject to the terms of any authorization issued under section 564(a) of the Act (21 U.S.C. § 360bbb-3(a)).

Having concluded that the criteria for issuance of this authorization under section 564(c) of the Act (21 U.S.C. § 360bbb-3(b)) are met, I am authorizing the emergency use of certain oseltamivir phosphate products[2] for the treatment and prophylaxis of influenza, subject to the terms of this authorization.

---

[1] Specifically, the letter was amended in the following two respects: (1) the reference on page 3 to "Fact Sheet for Patients and Recipients" was revised to read "Fact Sheet for Patients and Parents"; and (2) the correct authorized versions of the Tamiflu Fact Sheet for Health Care Providers and Tamiflu Fact Sheet for Patients and Parents were attached to the letter.

[2] FDA is authorizing the emergency use of Tamiflu (oseltamivir phosphate) (30 mg, 45 mg, and 75 mg) capsules and oral suspension for treatment and prophylaxis of influenza as described in the scope section of this letter (Section II). For ease of reference, this letter of authorization will use the terms "certain oseltamivir phosphate product(s)" and "authorized oseltamivir phosphate product(s)."

I. Criteria for Issuance of Authorization

I have concluded that the emergency use of certain oseltamivir phosphate products for the treatment and prophylaxis of influenza meets the criteria for issuance of an authorization under section 564(c) of the Act, because I have concluded that:

(1) Swine Influenza A can cause influenza, a serious or life-threatening disease or condition;

(2) based on the totality of scientific evidence available to FDA, it is reasonable to believe that certain oseltamivir phosphate products may be effective for the treatment and prophylaxis of influenza, and that the known and potential benefits of certain oseltamivir phosphate products, when used for the treatment and prophylaxis of influenza, outweigh the known and potential risks of such products; and

(3) there is no adequate, approved, and available alternative to the emergency use of certain oseltamivir phosphate products for the treatment and prophylaxis of influenza.[3]

Therefore, I have concluded that the emergency use of certain oseltamivir phosphate products for the treatment and prophylaxis of influenza meets the above statutory criteria for issuance of an authorization.

II. Scope of Authorization

I have concluded, pursuant to section 564(d)(1) of the Act, that the scope of this authorization is limited to the use of authorized oseltamivir phosphate products for the treatment and prophylaxis of influenza for individuals exposed to Swine Influenza A. The emergency use of authorized oseltamivir phosphate products under this EUA must be consistent with, and may not exceed, the terms of this letter, including the scope and the conditions of authorization set forth below.

The authorized oseltamivir phosphate products are as follows:

- Tamiflu (oseltamivir phosphate) (30 mg, 45 mg, and 75 mg) capsules
- Tamiflu (oseltamivir phosphate) oral suspension

Oseltamivir phosphate products are approved and indicated for the treatment of uncomplicated acute illness due to influenza infections in patients 1 year and older who have been symptomatic for no more than 2 days. Oseltamivir phosphate products are also approved and indicated for the prophylaxis of influenza in patients 1 year and older.[4]

---

[3] No other criteria of issuance have been prescribed by regulation under section 564(c)(4) of the Act.

[4] The approved labeling also states the following: "The following points should be considered before initiating treatment or prophylaxis with [oseltamivir phosphate products]: [Oseltamivir phosphate products are] not a substitute for early vaccination on an annual basis as recommended by the Centers for Disease Control and Prevention Advisory Committee on Immunization Practices. Influenza viruses change over time. Emergence of resistance mutations could decrease drug effectiveness. Other factors (for example, changes in viral virulence) might also diminish clinical benefit of antiviral drugs. Prescribers should consider available information on influenza drug susceptibility patterns and treatment effects when deciding whether to use [oseltamivir phosphate products.]"

1. The above oseltamivir phosphate products are authorized for use in patients less than 1 year old. Such products are also authorized for use at later time points (i.e., patients who are symptomatic for more than 2 days) and/or in patients sick enough to require hospitalization (i.e., patients who do not have "uncomplicated acute illness" per se).

2. The above oseltamivir phosphate products labeled consistent with the manufacturer's label are authorized to be distributed under this EUA. Such products are authorized to be distributed or dispensed without the requisite prescription label information under section 503(b)(2) of the Act (e.g., name and address of dispenser, serial number, date of prescription or of its filling, name of prescriber, name of patient, if stated on prescription, directions for use and cautionary statements, if contained in the prescription).

3a. The above oseltamivir phosphate products may include products that are deployed from the Strategic National Stockpile (SNS) and that are authorized to have their expiration date extended under the federal government's Shelf Life Extension Program (SLEP).

3b. Certain oseltamivir phosphate products that are: (i) identified by FDA, (ii) deployed from the SNS, and (iii) have passed SLEP testing are authorized to be distributed or dispensed without the SLEP-tested expiry on the label. The appropriate public health authority(ies) are authorized to label these products with the SLEP-tested expiry should the appropriate public health authority(ies) choose to do so.

4. The above oseltamivir phosphate products are authorized to be accompanied by the following written information pertaining to the emergency use, which are authorized to be made available to health care providers[5] and recipients:

- Fact Sheet for Health Care Provider
- Fact Sheet for Patients and Parents

CDC and the appropriate public health authority(ies) are also authorized to make available additional information relating to the emergency use of authorized oseltamivir phosphate products that is consistent with, and does not exceed, the terms of this letter of authorization. (See section IV).

I have concluded, pursuant to section 564(d)(2) of the Act, that it is reasonable to believe that the known and potential benefits of authorized oseltamivir phosphate products, when used for the treatment and prophylaxis of influenza, outweigh the known and potential risks of such products.

I have concluded, pursuant to section 564(d)(3) of the Act, based on the totality of scientific evidence available to FDA, that it is reasonable to believe that the authorized oseltamivir phosphate products may be effective for the treatment and prophylaxis of influenza pursuant to

[5] It is possible that public health officials or other volunteers might distribute authorized oseltamivir phosphate products to recipients, if permitted, in accordance with applicable state and local law and/or in accordance with the public health and medical emergency response of the Authority Having Jurisdiction to prescribe, administer, deliver, distribute, or dispense the covered countermeasures, and their officials, agents, employees, contractors, or volunteers following a declaration of an emergency. For ease of reference, this letter will use the term "health care provider(s)" to refer collectively to these individuals.

section 564(c)(2)(A) of the Act. FDA has reviewed the scientific information available, including the information supporting the conclusions described in Section I above, and concludes that the authorized oseltamivir phosphate products, when used for the treatment and prophylaxis of influenza in the specified population, meet the criteria set forth in section 564(c) of the Act concerning safety and potential effectiveness.[6]

Subject to the terms of this EUA and under the circumstances set forth in the Secretary of HHS's determination under section 564(b)(1)(C) described above and the Secretary of HHS's corresponding declaration under section 564(b)(1), the oseltamivir phosphate products described above are authorized for the treatment and prophylaxis of influenza for individuals exposed to Swine Influenza A.

This EUA will cease to be effective when the declaration of emergency is terminated under section 564(b)(2) of the Act or when the EUA is revoked under section 564(g) of the Act.

III. Current Good Manufacturing Practice

In the letter dated April 27, 2009, current good manufacturing practice (CGMP) requirements were waived with respect to the holding of authorized oseltamivir phosphate products by CDC and other public health authority(ies) for a period of ninety days (the "First Waiver"). As of the date of this letter, I terminate the First Waiver and replace it with the following waiver:

Although authorized oseltamivir phosphate products should be held in accordance with CGMP holding requirements, including appropriate product storage conditions[7], I am waiving CGMP requirements with respect to the holding of authorized oseltamivir phosphate products by CDC and other public health authority(ies) for a maximum of 90 days (consecutive or non-consecutive) from the date of shipment to the public health authority. However, this waiver is also limited in that the products may be stored with temperature excursions in excess of 40°C for a total cumulative period of 14 days (consecutive or non-consecutive) within that 90 days. Other temperature excursions outside labeled temperature storage conditions and not in excess of 40°C are permitted within the 90-day period.

IV. Conditions of Authorization

Pursuant to section 564 of the Act, I am establishing the following conditions on this authorization:

---

[6] Please note that with respect to authorized oseltamivir phosphate products for use in patients less than 1 year old, the conclusions above are based on limited data available for review under the limited timeframe given the circumstances of the emergency. The conclusions above may evolve as the emergency circumstances evolve and as more information becomes available.

[7] See Tamiflu Capsule and Oral Suspension product labeling or http://www.accessdata.fda.gov/drugsatfda_docs/label/2008/021087s047,%20021246s033lbl.pdf for oseltamivir phosphate product storage conditions.

CDC

A. CDC will verify that authorized oseltamivir phosphate products distributed to the Receive, Stage, Storage (RSS) sites are within unexpired labeled dates or within authorized SLEP-tested expiry dates whether relabeled or not.

B. For oseltamivir phosphate products identified in Section II.3.b. of this letter, information on the lot numbers of the oseltamivir phosphate products identified by FDA will be made available by CDC to the appropriate public health authority(ies), healthcare providers, and recipients (patients and parents) through appropriate means.

C. CDC will ensure that the appropriate public health authority(ies) are informed of this EUA, including the terms and conditions herein.

D. CDC will make available to the appropriate public health authority(ies) through appropriate means the authorized Fact Sheet for Health Care Providers, Fact Sheet for Patients and Parents, and at least one representative FDA-approved package insert that covers the dosage forms and strengths of authorized oseltamivir phosphate products.

E. Only CDC may request changes to the authorized Fact Sheet for Health Care Providers and authorized Fact Sheet for Patients and Parents. Such requests will be made by contacting FDA concerning FDA review and approval.

Public Health Authority(ies)

F. The appropriate public health authority(ies) will ensure that authorized oseltamivir phosphate products are distributed to recipients in accordance with applicable laws and/or in accordance with the public health and medical emergency response of the Authority Having Jurisdiction to prescribe, administer, deliver, distribute, or dispense the covered countermeasures, and their officials, agents, employees, contractors, or volunteers following a declaration of an emergency.

G. The appropriate public health authority(ies) will make available through appropriate means authorized Fact Sheet for Health Care Providers, Fact Sheet for Patients and Parents, and at least one representative FDA-approved package insert that covers the dosage forms and strengths of authorized oseltamivir phosphate products.

H. The appropriate public health authority(ies) are authorized to label the oseltamivir phosphate products identified in Section II.3.b. with the SLEP-tested expiry, should the appropriate public health authority(ies) choose to do so.

CDC and Public Health Authority(ies)

I. CDC and the appropriate public health authority(ies) are also authorized to make available additional information relating to the emergency use of authorized oseltamivir

phosphate products that is consistent with, and does not exceed, the terms of this letter of authorization.

The emergency use of authorized oseltamivir phosphate products as described in this letter of authorization must comply with the conditions above and all other terms of this authorization.

V. Duration of Authorization

This EUA will be effective until the declaration of emergency is terminated under section 564(b)(2) of the Act or the EUA is revoked under section 564(g) of the Act.

Joshua M. Sharfstein, M.D.
Principal Deputy Commissioner

cc: Administrator, Agency for Toxics Substance and Drug Registry
c/o Regulatory Affairs, SSPU/CCID
1600 Clifton Rd, MS C-12