DEPARTMENT OF HEALTH AND HUMAN SERVICES

Food and Drug Administration
Silver Spring MD 20993

October 30, 2009

Thomas R. Frieden, MD, MPH
Director
Centers for Disease Control and Prevention
1600 Clifton Rd, MS D-14
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Dear Dr. Frieden:

On April 27, 2009, a letter was issued authorizing the emergency use of certain zanamivir inhalation powder 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 October 29, 2009 request to address, among other things, issues that have arisen relating to certain zanamivir products deployed from the Strategic National Stockpile that are beyond or will be beyond their expiration date before the declaration of emergency underlying this EUA has terminated. FDA is issuing this amendment to address both categories of zanamivir products, as further described below. 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 zanamivir inhalation powder 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 (DHHS) determined that a public health emergency exists involving Swine Influenza A (now called 2009-H1N1 flu) 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 DHHS then declared an emergency justifying the authorization of the emergency use of certain zanamivir products subject to the terms of any authorization issued under section 564(a) of the Act (21 U.S.C. § 360bbb-3(a)). The Secretary's determination of emergency has been renewed. The Secretary's April 26, 2009 declaration of emergency justifying an EUA remains in effect.

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 zanamivir 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 respect: the correct authorized versions of the Zanamivir Fact Sheet for Health Care Providers and Zanamivir Summary Fact Sheet for Patients and Parents were attached to the letter.

[2] FDA is authorizing the emergency use of Relenza (zanamivir) inhalation powder 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 zanamivir product(s)" and "authorized zanamivir product(s)."

I. Criteria for Issuance of Authorization

I have concluded that the emergency use of certain zanamivir 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) 2009-H1N1 flu 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 zanamivir products may be effective for the treatment and prophylaxis of influenza, and that the known and potential benefits of certain zanamivir 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 zanamivir products for the treatment and prophylaxis of influenza.[3]

Therefore, I have concluded that the emergency use of certain zanamivir 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 zanamivir products for the treatment and prophylaxis of influenza for individuals exposed to 2009-H1N1 flu. The emergency use of authorized zanamivir 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.

<u>The authorized zanamivir products are as follows:</u>

- Relenza (zanamivir) Inhalation Powder

Zanamivir products are approved and indicated for the treatment of uncomplicated acute illness due to influenza A and B virus in adults and pediatric patients 7 years of age and older who have been symptomatic for no more than 2 days. Zanamivir products are also approved and indicated for prophylaxis of influenza in adults and pediatric patients 5 years of age and older.[4]

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

[4] Zanamivir products are not recommended for treatment or prophylaxis of influenza in individuals with underlying airways disease (such as asthma or chronic obstructive pulmonary disease) due to risk of serious bronchospasm. Zanamivir products have not been proven effective for treatment of influenza in individuals with underlying airways disease. Zanamivir products have not been proven effective for prophylaxis of influenza in the nursing home setting. Zanamivir 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

1. The above zanamivir products are 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 zanamivir 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), except for product described in paragraph 3c. below that is held by entities that are not public health authorities.

3. Certain zanamivir products that are (i) identified by FDA and (ii) are beyond or will be beyond their expiration dates before the declaration of emergency underlying this EUA has terminated are authorized to be distributed or dispensed subject to the terms and conditions of this authorization.

4. The above zanamivir 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/Caretakers

CDC and the appropriate public health authorities are also authorized to make available additional information relating to the emergency use of authorized zanamivir 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 zanamivir 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 zanamivir products may be effective for the treatment and prophylaxis of influenza pursuant to 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 zanamivir products, when used for the treatment and prophylaxis of influenza in the specified

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consider available information on influenza drug susceptibility patterns and treatment effects when deciding whether to use zanamivir products. There is no evidence for efficacy of zanamivir in any illness caused by agents other than Influenza A and B. Patients should be advised that the use of zanamivir products for treatment of influenza has not been shown to reduce the risk of transmission of influenza to others.

[5] It is possible that public health officials or other volunteers might distribute authorized zanamivir products to recipients (except as limited in IV.E below), 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.

population, meet the criteria set forth in section 564(c) of the Act concerning safety and potential effectiveness.

Subject to the terms of this EUA and under the circumstances set forth in the Secretary of DHHS's determination under section 564(b)(1)(C) described above and the Secretary of DHHS's corresponding declaration under section 564(b)(1), the zanamivir products described above are authorized for the treatment and prophylaxis of influenza for individuals exposed to 2009-H1N1 flu.

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 zanamivir products by CDC and other public health authorities 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 zanamivir products should be held in accordance with CGMP holding requirements, including appropriate product storage conditions,[6] I am waiving CGMP requirements with respect to the monitoring and calculating of mean kinetic temperature by CDC and other public health authorities so long as to the extent practicable given the circumstances of the emergency, temperature is monitored. I also am waiving CGMP requirements with respect to holding at the labeled storage conditions in that the products may be stored with temperature excursions up to 40°C for a total cumulative period of 7 days (consecutive or non-consecutive) from the date of shipment to the public health authority.

IV. Conditions of Authorization

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

CDC

A. CDC will verify that zanamivir products distributed to the Receive, Stage, Storage (RSS) sites are within their labeled expiration dates, or are beyond or will be beyond their expiration dates before the termination of the Secretary's declaration of emergency and have been identified by FDA under Section II.3.

B. For zanamivir products identified in Section II.3 of this letter, information on the lot numbers of the zanamivir products identified by FDA will be made available by CDC to

[6] See FDA-approved product labeling for zanamivir products storage conditions (http://www.accessdata.fda.gov/drugsatfda_docs/label/2008/021036s017lbl.pdf)

the appropriate public health authorities, healthcare providers, and recipients (patients and parents/caretakers) through appropriate means.

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

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

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

Public Health Authorities[7]

F. The appropriate public health authorities will ensure that authorized zanamivir 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.[8]

G. The appropriate public health authorities will make available through appropriate means authorized Fact Sheets for Health Care Providers, authorized Fact Sheets for Patients and Parents/Caretakers, and at least one representative FDA-approved package insert that covers the dosage forms and strengths of authorized zanamivir products.

Entities That Are Not Public Health Authorities

H. Entities acting under Section II.3 that are neither (a) public health authorities nor (b) acting in accordance with the Authority Having Jurisdiction to prescribe, administer, deliver, distribute, or dispense covered countermeasures will ensure that authorized zanamivir products are prescribed and dispensed to recipients in accordance with applicable laws that are consistent with this letter of authorization and with applicable federal public health guidelines that are consistent with this letter of authorization.

I. Entities acting under Section II.3 that are neither (a) public health authorities nor (b) acting 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 that dispense authorized zanamivir products, will make

[7] Conditions E and F apply to entities that are not public health authorities, but are acting under the public health and medical emergency response of the Authority Having Jurisdiction to prescribe, administer, deliver, distribute, or dispense the covered countermeasures.

[8] For more information about the terms "Authority Having Jurisdiction" and "covered countermeasures," see Public Readiness and Emergency Preparedness (PREP) Act, sections 319F-3 and 319F-4 of the Public Health Service Act (codified at 42 U.S.C. §§247d-6d, 247d-6e), and the PREP Act declaration regarding pandemic influenza antivirals. See http://www.hhs.gov/disasters/discussion/planners/prepact/.

available through appropriate means the authorized Fact Sheet for Health Care Providers, Fact Sheet for Patients and Parents/Caretakers, and at least one representative FDA-approved package insert that covers the dosage forms and strengths of authorized zanamivir products.

CDC and Public Health Authorities

J. CDC and the appropriate public health authorities are also authorized to make available additional information relating to the emergency use of authorized zanamivir products that is consistent with, and does not exceed, the terms of this letter of authorization.

The emergency use of authorized zanamivir 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.

Margaret A. Hamburg, M.D.
Commissioner of Food and Drugs