European Medicines Agency

London, 8 May 2009
Doc. Ref. EMEA/273535/2009

# Questions and answers on the use of antiviral medicines in case of novel influenza A/H1N1 pandemic

In view of the recent outbreak of the novel influenza virus A/H1N1, the European Medicines Agency has reviewed the use of the antiviral medicines Tamiflu (oseltamivir) and Relenza (zanamivir). The Agency's Committee for Medicinal Products for Human Use (CHMP) has recommended that during a declared pandemic:

- Tamiflu can be used in children younger than one year of age;
- Tamiflu and Relenza can be used in women who are pregnant or breastfeeding;
- Tamiflu capsules that have already been distributed may be used for an additional two years after the current expiry dates.

This review was carried out under an Article 5(3) procedure[1].

**What is Tamiflu?**
Tamiflu is currently authorised to treat or prevent influenza in adults and children over the age of one year. Tamiflu has been authorised in all countries of the European Union (EU) since June 2002. The company that makes Tamiflu is Roche Registration Limited.
The active substance in Tamiflu, oseltamivir, is a 'neuramidase inhibitor'. It acts specifically on the influenza virus, blocking some of the enzymes on its surface, known as neuramidases. When the neuramidases are blocked, the virus cannot spread.

**What is Relenza?**
Relenza is another neuramidase inhibitor currently authorised to treat or prevent influenza in adults and children from the age of five years. Relenza was first authorised in Sweden in 1999 and is currently authorised in all countries of the EU. The company that makes Relenza is GlaxoSmithKline.

**How can antiviral medicines be used in case of an influenza pandemic?**
In case of an influenza pandemic, the use of antiviral medicines, such as Tamiflu and Relenza, should be based on official recommendations. If an influenza pandemic is declared by the World Health Organization (WHO), antiviral medicines will be supplied through governmental organisations in accordance with national pandemic plans, together with instructions on when and how to use the medicines. In preparation for this, governments worldwide have been stockpiling antiviral medicines, such as Tamiflu.

**Why is the EMEA reviewing Tamiflu and Relenza?**
The current outbreak of novel influenza virus A/H1N1 has been classified by the WHO as being able to trigger a pandemic. The WHO also stated that the neuramidase inhibitors such as oseltamivir and zanamivir have shown effectiveness against the novel virus. In preparation for an influenza pandemic, the European Medicines Agency has been looking at a number of ways to ensure that antiviral medicines are available to those who might need them.

On 30 April 2009, the Executive Director of the Agency requested that the CHMP give its scientific opinion on the following issues:

[1] Article 5(3) of Regulation (EC) No 726/2004, opinion on any scientific matter concerning the evaluation of medicinal products for human use.

7 Westferry Circus, Canary Wharf, London E14 4HB, UK
Tel. (44-20) 74 18 84 00 Fax (44-20) 74 18 84 16
E-mail: mail@emea.europa.eu http://www.emea.europa.eu

- the possible use of Tamiflu capsules already on the market for two additional years after the current expiry dates, considering that the shelf life for newly manufactured Tamiflu capsules is being extended from five to seven years;
- the use of Tamiflu in children under the age of one year to prevent or treat the novel influenza A/H1N1;
- the use of Tamiflu and Relenza in women who are pregnant or breastfeeding to prevent or treat the novel influenza A/H1N1.

**Which data has the CHMP reviewed?**
To make a recommendation on the use of Tamiflu capsules beyond five years, the Committee looked at data on the condition of the capsules after seven years, in particular the impurities and degradation products that may develop during storage.
For the use of Tamiflu in infants below the age of one, the Committee looked at the interim results of an ongoing study in children under one year, two previous studies and a retrospective analysis in children.
Regarding the use of Tamiflu in pregnant women, the CHMP reviewed evidence from the published literature and data provided by the company on 232 cases of women who took the medicine during pregnancy.
For Relenza, the CHMP reviewed data previously provided by the company on women who took the medicine during pregnancy or while breastfeeding.

**What are the conclusions of the CHMP?**
Based on the data submitted by the company, the CHMP recommended an extension of the shelf life of Tamiflu capsules from five to seven years. During a novel influenza A/H1N1 pandemic, this extension will also apply to the capsules already distributed, including those that have already expired provided that they have been kept in appropriate conditions (at room temperature). This might help to prevent shortages.

In case of a pandemic, the Committee agreed that there is enough evidence to support the use of the Tamiflu for the treatment in children younger than one year of age. The Committee noted that there is less evidence to support the use of Tamiflu for the prevention of influenza. Therefore doctors should carefully consider the benefits and risks for each infant. Should Tamiflu be prescribed to children under the age of one, the recommended dosage is 2 to 3 mg per kg body weight.

In case of a pandemic, the Committee agreed that there is enough evidence to support the use of Tamiflu and Relenza in pregnant and breastfeeding women.

**What are the recommendations for patients?**
- Patients who have expired Tamiflu capsules should not dispose of them as they might be asked to use them in case of the A/H1N1pandemic;
- Patients must not take Tamiflu capsules unless they receive clear instructions from their doctor or health authorities;
- Patients who have any further questions should speak to their doctor or pharmacist.

**What are the recommendations for prescribers?**
- Doctors should follow official recommendation when prescribing antiviral medicines such as Tamiflu and Relenza during a pandemic;
- The current CHMP recommendation on the extended use of Tamiflu and Relenza will only apply in case of a influenza A/H1N1 pandemic;
- Doctors should continue to prescribe Tamiflu and Relenza for seasonal influenza according to the current prescribing information.

**What will happen next?**

The CHMP opinion will be communicated to the Member States, so that they act accordingly. For further information, see the scientific opinion adopted by the CHMP on 7 May 2009.