European Medicines Agency

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OPINION OF THE COMMITTEE FOR MEDICINAL PRODUCTS FOR HUMAN USE PURSUANT TO ARTICLE 5(3) OF REGULATION (EC) No 726/2004, ON
Novel Influenza (H1N1) outbreak
Tamiflu (oseltamivir)
Relenza (zanamivir)

Basis for opinion

On 30 April 2009, the EMEA requested the CHMP to give an opinion under Article 5(3) of Regulation (EC) No 726/2004 on the use of Tamiflu and Relenza in specific populations, as a result of the outbreak of the novel influenza A (H1N1).

Specifically, the Committee was requested to provide advice on the following four issues:

1. The potential usability of Tamiflu (oseltamivir) capsules already on the market in the EU for which the expiry date has already passed, taking into account
   - The outcome of the ongoing variation procedure to extend the shelf-life from 5 to 7 years, and
   - The exceptional potential health implications that may result from a shortage of Tamiflu available in the EU.

   Such recommendation should also elaborate on the conditions to be fulfilled, e.g. in terms of the storage conditions to be adhered to. The CHMP should also consider whether it is in a position to provide a recommendation regarding the usability of oseltamivir bulk over the extended period.

2. The appropriateness of administering Tamiflu (oseltamivir) to children younger than 1 year of age to treat or prevent the novel Influenza A (H1N1) in case of a pandemic. If appropriate, the CHMP should make dosing recommendations.

3. The use of Tamiflu (oseltamivir) during pregnancy and lactation to treat or prevent the novel Influenza A (H1N1) in case of a pandemic,

4. The use of Relenza (zanamivir) during pregnancy and lactation to treat or prevent the novel Influenza A (H1N1) in case of a pandemic.

On the basis of the request made by the EMEA, the CHMP considered that there were sufficient grounds to start the procedure.

The procedure started on 30 April 2009.

Opinion

The CHMP, having considered the matter as set out in the appended assessment report (Appendix 1), reviewed the available evidence and came to the conclusion that:

Due to the public health emergency linked to the current risk of pandemic influenza, and based on data made available regarding the stability of Tamiflu (Oseltamivir) 30mg, 45mg and 75mg capsules for an additional period of 2 years, the CHMP recommends that boxes of Tamiflu capsules should not

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be discarded where the expiry date has already passed. For these batches an updated expiry date should be determined by adding a further period of 2 years to the stated expiry date.
The conditions of storage play a role in the stability of medicinal products. It is of great importance that these boxes have always been kept and remains stored below 25°C.

It is acknowledged that limited data are available supporting the use of Tamiflu in children below 1 year of age. However considering the urgent need for recommendations to treat this population **in case of a pandemic influenza is declared by the WHO in the context of the Novel influenza A (H1N1) outbreak**, the CHMP recommends:
1. To treat children below 1 year of age with Tamiflu.
2. The appropriate dosage to treat children below 1 year of age is 2-3mg/kg twice daily during 5 days.
3. The post-exposure prophylaxis of children below 1 year of age should be very carefully considered by prescribers. If it is decided to prescribe Tamiflu to prevent influenza for children below 1 year of age who have been exposed to the virus, the appropriate dose should be 2-3mg/kg once a day during 10 days.
4. The paediatric suspension or dilution of the capsules of Tamiflu can be used to prepare the dose in children below 1 year of age.
5. Children below 1 year of age should be treated under medical supervision. However in case of pandemic influenza, this recommendation could potentially place huge burden on hospital resources and therefore, the CHMP strongly recommends that at least children below 3 months of age are treated under medical supervision in hospital.

This review seems to show that no new safety risks to foetus are connected to the use of Tamiflu in pregnant women. At the moment the statement in section 4.6. of the SPC "*Oseltamivir should not be used during pregnancy unless the potential benefit to the mother justifies the potential risk to the foetus*." remains valid for **seasonal influenza** epidemics.
However, the overall data suggest that the benefit of using Tamiflu in pregnant or breastfeeding women outweighs the risk in the context of a **novel influenza (H1N1) in a pandemic situation.**

At the moment the statement in section 4.6. of the SPC "*Relenza should not be used in pregnancy unless the expected benefit to the mother is thought to outweigh any possible risk to the foetus*." remains valid for **seasonal influenza** epidemics.
Zanamivir has in animal studies been shown to cross the placenta and to be secreted in breast milk. The non-clinical data are not indicative of any relevant cause for concerns regarding the safe use of Relenza at recommended doses.
Taken together the overall data suggest that the benefit of using Relenza in pregnant or breastfeeding women outweighs the risk in the context of a **novel influenza (H1N1) in a pandemic situation.**

The Icelandic and the Norwegian CHMP members agree with the above-mentioned recommendation of the CHMP.

This opinion is forwarded all Member States, Iceland, Norway and to the European Commission together with its appendix.

The opinion will be published on the EMEA website with its appendix.

London, 7 May 2009

On behalf of the CHMP
Dr Eric Abadie, Chairman

Appendix 1

CHMP Assessment Report on Article 5(3) of Regulation (EC) No 726/2004 for Tamiflu (oseltamivir) and Relenza (zanamivir)in the context of the Novel Influenza (H1N1) outbreak, dated 7 May 2009