Pandemic influenza

Recommendations on the use of antiviral medicines for pregnant women, women who are breastfeeding and children under the age of one year

Updated September 2009

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Author	DH
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Circulation List	Voluntary Organisations/NDPBs, Royal College of Obstetricians and Gynaecologists; Royal College of Midwifery; Royal College of Nursing; Royal College of General Practitioners; British Medical Association; Department of Health Maternity Matters Action Group
Description	This document identifies key issues and provides a guidance framework to enable and support the decisions on prioritisation that maternity services providers in hospitals, general practices and community care will need to take during a pandemic, covering the period from conception to just after birth. This supplementary information extends and updates the existing advice on the use of antiviral medicines in the maternity and neonatal setting.
Cross Ref	Pandemic flu: a national framework for responding to an influenza pandemic
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For Recipient's Use	

Background

As with most medicines with recently granted marketing authorisations there is only limited evidence to support the use of Tamiflu and Relenza in pregnant women, women who are breastfeeding and children under the age of one year.

Existing limited information on use in these groups was previously considered by the Department of Health scientific advisory group on pandemic influenza and the working group on influenza in pregnancy.

These groups found no evidence of harm to the fetus or to children in those known cases where antiviral medicines had been taken by pregnant women or by children under the age of one year.

Both groups recommended that **in a pandemic situation**, the use of antiviral medicines provides benefits which significantly outweigh any theoretical risks in these patient groups, and that antiviral medicines could be given, in appropriate doses, to treat pregnant women and children under the age of one year with clinically diagnosed influenza.

The Royal College of Paediatrics and Child Health has also developed a consensus statement on the use of oseltamivir in infants under one year of age, taking into account the use of the agent in Japan in recent outbreaks.

The situation regarding use by women who are breastfeeding was less clear, owing to very scanty scientific information, though animal studies suggested that the use of treatment doses in lactating animals did not cause harm to offspring.

The opinion of the European Medicines Agency (EMEA)

The licences for both oseltamivir and zanamivir were granted by the European Medicines Agency (EMEA) under the Central European Licensing Procedure, which licences a medicine for use in European countries. The EMEA has considered the latest available information on the use of these medicines in pregnancy, in women who are breastfeeding and in children under the age of one year.

They have based their opinions on:

Pregnancy and lactation:

- a review of over 200 case-reports of exposure to oseltamivir and just under 100 case-reports of exposure to zanamivir in pregnant women
- reports of effects on pregnancy and the offspring in other animal species during the initial investigational studies of both drugs
- knowledge of the concentrations of the two medicines in blood, tissues, placenta and the fetal compartment in investigational studies
- limited data on the concentration of the two drugs in the breast milk of lactating animals
- data on the safety of oseltamivir in children under the age of one year (see below).

There was no evidence of adverse effects on pregnancy or offspring; only the expected rate of events related to the progress of pregnancy, and the expected rates of congenital abnormality were seen in the relevant populations.

Children under the age of one year:

- data from ongoing studies of the use of oseltamivir treatment in children aged less than 24 months, including data on children aged below 12 months
- retrospective case-analyses of children aged below 12 months, treated with oseltamivir
- a prospective survey of the use of oseltamivir in children aged below one year in Japan.

Altogether, the cases of around three thousand children have been examined. EMEA found no evidence of adverse effects of treatment other than those already reported in the product literature. There was evidence of effectiveness of the treatment in this age group.

A summary of the opinions of EMEA, published on 8th May 2009

For seasonal (normal winter) influenza:

- the precautions indicated in the licence and in the Patient Information Leaflet for use of these medicines in pregnancy, by breastfeeding women and for children under the age of one *remain valid*.

In the context of a novel influenza virus in a pandemic situation:

- for pregnant or breastfeeding women: the benefit of using Tamiflu or Relenza outweighs the risk, for both treatment and prophylaxis
- for treatment of children under the age of one year: oseltamivir should be used, in a dose of 2 - 3 mg/kg twice daily for five days
- post-exposure prophylaxis for children under the age of one year requires very careful consideration: if it is decided to prescribe Tamiflu to prevent influenza for children below one year of age the appropriate dose should be 2 – 3 mg/kg once daily for 10 days.

The EMEA considers that children under one year of age should be treated under medical supervision and that, at least for children below three months of age, this should be in hospital; however, they realise that hospital resources may be under severe pressure.

European Commission decision on dosage change for children 6 months and over and up to 1 year of age, published on 18th Sep 2009

The European Commission has made a decision to change the dose of oseltamivir (Tamiflu) for children aged 6 months and over and up to 1 year of age from 2mg per kg to 3 mg per kg body weight twice daily for 5 days for treatment in an influenza pandemic, following advice from the European Medicines Agency. This is a result of the introduction of this dose to the Marketing Authorisation following the presentation of evidence from Roche, the manufacturer of Tamiflu.

Recommendations

The Department of Health's recommendations on the use of antiviral medicines in a pandemic situation for pregnant women, women who are breastfeeding and children under the age of one year:

Treatment of pregnant women

Early initiation of antiviral treatment for pregnant women with influenza is recommended.

Pregnant women presenting with uncomplicated illness due to influenza, and who have no evidence of systemic disease, can be offered either zanamivir (Relenza) or oseltamivir (Tamiflu). In view of the lower systemic exposure, zanamivir is recommended as first choice although either drug can be used. If the patient suffers with conditions such as asthma or chronic pulmonary disease, or may have difficulty with an inhaled preparation, oseltamivir should be used.

Pregnant women developing severe, systemic or complicated disease due to influenza will typically be treated as an inpatient and should be offered treatment with oseltamivir.

Post exposure prophylaxis of influenza in pregnant women exposed to a novel pandemic virus strain

If it is decided that a pregnant woman requires prophylaxis because of family or other contact with a novel pandemic virus strain, the preferred antiviral medicine is Relenza.

Treatment of women who are breastfeeding

Women who are breastfeeding and have symptoms of influenza should be treated with an antiviral medicine. The preferred medicine is Tamiflu, as for other adults. However, if a woman's baby is born and breastfeeding is started while the woman is taking Relenza, she should complete the course of Relenza; it is not necessary to switch to Tamiflu.

Post exposure prophylaxis for women who are breastfeeding

If it is decided that a woman who is breastfeeding requires prophylaxis because of family or other contact with a novel pandemic virus strain, the preferred antiviral medicine is Tamiflu.

Treatment of Children under the age of one year

Children under the age of one year who have symptoms of influenza should be treated with oseltamivir. In the UK, two preparations are available for this purpose: Tamiflu suspension 12 mg in one ml (manufactured by Roche and licensed for use in children over 1 year of age); and oseltamivir solution 15mg in one ml.

DH policy is not to stockpile the suspension manufactured by Roche (Tamiflu) because of its limited shelf life. Instead, the raw ingredient powder of pharmaceutical grade has been purchased from Roche to manufacture into a solution by designated licensed hospital pharmacy manufacturing units.

Children in this age-group with influenza symptoms will be assessed by a GP or other healthcare worker experienced in assessing children. At this assessment, the correct dose of antiviral medicine will be determined, and any other medical management requirements will be identified.

GPs will be available to review these children in the community, and will have a low threshold for seeking the advice of a specialist for further management decisions if severe or complicated influenza, or adverse effects of treatment are suspected.

Post-exposure prophylaxis for children under the age of one year

The balance of benefit and risk for using Tamiflu for the prophylaxis of influenza in children under the age of one year who are not currently suffering from influenza symptoms is not clear. A decision on whether prophylaxis with Tamiflu should be recommended should be taken with advice from a specialist in the care of young children.

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