

**MANAGEMENT OF PREGNANT WOMEN DURING AN
INFLUENZA A(H1N1) (Swine Flu) PANDEMIC**

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Related documents:

[Oseltamivir monograph](#)

[Zanamivir monograph](#)

[HPA Swine Flu information](#)

Please contact UKTIS on (0191) 232 1525 to report any pregnancy exposed to oseltamivir (Tamiflu®) or zanamivir (Relenza®).

SUMMARY: Influenza infection during pregnancy is associated with adverse maternal and fetal outcomes, including probable increases in the risk of pneumonia in the mother and possible increases in the risk of some congenital anomalies in the child.

The neuraminidase inhibitors oseltamivir (Tamiflu®, oral) and zanamivir (Relenza®, inhaled) are effective for prophylaxis and treatment of influenza. Although available data are limited, there is currently no evidence that these drugs are associated with adverse outcomes after use in pregnancy. When appropriately indicated, the benefits of neuraminidase inhibitors to mother and baby are likely to outweigh any risk that may be associated with use in pregnancy.

Because of the reduced systemic absorption associated with inhaled therapy, zanamivir may be preferred, especially in early pregnancy, but the orally administered agent oseltamivir is also a suitable option. Selection will also depend on availability, individual contraindications and patient preference.

If you require assistance in making a patient-specific risk assessment, please telephone UKTIS on (0191) 232 1525 to discuss the case with a teratology specialist.

It is important that all cases of exposure during pregnancy are reported to UKTIS on (0191) 232 1525. This will enable safer prescribing in the future.

Risks of influenza in pregnancy

Maternal risk

Pregnant women do not seem to be at an increased risk of contracting influenza than the general population. However, pregnant women, particularly in the third trimester of pregnancy, appear to be at a higher risk of developing influenza-associated pneumonia and cardio-respiratory complications.^{1, 2} In keeping with this, the incidence of acute cardio-respiratory hospitalisations during influenza season increases throughout pregnancy, the highest incidence being during the third trimester.

An increase in influenza associated mortality among pregnant women was documented during the influenza pandemics of 1918-1919 and 1957-1958, although a similar increase has not been noted during the inter-pandemic periods.^{2, 3}

Risk to the fetus

There are inconsistent data to suggest that maternal influenza may be associated with an increased risk of some congenital anomalies, including oesophageal atresia,⁴ or anophthalmos/microphthalmos;⁵ an increased risk of anencephaly was also reported following epidemics of Asian influenza.^{6, 7 8}

The Hungarian Case-Control Surveillance of Congenital Abnormalities reported an association between maternal influenza during the second and third month of pregnancy and congenital anomalies in the offspring, including cleft lip or palate, neural tube defects, and cardiovascular abnormalities.⁹ The use of antipyretics reduced the risk of congenital anomalies suggesting that they were due to fever. Use of folic acid supplements reduced or eliminated the apparent risk associated with influenza during pregnancy.

A further case-control study involving 363 infants with neural tube defects (NTD) and 523 normal newborns indicated an increased risk of NTDs associated with maternal influenza. In this study, risk was enhanced when antipyretics were used.¹⁰

There are, however, a number of studies that have not found any increased risk of congenital anomalies in association with maternal influenza.^{6, 11-13} Maternal influenza has not been associated with an increased risk of spontaneous abortion and intrauterine death.

An association has been reported between high fever-related maternal diseases (including influenza) and an increased risk of congenital anomalies in a case control study.^{9, 14, 15} During the first trimester of pregnancy a reduction in risk of congenital anomalies may be reduced by the administration of antipyretics. Fever associated with influenza can be reduced in pregnancy with the use of paracetamol; this antipyretic is suitable for use in all stages of pregnancy.

Sensitivity of currently circulating influenza A(H1N1) (Swine Flu)

The currently circulating swine influenza A(H1N1) virus has been shown to be sensitive to the neuraminidase inhibitor antiviral medications zanamivir and oseltamivir, but is resistant to amantadine and rimantadine.

Oseltamivir (Tamiflu®) & Zanamivir (Relenza®) in pregnancy

Oseltamivir (Tamiflu, ® Roche Products) and Zanamivir (Relenza, ® GlaxoSmithKline) are neuraminidase inhibitors effective as treatment and prophylaxis of influenza Types A and B. These drugs prevent viral release from infected cells and subsequent infection of adjacent cells. NICE has concluded that both are clinically effective treatments for influenza,¹⁶ with no clear distinctions between the two agents on the basis of clinical efficacy in different populations and that both are effective for seasonal or post-exposure prophylaxis.¹⁷

There are limited data available on the safety of oseltamivir and zanamivir in pregnancy, but the animal studies that are available have not demonstrated harm. To date there is no overall evidence of an increased risk of adverse human pregnancy outcomes following maternal antiviral treatment with oseltamivir or zanamivir. The European Medicines

Agency (EMA) have published an assessment report¹⁸ on oseltamivir and zanamivir which concludes that, in the context of a novel influenza (H1N1) in a pandemic situation, the overall data suggest that the benefit of using Tamiflu® or Relenza® in pregnant women outweighs the risk. The EMA report includes unpublished outcome data for both medications, which is included in the individual UKTIS [oseltamivir](#) and [zanamivir](#) monographs. It should be noted that neither drug is licensed for use in pregnancy.

A recent review from North America has concluded that, based on the relative amount of available safety data compared to zanamivir, oseltamivir appears to be the drug of choice for treatment or prophylaxis during pregnancy.¹⁹

Recommendations

Given the potential severity of influenza in pregnant women and the lack of evidence of harm from antiviral medications, pregnant women who meet current criteria for treatment in the context of a flu pandemic should be treated as if they were not pregnant. The risks to mother and baby of untreated influenza are likely to outweigh any possible risk associated with antiviral treatment.

Current algorithms for management of influenza A(H1N1) (swine flu) in the United Kingdom can be found at the [Health Protection Agency](#) website.

Zanamivir is administered by inhalation and is deposited at high concentrations throughout the respiratory tract with less systemic absorption;²⁰ for that reason it may be preferred for use in pregnant patients for prophylaxis or treatment, particularly in early pregnancy. However due to its route of administration, zanamivir may be associated with adverse respiratory effects such as bronchospasm and dyspnoea, which may be a concern in patients at risk of respiratory problems.

Oseltamivir is readily absorbed from the gastrointestinal tract following oral administration, and has significant systemic activity. It is recommended by the US Centres for Disease Control and Prevention for treatment of active influenza during pregnancy.²¹

Department of Health guidelines regarding pregnancy and swine flu²²

The Department of Health states:

As with many drugs, oseltamivir and zanamivir have not been specifically tested in pregnancy and breastfeeding and therefore are not licensed for this use. For both products (ie oseltamivir and zanamivir), use in pregnant and lactating women is only recommended based on the individual risk benefit assessment of the treating physician. Zanamivir results in significantly less systemic exposure than oseltamivir and therefore also significantly less potential exposure to the foetus. And therefore Relenza is the recommended antiviral for pregnant women.

Pregnant women should use paracetamol to control fever. Pregnant women should not take non-steroidal anti-inflammatory drugs for the treatment of flu symptoms, because they may interfere with the baby's pulmonary blood flow.

Conclusions

A pregnant patient should be managed using the same criteria as the general population. While there is a lack of information on oseltamivir and zanamivir use in pregnancy, either can be used when appropriately indicated, after discussing the risks and benefits with the patient:

- For prophylaxis or treatment of influenza A(H1N1), zanamivir (Relenza®) may be preferred because of its reduced systemic absorption. Oseltamivir (Tamiflu®) is a suitable alternative if zanamivir is unavailable or contraindicated.
- Risks of adverse fetal outcomes following influenza in pregnancy may be reduced by appropriate use of folic acid supplementation. Appropriate use of antipyretics (e.g. paracetamol) may also reduce risk the adverse fetal outcomes associated with fever.

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Disclaimer: Every effort has been made to ensure that this monograph is accurate and up-to-date. However it cannot cover every eventuality and the information providers cannot be held responsible for any adverse outcomes of the measures recommended. There is a background incidence of congenital malformations (2-3%) and spontaneous abortions (10-20%) irrespective of any drug or chemical exposure. The final decision regarding which treatment is used for an individual patient remains the clinical responsibility of the prescriber.