



## **Australian Government**

### **Department of Health and Ageing**

#### **PANDEMIC (H1N1) 2009 INFLUENZA AND OSELTAMIVIR RESISTANCE – 12 SEPTEMBER 2011**

Following uncharacteristically high out-of-season influenza levels in most states and territories, the 2011 influenza season commenced in early June. Over recent weeks influenza notifications have peaked and started to decrease in Queensland, New South Wales and South Australia but have continued to increase in all other states and territories.

Nationally, the majority of virus detections in 2011 have been pandemic (H1N1) 2009 with co-circulation of Influenza B, with proportions varying across jurisdictions. High levels of influenza Type A/H3N2 seen early in the season have dropped considerably with only Western Australia currently reporting significant numbers.

More than six percent of positive influenza samples in Australia have been sent to the WHO Collaboration Centre for Reference and Research on Influenza (WHOCC) for antigenic characterisation. The vast majority of these were antigenically similar to strains in the current trivalent influenza vaccine.

The WHOCC also tests isolates for antiviral resistance. Only one pandemic (H1N1) 2009 virus had tested resistant to oseltamivir until a recent cluster of cases was identified from the Newcastle region in NSW. This cluster consists of 25 cases, of which 6 were hospitalised and three were pregnant. None were treated with oseltamivir prior to their positive test for influenza. A further two oseltamivir-resistant pandemic (H1N1) 2009 viruses sampled in July and August have also been found to belong to the Newcastle cluster. These samples were both from untreated, otherwise healthy children, one from Sydney and the other from Orange. These are the first viruses of the cluster that have been received by the WHOCC from outside the Hunter New England region. Apparently neither the children nor their families had travelled recently to the Hunter New England area.

The potential spread of pandemic (H1N1) 2009 viruses resistant to oseltamivir will be monitored closely through the provision of a proportion of samples to the WHOCC for antigenic characterization and antiviral resistance testing from laboratories in all jurisdictions, and from a proportion of influenza positive samples collected from patients presenting with influenza-like illness to Australian Sentinel Practices Research Network (ASPREN) GPs.

The vast majority of the pandemic (H1N1) 2009 viruses received from around the country in August are still sensitive to oseltamivir (even from the Hunter New England area). Viruses of the other two circulating lineages (H3N2 and type B) are also sensitive. So at this stage the efficacy of oseltamivir should be unaffected in the great majority of cases. These viruses are also sensitive to zanamivir (Relenza) and they are not showing any antigenic changes that would affect their recognition by vaccine-induced antibodies.

Seasonal influenza vaccination remains the most effective preventative measure.

#### **BACKGROUND**

##### **Treatment with antiviral medication**

Oseltamivir and zanamivir act to reduce influenza virus replication by inhibiting the viral surface enzyme neuraminidase thus preventing release of the virus from cells. These medications are indicated for the treatment and prevention of influenza A and B. They are ineffective for influenza like illness. Guidelines

surrounding their use may vary depending on the local epidemiology and the local antiviral resistance profile.

Treatment with a neuraminidase inhibitor (oseltamivir or zanamivir) within 48 hours of symptom onset shortens duration by 0.5-1 day in both healthy and at-risk people. The earlier the treatment begins the shorter and less severe the illness.

Therapeutic Guidelines recommends the following indications for treatment of influenza with neuraminidase inhibitors<sup>1</sup>:

- **People with established complications / severe illness:** Where severe illness (eg pneumonitis) is already present, treatment should be offered regardless of the patient's risk group or duration of symptoms. In most cases, patients who require hospitalisation due to severe influenza should be treated.
- **High-risk groups:** Treatment should be prioritised for people with risk factors for poor outcomes. For these people treatment may be considered even if commenced more than 48 hours after the onset of symptoms.
- **People not in high-risk groups, and not severely unwell:** Treatment should be considered for people with severe symptoms (eg rigors) who present early. For an otherwise healthy person who is not in a high-risk group, and who is not severely unwell, treatment has a low likelihood of providing benefit if the patient's symptoms have been present for more than 48 hours.

## Resistance

Until 2008 emergence of resistance to neuraminidase inhibitors following clinical use had occurred only infrequently, though a higher incidence was reported for oseltamivir compared to zanamivir. However, in 2008 a variant of the seasonal H1N1 with a mutation in the neuraminidase gene (H275Y) that confers a high level of resistance to oseltamivir (but not zanamivir) was detected with increasing frequency. The spread of this oseltamivir resistant virus did not appear to correlate with use of oseltamivir.

The Australian Influenza Surveillance Report of March 2009 noted:

*'Although no new report on oseltamivir resistance has been released by the WHO since 18 March 2009, during the period 1 October 2008 to 31 January 2009, 95% of H1N1 viruses analysed from 30 countries were resistant to oseltamivir. Higher levels of oseltamivir resistance have been seen in Europe (98%), the United States (99%) and Canada (100%).'*

Thus resistance went rapidly from quite low levels in some parts of the world to very high levels.

The most recent report from the WHO<sup>2</sup> - Update on oseltamivir resistance in influenza A(H1N1)2009 viruses 24 August 2011 – notes:

*'There have been 570 cases of oseltamivir resistant H1N1 influenza viruses reported to the WHO since April 2009. Where clinical information is known, 132 (30%) have occurred in severely immunocompromised patients and 308 (70%) in non immunocompromised patients. Of the latter, 69% (211 cases) of the cases were associated with drug use, including cases occurring during or after oseltamivir treatment and/or peramivir treatment and associated with post-exposure prophylaxis, and 31% (97 cases) have occurred in patients who had not used antiviral drugs prior to occurrence of the resistant virus, including known or suspected cases of person to person transmission.'*

While the numbers of oseltamivir resistant viruses isolated from the Hunter New England region is currently very low this situation should be monitored closely to identify if an upward trend is occurring in a similar manner to 2008.

Clinicians should be alert for resistance and consider this where there are signs that oseltamivir may not be effective.

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1 Influenza . In: eTG complete [Internet]. Melbourne: Therapeutic Guidelines Limited; 2011 Jul. Accessed 2011 Sep 8 <http://www.tg.org.au>.

2 [http://www.who.int/influenza/surveillance\\_monitoring/updates/2011\\_08\\_26\\_weekly\\_web\\_update\\_oseltamivir\\_resistance.pdf](http://www.who.int/influenza/surveillance_monitoring/updates/2011_08_26_weekly_web_update_oseltamivir_resistance.pdf)

## **Links**

NSW Health Influenza Update – antiviral resistance seen in NSW.

[http://www.health.nsw.gov.au/PublicHealth/Infectious/professional\\_landing\\_page.asp](http://www.health.nsw.gov.au/PublicHealth/Infectious/professional_landing_page.asp)

WHO Summary of influenza antiviral susceptibility surveillance findings, September 2010 - March 2011.  
The WHO Global Influenza Surveillance and Response System

[http://www.who.int/influenza/gisrs\\_laboratory/updates/antiviral\\_susceptibility/en/index.html](http://www.who.int/influenza/gisrs_laboratory/updates/antiviral_susceptibility/en/index.html)

WHO Q&A re antiviral resistance

[http://www.who.int/csr/disease/influenza/oseltamivir\\_faqs/en/index.html#isit](http://www.who.int/csr/disease/influenza/oseltamivir_faqs/en/index.html#isit)

Australian Influenza Surveillance Report.

<http://www.health.gov.au/internet/main/publishing.nsf/Content/cda-surveil-ozflu-flucurr.htm>