Canterbury District Health Board
Te Poari Hauora ō Waitaha

Clinical Pharmacology Bulletin

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Oseltamivir (Tamiflu®)

Oseltamivir is an antiviral that has received extensive media coverage for treatment/prophylaxis of influenza. Concerns have arisen over the emergence of oseltamivir-resistant disease A(H5N1) 'bird flu' and more recently seasonal influenza A(H1N1) viruses.

Oseltamivir is a 'neuraminidase inhibitor' antiviral. It works by blocking the viral neuraminidase that cleaves and releases replicated virus from the infected cells. It is used in the treatment or prevention of influenza and is known to have activity against type A and B influenza viruses.

Dosage and administration

To maximise the effectiveness of the drug, oseltamivir should be initiated as soon as possible (ideally, within the first or second day) after the onset of symptoms or exposure to the influenza virus. Dosage recommendations are outlined in the table below.

	Treatment of seasonal influenza	Chemoprophylaxis/ post exposure
Adults & children >13yrs	75mg twice daily	75mg once daily
Children > 1 year		
> 40kg	75mg twice daily	75mg once daily
> 23-40kg	60mg twice daily	60mg once daily
> 15kg-23kg	45mg twice daily	45mg once daily
≤ 15 kg	30mg twice daily	30mg once daily
Children <1 year*		
6-11 months	25mg twice daily	25mg once daily
3-5 months	20mg twice daily	20mg once daily
<3 months	12mg twice daily	Not recommended unless situation judged critical
Duration of therapy	5 days	At least 7 days†

* Not registered for children <1yr. Dosage guidelines are from the US Centres for Disease Control and Prevention.
†Safety and efficacy data has been demonstrated for up to 6 weeks in adults and adolescents. The duration of protection lasts for as long as dosing is continued.

Adverse event profile

The most frequent reported side effects of oseltamivir are nausea, vomiting and abdominal pain, which are generally self limiting. Administration with food does not affect absorption of oseltamivir, and may help to reduce nausea and vomiting. The safety profile of oseltamivir in the elderly is similar to that of people less than 65 years. Neuropsychiatric events (e.g. abnormal thinking, delirium) have been reported during post-marketing surveillance, particularly in children and adolescents. Patients receiving oseltamivir should be monitored closely for these types of adverse effects.

Drug interactions

Oseltamivir generally has a low propensity for drug interactions, as it is predominantly eliminated renally (tubular secretion), is not protein bound and neither oseltamivir nor the active metabolite are substrates for, or inhibitors of, the cytochrome P450 system. However, oseltamivir has the potential to interact with other drugs that are eliminated via tubular secretion, such as probenecid. The interaction with probenecid can double the concentration of oseltamivir, which could be a dose saving device in a pandemic.

Efficacy in seasonal influenza

Oseltamivir is not a cure for influenza, but in some patient groups it has been shown to reduce the severity and duration of influenza symptoms. The duration of symptoms were reduced by 1.5 days in otherwise healthy adults and 0.5 days in those considered to be 'high risk' individuals.

Swine Influenza A(H1N1)

Swine influenza A(H1N1) is a variant of seasonal influenza. The viruses obtained from the recent human cases of swine influenza A (H1N1) in the United States have in-vitro sensitivity to oseltamivir but appear to be resistant to amantadine.

Oseltamivir-resistant influenza A(H1N1)

High rates of oseltamivir resistance to seasonal influenza A(H1N1) viruses were first detected during the Northern hemisphere 2007/08 influenza season. The resistance appears to be related to a specific mutation in viral neuraminidase (i.e. a histidine to tyrosine substitution at amino acid 274, referred to as the His274Tyr resistance mutation). So far, this mutation appears to be limited to seasonal H1N1 viruses and does not involve circulating H3N2 or influenza B viruses. H1N1 viruses containing the His274Tyr resistance mutation appear to be susceptible in-vitro to amantadine (Symmetrel®) and zanamivir (Relenza®). However, amantadine monotherapy is not recommended due to the rapid development of resistance, and zanamivir (an inhaled neuraminidase inhibitor) is not routinely recommended in New Zealand because of the high prevalence of individuals with asthma and the risk of bronchospasm associated with inhaled zanamivir.

Influenza A subtyping will be available through Canterbury Health Laboratories (CHL) this winter. Treatment decisions should be based on the knowledge of circulating influenza A strains, with treatment adjusted once the specific subtype is known. For patients who are severely compromised with influenza-like symptoms consider either zanamivir, or amantadine in addition to oseltamivir.

Efficacy against Influenza A(H5N1) 'bird flu'

Oseltamivir has shown activity in-vitro against the highly pathogenic influenza A (H5N1) virus. We are not aware of any randomised controlled trials in humans infected with this virus but there are at least 205 case reports in the literature. In the majority of these oseltamivir was initiated late (>48hrs after onset of symptoms) due to late diagnosis and/or hospitalisation. Despite treatment, the mortality rate remained high. Oseltamivir-resistance to highly pathogenic influenza A(H5N1) has also been reported, but is restricted to several A(H5N1) clades.

Availability without prescription

Oseltamivir is available without a prescription during the winter seasonal influenza season from 1st May to 30th September each year. It must be sold by a pharmacist to individuals 12 years of age and older presenting with symptoms of influenza. It cannot be purchased by individuals who are concerned that they may develop influenza.

The information contained within this bulletin is provided on the understanding that although it may be used to assist in your final clinical decision, the Clinical Pharmacology Department at Christchurch Hospital does not accept any responsibility for such decisions.