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Chapter 10a

Pandemic (H1N1) 2009

(formerly known as Swine flu or Influenza A (H1N1))

NOTIFIABLE

Date: 16/09/2010 Version 3

This chapter has been developed to provide current information on pandemic (H1N1) 2009 influenza, on vaccines available for use in Ireland and on vaccination recommendations. It also provides links to further information sources.

The information contained in this chapter is subject to change as more information becomes available or recommendations change.

Important updates on previous version

The influenza pandemic (H1N1) 2009 was declared over on August 10th 2010.

For the 2010/2011 influenza season NIAC has recommended that pandemic (H1N1) 2009 vaccine is not recommended for any at risk groups. The trivalent seasonal influenza vaccine contains the pandemic virus strain and will provide protection against the Pandemic (H1N1) 2009 virus (see updated Chapter 7).

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Introduction

Influenza pandemics occur when a new influenza virus (typically influenza A virus) appears, against which the human population has little or no immunity. Pandemic strains can result in a range of illness, from mild to severe, and a varying number of deaths associated with illness. The severity of a pandemic can change over the course of that pandemic. Three influenza pandemics occurred in the 20th century, in 1918-1919, 1957 and 1968. The pandemic in 1918-1919 was the most severe and is estimated to have been associated with between 20-40 million deaths worldwide.

Pandemic (H1N1) 2009, formerly known as swine flu or influenza A (H1N1), is a new type of flu virus that contains genes from pig, bird and human influenza viruses in a combination that has not been observed before. The virus was first recognised in April 2009 in Mexico and subsequently spread to all parts of the world. An influenza pandemic was declared by the World Health Organization (WHO) on June 11th 2009. The pandemic was declared over on August 10th 2010.

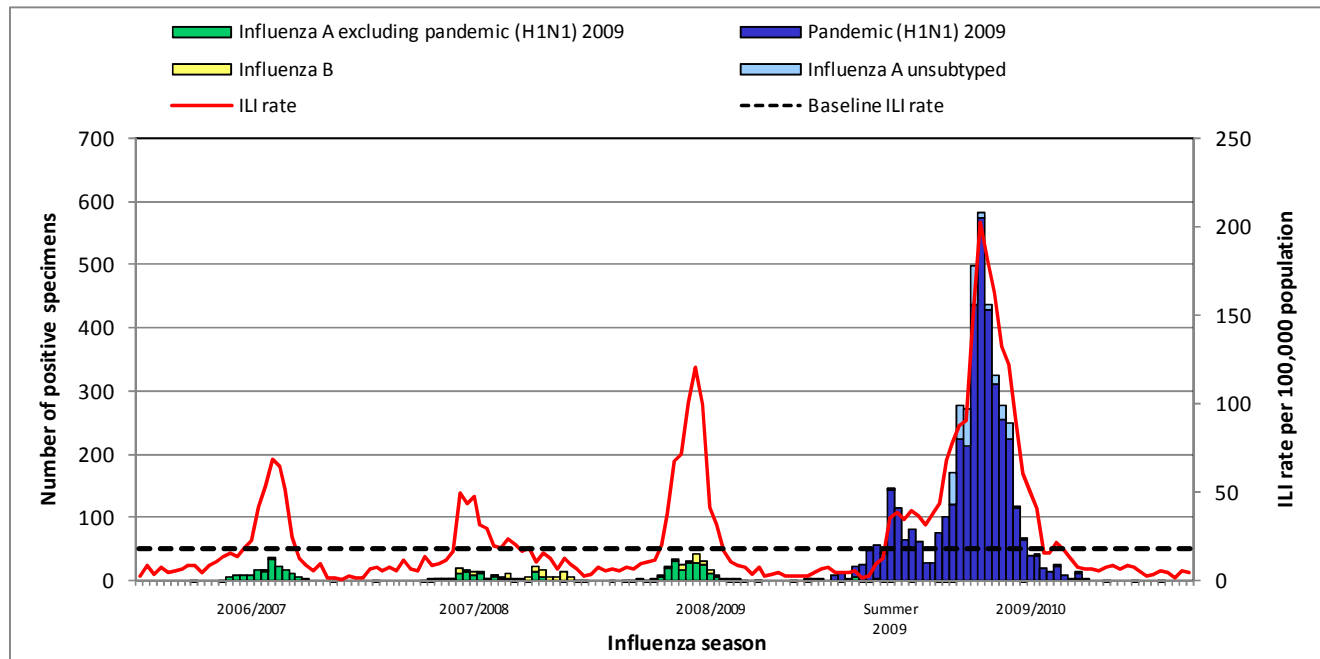
Epidemiology

Note: please see www.hpsc.ie for the most recent information on the evolving epidemiology of pandemic (H1N1) 2009.

WHO has called the new influenza A strain “Pandemic (H1N1) 2009”. This new strain appears to be more infectious than seasonal influenza, and has spread rapidly worldwide, particularly among young children, and those aged 10 to 45 years. As a result of this increased transmissibility the virus can spread rapidly in schools and closed institutions, causing rapidly escalating outbreaks in these settings. The severity of the disease ranges from very mild symptoms to severe illnesses that can result in death. The majority of people who contract the virus experience mild disease and recover without antiviral treatment or medical care.

Figure 10a.1 ILI GP consultation rates per 100,000 population, baseline ILI threshold rate, and number of positive influenza specimens, by influenza week and season¹

Source: NVRL, CUH and GUH laboratory data and ICGP clinical ILI data



Between July 2009 and early 2010, pandemic H1N1 (2009) circulated in Ireland. It predominantly affected young adults and children (Figure 10a.2) and the numbers hospitalised and those requiring intensive care increased as the virus spread (Figure 10a.3). By the end of December 2009 (week 53), 22.9% of H1N1 confirmed cases had been hospitalised, of whom 8.4% were admitted to ICU; 42.9% of hospitalised cases had pre-existing clinical conditions including chronic heart, liver, renal, respiratory and neurological disease, asthma, haemoglobinopathy, immunosuppression, diabetes mellitus, severe obesity (BMI \geq 40) and pregnancy.

From early 2010, influenza activity reduced with decreasing numbers of people with flu like illness, and correspondingly fewer confirmed cases of pandemic H1N1 (2009), (figure 10.a.2) hospitalisations due to H1N1 (figure 10.a.3) and deaths due to H1N1.

On 10th August 2010, the WHO declared that the global influenza situation no longer represented an extraordinary event requiring immediate emergency actions on an international scale. In their view, the public health emergency of international concern, recommended following the emergence of the H1N1 (2009) virus, should be considered over.

The Committee noted that the information from India, New Zealand and the Pacific Island countries, countries currently in their seasonal flu season, was consistent with the expectation that individual countries might experience significant levels of influenza associated with the H1N1 (2009) virus in the future, and expressed the need for national authorities to continue to implement outbreak response measures in those countries when such events occur. The Committee strongly emphasized the need for States to maintain vigilant disease surveillance and monitoring for influenza outbreaks and influenza-like illness as well as ensuring the availability of necessary public health measures for preventing and controlling influenza.

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Such measures include the continued use of H1N1 (2009) pandemic or seasonal influenza vaccines where appropriate and available.

Figure 10a.2

Age specific sentinel GP consultation rate for ILI per 100,000 population by week during the Summer 2009 and 2009/2010 influenza season

Source: ICGP ILI clinical data

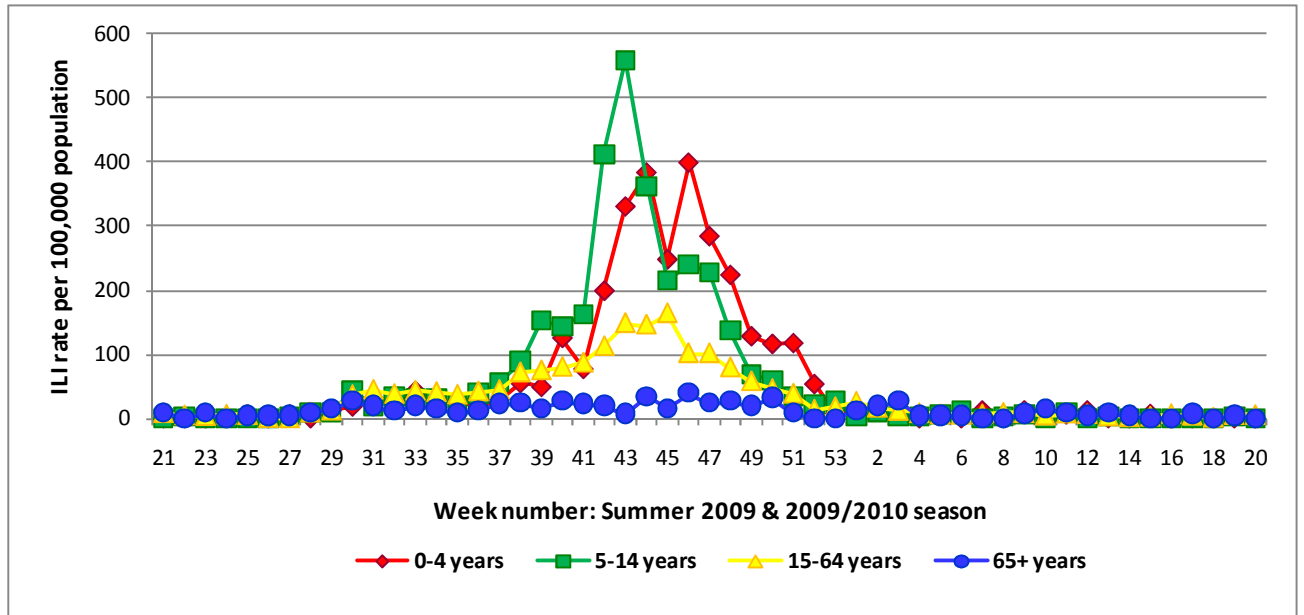
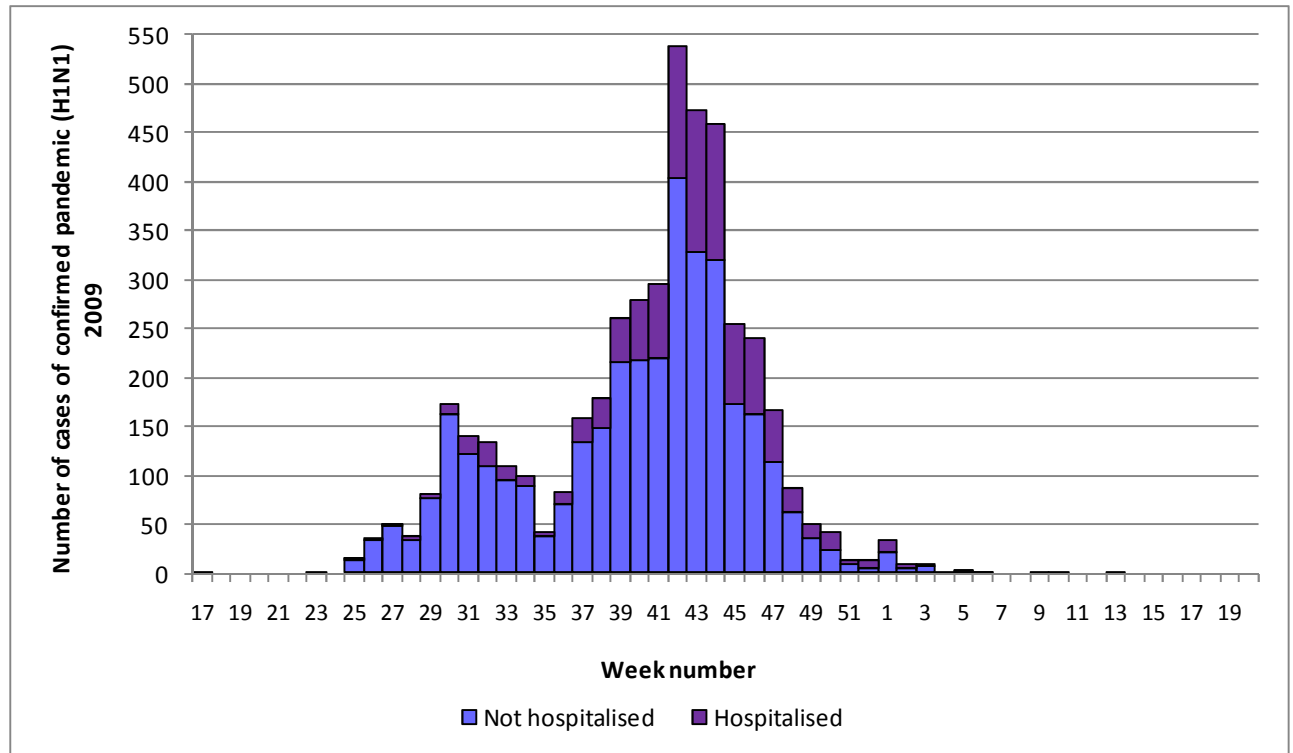


Figure 10a.3: Number of confirmed cases of pandemic (H1N1) 2009 by week of notification and hospitalisation status²

Source: CIDR



Transmission

Pandemic (H1N1) 2009 is spread from person to person by direct contact, by droplet infection or by contact with materials recently contaminated by nasopharyngeal secretions. Airborne spread can also occur. It is very contagious, especially in younger children in close contact environments such as day schools, and particularly residential schools or institutions. Virus can be detected in respiratory secretions from about one day before the onset of clinical illness to 7 days or longer after symptom onset. Shedding can be more prolonged in young children and in the immunocompromised.

Effects of pandemic influenza A (H1N1) 2009

For the most recent information on global epidemiology please refer to WHO website www.who.int.

The pandemic strain (H1N1) 2009 causes an acute illness of the upper and/or lower respiratory tracts similar to seasonal influenza in the majority of cases. It affects all age groups but the highest age-specific rates are in children and adults < 45 years of age. The illness is characterised by the abrupt onset of fever, headache, myalgia, cough, sore throat and malaise. For most people the illness is relatively mild and self-limited, with recovery in 2-7 days, but it can be severe. Individuals with pre-existing serious underlying illness are at increased risk of developing severe disease. Of the more serious cases who have been hospitalised, between one-third to more than half have had underlying health conditions.

² Week number on figure 10.3 is based on infectious disease notification week number, which was one week behind the international influenza week number during 2009. Therefore weeks 17-52 above are equivalent to weeks 18-53 on the influenza system. Epidemiological and influenza week numbering systems are the same for 2010.

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Small subsets of patients develop very severe progressive pneumonia either rapidly or over a period of days after the initial ILI. The severe viral pneumonia is often associated with failure of other organs, or marked worsening of underlying asthma or chronic obstructive airway disease. Many of the most severe cases develop an acute respiratory distress syndrome (ARDS) requiring high pressure ventilation and intensive care.

Primary viral pneumonia is the most common finding in severe cases and a frequent cause of death. Secondary bacterial infections have been found in approximately 30% of fatal cases. Respiratory failure and refractory shock have been the most common causes of death.

The clinical picture in severe cases is very different from that seen during epidemics of seasonal influenza. While people with certain underlying medical conditions, and pregnancy, are known to be at increased risk, many severe cases occur in previously healthy young people. In these patients, predisposing factors that increase the risk of severe illness are not currently understood.

In severe cases, patients generally begin to deteriorate around 3 to 5 days after symptom onset. Deterioration is rapid, with many patients progressing to respiratory failure within 24 hours, requiring immediate admission to an intensive care unit. Most of these patients need mechanical ventilation. Some do not respond well to conventional ventilatory support, further complicating the treatment.

Prompt treatment with the antiviral drugs, oseltamivir or zanamivir, reduces the severity of illness and improves the chances of survival. Early treatment with these drugs for people at risk of severe disease is recommended, even in the absence of a positive confirmatory test.

In addition to viral pneumonia, co-infection with bacteria can also contribute to a severe, rapidly progressive illness. Bacteria frequently reported include *Streptococcus pneumoniae* and *Staphylococcus aureus*, including methicillin-resistant strains in some cases. Infection with meningococcal disease is a recognised complication of influenza infection, and may appear in the weeks following infection.

Pandemic H1N1 2009 vaccine

Pandemic (H1N1) 2009 vaccine is NOT recommended for any at risk groups. The trivalent seasonal influenza vaccine contains the pandemic virus strain and will provide protection against the Pandemic (H1N1) 2009 virus (see updated Chapter 7).

A number of vaccine manufacturers produced pandemic vaccines for worldwide use. The licensing of vaccines to date by the European Medicines Agency (EMA) in conjunction with the Irish Medicines Board (IMB), including those used in Ireland (Celvapan and Pandemrix), was based on safety and immunogenicity data of similar vaccines developed with a strain of influenza virus other than that responsible for the H1N1 (2009) pandemic (the H5N1 strain). Clinical trials are on-going in adults and children with pandemic H1N1 2009 vaccines and the product information is updated regularly as data become available and these updates can be accessed on the IMB website at www.imb.ie. In line with this, the recommendations provided here are interim and may be subject to revision.

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Celvapan

All supplies of Celvapan vaccine expire at the end of September 2010 so this vaccine is no longer available in Ireland.

Pandemrix

Pandemrix vaccine is the only licensed pandemic vaccine available for use in Ireland. Pandemrix is a monovalent inactivated adjuvanted vaccine.

Adjuvants

Adjuvants are substances that enhance the immune response in vaccines and can make them more effective. They have been used for many years in some vaccines. Scientific data support the safety of adjuvants in pandemic influenza vaccine production.

The squalene-based adjuvant used in Pandemrix (the GSK vaccine used in Ireland) is AS03. It is an oil-in-water emulsion. The oil phase contains two oils, squalene and DL- α -tocopherol (vitamin E). WHO and EMEA have reviewed the safety of adjuvanted influenza vaccines in 2009 and reported that there were no significant concerns regarding using adjuvanted H1N1 vaccine.

Thiomersal

Thiomersal is present in Pandemrix. It has been used in vaccine production since the 1930s to protect against bacterial contamination of vaccines. It is broken down in the body and one of the products is ethyl mercury. There is no evidence that ethyl mercury in vaccines has any adverse effects apart from minor reactions such as swelling and redness at the site of injection.

Ethyl mercury should not be confused with methyl mercury. Methyl mercury can accumulate if consumed regularly over time, whereas ethyl mercury is rapidly excreted. Everybody in the population (including pregnant women) is likely to be exposed to small amounts of methylmercury via food, especially fish.

WHO has concluded that there is no evidence of mercury toxicity in infants, children or adults exposed to thiomersal in vaccines. The EMEA has acknowledged that the presence of thiomersal in some vaccines is necessary, including its use as a preservative in multidose vials. After evaluation of the scientific evidence, the EMEA has concluded that immunisation with vaccines containing thiomersal continues to offer benefits to the general population. While there are differences between the two vaccines in terms of their manufacture and constituents, the EMEA has concluded in licensing both vaccines that they are equally safe and effective.

Indications for pandemic (H1N1) 2009 vaccine

For the 2010/2011 influenza season pandemic (H1N1) 2009 vaccine is NOT recommended for any at risk groups.

The trivalent seasonal influenza vaccine contains the pandemic virus strain and will provide protection against the Pandemic (H1N1) 2009 virus (see updated Chapter 7).

Contraindications to Pandemrix

- There are very few people who cannot receive the pandemic (H1N1) 2009 vaccine.
- Anaphylactic reaction to a preceding dose or any of the constituents or trace residues of the vaccine.
- Pandemrix should not be given to persons with known anaphylactic hypersensitivity to eggs.
- History of Guillain-Barré Syndrome (GBS) within 6 weeks of influenza vaccination.

Precautions for Pandemrix

- Acute severe febrile illness, defer until recovery.
- Caution is required if vaccines are given intramuscularly to those with a bleeding disorder or receiving anticoagulant treatment as ecchymosis at the injection site is common, particularly in those with severe bleeding diatheses.
- History of sporadic Guillain-Barré Syndrome (GBS) within previous 12 months. However, the need for immunisation requires evaluation of the risks and benefits on an individual basis. The risk of GBS post pandemic vaccination should be considered in the context of the possible risk of GBS associated with influenza and the risk of severe illness and possible death from pandemic influenza.

Dose and route of administration for Pandemrix

Pandemrix is licensed for adults and for children 6 months of age and older.

Children aged from 6 months to 9 years

One dose of 0.25 ml (paediatric dose) at an elected date.

Children aged 9 years and older, and adults

One dose of 0.5 ml (adult dose) at an elected date.

Route of administration

The deltoid muscle is the recommended site for adults and older children and the anterolateral thigh for infants and young children.

Pandemrix is recommended for administration by intramuscular (IM) injection. There are no data with pandemic vaccines using the subcutaneous route. Immunogenicity of vaccines recommended for IM administration may not be as long-lasting if they are given subcutaneously. The patient or parent should be advised of this.

Bleeding disorders

In those with bleeding disorders it is prudent to use a 23-gauge needle, and to apply pressure to the vaccine site for 1-2 minutes after the injections. In those with a severe bleeding disorder (e.g. clotting factor deficiency or severe thrombocytopenia) vaccination

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can be scheduled shortly after administration of clotting factor replacement or similar therapy. Individuals with bleeding disorders are under the care of a specialist who can be consulted about vaccinations. The risks of pandemic influenza versus risks of IM injection should be considered. There are no data on subcutaneous administration of pandemic influenza vaccine and if this route is used consideration should be given to possible reduction of immunogenicity. The patient or parent should be advised of this.

Patients on warfarin should be having regular blood tests to check INR. It may be useful to ask when INR was last checked and if it was acceptable. If INR has not been checked for some time or was very high at the most recent test or warfarin dose was increased then the individual can be referred to their own GP for review. The usual precaution of applying pressure for 1-2 minutes and checking that bleeding has stopped before removing pressure should be sufficient for patients on warfarin.

Co-administration with other vaccines

Pandemrix is an inactivated vaccine and can be administered at the same time as other vaccines, but in separate limbs.

Storage and use of multidose pandemic vaccine vials

- Pandemrix should be stored in the original packaging in a refrigerator at +2°C to +8°C and protected from light.
- Pandemrix must be used within 24 hours after reconstitution. Once reconstituted Pandemrix should be stored at a temperature of +2°C to +25°C.
- Pandemrix vaccine must be reconstituted before administration.
- Pandemrix is provided in multi-dose vials. Appropriate infection control precautions should be taken at all times. Specific guidelines have been developed and are available on the NIO website at www.immunisation.ie.

Adverse reactions

At the time of licensing of the vaccines, data on adverse effects came from studies on the mock-up vaccines which used H5N1 influenza virus as well as preliminary results from trial data of the vaccines. Adverse effects were similar to those from seasonal flu vaccines. Since licensing, post-marketing surveillance data are available from mass-vaccination programmes in a number of EU Member States and to-date the adverse effects seen are those which were anticipated from clinical trials.

Local: local reactions are common and include pain, redness, swelling, or bruising at the injection site.

General: the more common generalised reactions include: headache, fever, fatigue, malaise, myalgia, arthralgia, vertigo, nasopharyngitis and lymphadenopathy. These reactions usually last 1 to 2 days.

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Allergic reactions and anaphylaxis are rare. As with all injectable vaccines, appropriate medical treatment and supervision should always be readily available.

Encephalomyelitis, neuritis, and Guillian-Barré syndrome have on very rare occasions been temporally associated with some seasonal influenza vaccines. Convulsions, transient thrombocytopenia and vasculitis have also been reported rarely. To date, there is no evidence of any association between sporadic GBS or encephalitis and pandemic vaccines.

For more details on potential side-effects please see the specification of product characteristics (SPC) for each vaccine which is available on the Irish Medicines Board (IMB) website www.imb.ie.

Postmarketing surveillance

The IMB evaluates and assesses all suspected adverse reactions reported and continues to monitor experience from other countries. This assists the IMB to make informed decisions and take measures as it deems appropriate to continue to safeguard public health safety in relation to medicines.

Suspected adverse reactions can be reported to the IMB by:

- Completing the online report on the IMB website (www.imb.ie)
- Downloading an adverse report form available on: <http://www.imb.ie/EN/Safety--Quality/Online-Forms/Human-Medicine-Adverse-Drug-Reaction.aspx>. Complete the form and send it to the IMB Pharmacovigilance Department
- Contacting the IMB's Pharmacovigilance Department on 01-676 4971.

Antiviral drugs

Anti-viral medicines are used for the early treatment of influenza infection. Early treatment is recommended for any patient who has severe symptoms, and for patients in defined risk groups (see below). Use clinical judgement. Treatment should be started as early as possible (preferably within 48 hours of onset) but may be started at any time if clinically indicated. Some of these patients may require hospitalisation.

Defined risk groups:

- Chronic respiratory, heart, kidney, liver or neurological disease
- Immunosuppression (whether caused by disease or treatment)
- Diabetes mellitus
- People aged 65 years and older
- Children <5 years (children <2 years are at higher risk for severe complications)
- People on medication for asthma
- Severely obese people (BMI \geq 40)
- Pregnant women
- Haemoglobinopathies (including thalassaemia, sickle cell disease).

Antiviral treatment can reduce the severity and duration of symptoms of influenza if started within 48 hours of illness onset, and limited data from observational studies among hospitalised patients with pandemic (H1N1) 2009 infection indicate that oseltamivir can reduce mortality, even when started > 48 hours after illness onset. The drug of first choice in the management of influenza pandemic (H1N1) 2009 is oseltamivir (Tamiflu®). Zanamivir (Relenza®) is available when clinically indicated. Both drugs

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have been used in young children, pregnant women and other individuals with risk conditions and have been shown to be safe, effective and associated with improved outcomes.

Chemoprophylaxis is no longer generally recommended for contacts except for exceptional individual cases or settings where it may be appropriate (e.g. nursing homes or special education residential centres – following discussion with local public health staff).

Guidelines on the use of antivirals are available from the Irish Medicines Board at www.imb.ie and HPSC at www.hpsc.ie.

Managing Outbreaks

In general, immunisation as a control measure has been shown to be effective in preventing ongoing transmission in outbreaks. If an outbreak occurs in an institution vaccination should be considered for all unvaccinated individuals.

The benefit of vaccinating individuals who have already had laboratory-confirmed disease is unclear.

Pandemic Surveillance

A number of surveillance activities are being implemented to monitor the impact of pandemic (H1N1) 2009 on the population. These include sentinel surveillance of ILI consultation rates, ILI calls to GP out-of-hour deputising services, hospitalised patient surveillance, surveillance of patients admitted to intensive care units, virological surveillance (NVRL), mortality surveillance of acute respiratory illness (General Register's Officer; GRO). Reports on the outcome of these surveillance activities are routinely published on the HPSC website and area available at www.hpsc.ie.

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