



IRISH MEDICINES BOARD

UPDATE ON NATIONAL MONITORING EXPERIENCE WITH PANDEMIC H1N1 VACCINES

Suspected Adverse Reactions to Pandemic (H1N1) 2009 Vaccines occurring in Ireland

1 April 2010

The H1N1 vaccines in use in Ireland are Pandemrix and Celvapan and it is estimated that 1.1 million doses have been administered in Ireland to date with Pandemrix used in the majority of cases. As of 31 March 2010, the HSE vaccination clinics have closed. Due to the decreasing numbers of patients being vaccinated, and an expected reduction in the number of adverse reaction reports, the IMB will discontinue publication of routine updates. The safety of the H1N1 vaccines will continue to be monitored and further safety updates will be provided as appropriate.

Suspected adverse reaction reporting rates are highly variable and are dependent on many factors. Therefore these data cannot be used to determine the frequency of occurrence of adverse reactions to the H1N1 vaccines. Additionally, the use of the two H1N1 vaccines available in Ireland varied in terms of the extent of use and the patient populations exposed. For these reasons, the data provided in this update should not be used to draw comparisons on the safety of the vaccines. Guidance on interpreting the data presented is provided at the end of this report.

Up to Tuesday 30 March 2010, 1633 reports of suspected adverse reactions to the Pandemic H1N1 vaccines (Pandemrix and Celvapan) have been received by the Irish Medicines Board (IMB). A single report may include more than one suspected reaction. The reports received to date remain consistent with the expected pattern of adverse effects for the pandemic vaccines. The balance of risks and benefits for the H1N1 vaccines remains positive.

Pandemrix

The IMB has received 1128 adverse reaction reports for Pandemrix. Frequently reported suspected adverse reactions were injection site reactions (e.g. pain, swelling, redness), gastrointestinal symptoms (e.g. nausea, vomiting, diarrhoea) and flu-like symptoms (e.g. pain, fever, fatigue, myalgia and swollen glands).

Other commonly reported effects included dizziness, syncope (fainting episodes), headache, paraesthesia and transient limb weakness, sometimes associated with pain.

The IMB has received 67 reports of allergic reactions to Pandemrix including 7 anaphylactic type reactions. Reported symptoms included rash, flushing and dyspnoea and less frequently urticaria, facial oedema (periorbital swelling/swelling of lips/tongue), hypotension, tachycardia and wheezing. Some of the allergic reactions occurred in patients without a history of anaphylactic reactions or known drug/food allergies. Allergic reactions are a recognised potential adverse reaction. The reports of allergic reactions indicate that not only allergy to substances in the vaccine such as egg may give rise to reactions, but also other forms of allergic tendency appear to contribute to the development of an allergic reaction.

The IMB has been made aware of the death of an elderly patient who had been vaccinated nine days previously. The patient had a history of respiratory problems, further information is awaited. There is no evidence of a causal relationship between vaccination and the patient's death.

There have been four reports of facial palsy occurring post-vaccination including three reports of Bell's Palsy. A causal relationship with vaccination has not been established. A case of facial weakness has also been reported and the patient recovered without sequelae.

There have been 13 reports of seizures received by the IMB. Three cases occurred in patients receiving treatment for epilepsy or with a history of seizures. A further two reports of seizures in adults have been received but follow up is ongoing to confirm the exact nature of the symptoms experienced.

There has been one report of febrile convulsion in a child and a further two reports of convulsions in children with a past history of febrile convulsion.

Four reports described fainting episodes in conjunction with seizure-like movements while another recent report of seizure in a child also occurred immediately post vaccination.

One report of suspected Guillain Barré Syndrome (GBS) was included in previous updates, however additional information received on the results of investigations undertaken are not suggestive of GBS. Experience to date does not suggest that the vaccine contributes to the occurrence of GBS.

The IMB has received 20 adverse reaction reports associated with the use of Pandemrix in pregnant women. The reactions reported included local injection-site reactions, gastrointestinal symptoms, flu-like symptoms (e.g. fever), vaccination-related events (such as syncope and dizziness) and one report of Bell's Palsy. The IMB has been notified of a case of spontaneous abortion (miscarriage) in a woman with a history of recurrent miscarriage. There is no evidence to suggest that the vaccine contributed to this event.

Six hundred and eighteen adverse reaction reports were associated with use of Pandemrix in children. These included injection site reactions and vaccination related events such as pallor, syncope and dizziness. Flu-like symptoms, gastrointestinal symptoms, skin reactions and irritability were also commonly reported reactions. To date, the IMB has received 34 reports of allergic reactions in children including four cases of suspected anaphylaxis. There have been nine reports of seizures in children. One of these occurred in a patient with epilepsy and another in a patient with a history of seizures. There was one case of febrile convulsion and a further two reports of seizure involved children with a past history of febrile convulsion. Three of the reports described fainting episodes in conjunction with seizure-like movements while a recent report of seizure in a child also occurred immediately post vaccination. There have been 50 reports of pyrexia (fever) in children, 17 of which occurred in children aged 11-18 years, 24 in children aged 3-10 years and nine reports in those aged 6-35 months.

Celvapan

The IMB has received 479 adverse reaction reports for Celvapan. These include injection site reactions, flu-like symptoms and allergic-type reactions. Headache, dizziness, paraesthesia and syncope were also among the commonly reported effects. There have also been reports of gastrointestinal symptoms, particularly nausea and vomiting.

There have been 51 reports of allergic reactions to Celvapan which included 8 cases reported as anaphylactic type reactions. Among the allergic reactions, the reported

symptoms most commonly included rash, urticaria and pruritis and in a smaller number of cases hypotension, tachycardia, oedema and respiratory effects. Serious allergic reactions have been reported in patients without a known history of allergy as well as in patients with a history of allergies or chronic conditions such as asthma and eczema.

The IMB has been made aware of the death of a patient 10 days post vaccination with Celvapan. The patient had a number of underlying conditions including severe cardiac disease and insulin-dependent diabetes. There is no evidence of a causal relationship between vaccination and the patient's death.

The IMB has received one report of Bell's palsy occurring some time after vaccination. Limited information is available however a causal relationship with vaccination has not been established.

The IMB has received five reports of seizures, three of which occurred in adults receiving treatment for epilepsy. Another case described a seizure in a patient who experienced pallor and felt faint after vaccination but recovered fully without treatment. The most recent case was reported as an afebrile seizure in a child occurring two days post-vaccination.

The IMB has received one report of a suspected exacerbation of an autoimmune disorder. Follow up information has indicated that an alternative aetiology may be likely and no association with vaccination has been established.

The IMB has been notified of one case of laboratory confirmed vaccination failure in an immunosuppressed patient where the interval between dose one and dose two was two weeks.

Forty eight reports were associated with use in pregnant women and included gastrointestinal reactions, flu-like symptoms (including fever), syncope and other vaccination related events (e.g. anxiety, palpitations, dizziness). There have been four reports of allergic-type reactions. There have also been reports of paraesthesia and hypoaesthesia including one case of facial hypoaesthesia which recurred following administration of the second dose. The IMB has been notified of a case of spontaneous abortion (miscarriage) in a woman with a history of recurrent miscarriages. There is no evidence to suggest that the vaccine contributed to this event.

One hundred and ninety seven reports were associated with the use of Celvapan in children and these included injection site reactions, gastrointestinal symptoms, flu-like symptoms, skin rashes and vaccination related events (e.g. feeling faint, pallor and syncope). The IMB has received 22 reports of allergic-type reactions in children including two anaphylactic type reactions. There have also been five reports of transient hypotonia, in some cases with other symptoms (i.e. post vaccination events such as syncope and/or allergic type reactions). A report of convulsions in a 3 year old child with no previous history of seizures has also been notified to the IMB. Thirteen reports of pyrexia (fever) in children have been received, 11 occurring in children aged 3 - 10 years and two in those aged 6 – 35 months.

Brand unknown

The vaccine brand was not reported in 26 cases and follow up to establish which product was used is underway. The reports include flu-like symptoms, injection site reactions, gastrointestinal symptoms, hypersensitivity reactions and vaccination-related events. Two of the reports related to seizures in children.

Advice to Healthcare Professionals and Caregivers

Vaccine Traceability:

- Wherever possible please include details of the brand name/manufacturer of the vaccine administered when submitting adverse reaction reports.
- It is also very important that the name of the vaccine administered is recorded in healthcare/patient records and that patients are provided with a copy of the package leaflet supplied with the vaccine to ensure that they are aware of the brand of vaccine administered and the safety profile.
- The IMB wishes to remind healthcare professionals that, as with all injectable vaccines, appropriate medical treatment and supervision should always be readily available in case of a serious allergic reaction and possibly a rare anaphylactic event following the administration of the vaccine. An appropriate post-vaccination monitoring period should be observed in line with local guidance and recommendations on vaccination.
- Monitoring of temperature is recommended in young children following vaccination. As with all vaccines, prescribers and parents should monitor the temperature of the vaccinated child and, if necessary, take measures to lower the fever (e.g. giving an antipyretic such as paracetamol).

Guidance on the interpretation of these data

These adverse reaction reports have been submitted to the IMB on a voluntary basis by healthcare professionals and members of the public, either through the online reporting tool available on the IMB website (www.imb.ie), or by post or telephone. This report also contains any Irish reports notified to the IMB by the Marketing Authorisation holders for Pandemrix (GSK) and for Celvapan (Baxter).

Reporters are encouraged to report *suspected* adverse reactions. In other words, the reporter does not have to be sure that the vaccine caused the reaction, a mere suspicion will suffice. Therefore the reports received may be true adverse reactions to the vaccine, they may be events related to the process of vaccination rather than to the specific vaccine itself, or they may be coincidental events which have occurred post-vaccination but which would have occurred anyway even if vaccination had not taken place (e.g. they may be due to an underlying medical condition).

All reports are carefully evaluated and one objective of this evaluation is to distinguish real side effects from coincidental medical events. Many people receiving the vaccine have serious and/or chronic underlying medical conditions which put them at greater risk of developing serious complications of swine flu. This is why it is important for these people to be vaccinated as a priority. Over the next few months, many of these patients may naturally suffer an exacerbation of their underlying illness and as a result some may subsequently die from their illness. Such events may coincidentally occur around the time of vaccination and as such, may be reported to the IMB. It is important to bear in mind that this temporal association does not in itself mean that the vaccine was responsible for the event and that the timing may be purely coincidental.

Complications can occur in any pregnancy and information from the Royal College of Obstetricians indicates that in Ireland up to 20% of pregnant women miscarry during the first 14 weeks of pregnancy, and still-births occur in 8-10 pregnancies per 1,000. Therefore, it is inevitable that some adverse pregnancy outcomes will occur with pregnant women, some of whom will have been vaccinated.

Guillain-Barré Syndrome is a spontaneously occurring condition so it is inevitable that cases will occur, and be reported as possible side effects, not long after vaccination, particularly over the winter period when many pathogens are circulating. It is important to understand that a temporal association alone does not mean that the vaccine caused the condition. There are excellent systems in place to detect if the vaccine may be causing conditions such as GBS and the IMB is working very closely with its European and international partners in monitoring vaccine safety. This issue is being closely followed. Specific studies on Guillain-Barré syndrome have also been initiated in some Member States and results are awaited. At least 42.3 million people have been vaccinated with the centrally authorised H1N1 vaccines in the European Economic Area and the balance of risks and benefits for the vaccines remains positive.

More information on Pandemrix and Celvapan, including information on recognised adverse effects, is provided in the product information, copies of which are available from the IMB (www.imb.ie) and European Medicines Agency (www.ema.europa.eu) websites.