IRISH MEDICINES BOARD

UPDATE ON NATIONAL MONITORING EXPERIENCE WITH PANDEMIC H1N1 VACCINES

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

21st January 2010

The H1N1 vaccines in use in Ireland are Pandemrix and Celvapan and it is estimated that approximately 1.6 million doses have been distributed. Some 800,000 doses have been administered in Ireland to date, with Pandemrix now being used in the majority of patients.

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 may differ 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 19th January 2010, 1080 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 Celvapan and Pandemrix remains positive.

Pandemrix

The IMB has received 655 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 49 reports of allergic reactions to Pandemrix including five suspected anaphylactic 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 recently 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 currently 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 five reports of seizures, one of which occurred in a patient receiving treatment for epilepsy. The second case was a febrile convulsion in a child with a history of previous febrile convulsions. Another case involved a patient with no prior history of epilepsy who had a recent pre-vaccination diagnosis of a neurological condition. Two recent reports described fainting episodes in conjunction with seizure-like movements and follow-up of these cases is underway.

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 15 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 currently no evidence to suggest that the vaccine contributed to this event.

Two hundred and eighty five adverse reaction reports were associated with use 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 25 reports of allergic reactions in children including two cases of suspected anaphylaxis. One case of a febrile convulsion and another of a fainting episode with associated seizure-like movements have been reported. There have been 38 reports of pyrexia (fever) in children, 10 of which occurred in children aged 11-18 years, 19 in children aged 3-10 years and nine reports in those aged 6-35 months.

Celvapan

The IMB has received 405 adverse reaction reports for Celvapan. These include injection site reactions, flu-like symptoms and allergic-type reactions. Headache, dizziness, paraesthesia and syncope were among the commonly reported effects. There have also been reports of gastrointestinal symptoms, particularly nausea and vomiting.

There have been 46 reports of allergic reactions to Celvapan which includes four reports of suspected anaphylactic 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 complex cardiac disorders and insulin-dependent diabetes. There is no evidence of a causal relationship between vaccination and the patient's death.

The IMB has received four reports of seizures, two 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 and follow up information is awaited.

The IMB has received one report of a suspected exacerbation of an autoimmune disorder – symptoms resolved with treatment.

Forty two 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 currently no evidence to suggest that the vaccine contributed to this event.

One hundred and sixty 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 20 reports of allergic-type reactions in children, some of which have been serious and required treatment. 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. Twelve reports of pyrexia (fever) in children have been received, 10 occurring in children aged 3 - 10 years and two in those aged 6 – 35 months.

Brand unknown
The vaccine brand was not reported in 20 cases and follow up to establish which product was used is underway. These include reports of flu-like symptoms, injection site reactions, gastrointestinal symptoms, hypersensitivity reactions, vaccination-related events and two reports of seizures.

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. It is estimated that 33.9 million patients have been vaccinated in Europe with one of the three centrally authorised H1N1 vaccines and there is no evidence to suggest that the vaccines are causing GBS.

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.