Analysis of suspected adverse events following vaccination against pandemic influenza (H1N1) 2009 in Switzerland

PaniFlow database 10 November - 11 December 2009

This document provides an analysis of the first month of reported suspected adverse events following vaccination against pandemic influenza (H1N1) 2009 in Switzerland.

In collaboration with The Uppsala Monitoring Centre and WHO, Swissmedic developed a spontaneous on-line reporting system known as PaniFlow which receives reports submitted by health professionals. Information on PaniFlow may be found on the Swissmedic Pandemic Portal (www.swissmedic.ch/pandemieportal.asp)

The first report was registered in PaniFlow on 10 November 2009. Up to and including 11 December 2009, a total of 360 reports have been entered and analysed in the PaniFlow database. The following table and summary of suspected adverse reactions indicate the support and commitment of health care professionals to report cases in the PaniFlow online system.

Figure 1
Overview of reports entered in the PaniFlow database

General Information
The reports listed are only for suspected adverse events that meet certain criteria. A case may have one or more suspected adverse reactions, thus the number of reactions exceeds the number of case reports. As currently no data are available on the number of people vaccinated, and because only a proportion of reactions that occurred are actually reported, no frequencies of reactions are calculated. Comparisons between the different vaccines cannot be made. Those reports that are not classified as serious are not listed separately, but are included in the total number of reports.

For pharmacovigilance purposes the term serious is defined as an event that is assessed to be medically important, or requiring (or prolonging) a hospital admission, or a persistent or significant disability, or a congenital birth defect, or life threatening or fatal. The term
expected is defined as an event described in the adverse reaction profile listed in the specified product monograph.

Important:
The single case reports describe suspected adverse events that occurred in a close time period following vaccination. The cause of the suspected adverse event(s) cannot be immediately assigned based on a case report. The event(s) may be related to the vaccine, or may have occurred as a coincidence following the vaccination. Determining causality for suspected adverse events requires careful further assessment. A causal relationship with the vaccine cannot be established without a confirmed diagnosis and full investigations to exclude other possible causes.

Summary of reports of suspected adverse events following vaccination with pandemic influenza vaccines

<table>
<thead>
<tr>
<th>Total number of reports</th>
<th>360</th>
</tr>
</thead>
<tbody>
<tr>
<td>Number of reports with serious and expected reactions</td>
<td>74</td>
</tr>
<tr>
<td>Number of reports with serious and unexpected reactions</td>
<td>69</td>
</tr>
<tr>
<td>Number of reports in pregnant women</td>
<td>7</td>
</tr>
<tr>
<td>Number of ongoing enquiries</td>
<td>54</td>
</tr>
</tbody>
</table>

Per: 11.12.2009

General Conclusions:

Up to 11 December 2009, a total of 2,968,880 million doses of vaccines were delivered to the Swiss cantons (286,250 doses of Focetria®, 985,330 doses of Celtura®, and 1,697,300 doses of Pandemrix®). Up to and including 11 December 2009, a total of 360 reports were received and which described a total of 1015 suspected adverse reactions. The majority of cases described self-limited and non-serious reactions occurring at the injection site, as well as generalized reactions such as headache, fever, nausea, muscle aches and joint pain.

69 reports were classified as serious and unexpected. 32/69 cases were medically important reactions that have been evaluated and assessed as unlikely to be related to the vaccination, due to other medical reasons and/or a temporal course that was implausible.

Swissmedic exchanges safety data of pandemic influenza vaccines with other national authorities on a weekly and confidential basis. Swissmedic is continuing to closely monitor the safety profile of all 3 vaccines, and in particular with close monitoring of allergic reactions, musculoskeletal and neurological system disorders and in special vaccinated groups including pregnant women and children. To date, the reported adverse reactions correspond with those described in clinical trials and with the profile from postmarketing experience with seasonal influenza vaccines. The reported adverse reactions of the pandemic influenza vaccines correspond to those observed in other countries using the same vaccine products.

Available mortality statistics indicate an average of 167 deaths per day in Switzerland and a background incidence rate of stillbirth of 4 per 1000 births in Western Europe. A temporal relationship with vaccination can therefore be purely coincidental.
In previous years, deaths have been reported to Swissmedic following seasonal influenza vaccination in Switzerland. Each of these reports is carefully investigated. In these cases, patients had serious underlying diseases such as heart or lung disease. A causal association with seasonal influenza vaccines and these reports was not established.

An evaluation of suspected adverse events reports for each vaccine is provided below. The different distribution of reports is expected, considering the different number of distributed doses and different public health recommendations for each of the 3 vaccines licensed in Switzerland.

I. Celtura®

Up to 11 December 2009, 15 reports (11 female, 4 male) and a total of 50 suspected adverse reactions were received for Celtura®.

2/15 reports described allergic reactions (urticarial rash), a known potential side effect of the vaccine.

6/15 reports described transient neurological symptoms such as visual disturbance, vertigo or a sensory disturbance. Paraesthesia (burning, tingling, reduced sensation) is a recognised potential adverse reaction of the vaccine. No cases had progression to a serious illness. 1/6 cases described an individual with a known history of multiple sclerosis who developed fever and sensory disturbances (diagnosed as a Uthoff phenomenon) which were transient following vaccination and with good recovery.

1/15 death was reported in an older individual (> 80 years old) with chronic medical conditions. A causal association with the vaccination was assessed as unlikely.

No reports were received in pregnant women or in children.

Figure 2: Celtura®
Suspected adverse drug reactions (ADRs) classified by system organ class (SOC)

Counts by SOC/ADRs

Notes on Figure 2: The SOC described as “Empty” refers to a free-text entry term that was not a standard SOC term.
II. Focetria®

Up to 11 December 2009, 33 reports (20 female, 13 male) and a total of 83 suspected adverse reactions were received for Focetria®.

4/33 reports described allergies (such as urticarial rash, swelling of lips and tongue, difficulty breathing) with the more severe cases requiring immediate medical attention. Allergic reactions are described in the product information of the vaccine.

1/33 report described a patient with a mild and transient thrombocytopenia (low platelets). This was detected by a blood test, with no clinical symptoms and resolved spontaneously. Thrombocytopenia is a described adverse reaction of the vaccine in the product information.

1/33 report described syncope (fainting) following vaccination related to the injection procedure. 5/33 reports described transient neurological symptoms such as visual disturbance, vertigo or paraesthesia (burning, tingling, reduced sensation). 1/5 cases described a pregnant woman with facial paralysis. A neuritis, such as a facial palsy, is described in the product information for the vaccine but other potential causes of facial paralysis should be considered, including infection.

1/33 report described a 15 year old boy who developed herpes zoster. Herpes zoster is not a described reaction. A causal association with the vaccine has not been established but these reports are being monitored closely.

2/33 cases described joint pains, 1/2 case described a new episode of arthritis in a patient with a pre-existing inflammatory arthritis.

7/33 reports were received in pregnant women. 1/7 reported premature labour which was medically treated and resolved in a patient with a history of premature labour in a prior pregnancy. 3/7 cases reported an intrauterine fetal death. Swissmedic has completed investigation of 2/3 cases. The 2 completed cases have indicated other plausible factors that may have led to the unfortunate event. An association with vaccination was assessed as unlikely in these 2 cases. The 3rd case is currently under investigation.

14/33 reports were in children under 16 years of age. 9/14 reports in children were under 3 years of age and described self-limited fever, vomiting, anxiety, and allergic reactions. 1/33 described a case of an afebrile convulsion in a child with a known chronic neurological disease. A causal association between this event and the vaccine was not established.
III. Pandemrix®

Up to 11 December 2009, 312 reports (191 female, 116 male, 5 unspecified) and a total of 882 suspected reactions were received for Pandemrix®. Pandemrix® accounts for the majority of reports (87%) entered in PaniFlow, which is most likely from the greater availability and use of this vaccine in Switzerland.

47/312 reports described allergies (such as urticarial rash, swelling of lips and tongue, difficulty breathing) with the more severe cases requiring immediate medical attention. Allergic reactions are described in the product information of the vaccine.

27/312 cases described arthralgia (joint pains), of which 6/27 cases described an episode of arthritis in patients with a pre-existing history of arthritis. 1/312 case was reported as allergic vasculitis in an older patient with history of rheumatological diseases and the patient is recovering after hospitalisation. Joint aches and swelling around joints are known and uncommon adverse reactions described in the product information for both seasonal and pandemic influenza vaccines. Vasculitis is also a known and very rare adverse event that has been described.

11/312 cases described syncope (fainting) following vaccination related to the injection procedure. 17/312 reports described transient neurological symptoms such as visual disturbance, vertigo or paraesthesia (burning, tingling, reduced sensation). 2/312 cases describe individuals with facial paralysis. A neuritis, such as a facial palsy, is described in the product information for the vaccine but other potential causes of facial paralysis should be considered, including infection. 2/312 reports were both in individuals with known diagnoses of multiple sclerosis, reporting neurological symptoms that were described as typical symptoms of pre-existing disease, with both patients responding to usual therapy.
6/312 reports describe adults who developed herpes zoster. Herpes zoster is not a described reaction. A causal association with the vaccine has not been established but these reports are being monitored closely.

1/312 report was a case of an abscess at the injection site following vaccination, which required and responded to antibiotic therapy. This highlights the importance of proper sterile technique in administering an injection.

12/312 reports were in children under 16 years of age. 2/12 reports in children were under 3 years of age and described self-limited fever, vomiting, anxiety, and allergic reactions. 1/2 cases described a febrile convulsion followed by good recovery in a 7-month old boy. A convulsion is a recognised complication of a fever in young children.

9/312 deaths were reported. All 9 individuals had chronic medical conditions and a causal association with the vaccination was assessed as unlikely.

Figure 4: Pandemrix®
Suspected adverse drug reactions (ADRs) classified by system organ class (SOC)

Counts by SOC/ADRs

Notes on Figure 4: The SOC described as “Empty” refers to a free-text entry term that was not a standard SOC term.