



European Medicines Agency
Patient Health Protection

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Pandemic pharmacovigilance weekly update
Status at 27 November 2009

This update has been prepared by the European Medicines Agency (EMA) to provide information on the evolution of the H1N1 pandemic, an estimate of how many doses of centrally authorised pandemic vaccines and antivirals have been distributed or administered in Europe, a summary of the adverse reactions reported to the Agency after use of the vaccines and antivirals, and other information on the benefits and risks of the vaccines and antivirals. Centrally authorised pandemic medicines concerned by this update are the vaccines Celvapan, Focetria and Pandemrix and the antiviral Tamiflu.

This report includes *suspected* reactions that were observed after the vaccine was administered. This does not mean they have been caused by the vaccine. They could be a symptom of another illness or they could be associated with another product taken by the patient. Healthcare professionals are actively encouraged to report events following vaccination.

The information has been obtained from EudraVigilance. EudraVigilance is a database and management system managed at the EMA for collecting and evaluating reports of suspected adverse reactions to medicinal products in the European Economic Area (EEA). It allows the transfer of reports from national regulatory agencies and marketing authorisation holders to the EMA, and the early detection and monitoring of possible safety signals in relation to reported adverse reactions.

Reports are collected on a continuous basis. This update includes reports received in Eudravigilance after the Marketing Authorization of the centrally authorised pandemic vaccines up to 27 November.

Note that a single patient may experience several reactions that will be included in a single report. Therefore the number of reactions may not be equal to the number of patients.

The weekly update may also include information on vaccine safety made available by Member States.

Key message:

The benefit/risk balance of the pandemic vaccines and antivirals used for the current H1N1 influenza pandemic continues to be positive. To date, no unexpected serious safety issues have been identified. The most frequent adverse reactions that have been reported are non-serious and as expected.

The EMA issued a press release on 20 November 2009 reaffirming the efficacy and safety of the centrally authorised vaccines. With vaccination campaigns ongoing in the European Union, it is estimated that about 10 million people have been vaccinated so far. The vaccine adverse effects reported so far have mainly been symptoms such as fever, nausea, headache, allergic reactions and injection site reactions, confirming the expected safety profile of the three vaccines.

New clinical trial data showed greater incidence of fever following the second dose of Pandemrix in infants from 6 months to 35 months. An assessment of these data is ongoing.

For further information on the established adverse reactions included in authorised product information for centrally authorised pandemic vaccines (Celvapan, Focetria, Pandemrix) and antivirals (Tamiflu), visit the [EMA Pandemic influenza \(H1N1\) website](http://www.emea.europa.eu/pdfs/vet/human/Pandemic_influenza_H1N1_website.pdf).

For information regarding products authorised at a national level, please contact the relevant National Competent Authority (see the [EMA website](#) for links).

Pandemic information:

According to the European Centre for Disease prevention and Control (ECDC) [latest report](#) of 27 November 2009, a total of 858 fatal H1N1 influenza cases in the European Union and EFTA countries and 7,710 in the rest of the world have been reported to date (see the [ECDC website](#)).

According to the World Health Organization (WHO) [latest report](#), as of 22 November 2009, worldwide more than 207 countries and overseas territories or communities had reported laboratory confirmed cases of pandemic influenza H1N1 2009.

As of 19 November, WHO had received vaccination information from 16 of around 40 countries conducting national H1N1 pandemic vaccine campaigns. Based on information in these 16 countries, WHO estimates that around 80 million doses of pandemic vaccine have been distributed and around 65 million people have been vaccinated (see the [WHO website](#)).

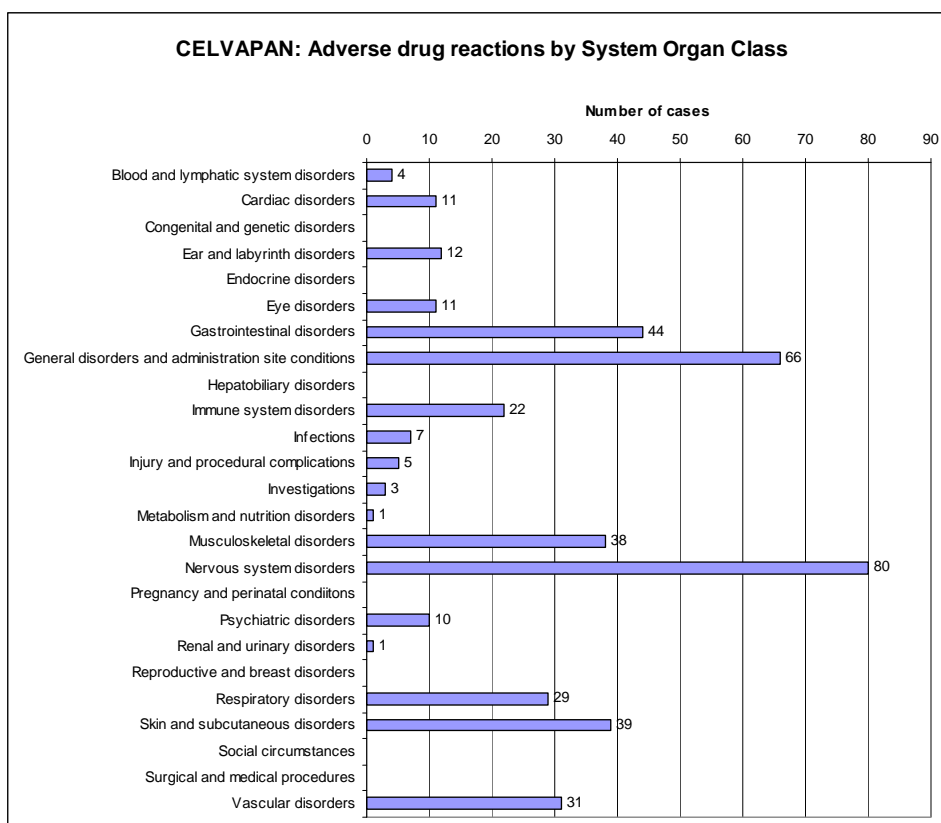
Overview of centrally authorised vaccines

As of 27 November, a total of 3,832 reports have been received by EudraVigilance since the authorisation of the three centrally-authorised vaccines. There has been an increase on the number of reports over time reflecting the increase in the take-up of vaccination. The graphs presented below include all reports received from the EEA. Updated safety information may include data received from outside the EEA.

Celvapan

As of 27 November, a total of 160 reports and 414 reactions have been received by EudraVigilance. According to company information, a total of 3,399,200 doses have been distributed to EU Member States through 16 November.¹ A current estimation of the number of doses administered was not available at the time of reporting.

¹ As stated by the marketing authorisation holder in the simplified Periodic Safety Update Report (S-PSUR) received 30 November 2009.
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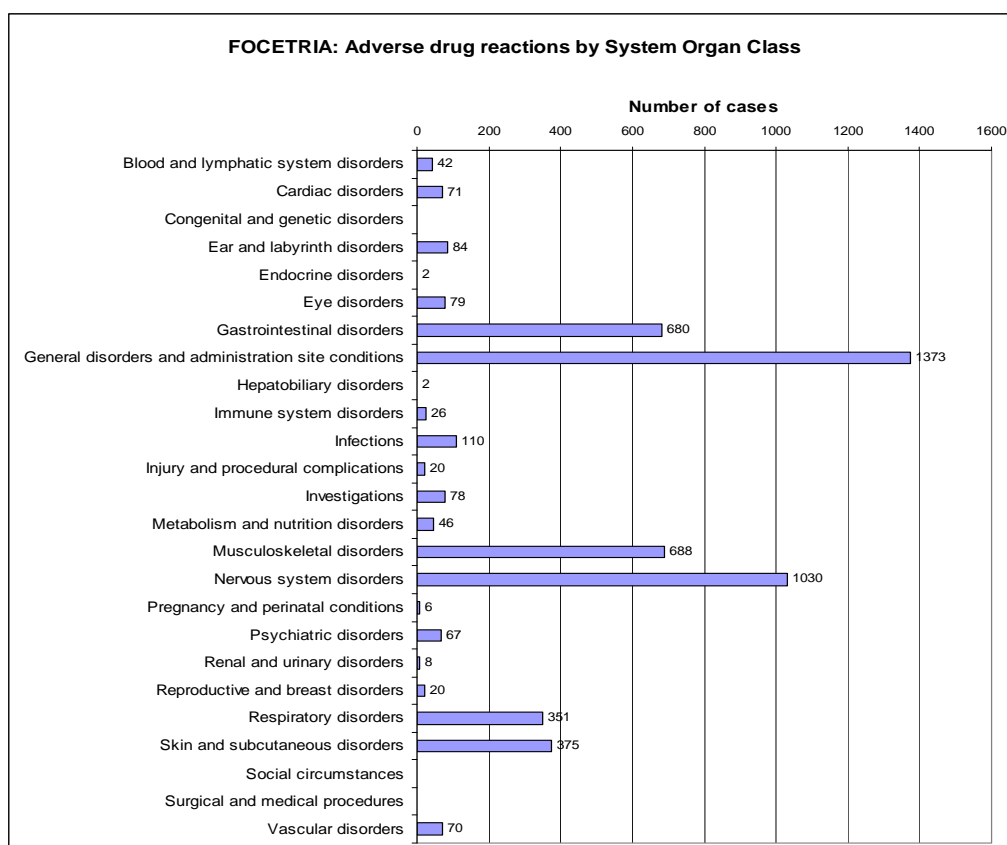
Updated safety information:

- Headache, nausea, malaise, vomiting, malaise, hypersensitivity, fever, paraesthesia, dyspnoea, arthralgia and myalgia have been among the most frequently reported suspected adverse reactions since the authorisation of the vaccine.
- Reports in children included anaphylactic reactions and hypersensitivity have been received.
- Since the start of use of Celvapan one case report has been received with a fatal outcome. There is no indication that the vaccine contributed to this death.
- No signal of a new safety issue has been detected since authorisation.

Focetria

As of 27 November, a total 1,371 reports and 5,228 reactions have been received by EudraVigilance. According to company information dated 16 November, 10 million doses have been distributed through 2 November 2009.² It is estimated that about 4.5 million of doses have been administered.

² As stated by the marketing authorisation holder in the S-PSUR received 16 November 2009.



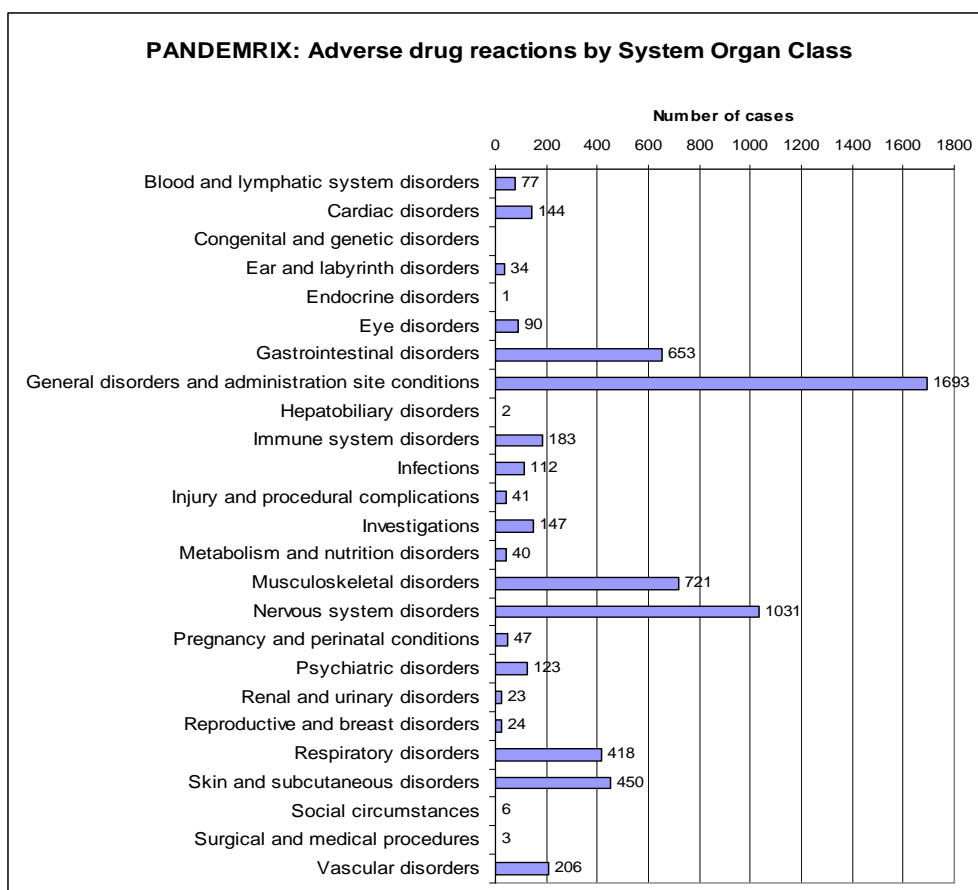
Updated safety information:

- Headache, fever, nausea, fatigue, dizziness, vomiting, chills, injection site reactions, myalgia, pain in extremity and dyspnoea have been among the most frequently reported suspected adverse reactions since the authorisation of the vaccine.
- Twelve reports have been received with a fatal outcome. There is no indication that the vaccine contributed to these deaths.
- One case of cerebral haemorrhage has been received. It concerned a patient of 76 years, and the information currently available does not suggest that the vaccine caused the event.
- Three cases of severe anaphylactic reactions have also been received.
- No signal of a new safety issue has been detected since authorisation.

Pandemrix

As of 27 November a total of 2,301 reports and 6,269 reactions have been received by EudraVigilance. According to information received from the marketing authorisation holder dated 19 November, the total number of doses distributed was 39.3 million and the total number of people vaccinated was estimated to be around 5.7 million through 17 November 2009.³

³ As stated by marketing authorisation holder in the S-PSUR received 19 November 2009.
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Updated safety information:

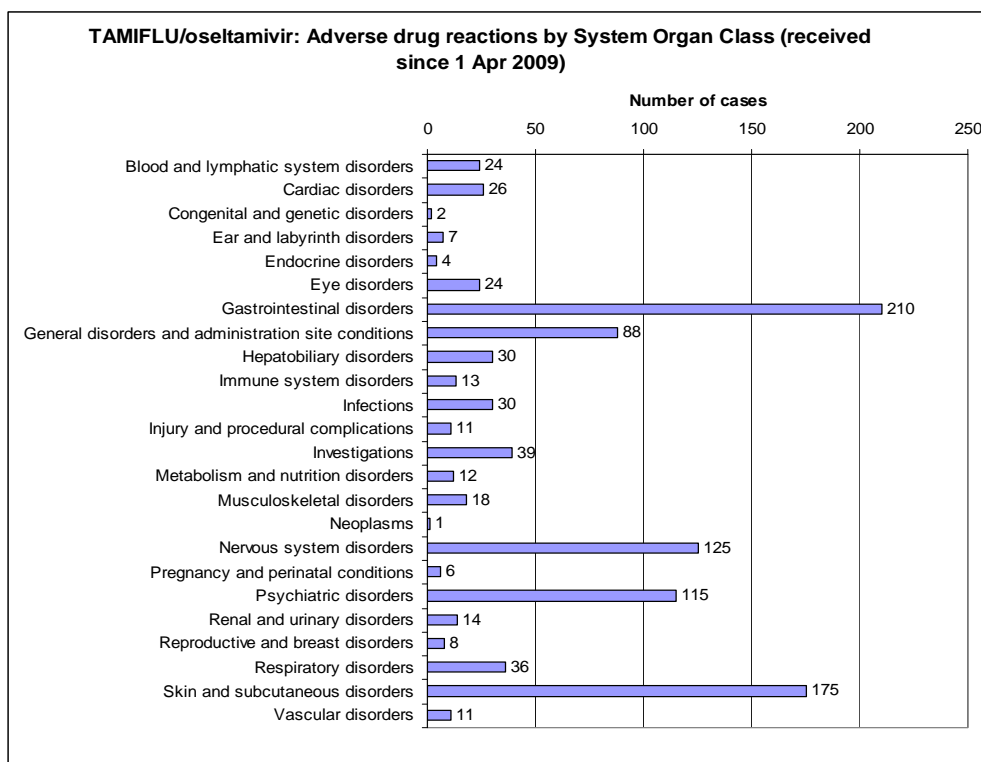
- Fever, headache, nausea, vomiting, fatigue, injection site reactions, myalgia, arthralgia, paraesthesia, dizziness, pain in extremity, diarrhoea, chills, dyspnoea, malaise, cough, anaphylactic reaction and hypersensitivity have been among the most frequently reported adverse reactions since the vaccine has been authorised.
- New clinical trial data showed greater incidence of fever ($\geq 38^{\circ}\text{C}$), local reactions (pain, redness, swelling) and drowsiness/irritability/loss of appetite following the second dose of Pandemrix in infants from 6 months to 35 months. An assessment of these data is ongoing.
- Since the start of use of Pandemrix as an authorised vaccine, a total of fifty-five case reports have been received by the EudraVigilance system which have a fatal outcome. There is no indication that the vaccine contributed to those deaths.
- EudraVigilance has received a total of 24 cumulative cases of pregnancy related events such as abortions, intrauterine deaths, stillbirths, foetal hypokinesia and premature birth. Those cases are being investigated further. There currently is no evidence of a causal link between the vaccine and reported events.
- EudraVigilance has received 26 paediatric cases of anaphylactic reactions/hypersensitivity (24 cases aged from 0 to 17 years, and 2 with age unknown). Anaphylaxis is a rare expected adverse reaction to Pandemrix.
- Up to 27 November, three reports of Guillain-Barré syndrome were received. Two were later not confirmed and one is under investigation. There is no evidence to suggest that the vaccine causes Guillain-Barré syndrome.
- A case of heart transplant rejection from Sweden was received. Further information was requested and health authorities are seeking advice from transplant immunologists.

Antiviral medicines:

Tamiflu

From 1 April to 27 November 2009, a total number of 705 reports and 1,029 reactions have been received in Eudravigilance.

According to information received from the marketing authorisation holder dated 5 November 2009, the patient exposure during the period October 2008 to September 2009 was 10.4 million patients.⁴



Updated safety information:

- The adverse reaction reports received are consistent with the safety profile described in the Product Information.
- Since April 2009, 137 case reports have been received by the EudraVigilance system with a fatal outcome following Tamiflu use. In the fatal cases, the causal association with oseltamivir treatment cannot be established. It should be noted that healthcare professionals are actively encouraged to report events following administration of medicinal products and purely coincidental events (e.g. due to underlying medical conditions) that would have occurred anyway, in the absence of therapy, will be reported.

⁴ As stated by marketing authorisation holder in the PSUR dated 5 November 2009.