EUROPEAN MEDICINES AGENCY
SCIENCE MEDICINES HEALTH

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Patient Health Protection

Sixteenth pandemic pharmacovigilance update

This report summarises the adverse drug reactions reported after the use of the centrally authorised pandemic vaccines Arepanrix, Celvapan, Focetria and Pandemrix and the antiviral Tamiflu. It also provides information on the evolution of the H1N1 pandemic, an estimate of how many doses of vaccines and antivirals have been distributed or administered in Europe, and other available information on the benefits and risks of the vaccines and antivirals. Humenza is a pandemic vaccine that received a positive opinion from the Committee for Medicinal Products for Human Use (CHMP), and the formal decision from the European Commission is expected shortly. As this vaccine is not marketed and no adverse reaction report has been received by EudraVigilance, this vaccine is not included in this update.

This update includes reports of *suspected* reactions that were observed after the medicines were administered. This does not mean that these reactions were caused by the medicines. 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 occurring after vaccination.

Due to different number of people receiving each vaccine, the number of reports for the four different vaccines cannot be used to compare the safety or the benefit-risk balance of the vaccines.

As a single patient may experience several reactions that will be included in a single report, the total number of reactions may not be equal to the total number of patients. In addition, as some patients have received two doses of the vaccines, the total number of doses administered is not necessarily equal to the total number of patients vaccinated.

Reports are collected in EudraVigilance, a database and management system administered by the European Medicines Agency for the collection and evaluation of reports of suspected adverse drug reactions to medicinal products. EudraVigilance allows the transfer of reports from national regulatory agencies and marketing authorisation holders to the Agency, and the early detection and monitoring of possible safety signals in relation to reported adverse reactions.

This update includes reports received by EudraVigilance up to 11 April 2010. Except for Arepanrix, which is not marketed in the European Economic Area (EEA), the graphs represent aggregated data related to the EEA only, and provide an overview of the reporting situation in the EEA. The updated safety information also considers worldwide cases from EudraVigilance.

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A list of the most frequently reported suspected adverse reactions is presented for the organ systems with the largest number of reports.

Key messages

The vast majority of the adverse reactions that had been reported as of 11 April 2010 are considered to be non-serious.

The benefit-risk balance of the centrally-authorised pandemic vaccines and antivirals for the current H1N1 influenza pandemic continues to be positive.

On 29 March 2010, a group of experts including neurologists and epidemiologists was convened to discuss the available information on the cases of Guillain-Barré syndrome reported in relation to A/H1N1 influenza pandemic vaccines. Based on the analysis of spontaneous reports, the experts concluded that the data are currently reassuring and there is no sign of a risk of a similar magnitude as that found in the pandemic situation of 1976. A possible association between the pandemic A/H1N1 vaccines and GBS cannot be totally ruled out given the uncertainties in the current information. However, if such an association exists, it would probably translate in a very small increase in the risk. The expert group also considered the ongoing epidemiological studies carried-out in several European countries. It concluded that the results of these studies should be awaited to obtain a valid estimate of the possible risk of GBS associated with A/H1N1 influenza vaccines. A summary of the meeting is at Appendix 1. Based on the recommendations of the report, the Committee for Medicinal Products for Human Use (CHMP) concluded at its April 2010 meeting that the benefit-risk balance of the A/H1N1 influenza vaccines remains positive and that no amendment of their Summary of Product Characteristics is necessary. The Committee will re-assess the issue as the preliminary results of the epidemiological studies become available (from June 2010).

For further information on the known adverse reactions included in the authorised product information for the centrally authorised pandemic vaccines Arepanrix, Celvapan, Focetria and Pandemrix and the antiviral Tamiflu, visit the Agency's pandemic influenza (H1N1) website.

For information regarding products authorised at a national level, please contact the relevant national competent authority (see regulatory bodies in the European Union for links).

Pandemic information

In its weekly influenza surveillance overview dated 16 April 2010, the European Centre for Disease Prevention and Control (ECDC) confirmed that all 24 reporting countries experienced low intensity of influenza activity for the sixth consecutive week.

The ECDC report also states that, even though, globally, the world remains in pandemic Phase 6, influenza activity caused by the 2009 pandemic influenza A(H1N1) virus is well past its winter peak in European Union (EU)/EEA countries. However, transmission associated with sporadic cases continues to occur whilst most cases of influenza-like illness in EU/EEA countries are not due to influenza virus infection.

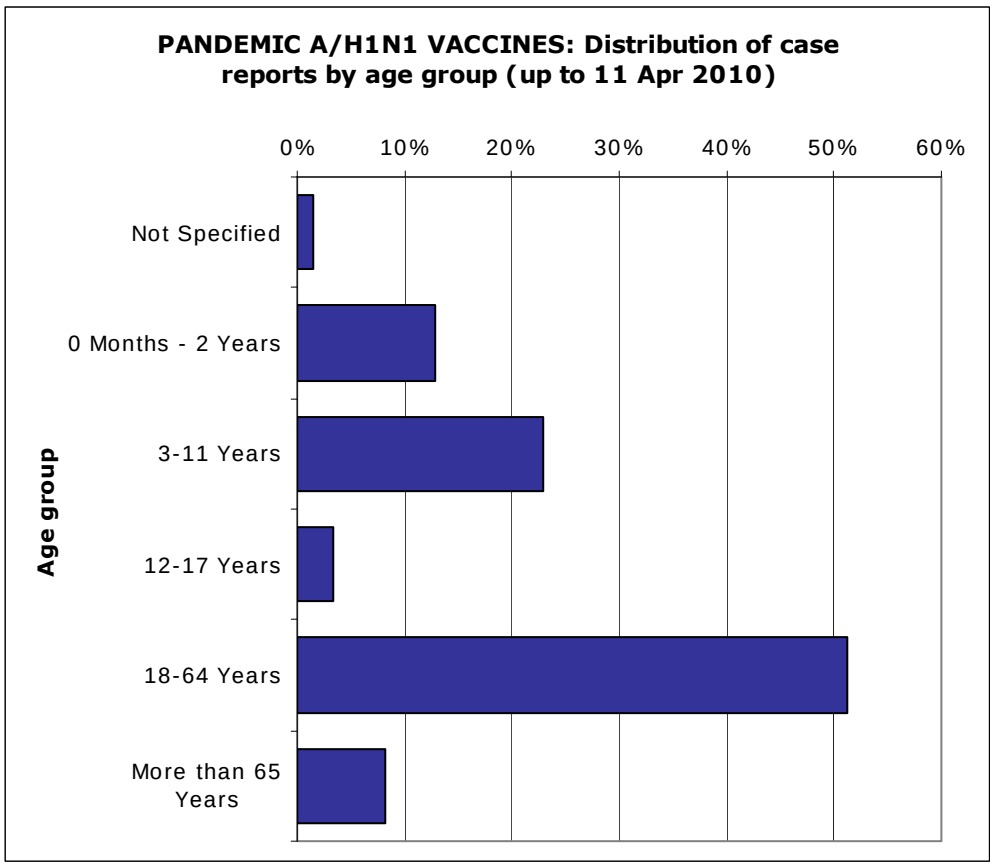
In the week ending April 19, EU/EFTA Member States announced three deaths on their national websites, meaning that as of April 19 there were 2,876 deaths due to the pandemic announced by these states. Click here for the breakdown by country.

See the ECDC pandemic website and its last weekly executive update for additional information

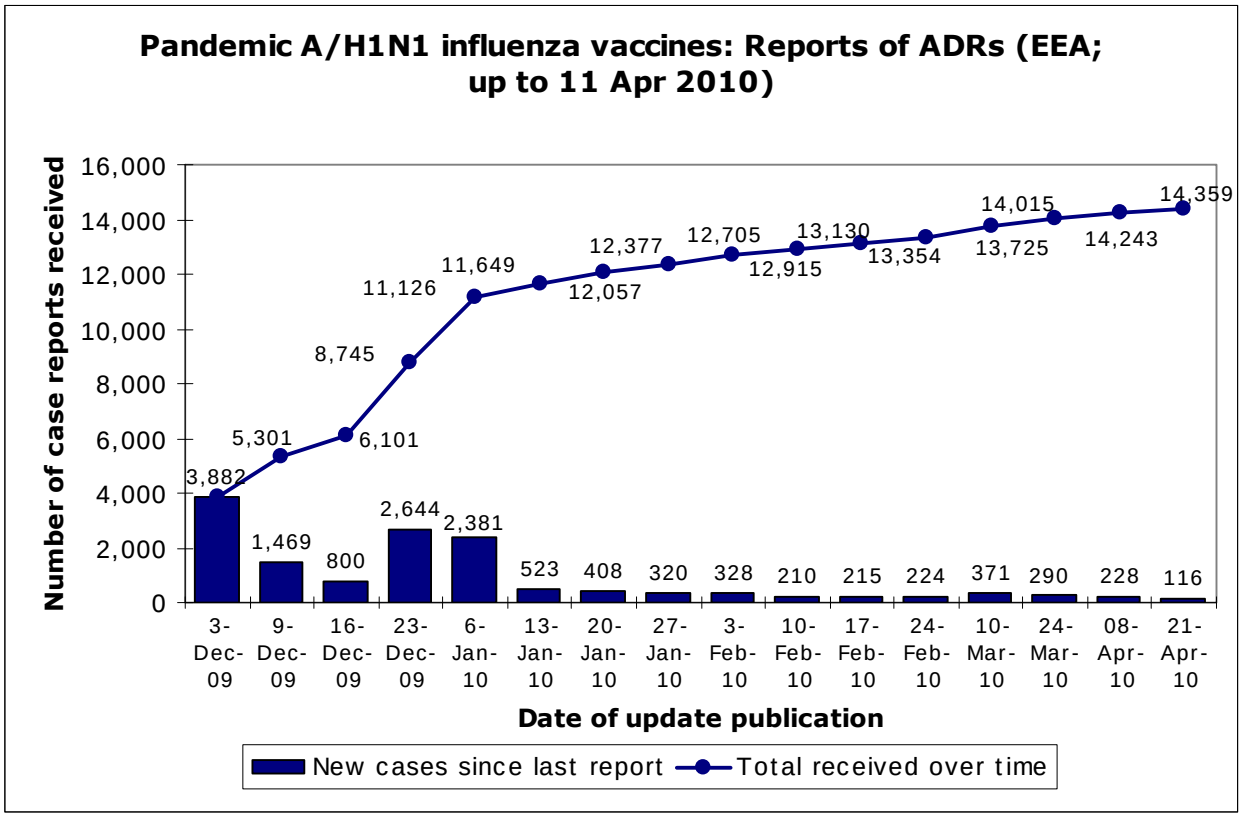
In its weekly update dated 16 April 2010, the World Health Organization (WHO) reports that, as of 11 April 2010, worldwide more than 214 countries and overseas territories or communities have reported laboratory confirmed cases of pandemic influenza H1N1 2009, including over 17,798 deaths.

Overview of centrally authorised vaccines

As of 11 April 2010, a total of 14,359 case reports had been received from the EEA by EudraVigilance since the authorisation of the centrally authorised vaccines in the EEA (Arepanrix, Celvapan, Focetria and Pandemrix). This represents an increase of 116 reports compared with the previous update. The graph below displays the age distribution of all the reports received by EudraVigilance.



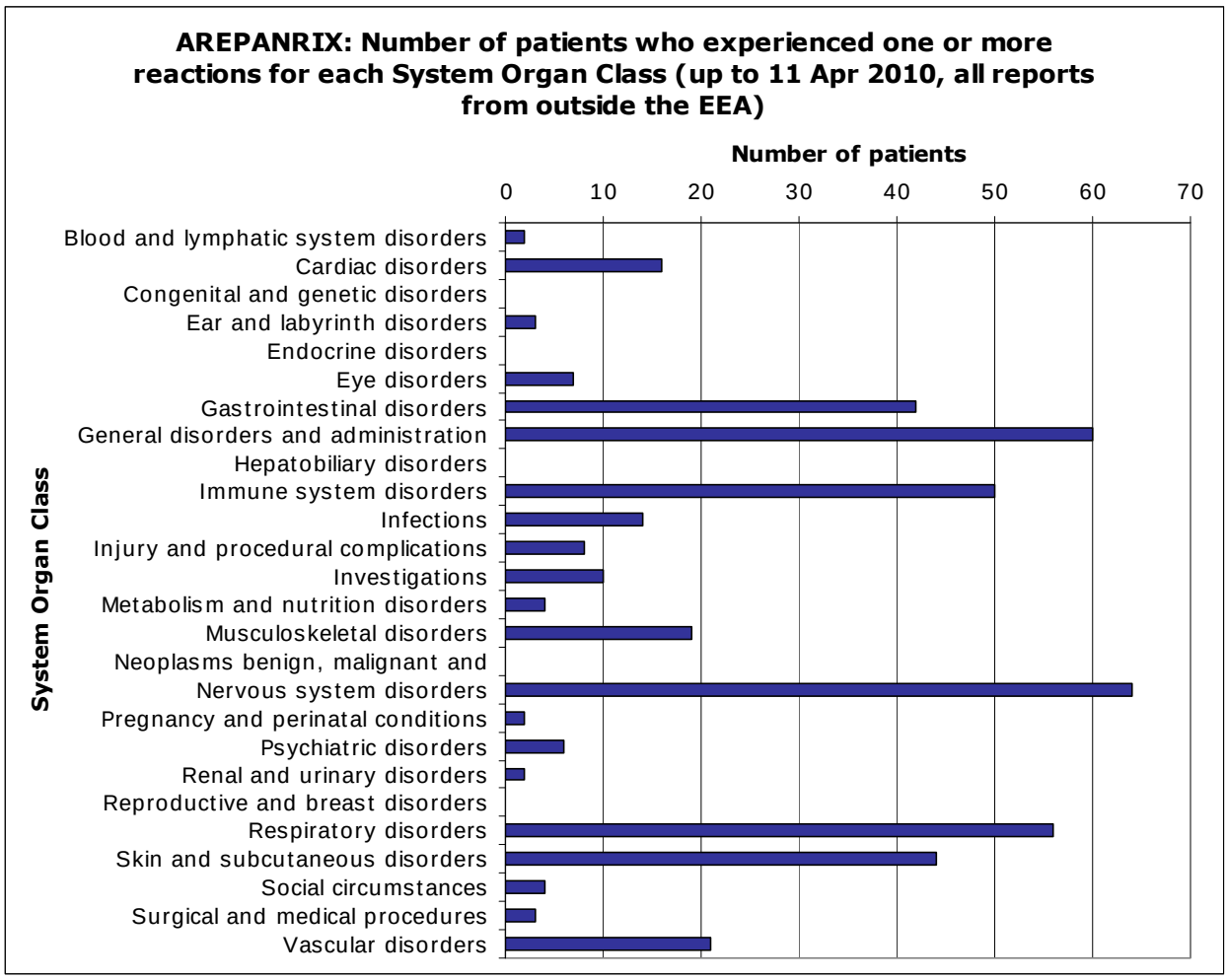
The graphs below display the cumulative numbers of adverse reaction reports received by EudraVigilance for the three centrally-authorised vaccines marketed in the EEA, as well as the number of new adverse reaction reports received between each update.



A list of specific topics discussed in previous updates is included at Appendix 2.

Arepanrix

Although authorised, Arepanrix is not marketed in the EEA but has been available in Canada since October 2009. In accordance with EU legislation, unexpected serious adverse reactions are reported from outside the EEA. As of 11 April 2010, a total of 116 reports had been received by EudraVigilance from outside the EEA. This represents an increase of three reports compared with the previous update.



Distribution of adverse reactions by system organ class

In reports of serious unexpected adverse reactions received from outside the EEA, the most frequently reported suspected adverse reactions in each system organ class (SOC) experienced by patients since the authorisation of the vaccine are listed below. Because known reactions to the vaccine are not reported from outside the EU, the profile of reports received for Arepanrix is different from those of the products marketed in the EU.

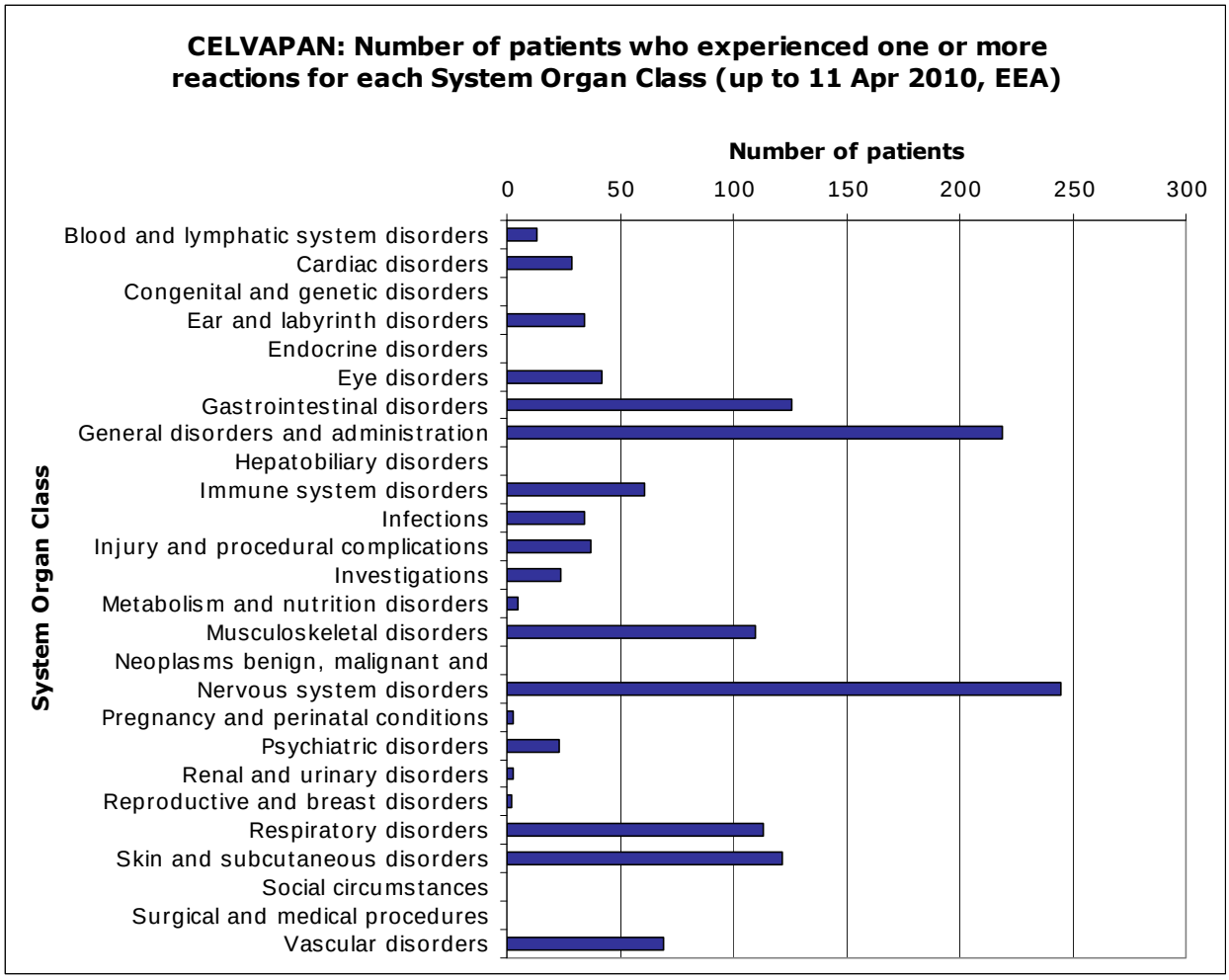
- Nervous-system disorders: Guillain-Barré syndrome, paraesthesia, dizziness, hyporeflexia, paralysis flaccid, hypoaesthesia, cranial nerve paralysis, headache;
- General disorders and administration-site conditions: asthenia, product quality issue, pyrexia, fatigue;
- Respiratory disorders: dyspnoea, throat tightness, cough, pharyngeal oedema, respiratory paralysis, respiratory disorder;
- Immune disorders: anaphylactic reaction, hypersensitivity;
- Skin and subcutaneous conditions: angioedema, urticaria, erythema;
- Gastrointestinal disorders: nausea;
- Vascular disorders: flushing, pallor;
- Musculoskeletal disorders: muscular weakness, pain in extremity, myalgia;

- Cardiac disorders: cyanosis, tachycardia;
- Infections: transmission of an infectious agent via a medicinal product.

- The most frequently reported suspected adverse reactions in children since authorisation included urticaria, angioedema, dyspnoea, anaphylactic reaction, cough, anaphylactic shock, erythema, cyanosis, flushing, hypersensitivity, pyrexia, rash, headache, nausea, pallor, pruritus, skin discolouration, throat tightness and tremor.

Celvapan

As of 11 April 2010, a total of 543 reports had been received by EudraVigilance (an increase of ten reports since the previous update). According to the information provided by the company[1] and Member States, at least 11.4 million doses had been distributed to EEA countries up to 22 March 2010. It is estimated that at least 659,400 patients have been vaccinated with Celvapan in the EEA.



Distribution of adverse reactions by system organ class

- In reports received from the EEA, the most frequently reported suspected adverse reactions in each system organ class (SOC) experienced by patients since the authorisation of the vaccine were:

[1] As stated by the marketing authorisation holder in the periodic safety update report dated 22 March 2010.

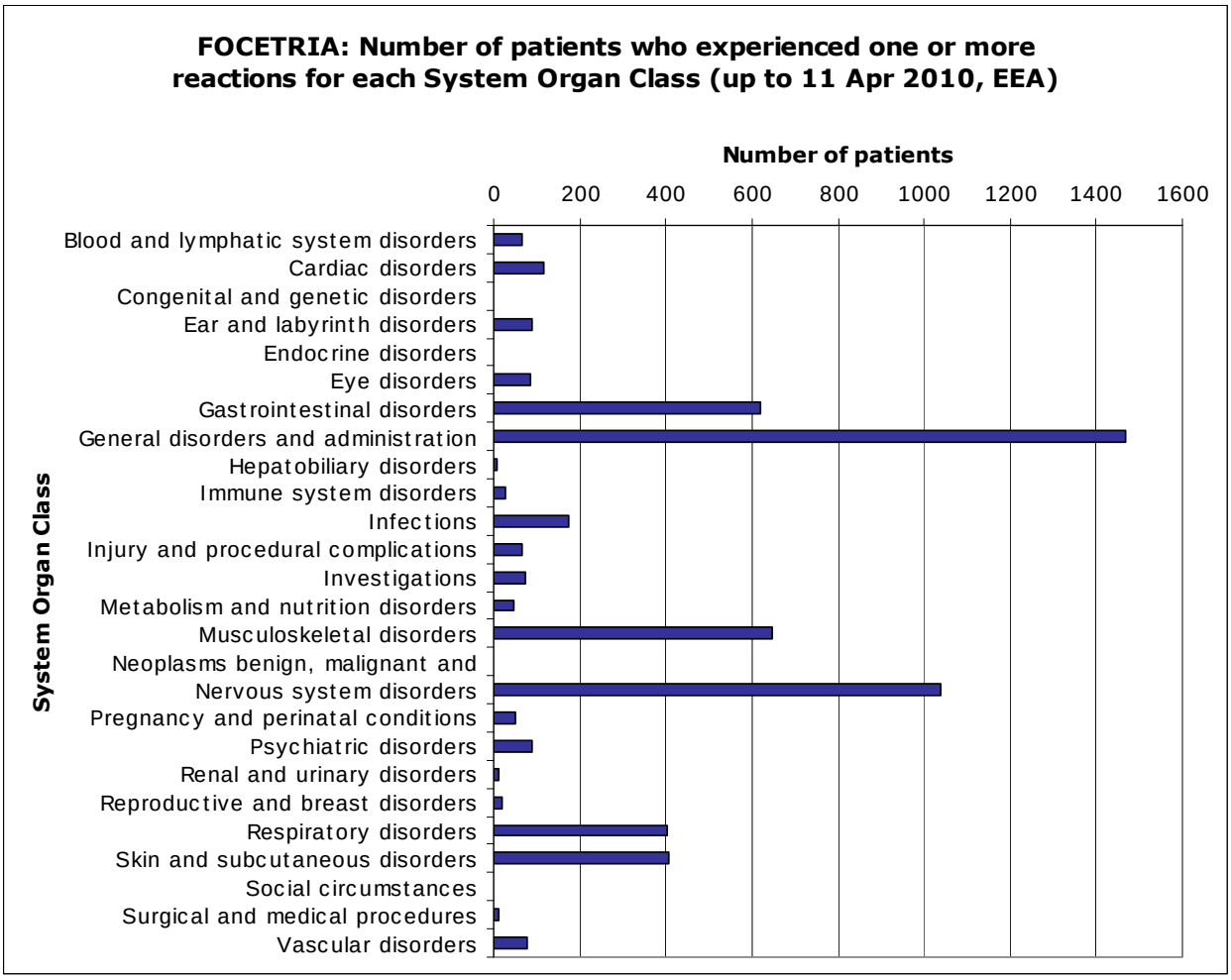
- Nervous-system disorders: headache, dizziness, syncope, paraesthesia, hypoaesthesia, lethargy;
- General disorders and administration-site conditions: pyrexia, malaise, fatigue, chills, asthenia, influenza-like illness, feeling hot, injection-site pain, chest discomfort, pain;
- Gastrointestinal disorders: nausea, vomiting, diarrhoea, abdominal pain, oral paraesthesia;
- Musculoskeletal disorders: myalgia, arthralgia, pain in extremity, muscular weakness;
- Skin and subcutaneous conditions: hyperhidrosis, pruritus, urticaria, rash, erythema;
- Respiratory disorders: oropharyngeal pain, cough, dyspnoea;
- Vascular disorders: pallor, flushing, hypotension;
- Immune disorders: hypersensitivity, anaphylactic reaction, anaphylactoid reaction;
- Eye disorders: vision blurred;
- Ear and labyrinth disorders: vertigo;
- Infections: rhinitis, nasopharyngitis;
- Cardiac disorders: tachycardia, palpitations;
- Investigations: body temperature increased;
- Psychiatric disorders: sleep disorder;
- Injury and procedural complications: medication error.

Updated safety information

- The most frequently reported suspected adverse reactions in children since authorisation included vomiting, hypersensitivity, medication error, syncope, pyrexia, dizziness, nausea, pallor, rash, headache, malaise, vision blurred, fatigue, urticaria, chills, cough, pruritus, dyspnoea, hyperhidrosis and somnolence.
- Since the last update, no fatal cases have been reported in people vaccinated with Celvapan.

Focetria

As of 11 April 2010, a total of 2,996 reports had been received by EudraVigilance (an increase of 24 reports since the previous update). Data available on 19 April 2010 from Member States and from the company[2] indicated that at least 36 million doses of Focetria had been distributed in the EEA, and at least 6.5 million patients had been vaccinated.



Distribution of adverse reactions by system organ class

- In reports received from the EEA, the most frequently reported suspected adverse reactions in each SOC experienced by patients since the authorisation of the vaccine were:
  - General disorders and administration-site conditions: pyrexia, fatigue, injection-site pain, influenza-like illness, malaise, chills, injection-site erythema, hyperpyrexia, injection-site swelling, injection-site induration, chest pain, asthenia, pain, injection-site pruritus, feeling cold, injection-site haematoma, injection-site warmth, oedema peripheral, feeling hot;
  - Nervous-system disorders: headache, dizziness, paraesthesia, somnolence, tremor, syncope, dysgeusia, hypoaesthesia, Guillain-Barré syndrome, presyncope, convulsion, migraine;

[2] According from the last periodic safety update report dated 31 March 2010.

- Musculoskeletal disorders: myalgia, pain in extremity, arthralgia, musculoskeletal stiffness, muscular weakness, neck pain, muscle spasms, musculoskeletal pain, back pain, sensation of heaviness, rheumatoid arthritis;
- Gastrointestinal disorders: nausea, diarrhoea, vomiting, abdominal pain, abdominal discomfort, upper abdominal pain, dyspepsia;
- Skin and subcutaneous conditions: rash, pruritus, urticaria, erythema, hyperhidrosis, rash pruritic, dermatitis allergic, angioedema, rash generalised, swelling face, eczema;
- Respiratory disorders: cough, dyspnoea, oropharyngeal pain, asthma, bronchospasm, dysphonia, productive cough, throat irritation;
- Infections: rhinitis, nasopharyngitis, pneumonia, influenza, herpes zoster, pharyngitis;
- Cardiac disorders: palpitations, tachycardia, atrial fibrillation, arrhythmia, cyanosis;
- Ear and labyrinth disorders: vertigo, tinnitus, ear pain;
- Psychiatric disorders: listlessness, insomnia, nightmare, restlessness, tearfulness;
- Eye disorders: visual impairment, eyelid oedema, eye irritation, eye swelling, vision blurred, conjunctivitis, diplopia, eye pain;
- Vascular disorders: hypotension, hypertension, flushing, pallor, haematoma, peripheral coldness;
- Investigations: body temperature increased, blood pressure increased, heart rate increased;
- Blood and lymphatic disorders: lymphadenopathy;
- Metabolism and nutrition disorders: decreased appetite;
- Immune system disorders: hypersensitivity, anaphylactic reaction.

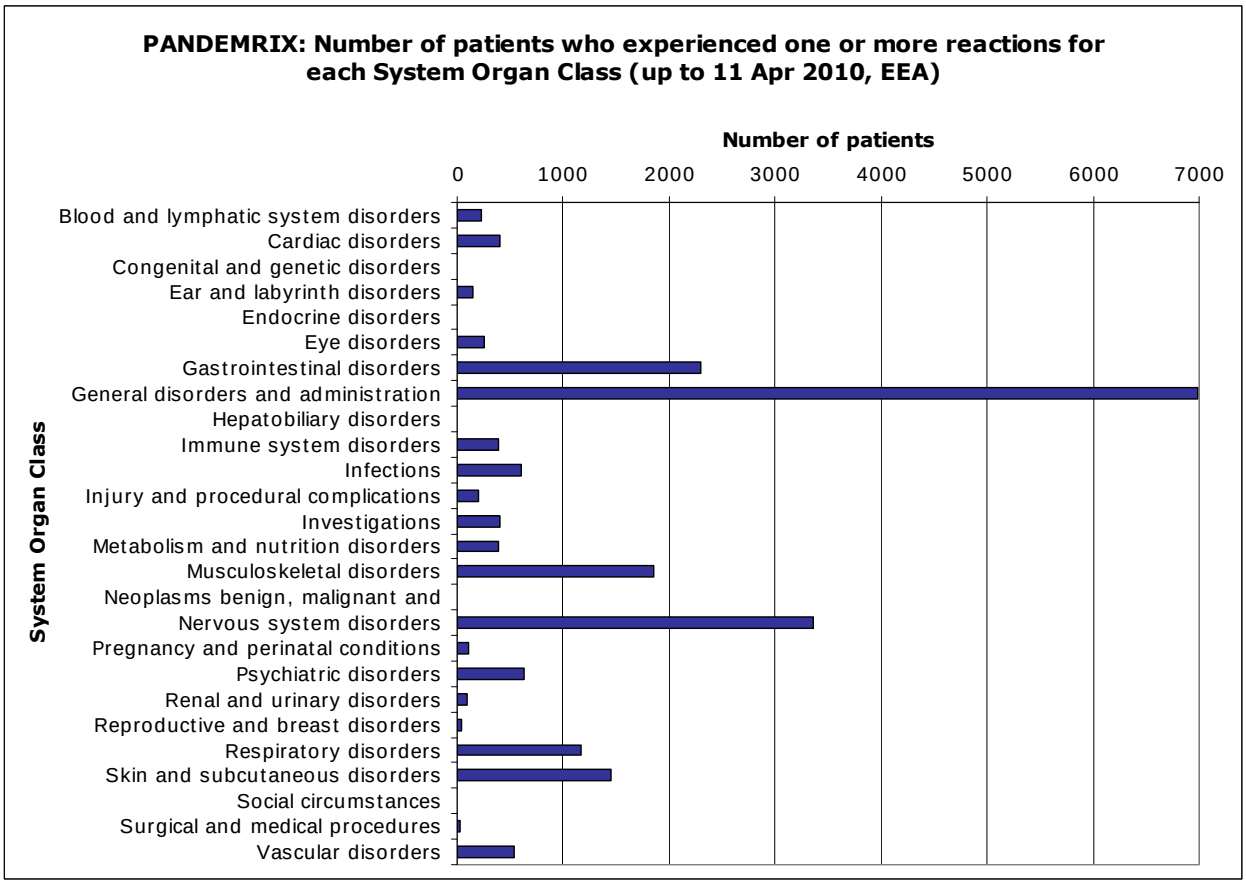
Updated safety information

- The most frequently reported suspected adverse reactions in children since authorisation included pyrexia, headache, hyperpyrexia, vomiting, cough, nausea, abdominal pain, diarrhoea, injection-site pain, myalgia, fatigue, influenza-like illness, drug exposure during pregnancy, rash, dyspnoea, urticaria, malaise, convulsion and asthma.
- Since the last update, three new fatal cases following vaccination with Focetria have been reported. They concerned a man aged 56 years who died for an unexpected cardiac death, a man aged 77 years with severe cardiac and lung disorders who died from an unreported cause stated to be related to his medication and a woman aged 51 years who had a terminal chronic obstructive pulmonary disease.

Pandemrix

As of 11 April 2010, a total of 10,845 reports had been received by EudraVigilance (an increase of 52 reports since the previous update). Data available on 19 April 2010 from Member States and from the company[3] indicate that at least 131 million doses of Pandemrix had been distributed in the EEA. It is estimated that at least 30.1 million patients have been vaccinated.

[3] As stated by the marketing authorisation holder in the periodic safety update report dated 9 April 2010.



Distribution of adverse reactions by system organ class

- In reports received from the EEA, the most frequently reported suspected adverse reactions in each SOC experienced by patients since the authorisation of the vaccine were:
  - General disorders and administration-site conditions: pyrexia, hyperpyrexia, injection-site pain, fatigue, influenza-like illness, malaise, chills, injection site erythema, injection-site swelling, pain, oedema peripheral, asthenia, injection-site induration, chest pain, injection-site inflammation, feeling hot, chest discomfort, local reaction;
  - Nervous-system disorders: headache, dizziness, paraesthesia, syncope, somnolence, hypoaesthesia, crying, febrile convulsion, convulsion, lethargy, tremor, loss of consciousness, Guillain-Barré syndrome, presyncope, hypersomnia, facial palsy, poor quality sleep, hypotonia;
  - Gastrointestinal disorders: vomiting, nausea, diarrhoea, abdominal pain, upper abdominal pain, paraesthesia oral, lip swelling, dysphagia, swollen tongue, abdominal discomfort, dry mouth, hypoaesthesia oral, lower abdominal pain;
  - Musculoskeletal disorders: myalgia, pain in extremity, arthralgia, muscular weakness, musculoskeletal stiffness, back pain, musculoskeletal pain, limb discomfort, neck pain, muscle spasms, arthritis;
  - Skin and subcutaneous conditions: rash, urticaria, erythema, hyperhidrosis, pruritus, rash generalised, angioedema, cold sweat, swelling face, rash erythematous, rash macular, rash pruritic, dermatitis allergic, pruritus generalised, rash maculo-papular, facial hypoaesthesia, petechiae, eczema, night sweats, vesicular rash, skin reaction;

- Respiratory disorders: dyspnoea, cough, oropharyngeal pain, asthma, rhinorrhoea, wheezing, epistaxis, throat tightness, pharyngeal oedema, tachypnoea, bronchospasm, respiratory failure, respiratory distress, sneezing, dysphonia, pulmonary embolism, productive cough, hyperventilation, stridor;
- Psychiatric disorders: listlessness, insomnia, tearfulness, sleep disorder, restlessness, hallucination, anxiety, confusional state, nightmare;
- Infections: rhinitis, pneumonia, nasopharyngitis, influenza, herpes zoster, swine influenza, cellulitis, bronchitis, lower respiratory tract infection, ear infection, gastroenteritis, respiratory tract infection;
- Vascular disorders: pallor, circulatory collapse, hypotension, flushing, hypertension, peripheral coldness, hot flush;
- Metabolism and nutrition disorders: decreased appetite, oligodipsia, dehydration, hypoglycaemia, polydipsia;
- Cardiac disorders: tachycardia, palpitations, cyanosis, myocardial infarction, cardiac failure, atrial fibrillation, cardiac arrest, bradycardia, myocarditis, angina pectoris;
- Immune disorders: hypersensitivity, anaphylactic reaction, anaphylactic shock, anaphylactoid reaction;
- Investigations: body temperature increased, blood pressure decreased, blood pressure increased, heart rate increased, heart rate decreased, weight decreased, body temperature decreased, C-reactive protein increased;
- Eye disorders: vision blurred, eye pain, eye swelling, visual impairment, ocular hyperaemia, photophobia, eyelid oedema, diplopia, conjunctivitis;
- Blood and lymphatic system disorders: lymphadenopathy, thrombocytopenia;
- Injury and procedural disorders: medication error, vaccination failure, fall, contusion;
- Ear and labyrinth disorders: vertigo, tinnitus, ear pain.

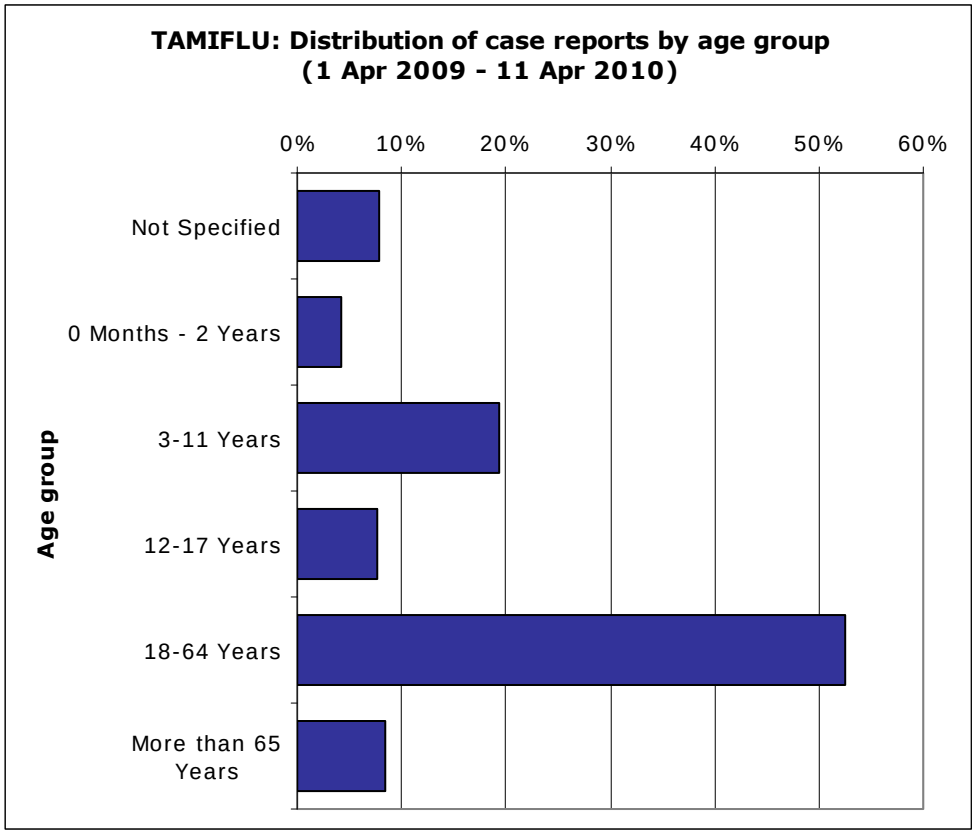
Updated safety information

- The most frequently reported suspected adverse reactions in children since authorisation were pyrexia, hyperpyrexia, vomiting, injection-site pain, headache, diarrhoea, cough, rash, fatigue, decreased appetite, nausea, abdominal pain, malaise, injection-site erythema, crying, somnolence, pallor, listlessness, injection site swelling, syncope, dyspnoea, influenza-like illness, pain in extremity, febrile convulsion, myalgia, urticaria, dizziness, tearfulness and erythema.
- Since the last update, four new fatal cases from the EEA have been received by EudraVigilance. They concerned two women aged 70 and 62 years old, one female infant aged one year old and one men aged 62 year old. All patients have medical history which might explain the fatalities. The infant has been reported with septicaemia meningococcal but no details have been reported.

Antiviral medicines

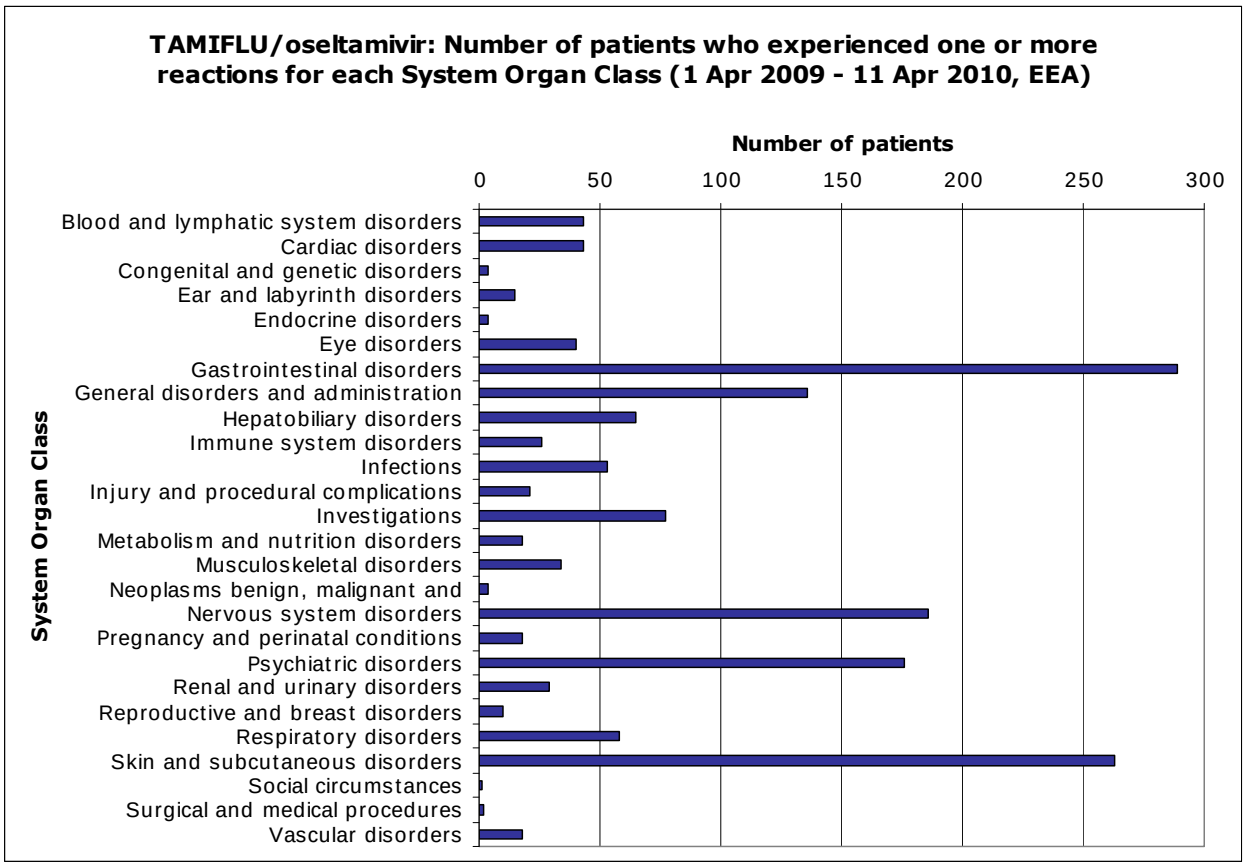
Tamiflu (oseltamivir)

From 1 April 2009 to 11 April 2010, a total of 1,085 reports worldwide were received by EudraVigilance (an increase of eight reports since the previous update). The graph below displays the age distribution of patients who experienced an adverse reaction reported to EudraVigilance.



According to information received from the marketing authorisation holder, exposure to Tamiflu is estimated to be at least 22.5 million patients during the pandemic period of 1 May 2009 to 28 February 2010[4].

[4] As stated by the marketing authorisation holder in the pandemic safety report dated 24 March 2010.



Distribution of adverse reactions by system organ class

- The adverse reaction reports received from the EEA are consistent with the safety profile described in the product information. The most frequently reported suspected adverse reactions experienced by patients in each SOC were as follows:
  - Gastrointestinal disorders: vomiting, nausea, diarrhoea, abdominal pain, upper abdominal pain, lip swelling, mouth ulceration, pancreatitis, pancreatitis acute, swollen tongue, dyspepsia, haematemesis, abdominal distension;
  - Skin and subcutaneous conditions: rash, rash generalised, urticaria, erythema, swelling face, pruritus, Stevens-Johnson syndrome, angioedema, rash erythematous, rash pruritic, erythema multiforme, dermatitis bullous, rash macular, blister, rash maculo-papular;
  - Nervous-system disorders: headache, convulsion, paraesthesia, dizziness, epilepsy, tremor, somnolence, syncope, burning sensation, nystagmus, psychomotor hyperactivity, balance disorder, cerebrovascular accident, coordination abnormal;
  - Psychiatric disorders: hallucination, confusional state, nightmare, anxiety, insomnia, delirium, hallucination visual, disorientation, abnormal behaviour, agitation, panic attack, sleep disorder, aggression, depression, depressed mood, mental disorder, psychotic disorder;
  - General disorders and administration-site conditions: malaise, death, pyrexia, influenza-like illness, chest pain, drug ineffective, oedema peripheral, condition aggravated, drug interaction, fatigue, pain, general physical health deterioration, face oedema, gait disturbance, multi-organ failure;

- Investigations: liver function test abnormal, hepatic enzyme increased, international normalised ratio increased, blood triglycerides increased, alanine aminotransferase increased, blood creatinine increased, gamma-glutamyltransferase increased, aspartate aminotransferase increased, hepatic enzyme abnormal, prothrombin time prolonged;
- Respiratory disorders: epistaxis, dyspnoea, chronic obstructive pulmonary disease;
- Infections: influenza, pathogen resistance, pneumonia, hepatitis A, bacterial infection, bronchitis;
- Hepatobiliary disorders: hepatitis, cholestasis, acute hepatic failure, hepatic failure, cytolytic hepatitis, jaundice.

Updated safety information

- The most frequently reported suspected adverse reactions reported in children since the beginning of the pandemic in April 2009 were vomiting, rash, hallucination, confusional state, convulsion, nightmare, epistaxis, urticaria, headache, diarrhoea, nausea and abdominal pain.
- Since the last update, two new case reports worldwide have been received by EudraVigilance with a fatal outcome following oseltamivir use. One case concerned a patient who died of fulminant group A streptococcal infection as a complication of an influenza A/H1N1 infection. In the other case, the cause of death has not been provided.

Appendix 1

Summary of the report of an expert group meeting regarding A/H1N1 influenza vaccines and Guillain-Barré syndrome

On 29 March 2010, a meeting of experts, including neurologists and epidemiologists, was convened by the European Medicines Agency to discuss the available data regarding the occurrence of Guillain-Barré syndrome (GBS) in patients vaccinated with an A/H1N1 influenza pandemic vaccine. The objectives of the meeting were to identify whether there is a possible association between the vaccine and the disease, to estimate the magnitude of the risk if any, to provide recommendations regarding further investigation of this issue and to advise on the need for collecting additional data.

From an analysis of spontaneous reports originating from European countries, the United-States and Canada, the experts concluded that the available data are reassuring and there is no sign of a risk of a similar magnitude as that found in the pandemic situation of 1976. A possible association between the pandemic A/H1N1 vaccines and GBS cannot be totally ruled out given the uncertainties in the current information. However, if this association exists, it would probably translate in a very small increase in the risk.

The experts identified several important factors limiting the interpretation of the data. These factors include an uncertainty regarding the completeness of the spontaneous reporting of adverse reactions by physicians, the variability of the underlying risk of GBS measured in different age groups of the general population, incomplete vaccination statistics in several countries and the lack of knowledge on the numbers of vaccinated people in different age categories. As the cases of GBS reported after the A/H1N1 vaccination were generally milder than those reported after the vaccination campaign of 1976, there is also a need to compare the severity of the cases observed in the current situation and that of the cases included in the calculation of the underlying risk in the general population. Given these limitations, the experts concluded that the possible association should be further investigated through epidemiological studies.

Many cases have been reported as having occurred between 4 and 29 days after the A/H1N1 vaccination. Additional investigations need therefore to also clarify if this observation reflects an increase of the risk in that time period or a preferential reporting of cases of GBS occurring in the month after the vaccination.

The experts reviewed the epidemiological studies currently being carried out in several Member States to estimate the risk of GBS associated with the A/H1N1 vaccines. They concluded that these studies will provide valid information provided there is a complete reporting of cases to the study. As the vaccination coverage may be lower than expected, a possible problem is the ability of these studies to detect if there is a small increase in the risk. Preliminary results from studies are expected in June 2010.

One of the studies is the VAESCO project which is recruiting GBS cases from eight EU countries, all using the same methodology and study protocol. As a possible problem of the ongoing studies may be the insufficient statistical power to detect small risks, the experts considered appropriate that studies not currently included in VAESCO could join the project either by pooling their data or by combining their results. Observational studies could also be extended to the next influenza vaccination campaign in order to increase the number of cases and improve the precision of the results.

As several studies are already ongoing in a large number of Member States, it was concluded that, at this stage, there is no need to start additional studies to address this issue. However, availability of

vaccination data was considered an essential element for a proper analysis of spontaneous reports of adverse reactions. If put in place before the next seasonal influenza vaccination campaign, a dedicated system such an immunisation registry would facilitate the estimation of the numbers of people vaccinated in different age categories and improve the assessment of vaccine safety by Member States.

Appendix 2

Specific topics discussed for H1N1 vaccines in previous updates

SOC	Topic	Update number		
		Celvapan	Focetria	Pandemrix
Blood and lymphatic system disorders	Haematopoietic cytopenias			8
	Idiopathic thrombocytopenic purpura (ITP)			4, 6
	Leucocytosis, lymphocytosis			8
	Thrombocytopenia		6	6
Cardiac disorders	Cardiovascular accidents		5	
Ear and labyrinth disorders	Sudden hearing loss			4
Eye disorders	Eye disorders	4, 7	7	7
	Photophobia			7
Gastrointestinal disorders	Necrotising oesophagitis and necrotising stomatitis			6
	Pancreatitis	7		10
General disorders and administration site conditions	Death, sudden death	10	10	10
	Fever, local reaction and drowsiness following 2nd dose in children 6-35 months old			1
	Injection site necrosis			3
Immune system disorders	Anaphylactic reactions in children			1
	Anaphylactic shock		2, 3	2
	Anaphylaxis, angioedema, hypersensitivity	2		
	Delayed hypersensitivity reaction type IV			4
	Serum sickness			6
	Transplant rejection			1, 2, 3

SOC	Topic	Update number		
		Celvapan	Focetria	Pandemrix
Infections and infestations	Herpes zoster	9	9	9
Injury, poisoning and procedural complications	Medication error	7, 10		7, 10
Nervous system disorders	Acute disseminated encephalomyelitis (ADEM)		2, 3	
	Cerebral haemorrhage or infarction		1	3
	Demyelinating disorders	11	11	11
	Encephalitis		3, 5	
	Facial palsy or paresis	8	4, 8	7
	Guillain-Barré syndrome	4, 5, 11	2, 4, 5, 11	1, 3, 4, 5, 6, 11
	Multiple sclerosis	11	5, 11	5, 11
	Neuralgic amyotrophy			9
	Neuritis, polyneuritis, polyradiculoneuritis, peripheral neuropathy, polyneuropathy			6
	Paraesthesia	2		
	Paralysis and paresis	7	8	3
	Seizures		8, 13	13
	Seizures with fatal outcome			4
Pregnancy, puerperium and perinatal conditions	Intra-uterine death		4	
	Pregnancy-related events	11	2, 11	1, 2, 11

SOC	Topic	Update number		
		Celvapan	Focetria	Pandemrix
Skin and subcutaneous tissue disorders	Bullous dermatitis		9	8
	Erythema multiforme, Stevens-Johnson syndrome (SJS) and toxic epidermal necrolysis (TEN)			3, 6
	Leukocytoclastic vasculitis		5	
	Photosensitivity reaction			2
	Systemic lupus erythematosus rash			8
Vascular disorders	Circulatory collapse	3		
	Vasculitis			6