

UK Suspected Adverse Drug Reaction (ADR) Analysis

Influenza antivirals - oseltamivir (Tamiflu) and zanamivir (Relenza)

15 October 2009

This report summarises all UK reports of suspected adverse drug reactions (ADRs)/side effects to influenza antiviral medicines Tamiflu (oseltamivir) and Relenza (zanamivir) received by MHRA between Wednesday 1st April 2009 and Thursday 8th October 2009 (inclusive)¹. These reports have been voluntarily submitted to MHRA by healthcare professionals and members of the public via the MHRA's 'Swine Flu ADR Portal' (www.mhra.gov.uk/swineflu) and the Yellow Card Scheme. It also includes all UK reports submitted by the Marketing Authorisation holders for Tamiflu and Relenza as part of their legal requirements. The suspected ADRs listed in the attached Drug Analysis Prints have been coded using 'MedDRA' terminology².

It is important to note that a report of a reaction does not necessarily mean that it has been caused by the drug in question. We encourage reporters to report *suspected* ADRs i.e. the reporter does not have to be sure of a causal association between the drug and the reaction – a mere suspicion will suffice. Therefore, reports submitted to MHRA may be true adverse effects of the drug or they may be coincidental events (e.g. due to underlying medical conditions) that would have occurred anyway in the absence of exposure to the drug in question. For this reason **this summary is not a list of known or proven adverse reactions to Tamiflu or Relenza and must not be interpreted and used as such.** A list of the recognised adverse effects is provided in the product information for Tamiflu and Relenza (see <http://emc.medicines.org.uk/>) or www.mhra.gov.uk/swineflu).

ADR reporting rates are highly variable and are dependent on many factors. Therefore these data cannot be used to determine the frequency of occurrence of ADRs to Tamiflu and Relenza. Furthermore, the fact that these two drugs are likely to be used in different patient populations during the current swine flu A/H1N1 pandemic, **a direct comparison of the relative safety of Tamiflu and Relenza can not be made using these data.**

All reports of suspected ADRs to Tamiflu and Relenza continue to be closely monitored by a dedicated team of drug safety specialists at the MHRA.

Headline summary:

- A total of 628,351 treatment courses of Tamiflu and 8,742 treatment courses of Relenza have been collected (via the National Pandemic Flu Service) in England between 23rd July 2009 and 6th October 2009 (inclusive)³. These data do not include courses of oseltamivir and zanamivir prescribed or obtained outside of the NPFS system, or courses of oseltamivir and zanamivir used in Scotland, Wales or Northern Ireland.
- Up to, and including Thursday 8th October 2009, the MHRA has received a total of **793** reports of suspected ADRs for Tamiflu and **17** reports for Relenza.
- The most frequently reported suspected ADRs are consistent with the signs and symptoms of recognised adverse effects of the antivirals or of flu-like illness.

¹ Suspected ADR data are released with a 1 week delay in order to ensure that MHRA has time to validate, extract and assess the data before publication.

² MedDRA - the Medical Dictionary for Regulatory Activities - is a standardised, medically validated adverse event terminology system used within the international medicines regulatory environment.

³ Data obtained from, and used with permission from the Department of Health, England.

- No new safety concerns have been identified for either drug and no changes to the product safety information are required. Patients should continue to take Tamiflu or Relenza as advised by their healthcare provider.
- The balance of risks and benefits for Tamiflu and Relenza within their licensed indications remains positive.
- For Tamiflu, we continue to closely monitor a number of recognised adverse effects. We also continue to closely monitor reports suggestive of a possible interaction between Tamiflu and warfarin resulting in an increased risk of bleeding. However, there is currently no strong evidence of an interaction between the two drugs (see below).
- When identified, information on new and emerging safety signals will be provided in this report together with details of any resulting regulatory action or changes to prescribing advice deemed necessary.

SUSPECTED ADR REPORTS RECEIVED FOR TAMIFLU

A total of 793 reports (including 1365 suspected adverse reactions⁴) have been reported for Tamiflu in the UK since 1st April 2009.

The most commonly reported suspected ADRs are consistent with the signs and symptoms of recognised side effects of Tamiflu such as mild allergic reactions as well as gastrointestinal events, headache and dizziness which can also be caused by flu-like illness.

No new safety issues have been identified.

Adverse events under close monitoring by MHRA

Possible Drug Interaction between Tamiflu and Warfarin

We continue to keep under review reports suggestive of a possible drug interaction between Tamiflu and warfarin (a drug used to prevent blood clotting) resulting in prolonged blood clotting time. Blood clotting control can be affected by infection and associated symptoms (e.g. decreased appetite and anorexia). Therefore it is very difficult to establish whether these cases represent a true drug interaction between Tamiflu and warfarin or whether blood clotting control in these patients may have been affected by underlying infection and associated symptoms.

Other data from clinical trials conducted by the Marketing Authorisation holder do not support the existence of an interaction between Tamiflu and warfarin.

Currently there is no strong evidence of an interaction between the two drugs. Patients should continue to take Tamiflu and warfarin as advised by their healthcare provider.

All reports of a possible interaction with warfarin remain under close review by the MHRA.

Suspected ADRs with a fatal outcome

We have received six reports in which the patient died following treatment with Tamiflu; two cases of unexplained death, one case of cardiac arrest, one case of acute hepatic failure; one case of pancreatitis; and one case of vomiting in a patient who was also receiving chemotherapy. These cases have been fully evaluated and in none of these is there evidence to confirm that Tamiflu was directly responsible for the fatal event. These were possibly due to underlying infection and illness.

⁴ A single report may contain more than one suspected adverse reaction

Neuropsychiatric adverse reactions

Neuropsychiatric adverse reactions, including convulsions and delirium (with symptoms such as confusion, abnormal behaviour, hallucinations, agitation, anxiety and nightmares) are listed as possible side effects in the Tamiflu product information.

However, influenza infection itself can be associated with a variety of neurologic and behavioural symptoms including the above, sometimes without obvious signs of a severe infection. Some studies have found that these types of event are no more frequent in influenza patients who have taken Tamiflu when compared to those who have not taken the drug. It therefore remains unclear whether these neuropsychiatric events may be a true side effect of Tamiflu or whether they are due to underlying infection (or a combination of both).

Reported cases of neuropsychiatric adverse effects will remain under close review by MHRA but those reported so far do not raise any new safety concerns. Nonetheless, patients should remain vigilant to the possibility of such events and discuss any serious concerns with their healthcare provider.

Serious skin reactions

Serious skin reactions including Erythema multiforme (EM), Stevens Johnson syndrome (SJS) and toxic epidermal necrolysis (TEN) are listed in the side effects section of the product information for Tamiflu. A number of such reactions have been reported for Tamiflu in the UK since 1st April but available epidemiological data suggest that these types of skin reactions can be caused by a number of different types of insults including viral infections. It therefore remains unclear whether reported cases of severe skin disorders are due to exposure to Tamiflu or to the underlying infection and associated illness.

The MHRA continues to keep such reports under close review.

Liver reactions

A Europe-wide review of Liver reactions reported for Tamiflu has previously been conducted; a causal association with Tamiflu could not be established. However as a precautionary measure, serious adverse effects on the liver including fulminant hepatic failure were added to side-effects section of the EU product information for Tamiflu as a result of isolated cases reported outside of the EU. MHRA has received a number of reports of liver reactions to Tamiflu since April 2009, including two reports of liver failure. However, more likely alternative explanations for the reported events (significant underlying illness; other medication) are present in both reports of liver failure.

SUSPECTED ADR REPORTS RECEIVED FOR RELENZA (zanamivir)

A total of 17 reports (including 32 suspected adverse reactions³) have been reported for Relenza in the UK since 1st April 2009. In one of these reports the suspected adverse reaction was fatal.

Most of the reported suspected ADRs are consistent with the signs and symptoms of known side effects of Relenza such as allergic reactions and bronchospasm. Most other reported events such as diarrhoea, nausea, vomiting, fatigue, headache and dizziness can be caused by flu-like illness.

No new safety issues have been identified.

Suspected ADRs with a fatal outcome

One suspected ADR with a fatal outcome has been reported for Relenza to date. This is a case of in-utero foetal death which occurred during the third trimester of pregnancy. We have very limited information regarding this case preventing full causality assessment. Further information has been requested. Currently there is no evidence to suggest that Relenza carries any risks (either to the mother or to the baby) when used during pregnancy (see safety in pregnancy below).

Safety in pregnancy

One case of spontaneous abortion occurring in the first trimester of pregnancy has been reported for Relenza. The report contains limited information which prevents full causality assessment; further information has been requested. Spontaneous abortion is not uncommon in early pregnancy – the available epidemiological data suggest that one in four women who become pregnant will suffer a spontaneous abortion and that the risk is greatest during the first trimester. Inevitably therefore spontaneous abortion may occur coincidentally following exposure to Relenza without the drug playing any causal role in the event. Other factors such as obstetric history, underlying medical conditions, and exposure to chemicals, smoking status and alcohol use can all influence the risk of spontaneous abortion.

Currently there is no evidence to suggest that Relenza carries any risks (either to the mother or to the baby) when used during pregnancy. A recent review of available evidence by European regulatory authorities led to a recommendation that, due to the potentially serious risks of H1N1 swine influenza in pregnancy, the benefits of using Relenza (and Tamiflu) in treating influenza in pregnant or breastfeeding women outweigh any known risks.

Drug Analysis Print
Drug Name: Tamiflu (oseltamivir)

Run Date: 1 April 2009 to 8 October 2009

Total number of reactions: 1365	Total number of ADR reports: 793	Total number of fatal ADR reports: 6
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System Organ Class	Reactions	Fatal Reactions
Blood and lymphatic system disorders	8	0
Cardiac disorders	18	1
Congenital, familial and genetic disorders	1	0
Ear and labyrinth disorders	6	0
Endocrine disorders	1	0
Eye disorders	32	0
Gastrointestinal disorders	441	2
General disorders and administration site conditions	80	2
Hepatobiliary disorders	18	1
Immune system disorders	7	0
Infections and infestations	13	0
Injury, poisoning and procedural complications	7	0
Investigations	44	0
Metabolism and nutrition disorders	9	0
Musculoskeletal and connective tissue disorders	21	0
Nervous system disorders	136	0
Pregnancy, puerperium and perinatal conditions	1	0
Psychiatric disorders	180	0
Renal and urinary disorders	11	0
Reproductive system and breast disorders	7	0
Respiratory, thoracic and mediastinal disorders	30	0
Skin and subcutaneous tissue disorders	286	0
Vascular disorders	8	0
Total	1365	6

Glossary/Abbreviations

ADR - Adverse Drug Reaction

Age group - lists which age groups are included in the Drug Analysis Print - either ALL, Adolescent, Adult, Child, Elderly, Infant or Neonate

Data lock date - shows data on the database at this specified date and time

HLT - High Level Term - see definition of MedDRA

MEDRA - this stands for Medical Dictionary for Regulatory Activities, which is the internationally agreed list of terms used for Medicines Regulation. MedDRA groups related adverse drug reaction terms in a hierarchical structure whereby the 'preferred term' (PT) (e.g. tunnel vision) is grouped under the broader heading the 'high level term' (HLT) (e.g. visual field disorders). 'High level terms' are contained within the 'system organ class' (SOC) (e.g. eye disorders). The 'preferred term' is the most specific term on the Drug Analysis Print, while the 'system organ class' is the most general

Multi active constituent products - contain the drug constituent of interest plus one or more other drug constituents (e.g. co-codamol contains paracetamol and codeine)

NEC - appears in MedDRA and stands for Not Elsewhere Classified

NOS - appears in MedDRA and stands for Not Otherwise Specified

PBG - Product Brand Generic - this means drug brand name e.g. Amoxil is a PBG for the drug substance amoxic

Products included in this print - this is a list of the products for which at least one suspected Adverse Drug Reaction (ADR) report has been received that specifies that product as a 'suspected drug' (i.e. suspected causal association with the reaction). It does not provide an exhaustive list of the products which contain the named drug substance

PT - Preferred Term - see definition of MedDRA

Reaction - defines which ADRs are included in the Drug Analysis Print - either ALL, Serious or Non-Serious

Reporter type - lists the reporter types which are included in the Drug Analysis Print - either Patient, Health Professional or ALL (i.e. both)

Report run date - the date the Drug Analysis Print was produced

Route of admin - lists the route of administration of the suspect drug for which reports are included in the Drug Analysis Print, e.g. ORAL only includes reports where the suspect drug was specified as having been taken by the oral route, or ALL which includes all routes of administration

Spontaneous - suspected ADR reports sent in to the Yellow Card Scheme are called spontaneous reports

Single active constituent products - contain only the drug substance of interest

System Organ Class (SOC) - this is the highest level in MedDRA which groups together reactions that affect similar systems/organs in the body

Drug Analysis Print
Drug Name: Tamiflu (oseltamivir)

Reaction Name	Reactions	Fatal Reactions
SOC		
<i>HLT</i>		
PT		
Blood and lymphatic system disorders		
<i>Anaemias haemolytic immune</i>		
Anaemia haemolytic autoimmune	1	0
<i>Haemolyses NEC</i>		
Haemolysis	1	0
<i>Lymphatic system disorders NEC</i>		
Lymphadenopathy	1	0
<i>Neutropenias</i>		
<i>Red blood cell abnormal findings NEC</i>		
Macrocytosis	1	0
<i>Thrombocytopenias</i>		
Thrombocytopenia	3	0
<i>Coagulopathies</i>		
Abnormal clotting factor	1	0
Blood and lymphatic system disorders SOC Total	8	0

Drug Analysis Print
Drug Name: Tamiflu (oseltamivir)

Reaction Name	Reactions	Fatal Reactions
SOC		
<i>HLT</i>		
PT		
Cardiac disorders		
<i>Cardiac signs and symptoms NEC</i>		
Cyanosis	1	0
Palpitations	8	0
<i>Cardiomyopathies</i>		
Congestive cardiomyopathy	1	0
<i>Noninfectious myocarditis</i>		
Myocarditis	1	0
<i>Rate and rhythm disorders NEC</i>		
Arrhythmia	1	0
Tachycardia	1	0
<i>Supraventricular arrhythmias</i>		
Atrial fibrillation	2	0
Sinus bradycardia	1	0
<i>Ventricular arrhythmias and cardiac arrest</i>		
Cardiac arrest	1	1
Ventricular arrhythmia	1	0
Cardiac disorders SOC Total	18	1

Drug Analysis Print
Drug Name: Tamiflu (oseltamivir)

Reaction Name	Reactions	Fatal Reactions
SOC		
<i>HLT</i>		
PT		
Congenital, familial and genetic disorders		
<i>Cerebral disorders congenital</i>		
Anencephaly	1	0
Congenital, familial and genetic disorders SOC Total	1	0

Drug Analysis Print
Drug Name: Tamiflu (oseltamivir)

Reaction Name	Reactions	Fatal Reactions
SOC		
<i>HLT</i>		
PT		
Ear and labyrinth disorders		
<i>Inner ear signs and symptoms</i>		
Tinnitus	2	0
Vertigo	3	0
<i>Inner ear disorders NEC</i>		
Meniere's disease	1	0
Ear and labyrinth disorders SOC Total	6	0

Drug Analysis Print
Drug Name: Tamiflu (oseltamivir)

Reaction Name	Reactions	Fatal Reactions
SOC		
<i>HLT</i>		
PT		
Endocrine disorders		
<i>Thyroid hyperfunction disorders</i>		
Hyperthyroidism	1	0
Endocrine disorders SOC Total	1	0

Drug Analysis Print
Drug Name: Tamiflu (oseltamivir)

Reaction Name	Reactions	Fatal Reactions
SOC		
<i>HLT</i>		
PT		
Eye disorders		
<i>Blindness (excl colour blindness)</i>		
Blindness transient	1	0
<i>Conjunctival infections, irritations and inflammations</i>		
Conjunctivitis	3	0
<i>Conjunctival and corneal bleeding and vascular disorders</i>		
Conjunctival haemorrhage	1	0
<i>Lacrimal disorders</i>		
Lacrimation increased	1	0
<i>Lid, lash and lacrimal infections, irritations and inflammations</i>		
Blepharitis	2	0
Eyelid oedema	2	0
<i>Ocular bleeding and vascular disorders NEC</i>		
Eye haemorrhage	1	0
<i>Ocular disorders NEC</i>		
Eye pain	1	0
Eye swelling	3	0
Ocular icterus	1	0
Eyelid disorder	2	0
<i>Ocular infections, inflammations and associated manifestations</i>		
Eye pruritus	2	0
<i>Ocular nerve and muscle disorders</i>		
Strabismus	1	0
<i>Ocular sensation disorders</i>		
Abnormal sensation in eye	1	0
Photophobia	4	0
<i>Visual disorders NEC</i>		
Diplopia	1	0
Vision blurred	2	0
Visual impairment	3	0
Eye disorders SOC Total	32	0

Drug Analysis Print
Drug Name: Tamiflu (oseltamivir)

Reaction Name	Reactions	Fatal Reactions
SOC		
<i>HLT</i>		
PT		
Gastrointestinal disorders		
<i>Colitis (excl infective)</i>		
Neutropenic colitis	1	0
<i>Diarrhoea (excl infective)</i>		
Diarrhoea	48	0
Diarrhoea haemorrhagic	4	0
<i>Duodenal ulcers and perforation</i>		
Duodenal ulcer	1	0
<i>Dyspeptic signs and symptoms</i>		
Dyspepsia	7	0
<i>Flatulence, bloating and distension</i>		
Flatulence	1	0
<i>Gastritis (excl infective)</i>		
Gastritis	1	0
<i>Gastrointestinal and abdominal pains (excl oral and throat)</i>		
Abdominal pain	29	0
Abdominal pain upper	26	0
Gastrointestinal pain	1	0
<i>Gastrointestinal atonic and hypomotility disorders NEC</i>		
Constipation	1	0
<i>Non-site specific gastrointestinal haemorrhages</i>		
Haematemesis	5	0
Lower gastrointestinal haemorrhage	1	0
<i>Gingival disorders NEC</i>		
Gingival disorder	1	0
Gingivitis	2	0
<i>Gingival pains</i>		
Gingival pain	1	0
<i>Intestinal haemorrhages</i>		
Rectal haemorrhage	5	0
<i>Gastrointestinal signs and symptoms NEC</i>		
Dysphagia	1	0
Stomach discomfort	2	0
<i>Nausea and vomiting symptoms</i>		

Nausea	71	0
Retching	1	0
Vomiting	167	1
Vomiting projectile	3	0
Regurgitation	1	0
<i>Oral dryness and saliva altered</i>		
Dry mouth	1	0
<i>Oral soft tissue disorders NEC</i>		
Cheilitis	2	0
Lip swelling	10	0
Lip ulceration	1	0
Chapped lips	1	0
<i>Oral soft tissue pain and paraesthesia</i>		
Oral pain	2	0
Paraesthesia oral	3	0
<i>Oral soft tissue swelling and oedema</i>		
Gingival swelling	1	0
<i>Acute and chronic pancreatitis</i>		
Pancreatitis	1	0
Pancreatitis acute	4	1
<i>Salivary gland disorders NEC</i>		
Salivary hypersecretion	1	0
<i>Stomatitis and ulceration</i>		
Mouth ulceration	17	0
Stomatitis	2	0
<i>Tongue disorders</i>		
Glossitis	1	0
Tongue ulceration	2	0
<i>Tongue signs and symptoms</i>		
Glossodynia	1	0
Swollen tongue	7	0
<i>Oesophagitis (excl infective)</i>		
Oesophagitis	1	0
Reflux oesophagitis	1	0
<i>Gingival haemorrhages</i>		
Gingival bleeding	1	0
Gastrointestinal disorders SOC Total	441	2

Drug Analysis Print
Drug Name: Tamiflu (oseltamivir)

Reaction Name	Reactions	Fatal Reactions
SOC		
<i>HLT</i>		
PT		
General disorders and administration site conditions		
<i>Asthenic conditions</i>		
Asthenia	2	0
Fatigue	12	0
Malaise	22	0
<i>Death and sudden death</i>		
Death	2	2
<i>Febrile disorders</i>		
Pyrexia	1	0
<i>Gait disturbances</i>		
Gait disturbance	4	0
Abasia	1	0
<i>General signs and symptoms NEC</i>		
Condition aggravated	1	0
Influenza like illness	2	0
General physical health deterioration	1	0
Secretion discharge	1	0
<i>Interactions</i>		
Drug interaction	4	0
<i>Mucosal findings abnormal</i>		
Mucosa vesicle	1	0
Mucosal inflammation	1	0
<i>Oedema NEC</i>		
Face oedema	2	0
Oedema peripheral	6	0
<i>Pain and discomfort NEC</i>		
Chest pain	7	0
Pain	4	0
<i>Feelings and sensations NEC</i>		
Chills	1	0
Feeling abnormal	4	0
Feeling of body temperature change	1	0
General disorders and administration site conditions SOC Total	80	2

Drug Analysis Print
Drug Name: Tamiflu (oseltamivir)

Reaction Name	Reactions	Fatal Reactions
SOC		
<i>HLT</i>		
PT		
Hepatobiliary disorders		
<i>Cholestasis and jaundice</i>		
Jaundice	2	0
Jaundice cholestatic	1	0
<i>Hepatic failure and associated disorders</i>		
Acute hepatic failure	2	1
<i>Hepatobiliary signs and symptoms</i>		
Hepatic pain	1	0
<i>Hepatocellular damage and hepatitis NEC</i>		
Hepatitis	7	0
Hepatitis acute	1	0
Hepatotoxicity	1	0
<i>Hepatic and hepatobiliary disorders NEC</i>		
Liver disorder	2	0
Liver injury	1	0
Hepatobiliary disorders SOC Total	18	1

Drug Analysis Print
Drug Name: Tamiflu (oseltamivir)

Reaction Name	Reactions	Fatal Reactions
SOC		
<i>HLT</i>		
PT		
Immune system disorders		
<i>Anaphylactic responses</i>		
Anaphylactic reaction	1	0
<i>Allergic conditions NEC</i>		
Hypersensitivity	6	0
Immune system disorders SOC Total	7	0

Drug Analysis Print
Drug Name: Tamiflu (oseltamivir)

Reaction Name	Reactions	Fatal Reactions
SOC		
<i>HLT</i>		
PT		
Infections and infestations		
<i>Bacterial infections NEC</i>		
Cellulitis	2	0
<i>Bone and joint infections</i>		
Bursitis infective	1	0
<i>Candida infections</i>		
Candidiasis	1	0
Vulvovaginal candidiasis	2	0
<i>Lower respiratory tract and lung infections</i>		
Lower respiratory tract infection	1	0
<i>Female reproductive tract infections</i>		
Vaginal abscess	1	0
<i>Skin structures and soft tissue infections</i>		
Impetigo	2	0
<i>Staphylococcal infections</i>		
Staphylococcal scalded skin syndrome	1	0
<i>Viral infections NEC</i>		
Viral labyrinthitis	1	0
<i>Vascular infections</i>		
Lymphangitis	1	0
Infections and infestations SOC Total	13	0

Drug Analysis Print
Drug Name: Tamiflu (oseltamivir)

Reaction Name	Reactions	Fatal Reactions
SOC		
<i>HLT</i>		
PT		
Injury, poisoning and procedural complications		
<i>Fractures and dislocations NEC</i>		
Joint dislocation	1	0
<i>Skin injuries NEC</i>		
Contusion	2	0
<i>Non-site specific procedural complications</i>		
Shunt occlusion	1	0
<i>Overdoses</i>		
Overdose	1	0
<i>Site specific injuries NEC</i>		
Head injury	1	0
<i>Maladministrations</i>		
Incorrect dose administered	1	0
Injury, poisoning and procedural complications SOC Total	7	0

Drug Analysis Print
Drug Name: Tamiflu (oseltamivir)

Reaction Name	Reactions	Fatal Reactions
SOC		
<i>HLT</i>		
PT		
Investigations		
<i>Carbohydrate tolerance analyses (incl diabetes)</i>		
Blood glucose decreased	1	0
Blood glucose increased	1	0
<i>Coagulation and bleeding analyses</i>		
Coagulation time prolonged	6	0
International normalised ratio increased	7	0
Prothrombin time prolonged	1	0
<i>Liver function analyses</i>		
Alanine aminotransferase increased	3	0
Blood bilirubin increased	3	0
Liver function test abnormal	15	0
Hepatic enzyme increased	2	0
Hepatic enzyme abnormal	1	0
<i>Mineral and electrolyte analyses</i>		
Blood sodium abnormal	1	0
<i>Platelet analyses</i>		
Platelet count decreased	1	0
<i>Urinalysis NEC</i>		
Urine colour abnormal	1	0
<i>White blood cell analyses</i>		
White blood cell count increased	1	0
Investigations SOC Total	44	0

Drug Analysis Print
Drug Name: Tamiflu (oseltamivir)

Reaction Name	Reactions	Fatal Reactions
SOC		
<i>HLT</i>		
PT		
Metabolism and nutrition disorders		
<i>Appetite disorders</i>		
Anorexia	2	0
Appetite disorder	1	0
Decreased appetite	1	0
<i>Diabetes mellitus (incl subtypes)</i>		
Diabetes mellitus inadequate control	1	0
<i>Food malabsorption and intolerance syndromes (excl sugar intolerance)</i>		
Fat intolerance	1	0
<i>Hypoglycaemic conditions NEC</i>		
Hypoglycaemia	2	0
<i>Total fluid volume decreased</i>		
Dehydration	1	0
Metabolism and nutrition disorders SOC Total	9	0

Drug Analysis Print
Drug Name: Tamiflu (oseltamivir)

Reaction Name	Reactions	Fatal Reactions
SOC		
<i>HLT</i>		
PT		
Musculoskeletal and connective tissue disorders		
<i>Arthropathies NEC</i>		
Arthritis	1	0
<i>Bone related signs and symptoms</i>		
Bone pain	1	0
<i>Joint related signs and symptoms</i>		
Arthralgia	4	0
Joint swelling	1	0
<i>Muscle pains</i>		
Myalgia	3	0
<i>Muscle related signs and symptoms NEC</i>		
Muscle spasms	2	0
Muscle twitching	1	0
<i>Musculoskeletal and connective tissue pain and discomfort</i>		
Back pain	5	0
Pain in extremity	3	0
Musculoskeletal and connective tissue disorders SOC Total	21	0

Drug Analysis Print
Drug Name: Tamiflu (oseltamivir)

Reaction Name	Reactions	Fatal Reactions
SOC		
<i>HLT</i>		
PT		
Nervous system disorders		
<i>Absence seizures</i>		
Petit mal epilepsy	2	0
<i>Central nervous system haemorrhages and cerebrovascular accidents</i>		
Cerebral haemorrhage	1	0
Cerebrovascular accident	5	0
Haemorrhage intracranial	1	0
<i>Cerebellar coordination and balance disturbances</i>		
Nystagmus	1	0
<i>Disturbances in consciousness NEC</i>		
Lethargy	5	0
Somnolence	4	0
Syncope	2	0
<i>Dyskinesias and movement disorders NEC</i>		
Psychomotor hyperactivity	3	0
<i>Headaches NEC</i>		
Headache	35	0
Tension headache	1	0
<i>Memory loss (excl dementia)</i>		
Amnesia	2	0
<i>Mental impairment (excl dementia and memory loss)</i>		
Disturbance in attention	2	0
<i>Migraine headaches</i>		
Migraine	1	0
<i>Myelitis (incl infective)</i>		
Myelitis transverse	1	0
<i>Narcolepsy and hypersomnia</i>		
Hypersomnia	1	0
<i>Neurological signs and symptoms NEC</i>		
Dizziness	19	0
Dizziness postural	2	0
Myoclonus	1	0
<i>Neuromuscular disorders NEC</i>		
Neuromyopathy	1	0

<i>Paraesthesias and dysaesthesias</i>		
Burning sensation	1	0
Paraesthesia	9	0
<i>Partial complex seizures</i>		
Complex partial seizures	1	0
<i>Seizures and seizure disorders NEC</i>		
Convulsion	14	0
Epilepsy	1	0
<i>Sensory abnormalities NEC</i>		
Ageusia	1	0
Dysgeusia	4	0
Hypoaesthesia	3	0
Sensory disturbance	1	0
Restless legs syndrome	1	0
<i>Sleep disturbances NEC</i>		
Poor quality sleep	1	0
<i>Speech and language abnormalities</i>		
Dysarthria	2	0
<i>Tremor (excl congenital)</i>		
Tremor	7	0
Nervous system disorders SOC Total	136	0

Drug Analysis Print
Drug Name: Tamiflu (oseltamivir)

Reaction Name	Reactions	Fatal Reactions
SOC		
<i>HLT</i>		
PT		
Pregnancy, puerperium and perinatal conditions		
<i>Abortions spontaneous</i>		
Abortion spontaneous	1	0
Pregnancy, puerperium and perinatal conditions SOC Total	1	0

Drug Analysis Print
Drug Name: Tamiflu (oseltamivir)

Reaction Name	Reactions	Fatal Reactions
SOC		
<i>HLT</i>		
PT		
Psychiatric disorders		
<i>Abnormal behaviour NEC</i>		
Breath holding	1	0
Abnormal behaviour	10	0
<i>Affect alterations NEC</i>		
Inappropriate affect	1	0
Affect lability	1	0
<i>Anxiety symptoms</i>		
Agitation	1	0
Anticipatory anxiety	1	0
Anxiety	8	0
<i>Attention deficit and disruptive behaviour disorders</i>		
Attention deficit/hyperactivity disorder	1	0
<i>Behaviour and socialisation disturbances</i>		
Aggression	3	0
Personality change	2	0
Social avoidant behaviour	1	0
<i>Confusion and disorientation</i>		
Confusional state	12	0
Disorientation	2	0
<i>Deliria</i>		
Delirium	4	0
<i>Delusional symptoms</i>		
Persecutory delusion	1	0
<i>Depressive disorders</i>		
Depression	5	0
<i>Dissociative states</i>		
Dissociation	1	0
<i>Disturbances in initiating and maintaining sleep</i>		
Insomnia	19	0
<i>Emotional and mood disturbances NEC</i>		
Anger	3	0
Emotional disorder	1	0
Emotional distress	1	0

Frustration	1	0
Fluctuating mood symptoms		
Mood swings	2	0
Increased physical activity levels		
Restlessness	1	0
Mental disorders NEC		
Mental disorder	1	0
Mood alterations with depressive symptoms		
Depressed mood	5	0
Tearfulness	2	0
Mood disorders NEC		
Apathy	1	0
Parasomnias		
Abnormal dreams	8	0
Nightmare	16	0
Sleep terror	4	0
Perception disturbances		
Hallucination	26	0
Hallucination, auditory	2	0
Hallucination, visual	7	0
Hallucinations, mixed	2	0
Personality disorders with dramatic behaviour (Cluster B)		
Histrionic personality disorder	1	0
Psychiatric symptoms NEC		
Psychiatric symptom	2	0
Psychotic disorder NEC		
Acute psychosis	1	0
Psychotic disorder	3	0
Sleep disorders NEC		
Sleep disorder	4	0
Speech articulation and rhythm disturbances		
Screaming	1	0
Dysphemia	1	0
Suicidal and self-injurious behaviour		
Suicidal ideation	2	0
Suicide attempt	1	0
Thinking disturbances		
Illogical thinking	1	0
Thinking abnormal	1	0
Panic attacks and disorders		
Panic attack	4	0

Panic reaction	1	0
Psychiatric disorders SOC Total	180	0

Drug Analysis Print
Drug Name: Tamiflu (oseltamivir)

Reaction Name	Reactions	Fatal Reactions
SOC		
<i>HLT</i>		
PT		
Renal and urinary disorders		
<i>Urinary abnormalities</i>		
Chromaturia	3	0
Haematuria	1	0
<i>Bladder and urethral symptoms</i>		
Dysuria	2	0
Pollakiuria	1	0
Urinary retention	1	0
<i>Renal failure and impairment</i>		
Renal failure acute	1	0
Renal impairment	1	0
<i>Urinary tract signs and symptoms NEC</i>		
Renal pain	1	0
Renal and urinary disorders SOC Total	11	0

Drug Analysis Print
Drug Name: Tamiflu (oseltamivir)

Reaction Name	Reactions	Fatal Reactions
SOC		
<i>HLT</i>		
PT		
Reproductive system and breast disorders		
<i>Erection and ejaculation conditions and disorders</i>		
Erectile dysfunction	1	0
<i>Menstruation and uterine bleeding NEC</i>		
Menstrual disorder	1	0
<i>Menstruation with decreased bleeding</i>		
Menstruation delayed	1	0
<i>Menstruation with increased bleeding</i>		
Polymenorrhoea	1	0
<i>Reproductive tract signs and symptoms NEC</i>		
Genital rash	1	0
<i>Vulvovaginal disorders NEC</i>		
Vaginal haemorrhage	1	0
<i>Breast signs and symptoms</i>		
Breast pain	1	0
Reproductive system and breast disorders SOC Total	7	0

Drug Analysis Print
Drug Name: Tamiflu (oseltamivir)

Reaction Name	Reactions	Fatal Reactions
SOC		
<i>HLT</i>		
PT		
Respiratory, thoracic and mediastinal disorders		
<i>Breathing abnormalities</i>		
Dyspnoea	6	0
Hypoventilation	1	0
<i>Bronchospasm and obstruction</i>		
Asthma	2	0
Wheezing	2	0
<i>Coughing and associated symptoms</i>		
Cough	1	0
<i>Lower respiratory tract inflammatory and immunologic conditions</i>		
Pneumonitis	1	0
<i>Nasal disorders NEC</i>		
Epistaxis	13	0
<i>Pharyngeal disorders (excl infections and neoplasms)</i>		
Pharyngeal inflammation	1	0
<i>Upper respiratory tract signs and symptoms</i>		
Throat irritation	1	0
Oropharyngeal pain	2	0
Respiratory, thoracic and mediastinal disorders SOC Total	30	0

Drug Analysis Print
Drug Name: Tamiflu (oseltamivir)

Reaction Name	Reactions	Fatal Reactions
SOC		
<i>HLT</i>		
PT		
Skin and subcutaneous tissue disorders		
<i>Acnes</i>		
Dermatitis acneiform	2	0
<i>Alopecias</i>		
Alopecia	2	0
<i>Angioedemas</i>		
Angioedema	2	0
<i>Apocrine and eccrine gland disorders</i>		
Cold sweat	2	0
Heat rash	1	0
Hyperhidrosis	2	0
Night sweats	3	0
<i>Bullous conditions</i>		
Blister	7	0
Dermatitis bullous	3	0
Erythema multiforme	4	0
Stevens-Johnson syndrome	4	0
Toxic epidermal necrolysis	2	0
<i>Dermal and epidermal conditions NEC</i>		
Scab	1	0
Skin discolouration	1	0
Skin discomfort	1	0
Skin disorder	1	0
Skin reaction	2	0
Swelling face	11	0
<i>Dermatitis and eczema</i>		
Dermatitis allergic	6	0
Dermatitis diaper	1	0
Eczema	2	0
<i>Erythemas</i>		
Erythema	11	0
Rash erythematous	13	0
<i>Exfoliative conditions</i>		
Skin exfoliation	3	0

<i>Panniculitides</i>		
Erythema nodosum	2	0
<i>Papulosquamous conditions</i>		
Rash papular	8	0
<i>Photosensitivity conditions</i>		
Photosensitivity reaction	1	0
<i>Purpura and related conditions</i>		
Purpura	2	0
<i>Skin injuries and mechanical dermatoses</i>		
Skin chapped	1	0
<i>Skin vasculitides</i>		
Vasculitic rash	2	0
<i>Urticarias</i>		
Urticaria	18	0
<i>Pruritus NEC</i>		
Pruritus	10	0
Rash pruritic	13	0
Pruritus generalised	10	0
<i>Rashes, eruptions and exanthems NEC</i>		
Rash	79	0
Rash generalised	26	0
Rash macular	16	0
Rash maculo-papular	11	0
Skin and subcutaneous tissue disorders SOC Total	286	0

Drug Analysis Print
Drug Name: Tamiflu (oseltamivir)

Reaction Name	Reactions	Fatal Reactions
SOC		
<i>HLT</i>		
PT		
Vascular disorders		
<i>Haemorrhages NEC</i>		
Haematoma	1	0
<i>Vascular hypertensive disorders NEC</i>		
Hypertension	1	0
<i>Peripheral vascular disorders NEC</i>		
Flushing	1	0
Hot flush	1	0
<i>Vascular hypotensive disorders</i>		
Hypotension	1	0
<i>Site specific vascular disorders NEC</i>		
Pallor	3	0
Vascular disorders SOC Total	8	0

Drug Analysis Print
Drug Name: Relenza (zanamivir)

Run Date: 1 April 2009 to 8 October 2009

Total number of reactions: 32	Total number of ADR reports: 17	Total number of fatal ADR reports: 1
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System Organ Class	Reactions	Fatal Reactions
Blood and lymphatic system disorders	2	0
Gastrointestinal disorders	3	0
General disorders and administration site conditions	3	0
Infections and infestations	1	0
Injury, poisoning and procedural complications	1	0
Investigations	1	0
Musculoskeletal and connective tissue disorders	4	0
Nervous system disorders	5	0
Pregnancy, puerperium and perinatal conditions	2	1
Respiratory, thoracic and mediastinal disorders	4	0
Skin and subcutaneous tissue disorders	5	0
Vascular disorders	1	0
Total	32	1

Glossary/Abbreviations

ADR - Adverse Drug Reaction

Age group - lists which age groups are included in the Drug Analysis Print - either ALL, Adolescent, Adult, Child, Elderly, Infant or Neonate

Data lock date - shows data on the database at this specified date and time

HLT - High Level Term - see definition of MedDRA

MEDRA - this stands for Medical Dictionary for Regulatory Activities, which is the internationally agreed list of terms used for Medicines Regulation. MedDRA groups related adverse drug reaction terms in a hierarchical structure whereby the 'preferred term' (PT) (e.g. tunnel vision) is grouped under the broader heading the 'high level term' (HLT) (e.g. visual field disorders). 'High level terms' are contained within the 'system organ class' (SOC) (e.g. eye disorders). The 'preferred term' is the most specific term on the Drug Analysis Print, while the 'system organ class' is the most general

Multi active constituent products - contain the drug constituent of interest plus one or more other drug constituents (e.g. co-codamol contains paracetamol and codeine)

NEC - appears in MedDRA and stands for Not Elsewhere Classified

NOS - appears in MedDRA and stands for Not Otherwise Specified

PBG - Product Brand Generic - this means drug brand name e.g. Amoxil is a PBG for the drug substance amoxic

Products included in this print - this is a list of the products for which at least one suspected Adverse Drug Reaction (ADR) report has been received that specifies that product as a 'suspected drug' (i.e. suspected causal association with the reaction). It does not provide an exhaustive list of the products which contain the named drug substance

PT - Preferred Term - see definition of MedDRA

Reaction - defines which ADRs are included in the Drug Analysis Print - either ALL, Serious or Non-Serious

Reporter type - lists the reporter types which are included in the Drug Analysis Print - either Patient, Health Professional or ALL (i.e. both)

Report run date - the date the Drug Analysis Print was produced

Route of admin - lists the route of administration of the suspect drug for which reports are included in the Drug Analysis Print, e.g. ORAL only includes reports where the suspect drug was specified as having been taken by the oral route, or ALL which includes all routes of administration

Spontaneous - suspected ADR reports sent in to the Yellow Card Scheme are called spontaneous reports

Single active constituent products - contain only the drug substance of interest

System Organ Class (SOC) - this is the highest level in MedDRA which groups together reactions that affect similar systems/organs in the body

Drug Analysis Print
Drug Name: Relenza (zanamivir)

Reaction Name	Reactions	Fatal Reactions
SOC		
<i>HLT</i>		
PT		
Blood and lymphatic system disorders		
<i>Leukopenias NEC</i>		
Lymphopenia	1	0
<i>Neutropenias</i>		
Neutropenia	1	0
Blood and lymphatic system disorders SOC Total	2	0

Drug Analysis Print
Drug Name: Relenza (zanamivir)

Reaction Name	Reactions	Fatal Reactions
SOC		
<i>HLT</i>		
PT		
Gastrointestinal disorders		
<i>Diarrhoea (excl infective)</i>		
Diarrhoea	1	0
<i>Nausea and vomiting symptoms</i>		
Nausea	1	0
Vomiting	1	0
Gastrointestinal disorders SOC Total	3	0

Drug Analysis Print
Drug Name: Relenza (zanamivir)

Reaction Name	Reactions	Fatal Reactions
SOC		
<i>HLT</i>		
PT		
General disorders and administration site conditions		
<i>Asthenic conditions</i>		
Fatigue	1	0
<i>Death and sudden death</i>		
<i>General signs and symptoms NEC</i>		
<i>Pain and discomfort NEC</i>		
Chest pain	1	0
<i>Feelings and sensations NEC</i>		
Feeling cold	1	0
General disorders and administration site conditions SOC Total	3	0

Drug Analysis Print
Drug Name: Relenza (zanamivir)

Reaction Name	Reactions	Fatal Reactions
SOC		
<i>HLT</i>		
PT		
Infections and infestations		
<i>Urinary tract infections</i>		
Kidney infection	1	0
Infections and infestations SOC Total	1	0

Drug Analysis Print
Drug Name: Relenza (zanamivir)

Reaction Name	Reactions	Fatal Reactions
SOC		
<i>HLT</i>		
PT		
Injury, poisoning and procedural complications		
<i>Pregnancy related accidental exposures and injuries</i>		
Drug exposure during pregnancy	1	0
Injury, poisoning and procedural complications SOC Total	1	0

Drug Analysis Print
Drug Name: Relenza (zanamivir)

Reaction Name	Reactions	Fatal Reactions
SOC		
<i>HLT</i>		
PT		
Investigations		
<i>Coagulation and bleeding analyses</i>		
International normalised ratio increased	1	0
Investigations SOC Total	1	0

Drug Analysis Print
Drug Name: Relenza (zanamivir)

Reaction Name	Reactions	Fatal Reactions
SOC		
<i>HLT</i>		
PT		
Musculoskeletal and connective tissue disorders		
<i>Joint related signs and symptoms</i>		
Arthralgia	1	0
<i>Muscle pains</i>		
Myalgia	1	0
<i>Musculoskeletal and connective tissue pain and discomfort</i>		
Neck pain	1	0
Pain in extremity	1	0
Musculoskeletal and connective tissue disorders SOC Total	4	0

Drug Analysis Print
Drug Name: Relenza (zanamivir)

Reaction Name	Reactions	Fatal Reactions
SOC		
<i>HLT</i>		
PT		
Nervous system disorders		
<i>Headaches NEC</i>		
Headache	1	0
<i>Neurological signs and symptoms NEC</i>		
Dizziness	2	0
<i>Paraesthesias and dysaesthesias</i>		
Paraesthesia	1	0
<i>Speech and language abnormalities</i>		
Dysarthria	1	0
Nervous system disorders SOC Total	5	0

Drug Analysis Print
Drug Name: Relenza (zanamivir)

Reaction Name	Reactions	Fatal Reactions
SOC		
<i>HLT</i>		
PT		
Pregnancy, puerperium and perinatal conditions		
<i>Abortions spontaneous</i>		
Abortion spontaneous	1	0
<i>Stillbirth and foetal death</i>		
Intra-uterine death	1	1
Pregnancy, puerperium and perinatal conditions SOC Total	2	1

Drug Analysis Print
Drug Name: Relenza (zanamivir)

Reaction Name	Reactions	Fatal Reactions
SOC		
<i>HLT</i>		
PT		
Respiratory, thoracic and mediastinal disorders		
<i>Bronchospasm and obstruction</i>		
Asthma	1	0
Bronchospasm	2	0
<i>Upper respiratory tract signs and symptoms</i>		
Oropharyngeal pain	1	0
Respiratory, thoracic and mediastinal disorders SOC Total	4	0

Drug Analysis Print
Drug Name: Relenza (zanamivir)

Reaction Name	Reactions	Fatal Reactions
SOC		
<i>HLT</i>		
PT		
Skin and subcutaneous tissue disorders		
<i>Dermatitis and eczema</i>		
Dermatitis allergic	1	0
<i>Erythemas</i>		
Rash erythematous	1	0
<i>Pruritus NEC</i>		
Pruritus	1	0
Rash pruritic	1	0
<i>Rashes, eruptions and exantheams NEC</i>		
Rash generalised	1	0
Skin and subcutaneous tissue disorders SOC Total	5	0

Drug Analysis Print
Drug Name: Relenza (zanamivir)

Reaction Name	Reactions	Fatal Reactions
SOC		
<i>HLT</i>		
PT		
Vascular disorders		
<i>Peripheral vascular disorders NEC</i>		
Hot flush	1	0
Vascular disorders SOC Total	1	0