

Suspected Adverse Drug Reaction (ADR) Analysis

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

21 August 2009

This report summarises all UK reports of suspected adverse drug reactions (ADRs) to influenza antiviral medicines received by MHRA between Wednesday 1st April 2009 and Thursday 13th August 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 reports submitted by the Marketing Authorisation holders for Tamiflu (oseltamivir) and Relenza (zanamivir) as part of their legal requirements. The attached listings of suspected ADRs are classified on the basis of 'MedDRA' terminology².

It is important to note that a report of a reaction to the MHRA 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 reactions – a mere suspicion will suffice. Therefore, reports submitted to MHRA may be true side-effects or they may be due to concurrent illness and therefore purely co-incidental events that would have occurred anyway in the absence of therapy. These reports remain under continual review by the MHRA.

This report therefore must not be interpreted as a list of known or proven side effects of Tamiflu or Relenza. The known side-effects of Tamiflu and Relenza are available in the product information (see <http://emc.medicines.org.uk/>) or www.mhra.gov.uk/swineflu.

As ADR reporting rates are dependent on many factors and are highly variable, these data cannot be used to determine the frequency of side effects. Due to the different routes of administration of Tamiflu and Relenza, and possible use in different patient populations, direct comparisons of the relative safety of Tamiflu and Relenza should not be made using these data.

Headline summary:

- As of 13th August 2009, the MHRA has received a total of **533** reports of suspected ADRs for Tamiflu and **12** reports for Relenza
- No new safety concerns have been identified for either drug and there is no change to the product information. Patients should continue to take Tamiflu or Relenza as advised by their healthcare provider.
- The balance of risks and benefits for Tamiflu and Relenza remains positive. We continue to closely monitor a number of potential safety signals for which an association with Tamiflu or Relenza has yet to be confirmed.
- All new and emerging safety signals will be identified in this report together with any regulatory action or changes to prescribing advice deemed necessary.

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.

SUSPECTED ADR REPORTS RECEIVED FOR TAMIFLU (oseltamivir)

A total of 533 reports (including 895 suspected adverse reactions³) have been reported in association with 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.

Specific events

Possible Drug Interaction between Tamiflu and Warfarin

We have received several reports suggestive of a possible drug interaction between Tamiflu and warfarin leading to prolonged blood clotting time. The available evidence is currently insufficient to establish whether such cases are 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 illness. Therefore, at present there is no change to the product information for Tamiflu and 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 two reports in which the patient died following treatment with Tamiflu; one case of unexplained death and one case of acute hepatic failure. These cases have been fully evaluated and in neither case is there evidence to confirm that Tamiflu was directly responsible for the fatal event. These were possibly due to underlying infection and illness.

Neuropsychiatric adverse events

Neuropsychiatric adverse effects, 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 events 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 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 disorders such as Toxic Epidermal Necrolysis (TEN), Stevens-Johnson Syndrome (SJS) and erythema multiforme are listed as possible side effects in the Tamiflu product information on the basis that some cases have occurred in patients following Tamiflu therapy.

³ One report may contain more than one suspected adverse reaction

Such conditions may also be caused by various infections including influenza. In patients being treated with Tamiflu for influenza, it therefore remains unclear whether reported cases of severe skin disorders are due to the drug or to the underlying infection and illness.

The MHRA will continue to keep such reports under close review.

SUSPECTED ADR REPORTS RECEIVED FOR RELENZA (zanamivir)

A total of 12 reports (including 19 suspected adverse reactions³) have been reported in association with Relenza in the UK since 1st April 2009.

Most 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 also be caused by flu-like illness.

No new safety issues have been identified.

Safety in pregnancy

There has been one reported case of miscarriage in early pregnancy. Cases of miscarriage are not uncommon in early pregnancy and some may inevitably occur by coincidence following Relenza therapy without the drug playing any role in the event. There is no evidence to indicate that Relenza carries any risks in pregnancy, to either the fetus or expecting mother.

This is supported by a recent review of available evidence by European regulatory authorities. Indeed, this review 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 13 August 2009

Total number of reactions: 895	Total number of ADR reports: 533	Total number of fatal ADR reports: 2
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System Organ Class	Reactions	Fatal Reactions
Blood and lymphatic system disorders	3	0
Cardiac disorders	11	0
Ear and labyrinth disorders	3	0
Eye disorders	23	0
Gastrointestinal disorders	294	0
General disorders and administration site conditions	46	1
Hepatobiliary disorders	12	1
Immune system disorders	5	0
Infections and infestations	7	0
Injury, poisoning and procedural complications	2	0
Investigations	25	0
Metabolism and nutrition disorders	7	0
Musculoskeletal and connective tissue disorders	11	0
Nervous system disorders	88	0
Pregnancy, puerperium and perinatal conditions	1	0
Psychiatric disorders	116	0
Renal and urinary disorders	9	0
Reproductive system and breast disorders	4	0
Respiratory, thoracic and mediastinal disorders	19	0
Skin and subcutaneous tissue disorders	204	0
Vascular disorders	5	0
Total	895	2

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>Haemolyses NEC</i>		
Haemolysis	1	0
<i>Lymphatic system disorders NEC</i>		
Lymphadenopathy	1	0
<i>Coagulopathies</i>		
Abnormal clotting factor	1	0
Blood and lymphatic system disorders SOC Total	3	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	5	0
<i>Cardiomyopathies</i>		
Congestive cardiomyopathy	1	0
<i>Rate and rhythm disorders NEC</i>		
Arrhythmia	1	0
Tachycardia	1	0
<i>Supraventricular arrhythmias</i>		
Atrial fibrillation	1	0
Sinus bradycardia	1	0
Cardiac disorders SOC Total	11	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	1	0
Vertigo	2	0
Ear and labyrinth disorders SOC Total	3	0

Drug Analysis Print
Drug Name: Tamiflu (oseltamivir)

Reaction Name	Reactions	Fatal Reactions
SOC		
<i>HLT</i>		
PT		
Eye disorders		
<i>Conjunctival infections, irritations and inflammations</i>		
Conjunctivitis	2	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 disorders NEC</i>		
Eye pain	1	0
Eye swelling	3	0
Eyelid disorder	2	0
<i>Ocular infections, inflammations and associated manifestations</i>		
Eye pruritus	2	0
<i>Ocular sensation disorders</i>		
Abnormal sensation in eye	1	0
Photophobia	2	0
<i>Visual disorders NEC</i>		
Diplopia	1	0
Vision blurred	2	0
Visual impairment	1	0
Eye disorders SOC Total	23	0

Drug Analysis Print
Drug Name: Tamiflu (oseltamivir)

Reaction Name	Reactions	Fatal Reactions
SOC		
<i>HLT</i>		
PT		
Gastrointestinal disorders		
<i>Diarrhoea (excl infective)</i>		
Diarrhoea	30	0
Diarrhoea haemorrhagic	1	0
<i>Dyspeptic signs and symptoms</i>		
Dyspepsia	5	0
<i>Flatulence, bloating and distension</i>		
Flatulence	1	0
<i>Gastrointestinal and abdominal pains (excl oral and throat)</i>		
Abdominal pain	19	0
Abdominal pain upper	19	0
Gastrointestinal pain	1	0
<i>Gastrointestinal atonic and hypomotility disorders NEC</i>		
Constipation	1	0
<i>Non-site specific gastrointestinal haemorrhages</i>		
Haematemesis	4	0
<i>Gingival disorders NEC</i>		
Gingivitis	1	0
<i>Gingival pains</i>		
Gingival pain	1	0
<i>Intestinal haemorrhages</i>		
Rectal haemorrhage	2	0
<i>Gastrointestinal signs and symptoms NEC</i>		
Dysphagia	1	0
Stomach discomfort	2	0
<i>Nausea and vomiting symptoms</i>		
Nausea	46	0
Retching	1	0
Vomiting	118	0
Vomiting projectile	3	0
<i>Oral dryness and saliva altered</i>		
Dry mouth	1	0
<i>Oral soft tissue disorders NEC</i>		
Cheilitis	1	0

Lip swelling	4	0
Oral soft tissue pain and paraesthesia		
Oral pain	2	0
Paraesthesia oral	3	0
Oral soft tissue swelling and oedema		
Gingival swelling	1	0
Acute and chronic pancreatitis		
Pancreatitis	1	0
Pancreatitis acute	2	0
Salivary gland disorders NEC		
Salivary hypersecretion	1	0
Stomatitis and ulceration		
Mouth ulceration	13	0
Tongue disorders		
Tongue ulceration	2	0
Tongue signs and symptoms		
Glossodynia	1	0
Swollen tongue	4	0
Oesophagitis (excl infective)		
Oesophagitis	1	0
Reflux oesophagitis	1	0
Gastrointestinal disorders SOC Total	294	0

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	1	0
Fatigue	10	0
Malaise	12	0
<i>Death and sudden death</i>		
Death	1	1
<i>Gait disturbances</i>		
Gait disturbance	2	0
<i>General signs and symptoms NEC</i>		
Condition aggravated	1	0
Influenza like illness	2	0
General physical health deterioration	1	0
<i>Interactions</i>		
Drug interaction	2	0
<i>Oedema NEC</i>		
Face oedema	2	0
Oedema peripheral	3	0
<i>Pain and discomfort NEC</i>		
Chest pain	3	0
Pain	2	0
<i>Feelings and sensations NEC</i>		
Chills	1	0
Feeling abnormal	2	0
Feeling of body temperature change	1	0
General disorders and administration site conditions SOC Total	46	1

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	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	4	0
Hepatitis acute	1	0
Hepatotoxicity	1	0
<i>Hepatic and hepatobiliary disorders NEC</i>		
Liver disorder	1	0
Liver injury	1	0
Hepatobiliary disorders SOC Total	12	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	4	0
Immune system disorders SOC Total	5	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	1	0
<i>Bone and joint infections</i>		
Bursitis infective	1	0
<i>Candida infections</i>		
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	1	0
Infections and infestations SOC Total	7	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	1	0
Injury, poisoning and procedural complications SOC Total	2	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
<i>Liver function analyses</i>		
Alanine aminotransferase increased	2	0
Blood bilirubin increased	2	0
Liver function test abnormal	4	0
<i>Platelet analyses</i>		
Platelet count decreased	1	0
<i>Urinalysis NEC</i>		
Urine colour abnormal	1	0
Investigations SOC Total	25	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
<i>Diabetes mellitus (incl subtypes)</i>		
Diabetes mellitus inadequate control	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	7	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>Joint related signs and symptoms</i>		
Arthralgia	3	0
<i>Muscle pains</i>		
Myalgia	1	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	1	0
Pain in extremity	2	0
Musculoskeletal and connective tissue disorders SOC Total	11	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	1	0
<i>Central nervous system haemorrhages and cerebrovascular accidents</i>		
Cerebrovascular accident	3	0
Haemorrhage intracranial	1	0
<i>Disturbances in consciousness NEC</i>		
Lethargy	1	0
Somnolence	2	0
Syncope	2	0
<i>Dyskinesias and movement disorders NEC</i>		
Psychomotor hyperactivity	2	0
<i>Headaches NEC</i>		
Headache	21	0
Tension headache	1	0
<i>Memory loss (excl dementia)</i>		
Amnesia	1	0
<i>Mental impairment (excl dementia and memory loss)</i>		
Disturbance in attention	1	0
<i>Migraine headaches</i>		
Migraine	1	0
<i>Narcolepsy and hypersomnia</i>		
Hypersomnia	1	0
<i>Neurological signs and symptoms NEC</i>		
Dizziness	14	0
Dizziness postural	1	0
Myoclonus	1	0
<i>Neuromuscular disorders NEC</i>		
Neuromyopathy	1	0
<i>Paraesthesias and dysaesthesias</i>		
Burning sensation	1	0
Paraesthesia	4	0
<i>Partial complex seizures</i>		
Complex partial seizures	1	0

<i>Seizures and seizure disorders NEC</i>		
Convulsion	10	0
<i>Sensory abnormalities NEC</i>		
Ageusia	1	0
Dysgeusia	2	0
Hypoaesthesia	4	0
Sensory disturbance	1	0
Restless legs syndrome	1	0
<i>Speech and language abnormalities</i>		
Dysarthria	2	0
<i>Tremor (excl congenital)</i>		
Tremor	6	0
Nervous system disorders SOC Total	88	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	7	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	4	0
<i>Attention deficit and disruptive behaviour disorders</i>		
Attention deficit/hyperactivity disorder	1	0
<i>Behaviour and socialisation disturbances</i>		
Aggression	1	0
Personality change	1	0
<i>Confusion and disorientation</i>		
Confusional state	8	0
Disorientation	2	0
<i>Deliria</i>		
Delirium	3	0
<i>Depressive disorders</i>		
Depression	4	0
<i>Dissociative states</i>		
Dissociation	1	0
<i>Disturbances in initiating and maintaining sleep</i>		
Insomnia	11	0
<i>Emotional and mood disturbances NEC</i>		
Anger	3	0
Emotional disorder	1	0
Frustration	1	0
<i>Fluctuating mood symptoms</i>		
Mood swings	1	0
<i>Increased physical activity levels</i>		

Restlessness	1	0
<i>Mood alterations with depressive symptoms</i>		
Depressed mood	4	0
Tearfulness	1	0
<i>Mood disorders NEC</i>		
Apathy	1	0
<i>Parasomnias</i>		
Abnormal dreams	3	0
Nightmare	13	0
Sleep terror	4	0
<i>Perception disturbances</i>		
Hallucination	17	0
Hallucination, auditory	1	0
Hallucination, visual	4	0
<i>Personality disorders with dramatic behaviour (Cluster B)</i>		
Histrionic personality disorder	1	0
<i>Psychiatric symptoms NEC</i>		
Psychiatric symptom	2	0
<i>Psychotic disorder NEC</i>		
Acute psychosis	1	0
Psychotic disorder	1	0
<i>Sleep disorders NEC</i>		
Sleep disorder	2	0
<i>Speech articulation and rhythm disturbances</i>		
Screaming	1	0
<i>Suicidal and self-injurious behaviour</i>		
Suicidal ideation	1	0
Suicide attempt	1	0
<i>Panic attacks and disorders</i>		
Panic attack	3	0
Psychiatric disorders SOC Total	116	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
<i>Bladder and urethral symptoms</i>		
Dysuria	3	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	9	0

Drug Analysis Print
Drug Name: Tamiflu (oseltamivir)

Reaction Name	Reactions	Fatal Reactions
SOC		
<i>HLT</i>		
PT		
Reproductive system and breast disorders		
<i>Menstruation with decreased bleeding</i>		
Menstruation delayed	1	0
<i>Menstruation with increased bleeding</i>		
Polymenorrhoea	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	4	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	5	0
Hypoventilation	1	0
<i>Bronchospasm and obstruction</i>		
Asthma	1	0
Wheezing	2	0
<i>Nasal disorders NEC</i>		
Epistaxis	8	0
<i>Pharyngeal disorders (excl infections and neoplasms)</i>		
Pharyngeal inflammation	1	0
<i>Upper respiratory tract signs and symptoms</i>		
Oropharyngeal pain	1	0
Respiratory, thoracic and mediastinal disorders SOC Total	19	0

Drug Analysis Print
Drug Name: Tamiflu (oseltamivir)

Reaction Name	Reactions	Fatal Reactions
SOC		
<i>HLT</i>		
PT		
Skin and subcutaneous tissue disorders		
<i>Alopecias</i>		
Alopecia	1	0
<i>Angioedemas</i>		
Angioedema	1	0
<i>Apocrine and eccrine gland disorders</i>		
Cold sweat	2	0
Heat rash	1	0
Hyperhidrosis	1	0
Night sweats	2	0
<i>Bullous conditions</i>		
Blister	3	0
Dermatitis bullous	2	0
Erythema multiforme	4	0
Stevens-Johnson syndrome	1	0
Toxic epidermal necrolysis	2	0
<i>Dermal and epidermal conditions NEC</i>		
Skin discolouration	1	0
Swelling face	6	0
Hypoaesthesia facial	1	0
<i>Dermatitis and eczema</i>		
Dermatitis allergic	4	0
Dermatitis diaper	1	0
Eczema	1	0
<i>Erythemas</i>		
Erythema	6	0
Rash erythematous	8	0
<i>Exfoliative conditions</i>		
Skin exfoliation	1	0
<i>Panniculitides</i>		
Erythema nodosum	1	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	1	0
<i>Urticarias</i>		
Urticaria	14	0
<i>Pruritus NEC</i>		
Pruritus	7	0
Rash pruritic	8	0
Pruritus generalised	10	0
<i>Rashes, eruptions and exantheams NEC</i>		
Rash	60	0
Rash generalised	23	0
Rash macular	10	0
Rash maculo-papular	9	0
Skin and subcutaneous tissue disorders SOC Total	204	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>Peripheral vascular disorders NEC</i>		
Hot flush	1	0
<i>Vascular hypotensive disorders</i>		
Hypotension	1	0
<i>Site specific vascular disorders NEC</i>		
Pallor	2	0
Vascular disorders SOC Total	5	0

Drug Analysis Print
Drug Name: Relenza (zanamivir)

Run Date: 1 April 2009 to 13 August 2009

Total number of reactions: 19	Total number of ADR reports: 12	Total number of fatal ADR reports: 0
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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	2	0
Infections and infestations	1	0
Injury, poisoning and procedural complications	1	0
Investigations	1	0
Nervous system disorders	2	0
Pregnancy, puerperium and perinatal conditions	1	0
Respiratory, thoracic and mediastinal disorders	3	0
Skin and subcutaneous tissue disorders	3	0
Total	19	0

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>Pain and discomfort NEC</i>		
Chest pain	1	0
General disorders and administration site conditions SOC Total	2	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		
Nervous system disorders		
<i>Headaches NEC</i>		
Headache	1	0
<i>Neurological signs and symptoms NEC</i>		
Dizziness	1	0
Nervous system disorders SOC Total	2	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
Pregnancy, puerperium and perinatal conditions SOC Total	1	0

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
Respiratory, thoracic and mediastinal disorders SOC Total	3	0

Drug Analysis Print
Drug Name: Relenza (zanamivir)

Reaction Name	Reactions	Fatal Reactions
SOC		
<i>HLT</i>		
PT		
Skin and subcutaneous tissue disorders		
<i>Erythemas</i>		
Rash erythematous	1	0
<i>Pruritus NEC</i>		
Pruritus	1	0
Rash pruritic	1	0
Skin and subcutaneous tissue disorders SOC Total	3	0