

## Suspected Adverse Reaction Analysis

### Human papillomavirus (HPV) vaccine (brand unspecified)

2 July 2009

This report summarises the reports of adverse reactions suspected to have been caused by human papillomavirus (HPV) vaccine for which information on the specific brand administered (whether Cervarix or Gardasil) is currently unavailable. This includes reports received up to 1 July 2009. Separate Adverse Reaction Analysis summaries exist for reports in which the brand was stated. These reports have been voluntarily submitted to the MHRA by healthcare professionals and members of the public via the Yellow Card Scheme (visit [www.yellowcard.gov.uk](http://www.yellowcard.gov.uk)) and by the manufacturers of the vaccine as part of their legal requirements.

It is essential to bear in mind that reports to the MHRA relate only to adverse medical events which the reporter considered could have been caused by the vaccine (i.e. if there was merely a **suspicion** of causality). Therefore, cases may be true side-effects or they may have been purely coincidental events due to underlying or undiagnosed illness that would have occurred anyway in the absence of vaccination. Events may also have been psychogenic<sup>1</sup> in origin. This report therefore cannot be considered to represent a list of known side-effects of the vaccine. These data also cannot be used to determine the frequency, or incidence, of known side-effects because they are often under-reported. The known side-effects, and their frequencies (based on clinical trial data), are available in the product information (see <http://emc.medicines.org.uk/>).

The reactions in this report have been broken down into 5 categories based on scientific assessment of individual cases by MHRA assessors: injection-site reactions; allergic reactions; 'psychogenic' events; other recognised reactions; and 'suspected adverse reactions not currently recognised' (reactions in this latter category are divided into the high-level classification of System Organ Class)<sup>2</sup>. The same event term may appear in more than one category (e.g. 'rash' may be associated with injection site, allergic or unrecognised suspected reactions and 'psychogenic' events). However, an event from a single report will appear in only one category.

A single report may contain more than one reaction, more than one sign or symptom of a single reaction or different reactions in more than one of the above categories. Therefore the total number of listed reactions is greater than the total number of reports and total reports in each of the 5 tables should not be added together.

#### Headline summary:

**To date, most suspected ADRs reported to MHRA in association with HPV vaccine have related to the signs and symptoms of recognised side effects listed in the product information or were due to the injection process and not the vaccine itself (i.e. 'psychogenic' in nature).**

**For the isolated case of other medical conditions reported, the available evidence does not suggest that the vaccine caused the condition and these may have been coincidental events.**

**Following administration of more than 1 million doses across the UK since last September, the balance of risks and benefits of Cervarix remains positive**

<sup>1</sup> For this analysis, defined as non-allergic events which occurred within minutes of, or soon after, vaccination and were most likely a psychogenic response to, or anticipation of, the injection. These are not side effects to the vaccine as such and can occur with any needle injection procedure.

<sup>2</sup> Using MedDRA terminology

## SUMMARY OF UK SAFETY EXPERIENCE

**Total number of reports received: 109**

**Total number of suspected reactions: 317**

**Estimated number of doses of Cervarix administered across the UK: at least 1 million doses<sup>3</sup>**

### A. Injection-site reactions

Injection-site reactions including redness, pain and swelling are recognised<sup>4</sup> side-effects of HPV vaccines and are listed in the product information. These may occur at a frequency<sup>5</sup> of more than 1 in 10 persons vaccinated.

The cases reported to the MHRA during use of the vaccine in the UK do not indicate any change in the severity or nature of injection site reactions.

Reported event (Preferred Term <sup>2</sup> )	Number of cases
Erythema	4
Pain in extremity	4
Oedema peripheral	3
Injection site coldness	2
Injection site discolouration	2
Injection site erythema	2
Pain	2
Pruritus	2
Skin reaction	2
Feeling hot	1
Injection site anaesthesia	1
Injection site haemorrhage	1
Injection site mass	1
Local swelling	1
Musculoskeletal stiffness	1
Peripheral coldness	1
Rash	1
Urticaria	1
Total reactions	32
Total reports	17

<sup>3</sup> Based on UK-wide vaccine uptake data to March 2009. As the Yellow Card data are up to the present date, the available uptake data should not be used to derive adverse reaction reporting rates (as this will result in an over-estimation)

<sup>4</sup> Known to be associated with either Cervarix or Gardasil

<sup>5</sup> Based on clinical trial data

## B. Allergic reactions (including skin reactions not directly related to an injection-site reaction)

Allergic reactions are a recognised<sup>4</sup> side-effect of HPV vaccines and are listed in the product information. These may occur at a frequency<sup>5</sup> between 1 in 10 persons (for non-serious types of allergic reaction such as rash and itching) to less than 1 in 10,000 persons vaccinated. Severe allergic reactions are very rare.

The cases reported to the MHRA during use of the vaccine in the UK do not indicate any change in the severity or nature of allergic reactions.

Reported event (Preferred Term <sup>2</sup> )	Number of cases
Rash	5
Erythema	3
Eyelid oedema	3
Hypersensitivity	3
Urticaria	3
Pharyngeal oedema	2
Rash pruritic	2
Anaphylactic reaction	1
Blister	1
Dysphagia	1
Dyspnoea	1
Heat rash	1
Laryngeal oedema	1
Lip swelling	1
Pruritus	1
Rash erythematous	1
Rash generalised	1
Rash macular	1
Stridor	1
Swelling	1
Throat irritation	1
Throat tightness	1
Total reactions	36
Total reports	20

### C. 'Psychogenic' events

Psychogenic events including vasovagal syncope, faints and panic attacks can occur with any injection procedure, not just vaccination, and can be common in adolescents. These are due to fear and/or anticipation of the needle injection and are not side-effects of HPV vaccine as such. Such events can be associated with a wide range of temporary signs and symptoms including loss of consciousness, vision disturbance, injury, limb jerking (often misinterpreted as a seizure/convulsion), limb numbness or tingling, difficulty in breathing, hyperventilation etc.

Reported event (Preferred Term <sup>2</sup> )	Number of cases
Syncope	19
Dizziness	9
Headache	8
Pallor	4
Nausea	3
Dyspnoea	2
Malaise	2
Presyncope	2
Rash	2
Vomiting	2
Abdominal pain	1
Asthenia	1
Back pain	1
Blindness transient	1
Blood pressure increased	1
Convulsion	1
Heart rate increased	1
Heart rate irregular	1
Hot flush	1
Hyperventilation	1
Hypoaesthesia	1
Muscular weakness	1
Paraesthesia	1
Sensory loss	1
Somnolence	1
Urticaria	1
Vision blurred	1
Visual impairment	1
Total reactions	71
Total reports	30

#### D. 'Other recognised' reactions

This section includes other events recognised<sup>4</sup> to be side-effects of HPV vaccine and not already included in sections A and B above. This also includes signs and symptoms of recognised side effects. The frequencies, where known, are listed in the product information.

The cases reported to the MHRA during use of the vaccine in the UK so far do not indicate any change in the severity or nature of these reactions.

Reported event (Preferred Term <sup>2</sup> )	Number of cases
Headache	10
Nausea	9
Pyrexia	8
Malaise	5
Vomiting	5
Fatigue	4
Abdominal pain	2
Abdominal pain upper	2
Body temperature increased	2
Dizziness	2
Limb discomfort	2
Somnolence	2
Asthenia	1
Diarrhoea	1
Lethargy	1
Lymphadenopathy	1
Musculoskeletal stiffness	1
Myalgia	1
Respiratory tract infection	1
Total reactions	60
Total reports	30

## E. 'Suspected adverse reactions not currently recognised'

This section includes reports which, based on MHRA assessment of the case details provided, do not fit into one of the above 4 categories.

These suspected ADRs are not currently recognised as side effects of HPV vaccine and the available evidence does not suggest a causal link with the vaccine. These are isolated medical events which may have been coincidental with vaccination. These reports are continually assessed by the MHRA.

System Organ Class	Reported event (Preferred Term <sup>2</sup> )	Number of cases
Ear and labyrinth disorders	Ear pain	1
	Hyperacusis	1
Eye disorders	Diplopia	1
	Photopsia	1
	Vision blurred	1
	Visual impairment	1
		1
Gastrointestinal disorders	Abdominal discomfort	1
	Abdominal pain	2
	Abdominal pain upper	1
	Diarrhoea	1
	Nausea	3
General disorders and administration site conditions	Abasia	1
	Chest pain	1
	Chills	1
	Discomfort	1
	Exercise tolerance decreased	1
	Fatigue	2
	Feeling abnormal	1
	Gait disturbance	1
	Influenza like illness	8
	Injection site swelling	1
	Local swelling	1
	Malaise	1
	Pain	2
	Pyrexia	2
	Temperature intolerance	1
	Thirst	1
Infections and infestations	Labyrinthitis	1
	Skin infection	1
Investigations	Body temperature increased	1
Musculoskeletal and connective tissue disorders	Arthralgia	2
	Back pain	1
	Joint stiffness	1
	Muscular weakness	1
	Musculoskeletal stiffness	1
	Pain in extremity	1
Nervous system disorders	Cerebellar ataxia	1
	Chorea	1

	Complex regional pain syndrome	1
	Convulsion	1
	Dizziness	5
	Dizziness postural	2
	Dyskinesia	1
	Epilepsy	1
	Grand mal convulsion	1
	Headache	7
	Hypoaesthesia	4
	Ivth nerve paralysis	1
	Lethargy	3
	Loss of consciousness	3
	Migraine	1
	Paraesthesia	2
	Syncope	1
	Tremor	1
Psychiatric disorders	Confusional state	2
	Depression	1
	Insomnia	1
Renal and urinary disorders	Neurogenic bladder	1
	Urinary retention	1
Respiratory, thoracic and mediastinal disorders	Dyspnoea	1
	Nasal congestion	1
	Oropharyngeal pain	1
	Wheezing	1
Skin and subcutaneous tissue disorders	Acne	1
	Alopecia	2
	Erythema	1
	Erythema multiforme	1
	Henoch-schonlein purpura	1
	Petechiae	1
	Photosensitivity reaction	1
	Purpura	2
	Rash	4
	Rash erythematous	1
	Skin discolouration	1
	Skin disorder	1
	Urticaria	1
Vascular disorders	Pallor	1
	Peripheral coldness	2
Total reactions		118
Total reports		35