

**Minutes of the
Adverse Drug Reactions
Advisory Committee**

319th meeting

11 December 2009

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8.1 PRR Report

The line listing of reports lodged in the period covered by this Meeting (10 September to 12 November 2009) with proportional reporting ratios was provided. The following associations were highlighted at the Meeting:

Medicine	Adverse reaction	Reports in database (sole suspected)	Comment
HPV vaccine	Anaphylactic reaction Autoimmune thyroiditis Coeliac disease Dermatomyositis Idiopathic thrombocytopenic purpura	14 (12) 1 (1) 2 (2) 1 (1) 1 (1)	Reports of autoimmune disorders are beginning to emerge, and first reports of some reactions were noted. (see also item 10)

10.2 Vaccine reports

During the period from 10 September to 12 November 2009, 1,228 reports of vaccine adverse reactions were lodged. This represents about 46% of the reports lodged for the period. [REDACTED] 51 relate to HPV vaccine alone.

The period covered by this Meeting is 11 days longer than the usual period covered by Meetings, resulting in 596 extra reports, including 50 extra vaccine reports.

Given that reports of [REDACTED] are subject to intense, weekly review, only the reports of vaccines other than [REDACTED] are considered at this Meeting.

Reports of vaccines other than HPV vaccine alone

278 of the vaccine reports describe reactions to vaccines other than single-injection HPV vaccine (including 17 where HPV vaccine was administered together with another vaccine – 12 with Hep B vaccine, 2 with varicella vaccine and 1 each with Hep A, PanVax and Boostrix vaccines).

183 of the reports were received from States, Territories or Local Government Councils, 26 were from sponsors, 28 were from members of the public and 40 were from healthcare professionals (nurse, GP, specialist or hospital staff) – including 4 from the AVN. 194 reports related to children, 77 related to adults and age was not stated in 7.

The case reports for vaccines other than HPV vaccine alone and a case line listing of these reports was provided.

HPV vaccine reports:

51 of the vaccine reports described reactions to HPV vaccine when given as a single vaccine. These were received from NSW (22), VIC (15), QLD (6), SA (1), WA (2), NT (1) or from an unidentified State *via* the sponsor (4).

Reports in association with HPV vaccine received from Sept 9 to Nov 12 2009 and a case line listing of these reports was provided.

Number of reports and events

The number of reports received in association with the majority of the vaccines is shown below:

Vaccine	No. reports	Vaccine	No. reports
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Human papilloma virus	68		
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Anaphylaxis (8 reports)

Note: onset time (if stated on report) is in days; an onset time of 0 indicates the reaction occurred on the day of vaccination

Number Source	Sex	Age	Onset Time	Outcome Description	Vaccine/s	Reactions, description
258533 (VIC)	F	12	10 mins	Unknown	██████ Gardasil	Vaccinated at 10.20am. At 10.35am - rash to chest (blotchy, raised edges) and red rashy face noticed. Patient also complained of heavy chest. At 10.40am, sore abdomen, pins & needles to hands, heavy chest, rash to chest subsiding, pale skin and hands clammy. No respiratory problems and patient alert. Ambulance called and adrenaline was given. ADRAC noted that the only ADR described in this report was of rash; 'heavy chest' was not a respiratory symptom according to Brighton criteria. The reporter (immunisation unit) had stated that the case was 'recoded following clinic review today to anaphylaxis', but the reason for the diagnosis was not clear. ADRAC suggested the basis for the diagnosis should be clarified before this is accepted as a case of anaphylaxis.

Seizures/convulsions (10 reports)

Note: onset time (if stated on report) is in days; an onset time of 0 indicates the reaction occurred on the day of vaccination

Number Source	Sex	Age	Onset Time	Outcome	Trade Name Description	Reactions
256905 (NSW)	F	15		Recovered	Gardasil	Grand mal convulsion
256907 (NSW)	F	40	6	Recovered	Gardasil	Convulsion
256966 (VIC)	F	12		Recovered	Gardasil, [REDACTED]	Presyncope Tonic convulsion
256940 (VIC)	F	12	0	Recovered	Gardasil [REDACTED]	Headache Tonic clonic movements
259677 (NSW)	F	17		Unknown	Gardasil	Autonomic thyroiditis Convulsion Diabetes mellitus Menstruation irregular Polycystic ovaries

10.3.1 Autoimmune disorders with HPV vaccine

A Member commented on the following auto-immune disorders reported in females vaccinated with HPV vaccine. Those emerging within 2-3 weeks after vaccination were of particular interest.

10.3.1.1 Idiopathic thrombocytopenic purpura with HPV vaccine (Gardasil)

Report 256779 (VIC)

This report described a previously healthy 19 year old female who received Gardasil in 2007. Two weeks after her second vaccination, she presented with the following: *“iron deficiency anaemia (Hb 10.1g) and her platelet count was 35. Her bone marrow showed a picture consistent with ITP and peripheral platelet destruction. Her platelet count subsequently fell to 5. Her ANA was positive to*

a titre of >1280 with a speckled pattern. The rheumatoid factor was borderline at 21; the ENA and DNA binding were negative. She responded to oral corticosteroid but thrombocytopenia recurred when this was weaned. She was subsequently treated with rituximab (on clinical trial) and has remained in haematological remission [at the time of reporting in Sept 2009]". The reporter (a specialist) was interested in this case "in light of recent reports from USA of a low incidence of severe autoimmune reactions to Gardasil."

10.3.1.2 Dermatomyositis with HPV vaccine (Gardasil)

Report 258071 (NSW)

A 29 year old female of ASTI background (with previously undiagnosed diabetes) was vaccinated with her first dose of Gardasil and 2 weeks later developed general muscle weakness and pains and rash. She was subsequently diagnosed by a hospital registrar as having dermatomyositis, treated with high dose steroids and was referred for care by a rheumatologist. Members commented on the detailed notes provided by the rheumatologist but it was notable that the report did not include mention of the vaccine 2 weeks prior to onset of symptoms.

10.3.1.3 Coeliac disease with HPV vaccine (Gardasil)

Report 258636 (QLD)

Three weeks after her third dose of Gardasil, a previously healthy 17 year old female experienced continuous nausea and weight loss. She was subsequently found (by gastroenterologist) to have coeliac disease and was put on a gluten-free diet.

10.3.1.4 Thyroiditis with HPV vaccine (Gardasil)

Report 259677 (NSW)

About 3 months after immunisation with Gardasil, a 17 year old female experienced lethargy, developed irregular menstruation, and experienced seizures. She was subsequently found to have Hashimoto's thyroiditis, polycystic ovary disease and insulin dependent diabetes mellitus.

10.3.2 Intracerebral haemorrhage and HPV vaccine (Gardasil)

Report 259677 (NSW)

Three months after her second dose of HPV vaccine, a 14 year old female developed dizziness and a cerebral bleed. She underwent emergency neurosurgery to drain the haematoma but no evidence of vascular malformation was detected (on CT and MRI scans). The reporter (immunisation unit) stated that "*3 months for onset of cerebral bleed post vaccination is difficult to explain plus patient was given the third dose of HPV 10 months after the 2nd dose with apparently no adverse event*".

10.3.3 Anaphylaxis and HPV vaccine (Gardasil)

Report 256897 (NSW)

A 17 year old female was immunised with Gardasil and experienced slight nausea immediately after, which worsened over the next 2 h. From 5 h after vaccination, she developed swollen eyes (which progressively worsened), hive-like rash over her head and neck (later extending to arms and

11.2.2 HPV vaccine and tracheo-oesophageal fistula

Report 256711

This sponsor report was reported to have been obtained from a pregnancy registry entry. It describes a female (no age details) who received Gardasil in early pregnancy (no specific details) and gave birth to a baby with tracheo-oesophageal fistula.

HPV vaccine is in pregnancy category B2 and is not cause to case untoward effects on the fetus. The vaccine is also not known to have genotoxicity activity.

An association between HPV vaccine and the physical defect described in case 256711 was considered unlikely.