

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

**314<sup>th</sup> meeting**

**17 April 2009**

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## 10 Vaccines

### 10.1 Vaccine issues and published articles

- Jeffrey S. AAN 2009: No increase in Guillain-Barré after HPV vaccination, but further monitoring warranted. Medscape Medical News Jan 2009.

This was a commentary on a study by Michas-Martin P *et al.* that was to be presented at the April 2009 meeting of the American Academy of Neurology. Based on data from the US passive surveillance monitoring centre, the authors had concluded there was no causal association between HPV vaccine and GBS. The commentary and study abstract contained insufficient information to allow an independent assessment of the data, including rates of GBS. **A Member requested a copy of the full study be provided to the Committee when it was published.**

- Gardasil Expert Panel. Final Report to the National Manager, Therapeutic Goods Administration, on the safety and efficacy of Gardasil, February 2009

This was provided to the Committee as a late paper. The report was also recently sent to the sponsor, who was expected to provide a response by end May. **The report, sponsor's response and any comments received in-between Meetings from Members were scheduled for discussion at the following ADRAC Meeting in May.**

### 10.2 Vaccine reports

During the period from 05 January to 23 February 2009, 165 reports of vaccine adverse reactions were lodged. This represents about 14% of the reports lodged for the period.

#### *Reports of vaccines other than HPV vaccine*

134 of the vaccine reports describe reactions to vaccines other than single-injection HPV vaccine (1 of these describes reactions to HPV vaccine plus Boostrix and hepatitis B vaccine).

97 of the reports were received from States, Territories or Local Government Councils, 30 were from health professionals, 4 were from sponsors; and 1 was from the AMEL and 2 were directly from consumers. 112 reports related to children, 21 related to adults and age was not stated in 1.

The case reports for vaccines other than HPV vaccine alone were provided.

#### *HPV vaccine reports:*

31 of the vaccine reports described reactions to HPV vaccine when given as a single vaccine. The reports were received from QLD (10, including 3 from the AME Line), VIC (8), NSW (4), WA (4), SA (2), ACT (1), NT (1; via the sponsor) and TAS (1).

Reports in association with HPV vaccine received from 4 Jan to 23 Feb 09 were 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 |
|---------|-------------|-----------------------|-------------|
|         |             | Human papilloma virus | 31          |

### **10.3.1 Rash and vasovagal episode after HPV vaccine – re-review**

Report 245830 was reviewed previously at the 312<sup>th</sup> (Dec 08) ADRAC Meeting. It was a detailed report of a 16 year old girl who felt faint after her 1<sup>st</sup> and 2<sup>nd</sup> doses of HPV vaccine and had a vasovagal episode, chest tightness, difficulty breathing and rash (possibly urticarial) after her 3<sup>rd</sup> dose. The girl had undergone extensive investigations and had been assessed in the hospital's allergy clinic, but there was no information on the outcome of and it was not know if this was or was not a case of anaphylaxis. The reporter noted that the head of the allergy team undertook to provide a report: *a Member requested that this report be obtained and presented to ADRAC at a later Meeting.*

Further information on report 245830 (and its associated sequenced report, 245829) was since obtained:

#### **Background:**

15 yo female with history of possible penicillin allergy and possible prawn allergy experienced three reproducible reactions post Gardasil vaccine:

1st dose – within 15 minutes fainted, 'blacked out' for 5 seconds before spontaneous recovery  
2nd dose - within 15 minutes fainted, 'blacked out' for 5 seconds before spontaneous recovery  
3rd dose- within 15 seconds fainted, developed throat discomfort, rash over neck and trunk: treated with adrenaline and recovered over the next 30 minutes.

#### **Discussion from allergy team:**

Skin prick test performed by immunologist was positive for prawn, negative to Gardasil (neat). Intradermal testing for Gardasil (1:10 dilution) was also negative. Patient reports no history of asthma, eczema or allergic rhinitis.

The immunologist states that the reactions are not convincing of an anaphylactic reaction and this has been supported by negative lab tests, which makes an IgE mediated reaction very unlikely. The possible explanations for these include a vasovagal reaction or possibly an idiosyncratic reaction. Due to the laryngeal involvement, previous history and IgE mediated response to prawns; she has been prescribed EpiPen in case of future exposures. A hospital based amoxicillin challenge is pending.

It was noted that the following coding/causality and reaction terms were assigned to these reports:

245829: dizziness, vasovagal reaction, fainting (certain: rechallenge)

245830: vasovagal reaction, breathing difficulty, urticarial rash and chest tightness (possible)

### **10.3.3 Systemic-like lupus disorder and HPV vaccine**

Report 247555

A 22 year old female developed arthritis typical of lupus, myalgia and fatigue at an unspecified time after her first dose of Gardasil. Her symptoms worsened within 2 weeks of her second dose and she was found to be strongly seropositive for anti-ANA.

This was the first report of lupus-like symptoms following HPV vaccine. While there was a positive re-challenge/flare in this case, it was not clear if there were other underlying, confounding factors. Comment on a possible causal relationship was not possible on the basis of this single report.

#### **10.3.4 Vaginal bleeding and HPV vaccine**

Report 248444/248449/248451

A 21 year old female experienced heavy vaginal bleeding and ‘period-type’ pain for 5 weeks after her first dose of HPV vaccine, again for 7 weeks after her second dose of HPV vaccine, and again for an unstated duration from 24 h after her 3<sup>rd</sup> vaccination with HPV vaccine. Onset time relative to vaccination was 24 h after the 3<sup>rd</sup> dose but this information was not provided for the 1<sup>st</sup> and 2<sup>nd</sup> doses. The girl was also taking citalopram but was on no other medications and the reporter notes that her period usually lasted 4 days, is painless and was not expected at the time she developed bleeding after her 3<sup>rd</sup> dose.

Members considered this a puzzling case: the temporal relationship and positive re-challenge on 2 occasions suggested a possible association, but there was no known biologically plausible mechanism. It was agreed a watch would be maintained for similar types of reports.

#### **10.3.5 Serum sickness and HPV vaccine**

Report 247559/247603

A 22 year old female developed serum sickness 84 h following HPV vaccination (dose number not stated). The reaction was described as “a rash on the lower trunk which spread over several hours. The patient then developed chills and felt worse when she was hot. Two days later, the rash became generalised and the patient was admitted to hospital with a possible diagnosis of scarlet fever. The patient was aching all over and her temperature was 38-39C.” The report also states “..skin biopsy demonstrated spongiotic epidermis likely due to a drug reaction, with serum sickness type hypersensitivity response...” although it was not specified whether a particular drug or HPV vaccine was the suspected causative agent.

This report was notable for the extensive and thorough histological follow-up.



### **11.2.11 HPV vaccine exposure during pregnancy**

Report 248518

This report was received from the sponsor, who received it from the Northern Territory HPV coordinator. It describes an 18 year old female who was vaccinated with HPV vaccine (2<sup>nd</sup> dose) when she was (unknowingly at the time) 10 weeks pregnant. The initial information was that the woman gave birth to a healthy baby boy at week 37 of gestation. Subsequent information indicated the baby was admitted to hospital “in the first few weeks of life due to sepsis”. Details of events surrounding the development of sepsis are not provided and no further information is expected.

The development of sepsis in the baby has been assessed by OMSM medical staff as being unrelated to HPV vaccination and this aspect of the report has been ‘general listed’. The Committee agreed this was appropriate.