Minutes of the

Adverse Drug Reactions

Advisory Committee

312th meeting

12 December 2008

[redacted]

- page 33: last paragraph: amend the following:

"The Committee agreed that the incident at the NSW school did not represent a cluster of hypersensitivity reactions that warranted broad, large-scale concern. Two students developed symptoms that would be classified as anaphylaxis with a Level 2 degree of certainty according to Brighton criteria; other reactions reported on the same day were minor skin reactions of various descriptions that occur typically after vaccination in a school-based setting. There were no certain (Level 1) cases of anaphylaxis. The events tended to confirm the known association between HPV vaccine and hypersensitivity reactions, although the rate of this association is yet to be been determined."

to read:

"The Committee noted that the incident at the NSW school generated a level of concern that had been appropriately documented and investigated by NSW Health and the sponsor. ADRAC considered the incident did not represent a cluster of hypersensitivity reactions. Two students developed symptoms that would be classified as anaphylaxis with a Level 2 degree of certainty according to Brighton criteria; other reactions reported on the same day were minor skin reactions of various descriptions that can occur after vaccination in a school-based setting. There were no certain (Level 1) cases of anaphylaxis. The events tended to confirm the known association between HPV vaccine and hypersensitivity reactions, although the rate of this association is yet to be been determined."

[redacted]

- page 34: amend the paragraph: *"ADRAC recommended that a template be developed within the HPV immunisation program (possibly with assistance from ATAGI) to facilitate the clear, accurate, unambiguous and definitive recording of clinical signs and symptoms occurring after vaccination."*

to

"ADRAC recommended that a template be developed within the HPV immunisation program (possibly with assistance from ATAGI) to facilitate the clear, accurate, unambiguous and definitive recording of clinical signs and symptoms occurring after vaccination, for use within the immunisation program."

- page 43: tabulated description of case 232885: Add, in the comments column: 'Possibly a case of anaphylaxis.'

- page 44: change the last sentence from *'It was anticipated this and the other cases would be reviewed by the GEP'* **to** 'It was anticipated this and the other cases would be reviewed by the Gardasil Expert Panel (see item 10.4, below).'

- page 45, 6th paragraph: Add the following: 'A request should be made to obtain further information, including hospital notes on this case, to determine if re-coding is warranted.'

[redacted]

10 Vaccines

10.1 Vaccine issues and published articles

10.1.1 Allergic reactions to HPV vaccine – cluster of reports: follow-up

At the 311th (Oct 08) Meeting ADRAC reviewed a series of 9 reports of suspected allergic reactions to HPV vaccine in girls from a NSW school. The final report of the sponsor's investigations into the incident was provided to the current Meeting. It focused only on quality aspects and concluded there was no evidence for anything untoward about the product used to vaccinate these girls. This was noted for information.

[redacted]

10.2 Vaccine reports

During the period from 10 September to 1 November 2008, 259 reports of vaccine adverse reactions were lodged. This represents about 23% of the reports lodged for the period.

Reports of vaccines other than HPV vaccine

163 of the vaccine reports describe reactions to vaccines other than single-injection HPV vaccine (4 of these describe reactions to HPV vaccine plus one other concomitant vaccine – pneumococcal polysaccharide, varicella, hep B or DTPa-Heb B).

115 of the reports were received from States, Territories or Local Government Councils, 37 were from health professionals, 8 were from sponsors; and 1 each was from the AVN, the AMEL and an unknown source. About 120 reports related to children, 31 related to adults and age was not stated in the remaining.

HPV vaccine reports:

94 of the vaccine reports described reactions to HPV vaccine when given as a single vaccine. The reports were received from NSW (44), VIC (29), QLD (10, including 3 from the AME Line), SA (5), WA (3), ACT (2), and Tas (1).

Note: These include the cluster of cases from the Country NSW School (numbers 244623, 244628, 244629, 244630, 244633, 244635, 244641, 244642, 244643) that were reviewed expeditiously at the last (311th) Meeting under item 10.2.1

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
[redacted]			
		Human papilloma virus	94

Anaphylaxis

Three reports received within the period had been coded 'anaphylaxis', all involve HPV vaccine: 244623, 244630 and 244642. These were part of the cluster of reports from a NSW school that were reviewed at the 311th Meeting. ADRAC considered there was a Level 2 degree of certainty, according to Brighton criteria, that cases 244630 and 244642 were anaphylaxis, but case 244623 was not considered to be anaphylaxis. The coding had not yet been updated to reflect this view.

Other events

Summarised details of other specific reactions associated with vaccines are shown below.

Seizures/convulsions (6 reports) Note: onset time is in days; an onset time of 0 indicates the reaction occurred on the day of vaccination						
Case Number	**Sex**	**Outcome Description**	**Onset Time**	**Age**	**Reactions/Report description**	**Trade Name Description**
244967	F	Unknown		13	Gardasil	Convulsion
[redacted]						

[redacted]

10.3.2 Pancreatitis and HPV vaccine

Three reports of pancreatitis in females given HPV vaccine were received in the period covered by the current Meeting:

Report 244981 described a 26 year old female who experienced severe abdominal and chest pain 5 days after her 2nd dose of HPV vaccine. The same symptoms were experienced again 4 months later and the girl was hospitalised with suspected gall stones and pancreatitis. Severe abdominal and chest pain also developed 3 days after her 3rd HPV vaccine. On this occasion, the patient's serum amylase was measured and found to be elevated, no gall stones were detected and she was placed on a waiting list to have her pancreas surgically removed. This turned out to be unnecessary as she later recovered fully.

Report 245551 described a 13 year girl who received her 3rd dose of HPV vaccine and the next day developed chronic pancreatitis requiring hospitalisation for 8 weeks.

Report 245713 involved a 19 year old female who experienced fever and sweating after her 2nd dose of HPV vaccine and the following week was hospitalised with severe back and gut pain that was later found to be due to pancreatitis.

Members note the recent publication of an Australian case of pancreatitis in a 26 year old female (Das A *et al*. Pancreatitis following human papillomavirus vaccination. *MJA* 2008; 189: 178). This publication referred to the background incidence of pancreatitis as 5.4-80 per 100,000, although the publication did not specify the background incidence in the target population for HPV vaccine (mainly teenage girls).

Members commented that the rates of pancreatitis in Australian paediatric populations had started to increase before the introduction of HPV vaccine. Reasons for the apparently increasing incidence were not clear but may include increased recognition of the disorder and increased inclusion of lipase assays in diagnostic testing; greater alcohol consumption by adolescents and changed dietary habits may also contribute. Nevertheless, pancreatitis was not a disorder associated usually with teenage girls.

To date, 7 cases of pancreatitis in females given HPV vaccine had been reported to ADRAC. However, Members were not convinced that there was evidence for a signal at this time and suggested that the question of whether HPV vaccine was associated with pancreatitis might be addressed by conducting a formal study, perhaps using data from the HPV vaccine registry.

10.3.3 Autoimmune disorders and HPV vaccine

Report 244770 described a 19 year old female who developed worsening headache and polyuria 13 days after receiving her 2nd HPV vaccine and 1 month later was found on MRI to have lymphocytic hypophysitis. Twenty days after the MRI and treatment with steroids, the girl continued to have diabetes insipidus but the headaches had resolved.

A Member commented that lymphocytic hypophysitis presents usually during pregnancy as a mass with autoimmune characteristics. It is rare but not unknown in women aged 20-30 years and can be associated with underlying autoimmune disease. There was not a clear association with HPV vaccine in this case, although the vaccine may have contributed by virtue of its immunogenic properties.

Report 244598 described the development of suspected Guillaine Barre syndrome in a 26 year old female who received her 2nd HPV vaccination 6 weeks previously.

A Member commented that autoimmune disorders in females receiving HPV vaccine were the subject of active investigation by various bodies in addition to the TGA. Formal data-linkage studies investigating various types of adverse events in those given HPV vaccine were planned. ADRAC endorsed moves to conduct formal studies investigating adverse events in those receiving HPV vaccine and anticipated these would enhance and complement current surveillance methods.

10.3.4 Optic disc swelling and HPV vaccine

Report 245766: One month after receiving HPV vaccine, a 20 year old female developed papilloedema and was under investigation for suspected benign intracranial hypertension as the girl had risk factors (obesity) for this condition. The reporter (State Health Department) noted that this was "an unusual event and unclear pathomechanism, but [the case was reported] for surveillance".

10.3.5 Rash and vasovagal episode after HPV vaccine

245830 was a detailed report of a 16 year old girl who felt faint after her 1st and 2nd doses of HPV vaccine and had a vasovagal episode, chest tightness, difficulty breathing and rash (possibly urticarial) after her 3rd 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.**

[redacted]

[redacted]

14 Australian media

A collection of newspaper clippings on the following subjects was noted for information:

[redacted]

- HPV vaccine

[redacted]