



Medicines Safety Update is the drug safety bulletin of the Therapeutic Goods Administration (TGA). It is published in each issue of *Australian Prescriber*. You can also read it and sign up for free Medicines Safety Update email alerts on the TGA website at [www.tga.gov.au/adr/msu.htm](http://www.tga.gov.au/adr/msu.htm)

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## Varenicline (Champix): an update

Dr Jennifer Elijah, Evaluator, Office of Product Review

### Summary

**Psychiatric symptoms, including suicidal behaviour, continue to be reported with varenicline. We ask health professionals to include relevant information from the patient's history in adverse reaction reports to help in our assessment of cases, and remind them to discuss the possibility of these events with patients and their families.**

The TGA has previously reported Australian experience with varenicline (Champix) up to October 2008.<sup>1</sup> In this update, we describe experience with varenicline to May 2010 – in particular, adverse reaction reports of psychiatric symptoms.

Varenicline is available on the Pharmaceutical Benefits Scheme (PBS) as an authority item for people in a comprehensive support and counselling program for smoking cessation. More than 900 000 PBS prescriptions for varenicline have been dispensed since January 2008.

### Psychiatric symptoms reported with varenicline

To May 2010 the TGA had received 1025 reports of suspected adverse reactions to varenicline, 691 (67%) of which describe psychiatric symptoms such as depression, agitation, anxiety, altered mood and aggression. There were reports of 206 suicide-related events in people taking varenicline, including 15 completed suicides.

We remind health professionals to discuss these possible adverse effects with patients taking or considering varenicline and their families, and to provide patients with the Consumer

Medicines Information leaflet. Health professionals should provide advice to patients and their families about how to recognise and respond to these possible adverse effects.

### What to include in adverse reaction reports

We ask health professionals to continue to report suspected adverse reactions to varenicline to the TGA. Please include in reports relevant information such as the patient's history of mental illness, concomitant psychotropic medicines and any reactions to previous quit attempts (See box). This information helps us to review cases and make a reasonable assessment of causality – particularly because the association of varenicline and neuropsychiatric symptoms may be confounded by factors such as the effects of nicotine withdrawal, the association of smoking and psychiatric conditions, and the effects of changes in smoking status on blood levels of some antipsychotics.

### Reference

1. Varenicline: the Australian experience so far. *Aust Adv Drug React Bull* 2008;27:22.

#### Box

#### Patient information to include in reports of possible adverse reactions to varenicline

- smoking, alcohol and substance use status
- any previous reactions to smoking cessation
- history of pre-existing psychiatric/mental illness
- past history of suicidal ideation/suicide attempt
- history of any recent psychosocial stresses
- history of concomitant medication especially psychotropic medications

## Australian experience with non-adjuvant H1N1 vaccine (Panvax and Panvax Junior)

Dr Jane Cook, Senior Medical Officer, Office of Product Review

### Summary

**The H1N1 influenza vaccination program used strategies to encourage consumers and health professionals to report adverse events to allow the TGA to closely monitor safety of the vaccine. Information is now available about the number and types of adverse reactions reported during the first six months of the program.**

The Australian national immunisation program with the non-adjuvant H1N1 vaccine (Panvax and Panvax Junior) began on 30 September 2009. The program was different from other national vaccination programs in several ways, including that it used strategies to stimulate adverse event reporting so that the TGA could closely monitor vaccine safety.

The program was aimed at certain groups at higher risk of exposure to H1N1 (such as healthcare workers) and those vulnerable to more severe outcomes (pregnant women, indigenous people and people with underlying chronic medical conditions) but was promoted and available to all Australians. Immunisation was provided via state and territory immunisation clinics and general practices.

### Information provided about vaccine safety and reporting mechanisms

The TGA worked closely with expert committees such as the Australian Technical Advisory Group on Immunisation (ATAGI) and the National Immunisation Committee (a subgroup of the

Australian Health Protection Principal Committee) to provide information to health practitioners and consumers on how to report adverse events. The TGA set up a telephone service to take adverse event reports and provided a web reporting tool on its website. Details of both ways to report adverse events and information about managing common, expected adverse effects of vaccination were included in fact sheets and consent forms provided to consumers (Fig. 1).

As the aim of a pandemic program is to immunise a large number of people as efficiently as possible, multidose vials were used. Multidose vials are not routinely used in Australia, although they are used in the United States to administer seasonal trivalent influenza vaccine. Information was developed to reassure consumers of the safety of thiomersal, the preservative in the vials, for pregnant women and children. Fact sheets were developed by ATAGI and distributed via the Department of Health and Ageing's Health Emergency website ([www.healthemergency.gov.au](http://www.healthemergency.gov.au)) and healthcare provider networks.

### Patterns of reporting

In the first six months of the program, from 30 September 2009 to 31 March 2010, approximately eight million doses of Panvax and 330 000 doses of Panvax Junior were distributed in Australia. During this period, the TGA received 1614 reports of adverse events associated with H1N1 vaccination.

The highest number of reports was received in October 2009, when there were 696 adverse event reports. By January 2010 numbers had fallen to around 80 reports per month. A second, smaller peak in reporting occurred in March, with 145 reports (Fig. 2). The TGA suspects the second peak was caused by a

Fig. 1

#### Information about adverse events included in the vaccination consent form and fact sheet

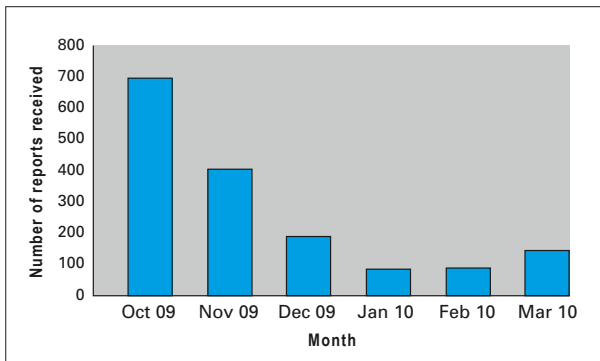
For further information about the Panvax® H1N1 vaccine, please contact the Pandemic Hotline on 180 2007

Care after vaccination	Possible side effects of vaccination
<ul style="list-style-type: none"><li>• For redness or swelling at the injection site, apply a cold compress</li><li>• To lower temperature or relieve discomfort, paracetamol can be taken</li><li>• If fever persists, consult your doctor</li><li>• Drink extra fluids and rest</li><li>• If any reaction occurs that you consider serious or unexpected, seek medical advice</li><li>• Contact your doctor if you have had a reaction following any dose of the vaccine or require further medical advice.</li></ul>	<p><i>Common:</i> About 1 in 10 people may have pain and redness at the injection site, drowsiness or tiredness, muscle aches; low grade fever</p> <p><i>Very Rare:</i> Severe allergic reaction (anaphylaxis)</p>

**You can report side effects online at [www.tga.gov.au](http://www.tga.gov.au)**  
You can also report side effects by calling the **Pandemic Hotline on 180 2007.**

Fig. 2

**Adverse event reports associated with H1N1 vaccination during the first six months of the Australian vaccination program**



second wave of promotion of the program by the Department of Health and Ageing, the start of school-based programs in some states and territories, and catch-up reporting following the vacation period.

**Types of reactions reported**

Most of the 1614 reports received were mild and common problems such as headache, gastrointestinal upset, and injection-site soreness, swelling or redness (Table 1). Most of the adverse effects reported were well recognised and listed in the Product Information for Panvax and Panvax Junior.

**Neurological events**

Several neurological adverse events of special interest were closely monitored. One of the concerns raised was a possible association between Guillain-Barré syndrome and vaccination. This concern arose from the observation that in the United States the 1976 influenza vaccine was associated with an excess risk of Guillain-Barré syndrome of nine

in every one million vaccinees in the six weeks following vaccination.<sup>1</sup> This association has not been seen since. The TGA convened an expert panel to assist in developing case definitions and clinical follow-up templates and to review cases. In total, 10 reports of Guillain-Barré syndrome were received by the TGA in the first six months of the program. This is within the background rate that would be expected for an unvaccinated population.

**Allergy and anaphylaxis**

The occurrence of allergy and anaphylaxis was also closely monitored by the TGA. Anaphylaxis and allergic reactions are not predictable and can occur in anyone regardless of whether they have a history of allergy or not. There were nine cases of anaphylaxis reported and all recovered without sequelae.

There was one case of anaphylaxis reported in a person with a latex allergy who had previously received seasonal trivalent vaccines without any allergic response. The TGA investigated whether latex may have been coming into contact with the vaccine, including commissioning studies in Europe. Investigations showed that latex was not detectable in the vaccine, even when the syringe was damaged or abnormal or the rubber bung of the syringe was crushed.

**Convulsions**

The number of reports of convulsion associated with H1N1 vaccination is of particular interest. The 2010 seasonal trivalent influenza vaccination program was suspended for children five years and under, following a higher than usual number of reports of febrile convulsion associated with vaccination. In the first six months of the H1N1 vaccination program there were seven reports of febrile convulsion, all of which were in children under five years. Two of these

Table 1

**Commonly reported reactions to H1N1 vaccination during the first six months of the Australian vaccination program**

Reaction	Number of cases	% reports containing one or more of these terms
Pain (excluding injection-site pain)	388	24%
Malaise, lethargy, fatigue, asthenia	360	22%
Influenza-like illness, cough, rhinorrhoea, oropharyngeal pain	346	21%
Vomiting, diarrhoea	317	20%
Headache	303	19%
Pyrexia	280	17%
Rash (any type), pruritus, urticaria	269	17%
Injection-site reaction or injection-site pain	240	15%
Nausea	203	12.5%

cases occurred in association with varicella vaccine. The Product Information documents for Panvax and Panvax Junior include the occurrence of convulsions as an uncommon event, occurring in 1 in 1000 to 1 in 10 000 cases. More than 300 000 doses of Panvax Junior have been distributed, and so these figures provide reassurance that the non-adjuvant H1N1 vaccine does not produce an excess risk of convulsions in children.

## Reference

1. Australian Technical Advisory Group on Immunisation (ATAGI) advice regarding influenza, influenza vaccines and Guillain-Barré Syndrome. Canberra: Australian Government Department of Health and Ageing; 2009. [www.healthemergency.gov.au/internet/healthemergency/publishing.nsf/Content/2723D54E78BF5739CA2576400027E1E9/\\$File/ATAGI-Infl\\_FluVac\\_GBS-Advice\\_091009.pdf](http://www.healthemergency.gov.au/internet/healthemergency/publishing.nsf/Content/2723D54E78BF5739CA2576400027E1E9/$File/ATAGI-Infl_FluVac_GBS-Advice_091009.pdf) [cited 2010 Jul 7]

## New structural arrangements

The TGA officially launched a new organisational structure on 1 July 2010. This new structure will support the TGA's delivery of appropriate, consistent, effective and efficient regulation into the future.

Postmarketing safety functions for all types of therapeutic products are managed by the Office of Product Review, which is part of the Monitoring and Compliance Group.

The implementation of the new structure is being carefully managed to ensure that current regulatory activities are maintained. The main contact points for reporting suspected reactions to medicines are unchanged, and information for health professionals and consumers – such as alerts, advisories and *Medicines Safety Update* – will continue to be published as usual.

Detailed information on the new structural arrangements is available at [www.tga.gov.au/about/structure-new.htm](http://www.tga.gov.au/about/structure-new.htm)

## What to report? (You do not need to be certain, just suspicious!)

The TGA encourages the reporting of all **suspected** adverse reactions to medicines, including vaccines, over-the-counter medicines, herbal, traditional or alternative remedies. The TGA particularly requests reports of:

- ALL suspected reactions to **new medicines**
- ALL suspected medicines interactions
- Suspected reactions causing
  - death
  - admission to hospital or prolongation of hospitalisation
  - increased investigations or treatment
  - birth defects

### For blue cards

Reports of suspected adverse drug reactions are best made by using a prepaid reporting form ('blue card') which is available from the website: [www.tga.gov.au/adr/bluecard.pdf](http://www.tga.gov.au/adr/bluecard.pdf) or from the Office of Product Review, phone 1800 044 114.

Reports can also be submitted:

- online [www.tga.gov.au](http://www.tga.gov.au) and click on 'Report a problem' on the left
- by fax 02 6232 8392
- by email [ADR.Reports@tga.gov.au](mailto:ADR.Reports@tga.gov.au)

**For further information** from the Office of Product Review:

Phone 1800 044 114 Fax 02 6232 8392 Email [ADR.Reports@tga.gov.au](mailto:ADR.Reports@tga.gov.au)

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