NAME OF THE MEDICINE

Panvax® H1N1 Vaccine
H1N1 Pandemic influenza vaccine (split virion, inactivated).

DESCRIPTION

Panvax® H1N1 Vaccine is a purified, inactivated, monovalent, split virion (split virus) vaccine. A single 0.5 mL dose contains antigen of the following type:

A/California/7/2009 (H1N1) (NYMC X-179A) (A/California/7/2009 (H1N1)v-like)
15 µg haemagglutinin (HA) per dose

Each 0.5 mL dose contains, nominally: sodium chloride 4.1 mg, sodium phosphate – dibasic anhydrous 0.3 mg, sodium phosphate – monobasic 0.08 mg, potassium chloride 0.02 mg, potassium phosphate – monobasic 0.02 mg, calcium chloride 1.5 µg and thiomersal 50 µg (for multi-dose vial presentation only).

The following are present in each 0.5 mL dose: sodium taurodeoxycholate $\leq$ 5 µg, ovalbumin ≤ 1.0 µg, sucrose < 10 µg, neomycin $\leq$ 0.7 ng, polymyxin B sulfate $\leq$ 0.11 ng and beta-propiolactone $\leq$ 1.4 ng.

The virus strain in this vaccine complies with the Australian Influenza Vaccine Committee (AIVC) decision, endorsing the World Health Organisation recommended virus for the influenza A(H1N1) vaccine.

Panvax® H1N1 Vaccine is prepared from influenza virus propagated in the allantoic fluid of embryonated chicken eggs. The virus is harvested from the eggs, purified by zonal centrifugation, inactivated with beta-propiolactone and disrupted with sodium taurodeoxycholate to produce split virion particles.

PHARMACOLOGY

Immunisation with inactivated influenza vaccines has been shown to induce antibodies to the viral surface glycoproteins, haemagglutinin and neuraminidase. These antibodies are important in the prevention of natural infection.

CLINICAL TRIALS

Clinical trials are being conducted to assess the immunogenicity and safety of the vaccine in healthy children and adults. Additionally, these trials will inform the dose and vaccination schedule for the vaccine. These studies are still ongoing; however preliminary data available from the study in adults have shown that a single dose of vaccine is sufficient to elicit a protective antibody response. Results from the trial in children are not yet available.

A total of 240 adult participants aged ≥ 18 to < 65 years were randomised to receive either a 15 µg or 30 µg HA per dose. The serum antibody response after of the first vaccine dose was assessed by the haemagglutination inhibition (HI) and viral microneutralisation (MN) assays. Similar immunogenicity results were observed for both antigen doses showing that the vaccine elicits a satisfactory immune response

in a large proportion of participants. Results are provided for the 15 µg HA antigen dose, with > 96% of participants by HI (Table 1a) and > 89% of participants by MN (Table 1b) achieving seroprotective antibody titres of ≥ 40.

Table 1a: Immunogenicity Results for Adult Population (HI assay)

Serum HI antibody	**15µg HA dose n=120 (95% CI)**
Fold increase in GMT[a]	10.6 (7.9,14.2)
Seroconversion or significant increase[b]	70.8% (61.8, 78.8)
Proportion with HI ≥ 40	96.7% (91.7, 99.1)

[a] Fold increase in GMT (geometric mean titre) is the fold increase in antibody titre over the pre-vaccination GMT. [b] 'Seroconversion' is defined as the number of participants with a pre-vaccination titre of < 1:10 achieving a post-vaccination titre value of at least 40 and 'significant increase' is defined as the number of participants with a pre-vaccination titre of ≥1:10 achieving at least a four fold increase over the pre-vaccination titre.

Table 1b: Immunogenicity Results for Adult Population (MN assay)

Serum HI antibody	**15µg HA dose n=120 (95% CI)**
Fold increase in GMT[a]	24.3 (17.2, 34.3)
Seroconversion or significant increase[b]	74.2% (65.4, 81.7)
Proportion with MN ≥ 40	89.2% (82.2, 94.1)

[a] Fold increase in GMT (geometric mean titre) is the fold increase in antibody titre over the pre-vaccination GMT. [b] 'Seroconversion' is defined as the number of participants with a pre-vaccination titre of < 1:20 achieving a post-vaccination titre of at least 40 and 'significant increase' is defined as the number of participants with a pre-vaccination titre of ≥ 1:20 achieving at least a four fold increase over the pre-vaccination titre.

INDICATIONS

For active immunisation to prevent influenza disease caused by the influenza A(H1N1) virus, in adults, adolescents and children 10 years of age and older.

CONTRAINDICATIONS

Anaphylactic hypersensitivity to previous influenza vaccination, or to eggs, chicken protein, thiomersal (for thiomersal-containing vaccine only), neomycin, polymyxin B sulfate or any of the constituents or trace residues (see Description section) of this vaccine.

Immunisation must be postponed in people who have febrile illness or acute infection.

PRECAUTIONS

As with all injectable vaccines, appropriate medical treatment and supervision should always be available to manage the rare event of an anaphylactic reaction following administration of the vaccine.

In immunocompromised patients, the antibody response may be lower.

Use in pregnancy: (Category B2)
The safety profile of the vaccine in pregnant women is unknown. Healthcare professionals should assess the potential benefits and risks of administering Panvax® H1N1 Vaccine to pregnant women on a case by case basis, taking into account Australian Health Authorities' recommendations.

Use in lactation:
The safety profile of the vaccine in lactating women is unknown Healthcare professionals should assess the potential benefits and risks of administering Panvax® H1N1 Vaccine to lactating women on a case by case basis, taking into account Australian Health Authorities' recommendations.

Paediatric use:
Data in children are not yet available.

Interactions with other medicines:
The immunological response may be diminished if the patient is undergoing corticosteroid or immunosuppressant treatment.

There are no data to assess the concomitant administration of Panvax® H1N1 Vaccine with other vaccines. If Panvax® H1N1 Vaccine is to be given at the same time as another injectable vaccine, the vaccines should be administered at different injection sites.

ADVERSE EFFECTS

Clinical Trials:

Clinical data specific to Panvax® H1N1 Vaccine show that the vaccine is safe and well tolerated in adults ≥ 18 to < 65 years of age. A total of 240 participants were administered a single dose of vaccine containing 15 µg or 30 µg HA. Data for solicited local and systemic and unsolicited adverse events for the 15 µg HA antigen dose are presented as this is the dosage to be administered.

The most common solicited local (injection-site) adverse events observed within 7 days of administration of the vaccine were injection-site tenderness, pain and induration, with the majority of reactions of mild intensity and self-limiting. The most common solicited systemic adverse reactions were headache, myalgia and malaise, with the majority of these events mild to moderate in intensity and similarly self-limiting (Table 2).

In addition, headache was identified as the most common unsolicited adverse event, reported in 11.7 % of participants. Other unsolicited adverse events, reported by

more than 2 % of participants, were back pain, arthralgia, seasonal allergy, cough, oropharyngeal pain, nasal congestion, diarrhoea and toothache. There were no reports of serious adverse events.

Table 2: Proportion of Adult Participants with Solicited Local and Systemic Adverse Events within 7 Days of Administration of Panvax® H1N1 Vaccine, Irrespective of Causality

Solicited Adverse Event	Proportion of Participants (%) Adults (n = 120) (≥ 18 to < 65 years)
Local (injection-site)	
Tenderness	30.8
Pain	20.8
Induration	10.0
Ecchymosis	5.0
Erythema	0.8
Systemic	
Headache	25.8
Myalgia	15.8
Malaise	11.7
Fever	5.8
Nausea	5.8
Chills	0.8
Vomiting	0

Post-marketing surveillance:
There are currently no post-marketing data for Panvax® H1N1 vaccine. It is anticipated that the adverse events after vaccination will be similar to those spontaneously reported during post-approval use of CSL's seasonal influenza vaccine, Fluvax® vaccine. The adverse events reported are presented below according to System Organ Class and frequency. These data reflect experience in children and adults with Fluvax® vaccine.

Adverse event frequencies are defined as follows:

Very common (≥ 1/10), common (≥ 1/100 and < 1/10), uncommon (≥ 1/1000 and < 1/100), rare (≥ 1/10 000 and < 1/1000) and very rare (< 1/10 000).

Blood and Lymphatic System Disorders

Rare: Transient thrombocytopenia

Immune System Disorders

Rare: Allergic reactions including anaphylactic shock

Nervous System Disorders

Rare: Neuralgia, paraesthesia and convulsions
Very rare: Encephalitis, neuritis or neuropathy and Guillain-Barré syndrome

Vascular Disorders

Very rare: Vasculitis with transient renal involvement

Skin and Subcutaneous Tissue Disorders

Uncommon: Pruritus, urticaria and rash

General Disorders and Administration Site Conditions

These reactions usually resolve within 1-2 days without treatment.

Very common:	Injection site inflammation
	Influenza-like illness (for thiomersal-containing vaccine only)
Common:	Injection site ecchymosis and induration
	Influenza-like illness (for thiomersal-free vaccine only)

Influenza-like illness may include pyrexia, chills, headache, malaise and myalgia.

DOSAGE AND ADMINISTRATION

Dosage:
Adults, adolescents and children from 10 years 0.5 mL

Administration:
The vaccine should be administered by intramuscular or deep subcutaneous injection.

It is important that the contents of the container be shaken thoroughly immediately before use. The vaccine should appear as a clear to slightly opaque liquid with some sediment that resuspends upon shaking.

The pre-filled syringe is for single use and any remaining contents should be discarded in accordance with local requirements.

For the multi-dose vials, the conditions for use are:

- the vaccine is stored at 2 - 8°C prior to and immediately after each use
- the vaccine is protected from light during storage
- the vaccine in the vial must be used **within 24 hours** once the stopper has been pierced
- the stopper is to be pierced no more than 18 times to ensure stopper integrity
- aseptic technique must be used to withdraw each dose, using a separate sterile needle and syringe
- following withdrawal of vaccine from the vial, the syringe must be used within the one vaccination session (up to a maximum time interval of 4 hours) and cannot be stored for use at a later date
- at the end of the 24 hour period, any remaining contents within the vials should be discarded in accordance with local requirements.

Ensuring the conditions for vial use are maintained is the responsibility of the healthcare professional administering the vaccine.

OVERDOSAGE

There is no specific information on overdose of Panvax® H1N1 Vaccine.

For general advice on overdose management, contact the Poisons Information Centre on 131 126.

PRESENTATION AND STORAGE CONDITIONS

Presentations:
Panvax® H1N1 Vaccine is presented in a single-dose pre-filled glass syringe with an attached needle for injection and a multi-dose glass vial.

Multi-dose Vial
Each multi-dose vial contains a nominal 5 mL or 10mL of vaccine and is closed with a latex-free stopper and sealed with an aluminium crimp seal. The aluminium seal has a plastic tear-away cap attached that is removed to gain access to the vial closure. The cap is present to protect the vial closure and to indicate if the vial has been tampered with. Once removed, the cap cannot be re-affixed to the vial. The sealed units are packed into a cardboard carton.

Pack size is 10 or 50 vials.

Pre-filled Syringe
Each disposable syringe contains a single 0.5 mL dose of vaccine and is supplied encased within a clear film wrapper. The presence of the film wrapper provides assurance that the product has not been opened. Do not use if the film wrap is damaged or missing.

Pack size is 1 or 10 syringes.

Storage Conditions:
Panvax® H1N1 Vaccine should be stored, protected from light, at 2°C to 8°C. IT MUST NOT BE FROZEN.

The shelf life of the vaccine is 12 months when stored at +2°C to +8°C. The expiry date is indicated on the container label.

NAME AND ADDRESS OF THE SPONSOR

Manufactured by:
CSL Limited ABN 99 051 588 348
45 Poplar Road, Parkville
VICTORIA 3052 AUSTRALIA

Distributed by:
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POISONS SCHEDULE

Prescription only medicine

DATE OF APPROVAL

Date of TGA approval: 18 September 2009

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