

NEW ZEALAND DATA SHEET

1. PRODUCT NAME

PANVAX® H5N8 pre-pandemic, Pre-pandemic influenza vaccine [split virion, inactivated], 30 micrograms per 0.5 mL dose, suspension for injection

2. QUALITATIVE AND QUANTITATIVE COMPOSITION

The vaccine is a purified, inactivated, monovalent, split virion (split virus), adjuvanted vaccine containing antigen of the following type:

A/Astrakhan/3212/2020 (H5N8)-like virus
30 microgram haemagglutinin (HA) per 0.5 mL dose

PANVAX® H5N8 pre-pandemic vaccine is prepared from influenza virus propagated in the allantoic fluid of embryonated chicken eggs. The virus is harvested from the eggs, purified, inactivated with beta-propiolactone and disrupted with sodium taurodeoxycholate to produce split virion particles which are further purified prior to formulation with 0.5 milligram aluminium phosphate adjuvant.

Excipient(s) with known effect
Thiomersal

For a full list of excipients, see **Section 6.1 LIST OF EXCIPIENTS**.

Each dose may also contain sodium taurodeoxycholate $\leq 5 \mu\text{g}$, ovalbumin $\leq 1.0 \mu\text{g}$, sucrose $< 10 \mu\text{g}$, neomycin $\leq 1 \text{ ng}$, polymyxin B sulfate $\leq 0.2 \text{ ng}$ and beta-propiolactone $\leq 2 \text{ ng}$.

3. PHARMACEUTICAL FORM

PANVAX® H5N8 pre-pandemic is a suspension for injection. It is a homogenous creamy/white opaque liquid suspension with no large clumps visible.

4. CLINICAL PARTICULARS

4.1 Therapeutic indications

For active immunisation in persons from 6 months of age, to prevent influenza disease caused by the influenza A virus. The use of this vaccine should be in accordance with official recommendations.

4.2 Dose and method of administration

Dosage

Two 0.5 mL doses, 21 days apart.

Method of administration

The vaccine should be administered by intramuscular injection.

The vaccine should be allowed to reach room temperature before use. It is important that the contents of the container be shaken thoroughly immediately before use. The vaccine should appear as a homogeneous creamy/white opaque liquid suspension with no large clumps visible.

Once opened, the vaccine is to be used immediately and within the one vaccination session, with any remaining contents discarded in accordance with local requirements. No additions should be made to the contents of the vial.

Please refer to the Ministry of Health *Immunisation Handbook* for recommendations regarding the appropriate vaccination technique and needle size.

4.3 Contraindications

History of an anaphylactic (i.e. life-threatening) reaction to any of the constituents or trace residues (e.g. eggs, chicken protein, refer to section **2 QUALITATIVE AND QUANTITATIVE COMPOSITION** and section **6.1 LIST OF EXCIPIENTS**) of this vaccine. However, in a pandemic situation, it may be appropriate to give the vaccine, provided that facilities for resuscitation are immediately available in case of need.

4.4 Special warnings and precautions for use

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.

Caution is needed when administering this vaccine to persons with a known hypersensitivity (other than anaphylactic reaction) to the active substance, to any of the excipients, to thiomersal and to residues e.g. eggs, chicken protein, neomycin or polymyxin B sulfate.

Antibody response in patients with endogenous or iatrogenic immunosuppression may be diminished.

If the pandemic situation allows, immunisation shall be postponed in patients with severe febrile illness or acute infection.

PANVAX® H5N8 pre-pandemic vaccine should under no circumstances be administered intravascularly.

Use in the elderly

Refer to sections 4.8 UNDESIRABLE EFFECTS – Clinical trials (Adults) and 5.1

PHARMACODYNAMIC PROPERTIES - Clinical trials for elderly data.

Paediatric use

PANVAX® H5N8 pre-pandemic vaccine may be used in children from 6 months of age (refer to section 4.8 UNDESIRABLE EFFECTS - Clinical trial (Paediatric) and 5.1 PHARMACODYNAMIC PROPERTIES - Clinical trials.

Effects on laboratory tests

No data available.

4.5 Interaction with other medicines and other forms of interaction

The vaccine should not be mixed with other injection fluids.

PANVAX® H5N8 pre-pandemic vaccine should not be given at the same time as other vaccines. However, if co-administration with another vaccine is indicated, immunisation should be carried out on separate limbs. It should be noted that the adverse reactions may be intensified.

The immunological response may be diminished if the patient is undergoing immunosuppressant treatment.

Influenza vaccines may impair the metabolism of warfarin, theophylline, phenytoin, phenobarbitone and carbamazepine by the hepatic P450 system. Results from studies showed conflicting evidence or found no evidence of an interaction. Studies which found a positive association have been variable in the degree of interaction and time after vaccination for the interaction to take effect. The interaction may be idiosyncratic.

4.6 Fertility, pregnancy and lactation

Effects on fertility

No data are available.

Use in pregnancy – Pregnancy Category B2

The effects of PANVAX® H5N8 pre-pandemic vaccine have not been studied in pregnant women. Therefore, health care providers should assess the risks and potential benefits of administering the vaccine to pregnant women on a case by case basis, taking into account New Zealand Health Authorities' recommendations. Data from vaccinations with inter-pandemic vaccines in pregnant women do not indicate that adverse foetal and maternal outcomes were attributable to the vaccine. Animal embryofoetal development studies have not been conducted with the vaccine.

Use in lactation

PANVAX® H5N8 pre-pandemic vaccine may be used during lactation.

4.7 Effects on ability to drive and use machines

The vaccine is unlikely to have an effect on the ability to drive and use machines.

4.8 Undesirable effects

Clinical trials (Adults)

Adverse reactions from the three clinical trials in adults 18 years and older with prototype pandemic vaccines (A/Vietnam/1194/2004; H5N1) are listed below (see Pharmacology for more information on the prototype vaccines). A total of 801 adult participants received the inactivated, split virion, monovalent, aluminium-adsorbed vaccine with different influenza HA antigen doses of 7.5 µg, 15 µg, 30 µg and 45 µg.

The frequency of adverse reactions observed in participants ≥ 65 years was lower compared to those in the 18 to 64 year age group.

Adverse effects are listed according to the following frequency: Very Common (≥ 1/10), Common (≥ 1/100 to < 1/10), Uncommon (≥ 1/1,000 to < 1/100), Rare (≥ 1/10,000 to < 1/1,000), Very Rare (< 1/10,000)

Infections and Infestations

Common - nasopharyngitis, upper respiratory tract infection

Nervous System Disorders

Very Common – headache

Respiratory, Thoracic and Mediastinal Disorders

Common - cough, nasal congestion, pharyngolaryngeal pain, rhinorrhoea

Gastrointestinal Disorders

Very Common – nausea

Common - diarrhoea, toothache, vomiting

Skin and Subcutaneous Tissue Disorders

Common – hyperhidrosis

Musculoskeletal and Connective Tissue Disorders

Very Common - myalgia

Common - arthralgia, back pain

Reproductive System and Breast Disorders

Common – dysmenorrhoea

General Disorders and Administration Site Conditions

Very Common - fatigue, injection site erythema, injection site induration, injection site pain, injection site swelling

Common - chills, injection site haemorrhage, pyrexia

These reactions generally resolve within 3 days.

Clinical trial (Paediatric)

Adverse reactions from the Paediatric clinical trial, in children aged 6 months to < 9 years, are listed below. The safety population consisted of a total of 149 participants who received the inactivated, split virion, monovalent, aluminium-adsorbed vaccine with 30 µg or 45 µg HA influenza antigen per dose.

Infections and Infestations

Common - upper respiratory tract infection, gastroenteritis, otitis media

Metabolism and Nutritional Disorders

Very common – decreased appetite

Nervous System Disorders

Very Common – headache

Eye Disorders

Common – conjunctivitis

Ear and Labyrinth Disorders

Common – ear pain

Respiratory, Thoracic and Mediastinal Disorders

Very common – rhinorrhoea, wheezing

Common – asthma, cough, pharyngolaryngeal pain

Gastrointestinal Disorders

Very Common – diarrhoea, vomiting

Common – abdominal pain

Skin and Subcutaneous Tissue Disorders

Common – rash

Musculoskeletal and Connective Tissue Disorders

Very Common – myalgia

General Disorders and Administration Site Conditions

Very Common - injection site pain, injection site erythema, injection site induration, injection site haemorrhage, injection site swelling, irritability, pyrexia

These reactions generally resolve within 3 days.

Injection site reactions occurred slightly less frequently in Group A (≥ 6 months to < 3 years) compared to Group B (≥ 3 years to < 9 years). Headache and myalgia was reported less frequently in Group A, while fever, irritability, reduced appetite, diarrhoea, wheezing and vomiting occurred less frequently in the Group B population.

Post-marketing surveillance

Post-marketing information is not available for PANVAX[®] H5N8 pre-pandemic vaccine, however similar adverse reactions to inter-pandemic influenza vaccines may be observed. From post marketing surveillance with inter-pandemic trivalent influenza vaccines, the following adverse reactions have been reported:

Uncommon ($\geq 1/1,000$ to $< 1/100$):

Generalised skin reactions including pruritus, urticaria or non-specific rash.

Rare ($\geq 1/10,000$ to $< 1/1000$):

Neuralgia, paraesthesia, convulsions, transient thrombocytopenia.

Allergic reactions, in rare cases leading to shock, have been reported.

Very rare ($< 1/10,000$):

Vasculitis with transient renal involvement.

Neurological disorders, such as encephalomyelitis, neuritis and Guillain Barré syndrome.

This medicinal product contains thiomersal (an organomercuric compound) as a preservative, and therefore, it is possible that sensitisation reactions may occur.

Reporting of suspected adverse reactions

Reporting suspected adverse reactions after authorisation of the medicine is important. It allows continued monitoring of the benefit/risk balance of the medicine. Healthcare professionals are asked to report any suspected adverse reactions <https://pophealth.my.site.com/carmreportnz/s/>

4.9 Overdose

There is no specific information on overdose of PANVAX[®] H5N8 pre-pandemic vaccine.

For advice on the management of overdose please contact the National Poisons Centre on 0800 POISON (0800 764 766).

5. PHARMACOLOGICAL PROPERTIES

5.1 Pharmacodynamic properties

Pharmacotherapeutic group: Influenza vaccines, ATC code: J07B B02

Mechanism of action

Prototype pandemic influenza vaccines contain influenza virus antigens that are different from those included in seasonal influenza vaccines and may also be substantially different from the virus which causes pandemic influenza. If a pandemic influenza virus emerges, the clinical efficacy and safety data obtained from clinical trials with prototype pandemic influenza vaccines are expected to be relevant for the pandemic vaccine made from the official pandemic influenza virus strain.

Clinical experience with prototype pandemic vaccines, following a two-dose primary vaccination course, has been derived from clinical trials in healthy adult, older adult and paediatric populations. The efficacy of prototype pandemic vaccines is assessed by serum immunogenicity, since clinical protection is not able to be evaluated.

The immunogenicity of prototype vaccines has been assessed in clinical trials by two serum antibody assays, the haemagglutination inhibition (HI) assay and a viral microneutralisation (MN) assay. There are currently no defined levels of serum antibody responses known to correlate with clinical protection against infection with pandemic influenza viruses. Guidelines for assessment of the pandemic influenza vaccines are based on those for inter-pandemic influenza vaccines developed by the European Medicines Agency (EMA) *Note for Guidance on Harmonisation of Requirements for*

Influenza Vaccines (CPMP/BWP/214/96) and the EMEA guidance document for pandemic vaccines (CPMP/VEG/4717/03).

A ferret efficacy challenge study using the prototype A/Vietnam/1194/2004 (H5N1) pandemic influenza vaccine has demonstrated that seroconversion (as measured by both HI and MN immune responses) in ferrets vaccinated with the 30 µg HA per dose adjuvanted formulation was associated with 100% survival following lethal challenge and also prevented serious morbidity. This data provides support for the assessment of HI and MN immune responses as a surrogate measure of clinical efficacy in human clinical trials.

Clinical trials

Four clinical trials have been conducted to assess the immunogenicity and safety of a prototype pandemic influenza vaccine in healthy persons aged 6 months and older.

The safety of the vaccine was assessed in 4 randomised Phase I or Phase II studies conducted in persons aged 6 months and older. A Phase I trial in 400 adults, 18 to 45 years of age, assessed vaccines formulated with lower HA antigen doses, with and without aluminium phosphate adjuvant. The data from this study demonstrated that higher antigen doses and an adjuvant were required, and that two doses of the vaccine elicited modest levels of cross-reactive neutralising antibodies against antigenically distinct H5N1 strains. The immunogenicity data from this study are not presented; however the safety data has been included in the overall safety analysis for the vaccine.

Three double blind, randomised Phase II clinical studies evaluated the immunogenicity of an inactivated, split virion, monovalent, aluminium phosphate-adjuvanted, prototype pandemic vaccine in adults aged 18 to 64 years, elderly adults aged 65 years and over, and children aged 6 months to less than 9 years. Two vaccinations were administered 21 days apart.

For the Adult Phase II study, immunogenicity was assessed by HI and MN approximately 21 days after each vaccination, and by MN only 6 months after the second vaccination to evaluate antibody persistence. For the older adult and paediatric studies, immunogenicity was assessed by MN only approximately 21 days after each vaccination and 6 months after the second vaccination.

The Adult Phase II study enrolled 400 participants, aged 18 to 64 years. Immunogenicity results for the 30 µg HA per dose vaccine are shown in Table 1 and 2.

Table 1: Immunogenicity (HI) Results for Adult Population (18 to 64 yrs)

Serum HI antibody	After Dose 1 n=200 (95% CI)	After Dose 2 n=197 (95% CI)
Fold increase in GMT ^a	2.8 (2.3,3.5)	6.8 (5.5,8.4)
Seroconversion or significant increase ^b	22.0% (16.5,28.4)	48.2% (41.1,55.4)
Proportion with HI ≥ 40	23.0% (17.4,29.5)	49.7% (42.6,56.9)

^a Fold increase in GMT (geometric mean titre) is the fold increase in antibody titre over the pre-vaccination GMT.

^b 'Seroconversion or significant increase' is defined as at least a four fold increase over the pre-vaccination GMT, and with a post-vaccination titre value of at least 40.

Table 2: Immunogenicity (MN) Results for Adult Population (18 to 64 yrs)

Serum viral neutralising antibody (MN)	After Dose 1 n=200 (95% CI)	After Dose 2 n=197 (95% CI)	6 months after Dose 2 n=192 (95% CI)
Fold increase in GMT ^a	1.8 (1.5,2.0)	4.3 (3.7,5.0)	3.4 (2.9,4.1)

Seroconversion or significant increase ^b	18.5% (13.4,24.6)	53.8% (46.6,60.9)	40.4% (33.4,47.7)
Proportion seropositive (MN ≥ 20)	28.0% (21.9,34.8)	72.6% (65.8,78.7)	60.1% (52.8,67.1)
Proportion with MN ≥ 40	18.5% (13.4,24.6)	53.8% (46.6,60.9)	40.4% (33.4,47.7)

^a Fold increase in GMT (geometric mean titre) is the fold increase in antibody titre over the pre-vaccination GMT.

^b 'Seroconversion or significant increase' is defined as at least a four fold increase over the pre-vaccination GMT, and with a post-vaccination titre value of at least 40.

The Older Adult Phase II study enrolled 201 participants, 65 years of age and older. Immunogenicity results for the 30 µg HA per dose vaccine are shown in Table 3.

Table 3: Immunogenicity (MN) Results for Older Adult Population (≥ 65 yrs)

Serum viral neutralising antibody (MN)	After Dose 1 n=100 (95% CI)	After Dose 2 n=101 (95% CI)	6 months after Dose 2 n=98 (95% CI)
Fold increase in GMT ^a	2.1 (1.6,2.7)	4.2 (3.2,5.4)	2.8 (2.2,3.5)
Seroconversion or significant increase ^b	22.0% (14.3,31.4)	47.5% (37.5,57.7)	38.8% (29.1,49.2)
Proportion seropositive (MN ≥ 20)	32.0% (23.0,42.1)	62.4% (52.2,71.8)	51.0% (40.7,61.3)
Proportion with MN ≥ 40	24.0% (16.0,33.6)	48.5% (38.4,58.7)	40.8% (31.0,51.2)

^a Fold increase in GMT (geometric mean titre) is the fold increase in antibody titre over the pre-vaccination GMT.

^b 'Seroconversion or significant increase' is defined as at least a four fold increase over the pre-vaccination GMT, and with a post-vaccination titre value of at least 40.

The Paediatric Phase II study enrolled 150 participants, aged 6 months to less than 9 years. Participants within this study were further defined into two age groups: Group A, 6 months to less than 3 years, and Group B, 3 years to less than 9 years. Immunogenicity results were comparable across these age groups and are presented for the 30 µg HA per dose vaccine as combined results in Table 4.

Table 4: Immunogenicity (MN) Results for Paediatric Population (6 months to < 9yrs)

Serum viral neutralising antibody (MN)	After Dose 1 n=55 (95% CI)	After Dose 2 n=66 (95% CI)	6 months after Dose 2 n=67 (95% CI)
Fold increase in GMT ^{a, 1}	1.6 (1.2, 2.2)	40.2 (30.6, 52.8)	5.4 (4.3, 6.8)
Seroconversion or significant increase ^{b, 1}	12.7% (5.3, 24.5)	98.3% (91.1, 100.0)	66.7% (53.3, 78.3)
Proportion seropositive (MN ≥ 20)	25.5% (14.7, 39.0)	98.5% (91.8, 100.0)	85.1% (74.3, 92.6)
Proportion with MN ≥ 40	14.5% (6.5, 26.7)	98.5% (91.8, 100.0)	67.2% (54.6, 78.2)

^a Fold increase in GMT (geometric mean titre) is the fold increase in antibody titre over the pre-vaccination GMT.

^b 'Seroconversion or significant increase' is defined as at least a four fold increase over the pre-vaccination GMT, and with a post-vaccination titre value of at least 40.

¹ The number of participants assessed for Fold Increase in GMT and Seroconversion or significant increase, after Dose 2 and 6 months after Dose 2, was 60.

This medicine has been given a provisional consent under Section 23 of the Act. This means that further evidence on this medicine is awaited or that there are specific conditions of use.

The vaccine may only be marketed or distributed in accordance with the directives contained in the current version of the New Zealand Pandemic Plan.

5.2 Pharmacokinetic properties

Not applicable.

5.3 Preclinical safety data

Genotoxicity

No data available.

Carcinogenicity

No data available.

6. PHARMACEUTICAL PARTICULARS

6.1 List of excipients

Each 0.5 mL dose of PANVAX® H5N8 pre-pandemic also contains nominally:

Table 5: List of excipients

sodium chloride	4.1 milligram
sodium phosphate – dibasic anhydrous	3.0 milligram
sodium phosphate - monobasic	12 microgram
potassium chloride	10 microgram
potassium phosphate - monobasic	10 microgram
calcium chloride	0.2 microgram
thiomersal	0.01% w/v
water for injections	Up to 0.5mL

Table 6: Adjuvants

aluminium (as aluminium phosphate adjuvant)	0.5 milligram
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Excipient(s) with known effect

Thiomersal

6.2 Incompatibilities

Incompatibilities were either not assessed or identified as part of the registration of the medicine.

6.3 Shelf life

The shelf life of the vaccine is 24 months when stored at 2°C to 8°C. The expiry date is indicated on the container label. Once opened, the vaccine is to be used immediately and within the one vaccination session, with any remaining contents discarded in accordance with local requirements. See section 4.2 DOSE AND METHOD OF ADMINISTRATION.

6.4 Special precautions for storage

PANVAX® H5N8 pre-pandemic vaccine should be stored, protected from light, at 2°C to 8°C. IT MUST NOT BE FROZEN. Store in the original package in order to protect from light.

6.5 Nature and contents of container

Multi-dose Vial

Multi-dose type 1 glass vial containing 10 mL of PANVAX® H5N8 pre-pandemic.

The multi-dose vial is closed with a latex-free stopper and sealed with an aluminium crimp seal. The aluminium seal has attached a plastic tear-away cap 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.

Vials are packed into a cardboard carton (pack size 50).

6.6 Special precautions for disposal

Any unused medicine or waste material should be disposed of in accordance with local requirements.

7. MEDICINE SCHEDULE

Prescription Only Medicine

8. SPONSOR

Seqirus (NZ) Ltd

PO Box 62590

Greenlane

Auckland 1546

New Zealand

Telephone: 0800 502 757

9. DATE OF FIRST APPROVAL

Date of publication in the New Zealand Gazette of consent to distribute the medicine: 07 November 2024

10. DATE OF REVISION OF THE TEXT

07 November 2024

SUMMARY TABLE OF CHANGES

Section Changed	Summary of new information