VAXIGRIP®

INACTIVATED INFLUENZA VACCINE (SPLIT VIRION)

Description

VAXIGRIP® is a sterile suspension of influenza virus for intramuscular or deep subcutaneous injection. It is a purified, inactivated, split virion vaccine.

VAXIGRIP® contains the following strains of influenza virus:

- A/ California/7/2009 NYMC X-179A (A/California/7/2009 [H1N1] - like),
- A/ Wisconsin/15/2009 NYMC X-183 (A/Perth/16/2009 [H3N2] – like), and
- B/ Brisbane/60/2008 (B/Brisbane/60/2008 - like)

Each 0.5 mL pre-filled syringe contains 15 mcg haemagglutinin of each of the 3 strains in a buffered saline solution. A buffered saline solution contains the following excipients – sodium chloride, potassium chloride, sodium phosphate – dibasic dihydrate, potassium phosphate – monobasic and water for injection.

The vaccine is prepared from virus grown in the allantoic cavity of embryonated eggs, concentrated, purified by zonal centrifugation in a sucrose gradient, split by octoxinol 9 (Triton X-100), inactivated by formaldehyde and then diluted in phosphate buffered saline solution to the required concentration. No adjuvant or preservative is added. The vaccine may contain traces of formaldehyde (≤ 30 mcg), octoxinol 9 (≤ 150 mcg) and neomycin (< 20 picogram). VAXIGRIP® does not contain more than 0.05 mcg ovalbumin per dose.

The type and amount of viral antigens contained in VAXIGRIP® conform to the annual requirements of the Australian Influenza Vaccine Committee (AIVC) and the World Health Organization (WHO) recommendations for the season. VAXIGRIP® conforms in safety and sterility to the requirements of the British Pharmacopoeia.

Pharmacology

Influenza vaccines have been shown to give antibody responses and to provide protection against clinical illness in a proportion of vaccinees. Because the influenza virus is capricious antigenically and because significant changes in its antigenic behaviour may occur from time to time, protection afforded by VAXIGRIP® is limited to the strains from which the vaccine has been prepared or to closely related strains.

Seroprotection is generally obtained within 2 to 3 weeks. The duration of post vaccinal immunity varies and is usually 6 to 12 months

Indications

VAXIGRIP® is indicated for the prevention of influenza caused by Influenza Virus types A and B in adults and children aged 6 months and over.

The current New Zealand Immunisation Handbook recommends annual vaccination for the following persons:

1. All people over the age of 65 years.

2. People under 65 years of age with:

- Cardiovascular disease - ischaemic heart disease, congestive heart failure, rheumatic heart disease, congenital heart disease, cerebrovascular disease.
- Chronic respiratory disease - Asthma if on regular preventative therapy; other chronic respiratory disease with impaired lung function.
- Diabetes.
- Chronic renal disease.
- Any cancer, excluding basal or squamous skin cancers if not invasive.
- Other conditions - autoimmune disease, immune suppression, HIV, transplant recipients, neuromuscular and CNS diseases, haemoglobinopathies, children on long-term aspirin.

Pregnant women

Influenza vaccine should be offered, and is funded, for pregnant women with a medical condition (as above). The vaccine should be given before the influenza season. Although the inactivated influenza vaccine is considered by many experts to be safe at any stage of pregnancy, others prefer to administer the influenza vaccine in the second trimester to avoid a coincidental association with spontaneous abortion. Practitioners should assess the risks for individual women. Although the publicly funded vaccine is not yet available for pregnant women (without a risk condition) the Immunisation Technical Working Group to the Ministry of Health makes the following recommendations for pregnant women:

- Influenza vaccination is recommended for women who are beyond the first trimester of pregnancy (ie, greater than 14 weeks gestation) during the influenza season.

Other adults

Healthy individuals should also consider the use of the vaccine, especially if they are in close contact with individuals at high risk of complications. Employers should consider providing influenza vaccine to avoid illness in their employees, especially those engaged in health care and other essential community services. Immunizing healthy individuals has been shown to be cost effective.

For full details regarding these recommendations for influenza vaccination, refer to the current New Zealand Immunisation Handbook.

Contraindications

VAXIGRIP® should not be given to persons with known anaphylactic hypersensitivity reactions to egg proteins (eggs or egg products), chicken proteins, or any other component of the vaccine including traces (formaldehyde, octoxinol 9 (Triton X-100) and neomycin)..

Immunisation should not be performed during an acute febrile illness.

Precautions

Since this vaccine contains traces of formaldehyde, octoxinol 9 (Triton X-100) and neomycin due to the use of these substances during production, it should be used with caution in subjects with a hypersensitivity to any of these substances.

Patients with a history of Guillain-Barré Syndrome (GBS) with an onset related in time to influenza vaccination may be at increased risk of again developing GBS if given influenza vaccine. While this risk should be weighed against the benefits to the individual patient of influenza vaccination, it would seem prudent to avoid subsequent influenza vaccination in this group. Because patients with a history of GBS have an increased likelihood of again developing the syndrome, the chance of them coincidentally developing the syndrome following influenza vaccination may be higher than in individuals with no history of GBS.

The immune response to this vaccine may be insufficient in persons deficient in producing antibodies, whether due to genetic defect, immunodeficiency disease, or immunosuppressive therapy.

Do not administer by intravascular route. Ensure that the needle does not penetrate a blood vessel.

As with all injectable vaccines, the vaccine must be administered with caution to subjects with thrombocytopenia or a bleeding disorder since bleeding may occur following an intramuscular administration to these subjects.

As with other injectable vaccines, appropriate medical treatment and supervision should always be available in case of anaphylactic reactions. Adrenaline should always be ready for immediate use whenever any injection is given.

Use in Pregnancy (Category B2)

There is no convincing evidence of risk to the foetus from immunisation of pregnant women using inactivated virus vaccines, bacterial vaccines, or toxoids.

Safety of use during pregnancy has not been established; benefits of vaccination should be weighed against potential risks. However, as VAXIGRIP® is an inactivated vaccine, it does not share the theoretical risks associated with live vaccines.

Use in Lactation

It is not known if VAXIGRIP® is excreted in human milk; hence, caution should used when administering vaccine to breastfeeding women. However, as VAXIGRIP® is an inactivated vaccine, it does not share the theoretical risks associated with live vaccines.

Interactions

Influenza vaccine can impair the metabolism of warfarin, theophylline, phenytoin, phenobarbitone and carbamazepine by the hepatic P450 system. Results from studies have been variable in degree of interaction and time after vaccination for the interaction to take effect. The interaction may be idiosyncratic. Patients taking warfarin, theophylline, phenytoin, phenobarbitone or carbamazepine should be advised of the possibility of an interaction and told to look out for signs of elevated levels of medication..

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

Following influenza vaccination, false positive results in serology tests using the ELISA method to detect antibodies against HIV1, Hepatitis C and especially HTLV1 have been observed. The Western Blot technique can be used to disprove these results. The transient false positive reactions could be due to IgM response by the vaccine.

Adverse Reactions

In children under 5 years of age, systemic reactions (e.g. fever, malaise, myalgia) may be more pronounced.

Clinical Trial Experience

The strain composition of the influenza virus vaccines is subject to annual changes, and clinical studies, including at least 50 adults 18-60 years of age and at least 50 elderly aged 60 years or older, are conducted annually in Europe to assess the safety and immunogenicity of VAXIGRIP®.

For the purpose of the cumulative safety analysis, clinical data collected over five years were considered. A total number of 779 vaccinees received an intramuscular injection of VAXIGRIP®.

The most common reactions occurring after vaccine administration were local reactions at injection site; mainly pain and erythema, asthenia and headache. Most of the adverse events were of mild to moderate intensity, usually occurring within one day of vaccination and resolving within 3 days.

The table below summarizes the frequencies (range across individual trials) of the solicited adverse events that were recorded within 3 days following the vaccination.

Table 1: Adverse events within 3 days after vaccination of 779 patients with VAXIGRIP®

Adverse events	Adult 18-59Years (N=393)	Elderly > 60Years (N=386)
General Disorders and Administration Site Conditions		
Local reactions: Injection site pain	27 to 57%	11.5 to 23.7%

Injection site erythema Injection site induration Injection site oedema Injection site bruising Injection site pruritus	7.1 to 29.1% 4.5 to 17.3% 2.2 to 21.5% 1.1 to 7.4%* 1.1 to 4.9%*	7.1 to 29.9% 3.8 to 10.5% 5.8 to 14.5%* 1.9 to 4.5%* 1.9 to 3%*
Systemic complaints: Asthenia Pyrexia (oral temperature > 38C) Rigors Malaise	 4.3 to 14.8% 1.2 to 1.4%* 1.4 to 6.7% 1.1 to 1.3%*	 1.4 to 7.9% 1 to 1.5%* 1 to 3%* 1.3%*
Nervous system disorders: Headache	 1.4 to 10%	 2.9 to 6%*
Musculoskeletal and connective tissue disorders: Arthralgia Myalgia	 1.4 to 3.8%* 1.1 to 8.9%	 1.5 to 2.6%* 1.4 to 3%*
Skin and subcutaneous tissue disorders		
Sweating increased	1.4 to 4.9%*	6%*

* Adverse event not reported in all studies.

Post-Marketing Experience

Based on spontaneous reporting, the following additional adverse events have been reported during the commercial use of VAXIGRIP® and VAXIGRIP® Junior. These events have been very rarely reported, however exact incidence rates cannot be precisely calculated.

Blood and lymphatic system disorders

Transient thrombocytopenia, lymphadenopathy

Immune system disorders

Allergic reactions: pruritus, rash erythematous, urticaria, dyspnoea, angioneurotic oedema, or shock

Nervous system disorders

Paraesthesia, Guillain-Barre Syndrome (GBS)*, neuritis, neuralgia, convulsions, encephalomyelitis.

* Post vaccination neurological disorders have been reported following the use of almost all biological products. Guillain-Barré Syndrome (GBS) has been very rarely reported in temporal association with administration of influenza vaccines. In the 1976 swine influenza vaccination program the U.S. Public Health Advisory Committee on Immunisation Procedures (ACIP) found that GBS occurred at an incidence of approximately 1 in 100,000 after immunisation and that the death rate in this 'series' was approximately 1 in 2,000,000. Such an excess incidence of GBS has not been demonstrated in subsequent years when recipients of the 1978 and 1979 vaccines were studied. An association between Guillain-Barré Syndrome and the Influenza vaccines used in the Northern Hemisphere USA in the 1992-93 and 1993-

94 seasons has been reported. The excess cases of Guillain-Barré Syndrome attributed to Influenza vaccination was 1 to 2 cases for each million persons vaccinated.

Vascular disorders
Vasculitis, such as Henoch-Schonlein purpura, with transient renal involvement in certain cases.

Dosage and Administration

Immunisation is normally undertaken in the autumn, in anticipation of winter outbreaks of influenza.

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

Table 2: Dosage recommendations

Age	Dose	No. of doses (first vaccination)	No. of doses[(1)] (subsequent years)
6 months to 35 months	0.25 mL	2*	1
3 to 9 years	0.5 mL	2*	1
> 9 years	0.5 mL	1	1

(1) Where children 6 months to ≤ 9 years of age receiving influenza vaccine for the first time have not received the second dose within the same year, they should be given 2 doses the following year.
* For children aged ≤ 9 years who are receiving influenza vaccine for the first time, it is recommended that they receive 2 doses at least 1 month apart.

Note: VAXIGRIP® should be administered to children under 5 years of age with care (see INDICATIONS; ADVERSE REACTIONS).

When using the single dose 0.5 mL syringe for administering a 0.25 mL dose, push the plunger to the edge of the black mark on the glass syringe so that half of the volume is eliminated. Inject the remaining volume.

The contents of the syringe must be shaken thoroughly immediately before use. After shaking, the vaccine is a slightly whitish and opalescent liquid.

Syringes are for single use only and must not be used in more than one individual.

The current New Zealand Immunisation Handbook recommends that influenza vaccine can be administered concurrently with other vaccines, including pneumococcal polysaccharide vaccine and all the scheduled childhood vaccines. When administering VAXIGRIP® concurrently with other vaccines, separate syringes and different injection sites should be used.

Overdosage

No specific information exists on overdosage with VAXIGRIP®.
For general advice on overdose management, contact the New Zealand National Poisons Centre on 0800 764 766.

Presentation

Prefilled syringe containing 0.5 mL of vaccine.
Packs of 1 or 10 syringes

Storage

Store at 2°C to 8°C. Do not freeze. Protect from light.

Manufacturer

Sanofi Pasteur S.A.
Lyon, France

Distributor

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Medicines Classification

PRESCRIPTION ONLY MEDICINE

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