

PRODUCT MONOGRAPH

VAXIGRIP®

Inactivated Influenza Vaccine Trivalent Types A and B (Split Virion)

Suspension for Injection

Active Immunizing Agent for the Prevention of Influenza

ATC Code: J07BB02

Manufactured by:
Sanofi Pasteur SA
Lyon, France

Distributed by:
Sanofi Pasteur Limited
Toronto, Ontario, Canada

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VAXIGRIP®

Inactivated Influenza Vaccine Trivalent Types A and B (Split Virion)

PART I: HEALTH PROFESSIONAL INFORMATION

SUMMARY PRODUCT INFORMATION

Route of Administration: Intramuscular injection.

Dosage Form/Strength: Suspension for injection.

Active Ingredients:

Each 0.5 mL dose is formulated to contain: 15 µg of haemagglutinin (HA) for each strain listed below. (See [DESCRIPTION](#).)

Each 0.25 mL dose is formulated to contain: 7.5 µg of haemagglutinin (HA) for each strain listed below. (See [DESCRIPTION](#).)

Clinically Relevant Non-medicinal Ingredients: thimerosal^{*}, formaldehyde, Triton® X-100[†], neomycin

* multidose presentation only

† Triton® X-100 is a registered trademark of Union Carbide, Co.

For a complete listing see [DOSAGE FORMS, COMPOSITION AND PACKAGING](#) section.

DESCRIPTION

VAXIGRIP® [Inactivated Influenza Vaccine Trivalent Types A and B (Split Virion)] for intramuscular use, is a sterile suspension containing 3 strains of influenza virus cultivated on embryonated eggs, concentrated, purified by zonal centrifugation in a sucrose gradient, split by Triton® X-100, inactivated by formaldehyde and then diluted in phosphate buffered saline solution. The type and amount of viral antigens contained in VAXIGRIP® conform to the current requirements of the World Health Organization (WHO). (1) The strains for the 2013 – 2014 season are: A/California/7/2009 (H1N1)pdm09-like strain, A(H3N2) strain antigenically like the cell-propagated prototype strain A/Victoria/361/2011 and B/Massachusetts/2/2012-like strain.

INDICATIONS AND CLINICAL USE

VAXIGRIP® is indicated for active immunization against influenza caused by the specific strains of influenza virus contained in the vaccine in adults and children 6 months of age and older.

Although the current influenza vaccine can contain one or more of the antigens administered in previous years, annual vaccination using the current vaccine is necessary because immunity declines in the year following vaccination.

The National Advisory Committee on Immunization (NACI) encourages annual influenza vaccination for all Canadians who have no contraindications. (2)

Vaccine should be offered to both children and adults up to and even after influenza virus activity is documented in a community. (2) (3)

CONTRAINDICATIONS

Hypersensitivity

VAXIGRIP® should not be administered to anyone with a history of severe allergic reaction to egg protein or any component of the vaccine (see [DOSAGE FORMS, COMPOSITION AND PACKAGING - Composition](#)) or after previous administration of the vaccine or a vaccine containing the same components or constituents.

WARNINGS AND PRECAUTIONS

General

Before administration of VAXIGRIP®, health-care providers should inform the recipient, or parent / guardian of the recipient of the benefits and risks of immunization, inquire about the recent health status of the recipient, review the recipient's history concerning possible hypersensitivity to the vaccine or similar vaccine, previous immunization history, the presence of any contraindications to immunization and comply with any local requirements regarding information to be provided to the recipient/guardian before immunization.

As with any vaccine, immunization with influenza vaccine may not protect 100% of individuals.

Influenza virus is remarkably unpredictable in that significant antigenic changes may occur from time to time. It is known that VAXIGRIP® as now constituted is not effective against all possible strains of influenza virus. Protection is limited to those strains of virus from which the vaccine is prepared or against closely related strains.

Administration-route Related Precautions: Do not administer by intravascular injection: ensure that the needle does not penetrate a blood vessel.

VAXIGRIP® should not be administered into the buttocks.

Aseptic technique must be used for withdrawal of each dose from a multidose vial. Use a separate, sterile needle and syringe or a sterile disposable unit for each individual patient and for each entry into a multidose vial, to prevent disease transmission. In particular, the same needle and/or syringe must never be used to re-enter a multidose vial to withdraw vaccine even when it is to be used for inoculation of the same patient. This may lead to contamination of the vial contents and infection of patients who subsequently receive vaccine from the vial. (5)

The syringe presentations of VAXIGRIP® should be used for single-dose administration only. When a pre-filled syringe containing 0.5 mL of VAXIGRIP® is used to administer a dose of 0.25 mL to children from 6 to 35 months of age, half of the volume of vaccine should be discarded before administration and the remaining volume should be injected. (See [DOSAGE AND ADMINISTRATION - Administration](#)). However, NACI recommends that children 6 to 35 months of age should be given a full dose (0.5 mL). (2)

Febrile or Acute Disease

Persons with serious acute febrile illness usually should not be vaccinated until their symptoms have abated. Those with mild non-serious febrile illness (such as mild upper respiratory tract infections) may be given influenza vaccine. (2) (3)

Hematologic

Because any intramuscular injection can cause an injection site haematoma in persons with any bleeding disorders, such as haemophilia or thrombocytopenia, or in persons on anticoagulant therapy, intramuscular injections with VAXIGRIP® should not be administered to such persons unless the potential benefits outweigh the risk of administration. If the decision is made to administer any product by intramuscular injection to such persons, it should be given with caution, with steps taken to avoid the risk of haematoma formation following injection.

NACI has recommendations for giving vaccinations to persons with bleeding disorders. (3)

Immune

As with all products, epinephrine hydrochloride solution (1:1,000) and other appropriate agents should be available for immediate use in case an anaphylactic or acute hypersensitivity reaction occurs. Health-care providers should be familiar with current recommendations for the initial management of anaphylaxis in non-hospital settings including proper airway management. For instructions on recognition and treatment of anaphylactic reactions see the current edition of the Canadian Immunization Guide or visit the Health Canada website. (3)

As each dose may contain traces of formaldehyde, Triton® X-100 and undetectable traces of neomycin, which are used during vaccine production, caution should be exercised when the vaccine is administered to subjects with hypersensitivity to any of these substances. (See [CONTRAINDICATIONS](#)). (6) The multidose vial of this vaccine contains thimerosal as a preservative. Thimerosal has been associated with allergic reactions. (7)

Immunocompromised persons (whether from disease or treatment) may not achieve the expected immune response. Nevertheless, as recommended by NACI, the possibility of lower efficacy should not prevent immunization in those at high risk of influenza-associated morbidity, since protection is still likely to occur. (2)

According to NACI, egg-allergic individuals may be vaccinated against influenza, without a prior influenza skin test, based on an assessment of risk for a severe allergic reaction to guide the method of vaccination. (2)

Neurologic

Immunization should be delayed in a patient with an active neurologic disorder, but should be considered when the disease process has been stabilized.

Guillain-Barré syndrome has been reported after influenza vaccination. However, it is not known whether influenza vaccination specifically might increase the risk for recurrence of GBS. Therefore, the NACI and the Advisory Committee on Immunization Practices (ACIP) state it is prudent to avoid vaccinating persons who are known to have experienced GBS within 6 weeks after a previous influenza vaccination. (2) (3)

Respiratory

According to NACI, persons who have experienced oculorespiratory syndrome (ORS) symptoms including severe ORS consisting of non-lower respiratory symptoms (bilateral red eyes, cough, sore throat, hoarseness, facial swelling), may be safely reimmunized with influenza vaccine. (3) Please refer to the most current NACI recommendations regarding revaccination of subjects who experienced more severe ORS. (3)

Special Populations

Pregnant Women

Animal reproduction studies have not been conducted with VAXIGRIP®. It is not known whether VAXIGRIP® can cause fetal harm when administered to a pregnant woman or can affect reproductive capacity.

Data on the use of this vaccine in pregnant women are limited. VAXIGRIP® should be given to pregnant women only if clearly needed and following an assessment of the risks and benefits. (3)

NACI states that influenza vaccination is recommended for all pregnant women. (2)

Nursing Women

It is not known whether VAXIGRIP® is excreted in human milk. Caution must be exercised when VAXIGRIP® is administered to a nursing mother.

NACI states that influenza vaccination is considered safe for breastfeeding women.

Pediatrics

The use of VAXIGRIP® in infants under 6 months of age is not recommended.

ADVERSE REACTIONS

Adverse Drug Reaction Overview

Adverse event information is derived from uncontrolled clinical trials and worldwide post-marketing experience.

Because VAXIGRIP® does not contain infectious viral particles, it cannot cause influenza.

The most common reactions occurring after vaccine administration are injection site pain, erythema and edema. The most common systemic reactions observed after vaccine administration are asthenia, headache and myalgia. Most of the adverse events reported after influenza vaccination are mild to moderate in intensity, resolving within 3 days.

Clinical Trial Adverse Drug Reactions

Because clinical trials are conducted under very specific conditions, the adverse reaction rates observed in the clinical trials of a vaccine cannot be directly compared to the rates in the clinical trials of another vaccine and may not reflect rates observed in practice. The adverse reaction

information from clinical trials does, however, provide a basis for identifying the adverse events that appear to be related to vaccine use and for approximating rates of those events.

The strain composition of the influenza virus vaccines is subject to annual changes and corresponding clinical studies, including at least 50 adults 18-60 years of age and at least 50 elderly aged 60 years or older, are conducted as annual update requirements in Europe to assess the safety and immunogenicity of VAXIGRIP®. (8)

For the purpose of cumulative analysis, five years of annual clinical safety data were considered. (See Table 1). (9) (10) (11) (12) (13) A total of 779 vaccinees received an intramuscular injection of VAXIGRIP®. Table 1 summarizes the frequencies (range across individual trials) of the solicited adverse events that were recorded within 3 days following the vaccination.

Data are categorized by age group and by MedDRA system organ class.

Table 1: Adverse Events within 3 Days after Vaccination of 779 Patients with VAXIGRIP®

Adverse Events	Adult 18-59 years (N = 393)	Elderly >60 years (N = 386)
General Disorders and Administration Site Conditions		
Injection Site Reactions		
Pain	27 to 57%	11.5 to 23.7%
Erythema	7.1 to 29.1%	7.1 to 29.9%
Induration	4.5 to 17.3%	3.8 to 10.5%
Edema	2.2 to 21.5%	5.8 to 14.5%*
Bruising	1.1 to 7.4%*	1.9 to 4.5%*
Pruritus	1.1 to 4.9%*	1.9 to 3%*
Systemic Reactions		
Asthenia	4.3 to 14.8%	1.4 to 7.9%
Pyrexia (oral temperature >38°C)	1.2 to 1.4%*	1 to 1.5%*
Rigors	1.4 to 6.7%	1 to 3%*
Malaise	1.1 to 1.3%*	1.3%*
Nervous System Disorders		
Headache	1.4 to 10%	2.9 to 6%*
Musculoskeletal And Connective Tissue Disorders		
Arthralgia	1.4 to 3.8%*	1.5 to 2.6%*
Myalgia	1.1 to 8.9%	1.4 to 3%*
Skin And Subcutaneous Tissue Disorders		
Sweating increased	1.4 to 4.9%*	6%*

* Adverse events not reported in all studies.

Data from Post-marketing Experience

The following additional adverse events have been spontaneously reported during the post-marketing use of VAXIGRIP®. Because these events are reported voluntarily from a population of

uncertain size, it is not possible to reliably estimate their frequency or establish a causal relationship to vaccine exposure.

Blood and Lymphatic System Disorders

Transient thrombocytopenia, lymphadenopathy

Immune System Disorders

Allergic reactions: pruritus, erythematous rash, urticaria, dyspnea, angioneurotic edema, or anaphylaxis (including shock)

Nervous System Disorders

Paraesthesia, Guillain-Barré syndrome (GBS), neuritis, neuralgia, convulsions, encephalomyelitis

Vascular Disorders

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

Additional Adverse Reactions

The following adverse events not listed above have been reported with influenza vaccines:

During the 2000-2001 influenza season, the Public Health Agency of Canada (PHAC) received an increased number of reports of influenza vaccine-associated symptoms and signs that were subsequently described as ORS. The pathophysiologic mechanism underlying ORS remains unknown, but it is considered distinct from IgE-mediated allergy. (3) Since the 2000-2001 influenza season fewer ORS cases have been reported to PHAC.

Neurological disorders temporally associated with influenza vaccination such as encephalopathy (with or without permanent neurological - motor and/or sensory - deficit and/or intellectual impairment), optic neuritis, facial paralysis, labyrinthitis and brachial plexus neuropathy have been reported. However, no cause-and-effect relationships have been established. (14)

Physicians, nurses and pharmacists should report any adverse occurrences temporally related to the administration of the product in accordance with local requirements and to the Global Pharmacovigilance Department, Sanofi Pasteur Limited, 1755 Steeles Avenue West, Toronto, ON, M2R 3T4, Canada. 1-888-621-1146 (phone) or 416-667-2435 (fax).

DRUG INTERACTIONS

Concomitant Vaccine Administration

Clinical studies show that influenza vaccine may be administered with pneumococcal polysaccharide vaccine using separate syringes at different sites. (15) (16)

No studies regarding the concomitant administration of inactivated influenza vaccine and other childhood vaccines have been conducted.

NACI states that influenza vaccine may be given at the same time as other vaccines. The same limb may be used if necessary, but different sites on the limb should be chosen. Different administration sets (needle and syringe) must be used. (3)

VAXIGRIP® must not be mixed in the same syringe with other parenterals.

Vaccine-Drug Interactions

Immunosuppressive treatments may interfere with the development of the expected immune response. (See WARNINGS AND PRECAUTIONS).

DOSAGE AND ADMINISTRATION

Recommended Dose

The recommended dosage schedule is presented in Table 2.

Table 2: Recommended Influenza Vaccine Dosage, by Age

Age Group	Dose	No. of Doses
6 to 35 months	0.25 mL* or 0.5 mL†	1 or 2‡
3 to 8 years	0.5 mL	1 or 2‡
≥9 years	0.5 mL	1

* In clinical studies conducted by Sanofi Pasteur children 6 to 35 months of age received 0.25 mL dose.

† NACI recommends that children 6 to 35 months of age should be given a full dose (0.5 mL) of influenza vaccine. (2)

‡ Previously unvaccinated children 6 months to <9 years of age require 2 doses of seasonal influenza vaccine with an interval of weeks. Eligible children <9 years of age who have properly received one or more doses of seasonal influenza vaccine in the past are recommended to receive one dose per season thereafter. (2)

Fractional doses (doses of less volume than indicated for each age group in [Table 2](#)) should not be given. The effect of fractional doses on the safety and efficacy has not been determined. (3)

Administration

Inspect for extraneous particulate matter and/or discolouration before use. If these conditions exist, the product should not be administered.

Administer the vaccine **intramuscularly**. The preferred site is into the deltoid muscle, in adults and children >1 year of age. The preferred site for infants and young children (<1 year of age) is the anterolateral aspect of the mid-thigh (vastus lateralis muscle).

SHAKE THE PRE-FILLED SYRINGE WELL to uniformly distribute the suspension before administration.

If using a pre-filled syringe with two needles, select a needle of appropriate length to ensure that the vaccine will be delivered intramuscularly. Remove the tip cap from the syringe, take the chosen needle from the blister pack and fix to the tip of the pre-filled syringe.

For children, when a single dose 0.5 mL syringe is to be used for administration of a 0.25 mL dose, push the plunger exactly to the edge of the mark so that half of the volume is eliminated.

The remaining volume should be injected. However, NACI recommends that children 6 to 35 months of age should be given a full dose (0.5 mL). (2)

If using a multidose vial, SHAKE THE VIAL WELL to uniformly distribute the suspension before withdrawing each dose. When administering a dose from a stoppered vial, do not remove either the stopper or the metal seal holding it in place. Aseptic technique must be used for withdrawal of each dose. (See WARNINGS AND PRECAUTIONS).

Aseptic technique must be used. Use a separate sterile needle and syringe, or a sterile disposable unit for each individual recipient, to prevent disease transmission. Needles should not be recapped and should be disposed of according to biohazard waste guidelines.

Give the patient a permanent personal immunization record. In addition, it is essential that the physician or nurse record the immunization history in the permanent medical record of each patient. This permanent office record should contain the name of the vaccine, date given, dose, manufacturer and lot number.

OVERDOSAGE

Not applicable.

For management of a suspected drug overdose, contact your regional Poison Control Centre.

ACTION AND CLINICAL PHARMACOLOGY

Mechanism of Action

The inoculation of antigen prepared from inactivated influenza virus stimulates the production of specific antibodies. Protection is afforded only against those strains of virus from which the vaccine is prepared or closely related strains.

Immunity to the surface antigens, particularly the haemagglutinin, reduces the likelihood of infection. Antibody against one influenza virus type or subtype confers limited or no protection against another type or subtype of influenza. Furthermore, antibody to one antigenic type or subtype of influenza virus might not protect against infection with a new antigenic variant of the same type or subtype. Frequent emergence of antigenic variants through antigenic drift is the virologic basis for seasonal epidemics and is the reason for the usual incorporation of one or more new strains in each year's influenza vaccine. (17)

Each year's influenza vaccine contains three virus strains (usually two type A, and one type B) representing the influenza viruses that are believed likely to circulate in the coming winter. (1) (3) The antigenic characteristics of current and emerging influenza virus strains provide the basis for selecting the strains included in each year's vaccine. (1) (3)

Pharmacodynamics

Seroprotection is expected within 2 to 3 weeks following influenza vaccination. (18)

Pharmacokinetics

No pharmacokinetic studies have been performed.

Duration of Effect

The duration of post-vaccinal immunity varies and is usually 6-12 months. (18)

STORAGE AND STABILITY

Store at 2° to 8°C (35° to 46°F). **Do not freeze.** Discard product if exposed to freezing.

Protect from light. Do not use vaccine after expiration date.

SPECIAL HANDLING INSTRUCTIONS

A multidose vial of VAXIGRIP® which has been entered must be stored at 2° to 8°C and used within 7 days. Seven days after first entry, it must be discarded.

DOSAGE FORMS, COMPOSITION AND PACKAGING

Dosage Forms

VAXIGRIP® is supplied as a slightly whitish, opalescent suspension in a vial, prefilled syringe or ampoule.

Composition

For the 2013-2014 season, VAXIGRIP® contains the following:

Active Ingredients

0.5 mL dose: 15 µg per strain of HA of split inactivated influenza virus of each strain listed below:

0.25 mL dose: 7.5 µg per strain of HA of split inactivated influenza virus of each strain listed below:

A/California/7/2009 (H1N1)pdm09-like strain, A(H3N2) strain antigenically like the cell-propagated prototype strain A/Victoria/361/2011 and B/Massachusetts/2/2012-like strain.

Other Ingredients

0.5 mL dose: 2 µg thimerosal*, up to 0.5 mL sodium phosphate buffered isotonic sodium chloride solution, formaldehyde (≤30 µg), 0.25 mL dose: 1 µg thimerosal*, up to 0.25 mL sodium phosphate buffered isotonic sodium chloride solution, formaldehyde (≤15 µg)

Triton® X-100 and trace amounts of sucrose and neomycin

* added as a preservative in multidose presentation only

After shaking, VAXIGRIP® is slightly whitish and opalescent in colour.

Packaging

VAXIGRIP® is supplied in multidose vials, single dose prefilled syringes or single dose ampoules.

The vials and syringes are made of Type 1 glass. The container closure system for all presentations of VAXIGRIP® does not contain latex (natural rubber).

VAXIGRIP® is available in packages of:

- 1 x 5 mL (Multidose) vial
- 1 x 0.25 mL (Single Dose) syringe with an attached (25G, 16 mm) needle
- 1 x 0.5 mL (Single Dose) syringe with an attached (25G, 16 mm) needle
- 1 x 0.5 mL (Single Dose) syringe co-packaged with two 25G needles of different lengths (16 mm and 25 mm)
- 1 x 0.5 mL (Single Dose) syringe without needle

Not all pack sizes may be marketed.

The vial stopper, plunger stopper and the needle shield of the pre-filled syringe do not contain latex (natural rubber).

Vaccine Information Service: 1-888-621-1146 or 416-667-2779.

Business hours: 8 a.m. to 5 p.m. Eastern Time, Monday to Friday.

Full product monograph available on request or visit us at www.sanofipasteur.ca

Product information as of May 2013.

Manufactured by:
Sanofi Pasteur SA
Lyon, France

Distributed by:
Sanofi Pasteur Limited
Toronto, Ontario, Canada

R19-0513 Canada

PART II: SCIENTIFIC INFORMATION

PHARMACEUTICAL INFORMATION

Drug Substance

VAXIGRIP® [Inactivated Influenza Vaccine Trivalent Types A and B (Split Virion)]

For the 2013-2014 season VAXIGRIP® contains the following strains:

A/California/7/2009 (H1N1)pdm09-like strain [A/California/7/2009 (NYMC X-179A)]

A(H3N2) strain antigenically like the cell-propagated prototype strain A/Victoria/361/2011 [A/Texas/50/2012 (NYMC X-223A)]

B/Massachusetts/2/2012-like strain [B/Massachusetts/2/2012]

The type and amount of viral antigens contained in VAXIGRIP® conform to the current requirements of the World Health Organization (WHO). (1)

Product Characteristics

VAXIGRIP® for intramuscular use is a sterile suspension prepared from influenza viruses cultivated in embryo-containing hens' eggs. Each of the strains is separately inoculated into the allantoic cavity of chicken embryos aged 11 days with neomycin solution equivalent to 0.5 mg per egg. Following incubation, the allantoic fluid is collected and clarified, and the viruses are concentrated, and then purified by zonal centrifugation using a sucrose density gradient. Subsequent stages consist of treatment with Triton® X-100 to obtain split antigens, then inactivation using formaldehyde solution. The final vaccine is obtained by mixing the three strains in a buffer. Thimerosal is then added for the multidose presentation only.

After shaking, VAXIGRIP® is slightly whitish and opalescent in colour.

CLINICAL TRIALS

Study Demographics and Trial Design

The immunogenicity of VAXIGRIP® has been demonstrated in clinical trials in adults (age 18-60 years), elderly (age >60 years), and young children (age 6-36 months and 3-10 years). The strain composition of influenza virus vaccines is subject to annual changes, and annual studies in adults to verify the immunogenicity are performed. (See [Table 3](#).) In the annual studies (19) and in study 3 (20), a single dose of VAXIGRIP® was given and antibody titres were assessed immediately before vaccination and 21 days later. In study 2 (21), antibody titres were assessed immediately before the first dose and 27-33 days following the second vaccine dose.

Table 3: Summary of Patient Demographics for Clinical Trials

Study #	Trial design	Dosage, route of administration and duration	Study subjects (n = number)	Mean age (Range)	Gender
Annual Study (19)	Open	0.5 mL IM	n >50 n >50	18-60 years >60 years	--
Study 2 (19) (21)	Open	0.25 mL IM; 2 doses 1 month apart	n = 65	6 months to 3 years	Male 37 Female 28
Study 3 (20)	Open	0.5 mL	n = 42 (12 had received prior influenza vaccination)	8-10 years	Male 19 Female 23

Study Results

The efficacy of influenza vaccine is assessed using a surrogate for protection defined as the immune response elicited by the vaccine (haemagglutination inhibition). In the annual studies, the serologic responses of both adult age groups to all antigens must meet the assessment criteria as defined in the European Requirements for Influenza Vaccines (i.e., for subjects 18-60 years - at least one of seroconversion or significant increase in antihaemagglutinin antibody titre in >40%, mean GMT increase >2.5, proportion of subjects achieving HI (haemagglutination inhibition) titre or seroprotection >70%, and for subjects >60 years at least one of seroconversion or significant increase in antihaemagglutinin antibody titre in >30%, mean GMT increase >2.0, proportion of subjects achieving HI titre >60%.) (8) Elderly subjects generally respond less well to influenza vaccines than young healthy adults, and those with chronic debilitating medical conditions generally respond less well than healthy subjects of similar age. (22)

The results in children met the criteria defined for young adults; no criteria for children have been set.

ADDITIONAL RELEVANT INFORMATION

Influenza A and B are the two types of influenza viruses that cause epidemic human disease. Influenza A viruses are further categorized into subtypes on the basis of two surface antigens: haemagglutinin (H) and neuraminidase (N). Influenza B viruses are not categorized into subtypes. (3) Since 1977, influenza A (H1N1) viruses, influenza A (H3N2) viruses and influenza B viruses have been in global circulation. (3) Influenza A (H1N2) has been circulating widely since 2001. (3) Because circulating influenza A (H1N2) viruses are a reassortant of influenza A (H1N1) and (H3N2) viruses, antibody directed against influenza A (H1N1) and (H3N2) vaccine strains will provide protection against circulating influenza A (H1N2) viruses. (3)

In the tropics, influenza can occur throughout the year. In the southern hemisphere, peak activity occurs from April through September.

Uncomplicated influenza illness is characterized by the abrupt onset of constitutional and respiratory signs and symptoms (e.g., fever, myalgia, headache, malaise, non-productive cough, sore throat and rhinitis). Illness typically resolves after a limited number of days for the majority of persons, although cough and malaise can persist for two or more weeks. Among certain persons, influenza can exacerbate underlying medical conditions (e.g., pulmonary or cardiac disease), lead to secondary bacterial pneumonia or primary influenza viral pneumonia, or occur as

part of a coinfection with other viral or bacterial pathogens. (3) The spectrum of influenza in children ranges from asymptomatic infection to influenza illness with or without complications. In addition to febrile upper respiratory tract infection, common clinical presentations of influenza in children include lower respiratory tract infection (croup, bronchiolitis, primary viral, or secondary bacterial pneumonia), otitis media, diarrheal illness, and febrile seizures. Influenza infection has also been associated with encephalopathy, transverse myelitis, Reye syndrome, myositis, myocarditis, and pericarditis. (3) The risks of complications, hospitalizations and deaths from influenza are higher among persons 65 years of age or older, young children and persons of any age with some underlying health conditions than among healthy older children and younger adults. (3)

In Canada approximately 4,000 deaths can be attributed to influenza annually. (23) Over 95% of these deaths occur in individuals over 65 years of age. Up to 17,000 hospitalizations can be attributed annually to influenza. (24) The rate of hospitalizations in older adults ≥ 65 Years attributable to influenza can be as high as 3.4 per 1000 individuals.

Vaccination is recognized as the single most effective way of preventing or attenuating influenza for those at high risk of serious illness or death from influenza infection and related complications. (3) The national goal of influenza immunization programs is to prevent serious illness caused by influenza and its complications, including death. NACI therefore recommends that immunization programs target vaccine delivery, as a priority, to those persons at high risk of complications and those who provide essential community services; however, NACI encourages annual vaccine for all Canadians.

The inoculation of antigen prepared from inactivated influenza virus stimulates the production of specific antibodies. Protection is afforded only against those strains of virus from which the vaccine is prepared or closely related strains.

Immunity to the surface antigens, particularly the haemagglutinin, reduces the likelihood of infection. Antibody against one influenza virus type or subtype confers limited or no protection against another type or subtype of influenza virus. Furthermore, antibody to one antigenic type or subtype of influenza virus might not protect infection. Frequent emergence of antigenic variants through antigenic drift is the virologic basis for seasonal epidemics and is the reason for annually reassessing the need to change one or more of the recommended strains for influenza vaccines. (17)

Each year's influenza vaccine contains three virus strains (usually two types A and one type B) representing the influenza viruses that are believed likely to circulate in the coming winter. (1) (3) The antigenic characteristics of current and emerging influenza virus strains provide the basis for selecting the strains included in each year's vaccine. (1) (3) The WHO reviews the world epidemiological situation annually and if necessary recommends new strains based on the current epidemiological evidence.

The majority of vaccinated children and young adults develop high post-vaccination haemagglutination inhibition antibody titres. These antibody titres are protective against illness caused by strains similar to those in the vaccine. Older persons and persons with certain chronic diseases might develop lower post-vaccination antibody titres than healthy young adults and thus can remain susceptible to influenza-related upper respiratory tract infection. The vaccine can also be effective in preventing secondary complications and reducing the risk for influenza-related hospitalization and death among adults 65 years and older with and without high-risk medical conditions (e.g., heart disease and diabetes). (17)

The effectiveness of influenza vaccine varies depending upon the age and immunocompetence of the vaccine recipient, the degree of similarity between the virus strain included and the characteristics of the strain of circulating virus during the influenza season. With a good match, influenza vaccination has been shown to prevent laboratory-confirmed influenza illness in approximately 70% or more of healthy individuals. (25) In the elderly, vaccination against influenza is associated with reductions in the risk of hospitalization for heart disease, cerebrovascular disease, and pneumonia or influenza as well as the risk of death from all causes during influenza season. (26) In older persons living in residential facilities influenza vaccine prevents pneumonia, hospital admission, death from pneumonia (vaccine effectiveness 42% to 46%), and all-cause mortality (vaccine effectiveness 60%). (26)

Children aged as young as 6 months can develop protective levels of antibody after influenza vaccination, although the antibody response among children at high risk of influenza-related complications might be lower than among healthy children. In a randomized study among children aged 1 - 15 years, inactivated influenza vaccine was 77% - 91% effective against influenza respiratory illness. (17) Vaccination of health-care workers has been associated with reduced work absenteeism (17) (27) and decreased deaths among nursing home patients. (17) (28)

Vaccination is associated with reductions in influenza-related respiratory illness and physician visits among all age groups, hospitalization and death among persons at high risk, otitis media among children and work absenteeism among adults. (17) (29)

Although the current influenza vaccine can contain one or more of the antigens administered in previous years, annual vaccination using the current vaccine is necessary because immunity declines in the year following vaccination.

TOXICOLOGY

Data in animals revealed no unexpected findings and no target organ toxicity. (30) (31) (32)

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Vaccine Information Service: 1-888-621-1146 or 416-667-2779.

Business hours: 8 a.m. to 5 p.m. Eastern Time, Monday to Friday.

Full product monograph available on request or visit us at www.sanofipasteur.ca.

Product information as of May 2013.

Manufactured by:

Sanofi Pasteur SA

Lyon, France

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Toronto, Ontario, Canada

R19-0513 Canada

IMPORTANT: PLEASE READ

PART III: CONSUMER INFORMATION

VAXIGRIP®

**Inactivated Influenza Vaccine Trivalent
Types A and B (Split Virion)**

This leaflet is part III of a three-part "Product Monograph" published when VAXIGRIP® was approved for sale in Canada. It provides important information about the product for Consumers. This leaflet is a summary and it does not tell you everything about VAXIGRIP®. Contact your doctor, nurse or pharmacist if you have any questions about the vaccine.

ABOUT THIS VACCINE

What the vaccine is used for:

VAXIGRIP® is a vaccine used to prevent influenza. Influenza (or flu) is an infection caused by the influenza virus.

This vaccine may be given to adults and children 6 months of age and older.

Flu symptoms can include fever, headache, muscle pain, runny nose, sore throat, extreme tiredness and cough. Some people get much sicker.

The influenza virus spreads when a person who has the flu coughs or sneezes into the air. Small droplets of the flu virus stay in the air for a short time then fall onto surfaces nearby. You can get the flu by:

- breathing in these droplets through your nose or mouth.
- the droplets landing directly on your eyes.
- touching the hands of a person who has the flu and then touching your eyes, nose or mouth.
- touching surfaces that have been contaminated with flu virus and then touching your eyes, nose or mouth.

What it does:

VAXIGRIP® causes your body to produce its own protection against influenza virus. After you get a flu shot, your immune system produces antibodies against the strains of virus that are in the vaccine. The antibodies are effective for six to 12 months. When you are exposed to the virus, the antibodies will help to keep you from getting sick. If you do get the flu, you may not be as sick.

When it should not be used:

VAXIGRIP® should not be used in the following situations:

Do not give VAXIGRIP® to anyone who has ever had a severe allergic reaction to:

- egg or egg products
- chicken protein
- any component of VAXIGRIP® or its container.

What the medicinal ingredient is:

Each 0.5 mL dose of VAXIGRIP® contains killed split viruses from three strains of influenza virus for the 2013-2014 season. The viruses in VAXIGRIP® are:

- A/California/7/2009 (H1N1)pdm09-like strain
- A(H3N2) strain antigenically like the cell-propagated prototype strain A/Victoria/361/2011
- B/Massachusetts/2/2012-like strain.

What the important nonmedicinal ingredients are:

Thimerosal (only in the multidose vial), sodium phosphate-buffered, isotonic sodium chloride solution, formaldehyde, Triton® X-100, sucrose and neomycin

What dosage forms it comes in:

Individual doses in a prefilled syringe or a vial that contains enough vaccine for many doses.

WARNINGS AND PRECAUTIONS

VAXIGRIP® will only protect against the strains of flu virus contained in the vaccine or those that are closely related.

VAXIGRIP® will not protect against any other strains of flu virus.

If you have any of the following conditions, talk to your doctor, nurse or pharmacist BEFORE you use VAXIGRIP®:

- **Diseases of the immune system or who are having treatment that affects the immune system.** The vaccine may provide you with a lower level of protection than it does for people with healthy immune systems.
- **A bleeding disorder or taking blood-thinning medications.** Tell the person giving you the injection about your condition. There is a risk of excessive bleeding at the injection site if it is not done carefully.
- **Pregnant or breast-feeding women.** It is important that you understand the risks and benefits of vaccination. VAXIGRIP® should be given to a pregnant or nursing woman only if it is clearly needed. Tell the person giving you the injection if you are pregnant or breast-feeding.
- **Allergy to egg protein or to any component of the vaccine or the container.**
- **Fever or serious illness.** Wait until the person is better before giving the flu shot. A person who has a mild illness (such as a mild cold) may have the flu shot. Ask your doctor, nurse or pharmacist for advice.

- **A history of Guillain-Barré syndrome (GBS) within 6 weeks of a previous influenza vaccination.**

The use of VAXIGRIP® in infants under 6 months of age is not recommended.

As with all vaccines, VAXIGRIP® does not protect 100% of people immunized.

INTERACTIONS WITH THIS MEDICATION

VAXIGRIP® must not be mixed with other vaccines or medicinal products in the same syringe.

PROPER USE OF THIS MEDICATION

Usual dose:

For children 6 to 35 months - recommended dose is 0.25 mL or 0.5 mL. The National Advisory Committee on Immunization (NACI) now recommends that children 6 to 35 months of age should be given a full dose (0.5 mL).

For persons 3 years or older - recommended dose is 0.5 mL.

Children under 9 years of age who have not received a previous vaccination - 2 doses are required 4 weeks apart. The second dose is not needed if the child received one or more doses of influenza vaccine in a previous season.

For adults and children older than 1 year, inject the vaccine into the deltoid (shoulder) muscle.

For infants and children less than 1 year inject the vaccine into the mid-thigh muscle.

Overdose:

In case of drug overdose, contact a health care practitioner, hospital emergency department or regional Poison Control Centre immediately, even if there are no symptoms.

Missed Dose: If a child's second dose is missed, it can be given at any time.

SIDE EFFECTS AND WHAT TO DO ABOUT THEM

A vaccine, like any medicine, may cause serious problems, such as severe allergic reactions. The risk of VAXIGRIP® causing serious harm is extremely small. The small risks associated with VAXIGRIP® are much less than the risks associated with getting the disease against which it protects.

The flu vaccine cannot cause influenza because it does not contain any live virus. The most common side effect is soreness where you got the injection. It may last a couple of days. You might also notice fever, fatigue and

muscle aches within 6 to 12 hours after your shot. These side effects may last a day or two.

Severe allergic reactions to the flu shots are very rare. A very rare but possible side effect of influenza vaccination is Guillain-Barré syndrome (GBS). This is an autoimmune disease that attacks the nervous system. GBS causes weakness and abnormal sensations. Most patients recover fully. This is not a complete list of side effects. Talk to your doctor or nurse before receiving VAXIGRIP®.

Tell your doctor, nurse or pharmacist as soon as possible if you do not feel well after having VAXIGRIP®.

For any unexpected effects after having VAXIGRIP®, contact your doctor, nurse or pharmacist.

HOW TO STORE IT

Store in a refrigerator at 2° to 8°C (35° to 46°F). **Do not freeze.** Protect from light. Discard product if it has been exposed to freezing.

Do not use vaccine after expiration date.

Discard multidose vials of VAXIGRIP® 7 days after first use.

Keep VAXIGRIP® out of children's reach.

REPORTING SUSPECTED SIDE EFFECTS

To monitor vaccine safety, the Public Health Agency of Canada collects case reports on adverse events following immunization.

For Health Care Professionals:

If a patient experiences an adverse event following immunization, please complete the appropriate Adverse Events following Immunization (AEFI) Form and send it to your local Health Unit in **your province/territory**.

For the General Public:

Should your child experience an adverse event following immunization, please ask your doctor, nurse, or pharmacist to complete the Adverse Events following Immunization (AEFI) Form.

If you have any questions or have difficulties contacting your local health unit, please contact Vaccine Safety Section at Public Health Agency of Canada:

By toll-free telephone: (1-866-844-0018)

By toll-free fax: (1-866-844-5931)

By email: caefi@phac-aspc.gc.ca

Web: <http://www.phac-aspc.gc.ca/im/vs-sv/index-eng.php>

By regular mail:
The Public Health Agency of Canada
Vaccine Safety Section
130 Colonnade Road
A/L 6502A
Ottawa, Ontario
K1A 0K9

NOTE: Should you require information related to the management of the side effect, please contact your health-care provider before notifying the Public Health Agency of Canada. The Public Health Agency of Canada does not provide medical advice.

MORE INFORMATION

This document plus the full product monograph, prepared for health professionals can be found at: <http://www.sanofipasteur.ca> or by contacting the vaccine producer, Sanofi Pasteur Limited, 1755 Steeles Avenue West, Toronto, Ontario, M2R 3T4.

Phone: 1-888-621-1146 or 416-667-2779.

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