1 NAME OF THE MEDICINAL PRODUCT

VAXIGRIP, suspension for injection in prefilled syringe.
Influenza vaccine (split virion, inactivated).

2 QUALITATIVE AND QUANTITATIVE COMPOSITION

Split influenza virus*, inactivated containing antigens equivalent to the following strains:

- A/California/7/2009 (H1N1)pdm09– like virus ….15 micrograms HA**
- A/Hong Kong/4801/2014 (H3N2) -like virus 15 micrograms HA**
- B/Brisbane/60/2008 –like virus 15 micrograms HA**

per 0.5 ml dose.

* propagated in fertilized hens' eggs from healthy chicken flocks
** haemagglutinin

This vaccine complies with the WHO recommendations (Northern Hemisphere) and EU decision for the 2016-2017 season.
For a full list of excipients, see section 6.1.

VAXIGRIP may contain traces of eggs, such as ovalbumin, traces of neomycin, of formaldehyde and of octoxinol-9, which are used during the manufacturing process (see Section 4.3.).

3 PHARMACEUTICAL FORM

Suspension for injection in prefilled syringe.
The vaccine, after shaking gently, is a slightly whitish and opalescent liquid.

4 CLINICAL PARTICULARS

4.1 Therapeutic indications

For the prevention of influenza.
VAXIGRIP is indicated in adults and children from 6 months of age.

The use of VAXIGRIP should be based on official recommendations.

4.2 Posology and method of administration

Posology

Adults: 0.5 ml.

Paediatric population

Children aged 36 months onwards: 0.5 ml.
Children aged 6 to 35 months: 0.25 ml. Clinical data are limited. See Section 6.6 for more information on administration of the 0.25 ml dose.
A 0.5 ml dose may be given, if this is required by national recommendations.
For children aged less than 9 years who have not previously been vaccinated, a second dose should be given after an interval of at least 4 weeks.
Children aged less than 6 months: the safety and efficacy of VAXIGRIP in children aged less than 6 months have not been established. No data are available.

Method of administration

To be administered via intramuscular or deep subcutaneous route.
For adults and children from 36 months of age: the preferred site for intramuscular injection is the deltoid muscle.
For children from 12 to 35 months of age: the preferred site for intramuscular injection is the anterolateral aspect of the thigh (or the deltoid muscle if muscle mass is adequate).
For children from 6 to 11 months of age: the preferred site for intramuscular injection is the anterolateral aspect of the thigh.
Precautions to be taken before handling or administering the medicinal product.
For instructions for preparation of the medicinal product before administration, see Section 6.6.

4.3 Contraindications

Hypersensitivity to the active substances, to any of the excipients listed in Section 6.1 or to any component that may be present as traces such as eggs, (ovalbumin, chicken proteins),neomycin, formaldehyde and octoxinol -9.
Immunisation shall be postponed in patients with febrile illness or acute disease.

4.4 Special warnings and precautions for use

As with all injectable vaccines, appropriate medical treatment and supervision should always be readily available in case of an anaphylactic reaction , although rare,following the administration of the vaccine.
VAXIGRIP should under no circumstances be administered intravascularly.

As with other vaccines administered intramuscularly the vaccine should be administered with caution to subjects with thrombocytopenia or bleeding disorders since bleeding may occur following intramuscular administration to these subjects.
As with any vaccine, vaccination with VAXIGRIP may not protect 100% of susceptible subjects
Antibody response in patients with congenital or acquired immunosuppression may be insufficient.
Interference with serological testing

4.5 Interaction with other medicinal products and other forms of interaction

VAXIGRIP may be given at the same time as other vaccines. However injections
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.
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 disproves the false-positive ELISA test results. The transient false positive reactions could be due to the IgM response by the vaccine.

4.6 Pregnancy and lactation

Pregnancy

Inactivated influenza vaccines can be used in all stages of pregnancy. Larger datasets on safety are available for the second and third trimester, compared with the first trimester, however, data from worldwide use of Inactivated influenza vaccines do not indicate any adverse foetal and maternal outcomes attributable to the vaccine.

Breastfeeding

VAXIGRIP may be used during Breastfeeding

Fertility

No fertility data are available.

4.7 Effects on ability to drive and use machines

The vaccine has no or negligible influence on the ability to drive and use machines.

4.8 Undesirable effects

a. Summary of the safety profile

In recent clinical trials approximately 10,000 subjects from 6 months of age received VAXIGRIP.
Depending on immunization history and the age of the children, the dosage and the number of doses were different (see Paediatric population in subsection b.
Tabulated list of adverse reactions).
Solicited reactions usually occurred within the first 3 days following VAXIGRIP, resolved spontaneously within 1 to 3 days after onset. Most of the solicited adverse reactions were of mild to moderate intensity.

The most frequently reported solicited adverse reaction within 7 days following injection of VAXIGRIP was injection site pain in all population except in children aged 6 to 35 months in whom irritability was the most frequently reported.
The most frequently reported solicited systemic adverse reaction within 7 days following injection of VAXIGRIP was headache in adults, elderly and children aged 9 to 17 years and malaise in children aged 3 to 8 years.
Solicited adverse reactions were generally less frequent in elderly than in adults.

b. Tabulated list of adverse reactions

The data below summarize the frequencies of the adverse reactions that were recorded following vaccination with VAXIGRIP during clinical trials and worldwide post-marketing experience.

Adverse events are ranked under headings of frequency using the following convention:
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);
Not known: cannot be estimated from available data.

Adult and elderly

ADVERSE REACTIONS	FREQUENCY
Blood and Lymphatic System Disorders	
Lymphadenopathy [1]	Uncommon
Transient thrombocytopenia	Not known
Immune System Disorders	
Allergic reactions such as swelling face [6], urticaria [6], prurit, generalized prurit [6], erythema, generalized erythema [6], rash	Rare
Severe allergic reactions such as dyspnoea, angioedema, shock	Not known
Nervous System Disorders	
Headache	Very common
Dizziness [3], somnolence [2]	Uncommon
Hypoaesthesia [2], paresthesia, neuralgia [5], brachial radiculitis [3]	Rare
Convulsions, neurological disorders such as encephalomyelitis, neuritis, Guillain Barré syndrome	Not known
Vascular disorders	
Vasculitis such as Henoch-Schonlein purpura, with transient renal involvement in certain cases	Not known
Gastrointestinal Disorders	
Diarrhoea, nausea [2]	Uncommon
Skin and Subcutaneous System Disorders	
Sweating increased	Common
Musculoskeletal and Connective Tissue Disorders	
Myalgia	Very common
Arthralgia	Common
General Disorders and Administration Site Conditions	
Injection site pain/tenderness, injection site erythema/redness, injection site oedema/swelling, injection site induration, malaise [4], asthenia [4], injection site pruritus [4]	Very common
Fever, shivering/rigors, injection site ecchymosis	Common
Flu-like syndrome [2], injection site warmth [2], injection site discomfort [2]	Uncommon

[1] Rare in elderly
[2] Reported during clinical trials in adults
[3] Reported during clinical trials in elderly
[4] Common in elderly
[5] Not known in adults
[6] Not known in elderly

Paediatric population

Depending on immunization history, children aged 6 months to 8 years received one or two doses of VAXIGRIP. Children aged 6 to 35 months received the 0.25 ml formulation, and children from 3 years of age received the 0.5 ml formulation.

- Children/adolescents aged 3 to 17 years:

The safety profile presented below is based on data from more than 300 children aged 3 to 8 years and around 70 children/adolescents aged 9 to 17 years.

In children aged 3 to 8 years, the most frequently reported solicited reactions within 7 days following injection of VAXIGRIP were as follows: injection site pain/tenderness (56.3%), malaise (27.3%), myalgia (25.5%) and injection site erythema/redness (23.4%).

In children/adolescents aged 9 to 17 years, the most frequently reported solicited reactions within 7 days following injection of VAXIGRIP were as follows: injection site pain/tenderness (54.5% to 70.6%), cephalalgia (22.4% to 23.6%), myalgia (12.7% to 17.6%) and injection site erythema/redness (5.5% to 17.6%).

The data below summarize the frequencies of the adverse reactions that were recorded in children/adolescents aged 3 to 17 years following vaccination with VAXIGRIP during clinical trials and worldwide post-marketing experience.

ADVERSE REACTIONS	FREQUENCY
Blood and Lymphatic System Disorders	
Lymphadenopathy [5]	Uncommon
Transient thrombocytopenia	Not known
Immune System Disorders	
Urticaria [5]	Uncommon
Allergic reactions such as pruritus, rash erythematous, dyspnoea, angioedema, shock	Not known
Nervous System Disorders	
Cephalalgia	Very common
Dizziness [2]	Common
Neuralgia, paresthesia, convulsions, neurological disorders, such as encephalomyelitis, neuritis and Guillain Barré syndrome	Not known
Vascular disorders	
Vasculitis such as Henoch-Schonlein purpura, with transient renal involvement in certain cases	Not known
Gastrointestinal Disorders	
Diarrhoea [1]	Uncommon
Musculoskeletal and Connective Tissue Disorders	
Myalgia	Very common
General Disorders and Administration Site Conditions	
Injection site pain/tenderness, injection site erythema/redness, injection site oedema/swelling, injection site induration [3], malaise	Very common
Fever, shivering/rigors [4], injection site ecchymosis, injection site discomfort [2], injection site pruritus	Common
Injection site warmth [3], injection site haemorrhage [1]	Uncommon

[1] Reported during clinical trials in children aged 3 to 8 years
[2] Reported during clinical trials in children/adolescents aged 9 to 17 years
[3] Common in children/adolescents aged 9 to 17 years
[4] Very common in children/adolescents aged 9 to 17 years
[5] Not known in children/adolescents aged 9 to 17 years

- Children aged 6 to 35 months:

The safety profile presented below is based on data from around 50 children aged 6 to 35 months.

In one clinical trial, the most frequently reported solicited reactions within 3 days following injection of VAXIGRIP were as follows: injection site pain (23.5%), irritability (23.5%), fever (20.6%) and abnormal crying (20.6%).

In another trial, the most frequently reported solicited reactions within 7 days following injection of VAXIGRIP were as follows:

irritability (60%), fever (50%), decreased appetite (35%) and abnormal crying (30%).

The data below summarize the frequencies of the adverse reactions that were recorded in children aged 6 to 35 months within 3 or 7 days following one or two 0.25 ml doses of VAXIGRIP during these two clinical trials and worldwide post-marketing experience:

ADVERSE REACTIONS	FREQUENCY
Blood and Lymphatic System Disorders	
Transient thrombocytopenia, lymphadenopathy	Not known
Immune System Disorders	
Urticaria	Not known
Allergic reactions such as pruritus, rash erythematous, dyspnoea, angioedema, shock	Not known
Metabolism and nutrition Disorders	
Decreased appetite, anorexia [1]	Very common
Psychiatric Disorders	
Crying abnormal, irritability	Very common
Insomnia [1]	Common
Nervous System Disorders	
Drowsiness	Very common
Paresthesia, convulsions, neurological disorders such as encephalomyelitis	Not known
Vascular disorders	
Vasculitis such as Henoch-Schonlein purpura, with transient renal involvement in certain cases	Not known
Gastrointestinal Disorders	
Diarrhoea [1]	Very common
Vomiting	Common
General Disorders and Administration Site Conditions	
Injection site pain/tenderness, injection site erythema/redness, injection site oedema/swelling, injection site induration, fever	Very common
Injection site pruritus [1], injection site ecchymosis [1]	Common

[1] Reported within 3 days after injection of VAXIGRIP

c. Other special populations

Although only a limited number of subjects with co-morbidities were enrolled, studies conducted in renal transplant patients, asthmatic patients, or children aged 6 months to 3 years with medical conditions being at especially high risk of developing serious flu-related complications showed no major differences in terms of safety profile of VAXIGRIP in these populations.

Reporting of suspected adverse reactions

Reporting suspected adverse reactions after authorisation of the medicinal product is important. It allows continued monitoring of the benefit/risk balance of the medicinal product.

Any suspected adverse events should be reported to the Ministry of Health according to the National Regulatorybyusinganonlineform http://forms.gov.il/globaldata/getsequence/getsequence.aspx?formType=AdversEffectMedic@moh. gov.il

4.9 Overdose

Cases of administration of more than the recommended dose (overdose) have been reported with VAXIGRIP. When adverse reactions were reported, the information was consistent with the known safety profile of VAXIGRIP described in Section 4.8.

5 PHARMACOLOGICAL PROPERTIES

5.1 Pharmacodynamic properties

Pharmacotherapeutic group: INFLUENZA VACCINE
ATC code: J07BB02
An antibody immune response is generally obtained within 2 to 3 weeks. The duration of postvaccinal induced immunity varies but is usually 6-12 months.

5.2 Pharmacokinetic properties

Not applicable.

5.3 Preclinical safety data

Not applicable.

6 PHARMACEUTICAL PARTICULARS

6.1 List of excipients

Buffer solution:
- Sodium chloride
- Potassium chloride
- Disodium phosphate dihydrate
- Potassium dihydrogen phosphate
- Water for injections

6.2 Incompatibilities

In the absence of compatibility studies, this medicinal product must not be mixed with other medicinal products.

6.3 Shelf life

1 year.

6.4 Special precautions for storage

Store in a refrigerator (2°C – 8°C). Do not freeze. Keep the syringe in the outer carton in order to protect from light.

6.5 Nature and contents of container

0.5 ml of suspension in prefilled syringe (type I glass) with attached needle, equipped with a plunger stopper (elastomer chlorobromobutyl or chlorobutyl or bromobutyl) – pack size of 1, 10, 20 or 50.
0.5 ml of suspension in prefilled syringe (type I glass) without needle, equipped with a plunger stopper (elastomer chlorobromobutyl or chlorobutyl or bromobutyl) and a tip cap (chlorobromobutyl) – pack size of 1, 10, 20 or 50.

6.6 Special precautions for disposal and other handling

Any unused product and or waste material should be disposed of in accordance with local requirements.
The vaccine should not be used if foreign particles are present in the suspension.
The vaccine should be brought to reach room temperature before use.
Shake before use. Inspect visually prior to administration.

Instructions for the administration of a dose of 0.25 ml in children aged 6 to 35 months
When one dose of 0.25 ml is indicated, in order to eliminate half of the volume of the 0.5 ml syringe: the syringe should be held in an upright position and the plunger stopper should be pushed until it reaches the fine black line printed on the syringe. The remaining volume of 0.25 ml should be injected. See also Section 4.2.

Manufacturer:
SANOFI PASTEUR SA 2, avenue Pont Pasteur 69007 Lyon, France

License Holder:
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