# PRODUCT INFORMATION

## VaxigripTetra, suspension for injection in pre-filled syringe

## Quadrivalent influenza vaccine (split virion, inactivated)

## ENGLISH TRANSLATION

## SOUTHERN HEMISPHERE

| French MA approval | Modified sections |
|---|---|
| 11 August 2016 | Full text |
| 13 July 2017 | Full text – Strain variation |
| 31 January 2018 | Full text – variation « 6-35 months » + HQ address and Template 10 changes |
| 07 August 2018 | Full text – Strain variation |
| 27 May 2019 | Full document – « Maternal immunisation » variation |
| 01 August 2019 | Full text – Strain variation |
| 06 August 2020 | Full text – Strain variation |
| 8 March 2021 | Full text – «Deletion of black symbol and explanatory statements for medicinal products in the list of medicinal products that are subject to additional monitoring» variation + Renewal |
| 05 August 2021 | Full text – Strain variation |
| 02 June 2022 | Full text – Strain variation |

Differences between French MA and SH Product Information (other than strains and year):

| French MA - NH | Product Information - SH |
|---|---|
| **RCP** | |
| **Section 2.** | |
| This vaccine complies with the WHO recommendations (Northern Hemisphere) and European Union decision for the 2022/2023 season. | This vaccine complies with the WHO recommendations (Southern Hemisphere) for the 2023 season. |
| **Section 9.** | |
| [to be completed later by the holder] | Date of first authorisation: 11 August 2016<br>Renewal date of the authorisation: 21 June 2021 |
| **Section 10.** | |
| [to be completed later by the holder] | 02 June 2022 |
| **LABELLING - OUTER PACKAGING** | |
| **Section 5.** | |
| <<Scan here QR code to be included or > visit https://vaxigriptetra-nh.info.sanofi > | **/** |
| **LEAFLET** | |
| **Section 1.** | |
| The greatest risk of catching flu is during the coldest months, between October and March. | The greatest risk of catching flu is during the coldest months. |
| **Section 6.** | |
| This vaccine complies with the WHO (World Health Organisation) recommendations (Northern Hemisphere) and European Union decision for the 2022/2023 season. | This vaccine complies with the WHO (World Health Organisation) recommendations (Southern Hemisphere) for the 2023 season. |
| **Names of the medicinal product in the Member States of the European Economic Area**<br>**This medicinal product is authorised in the Member States of the European Economic Area under the following names: In accordance with local requirements.**<br>[To be completed later by the holder] | **Names of the medicinal product in the Member States of the European Economic Area**<br>**This medicinal product is authorised in the Member States of the European Economic Area under the following names: In accordance with local requirements.**<br>Not applicable. |
| **This leaflet was last revised in:**<br>[to be completed later by the holder]<br>**{month YYYY}.** | **This leaflet was last revised in:**<br>**06/2022.** |
| **Other**<br><Latest approved information on this product is available < by scanning the QR code on the outer carton with a smartphone or > on the following URL: https://vaxigriptetra-nh.info.sanofi ><br>Detailed information on this medicine is available on the website of ANSM (France). | **Other**<br>Detailed information on this medicine is available on the website of ANSM (France). |

# ANNEX I

# SUMMARY OF PRODUCT CHARACTERISTICS

## 1. NAME OF THE MEDICINAL PRODUCT

**VAXIGRIPTETRA, suspension for injection in pre-filled syringe**

**Quadrivalent influenza vaccine (split virion, inactivated)**

## 2. QUALITATIVE AND QUANTITATIVE COMPOSITION

Influenza virus (inactivated, split) of the following strains*:

A/Sydney/5/2021 (H1N1)pdm09 - like strain (A/Sydney/5/2021, SAN-013) .....
.....15 micrograms HA**

A/Darwin/9/2021 (H3N2) - like strain (A/Darwin/9/2021, IVR-228) .....
.....15 micrograms HA**

B/Austria/1359417/2021 - like strain (B/Michigan/01/2021, wild type) .....
.....15 micrograms HA**

B/Phuket/3073/2013 - like strain (B/Phuket/3073/2013, wild type) .....
.....15 micrograms HA**

For one 0.5 mL dose

* propagated in fertilised hens' eggs from healthy chicken flocks

** haemagglutinin

This vaccine complies with the WHO recommendations (Southern Hemisphere) for the 2023 season.

For the full list of excipients, see section 6.1.

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

## 3. PHARMACEUTICAL FORM

Suspension for injection in pre-filled syringe.

The vaccine, after shaking gently, is a colourless opalescent liquid.

## 4. CLINICAL PARTICULARS

### 4.1. Therapeutic indications

VAXIGRIPTETRA is indicated for the prevention of influenza disease caused by the two influenza A virus subtypes and the two influenza B virus types contained in the vaccine for:

- active immunisation of adults, including pregnant women, and children from 6 months of age.
- passive protection of infants less than 6 months of age and born to women vaccinated during pregnancy (see Sections 4.4, 4.6 and 5.1).

The use of VAXIGRIPTETRA should be based on official recommendations.

### 4.2. Posology and method of administration

**Posology**

Based on clinical experience with the trivalent vaccine, annual revaccination with influenza vaccine is recommended given the duration of immunity provided by the vaccine and because circulating strains of influenza virus might change from year to year.

Adults: one dose of 0.5 mL.

*Paediatric population*

- Children from 6 months to 17 years of age: one dose of 0.5 mL.
  - For children less than 9 years of age who have not previously been vaccinated, a second dose of 0.5 mL should be given after an interval of at least 4 weeks.
- Infants less than 6 months of age: the safety and efficacy of VAXIGRIPTETRA administration (active immunisation) have not been established. No data are available.
  - Regarding passive protection, one 0.5 mL dose administered to a pregnant woman may protect infants from birth to almost 6 months of age; however, not all infants may be protected (see section 5.1).

**Method of administration**

The vaccine should be given by intramuscular or subcutaneous injection.

The preferred site for intramuscular injection is the anterolateral aspect of the thigh (or the deltoid muscle if muscle mass is adequate) in children 6 months through 35 months of age, or the deltoid muscle in children from 36 months of age and adults.

*Precautions to be taken before handling or administering the medicinal product*

For instructions on 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.

Vaccination should be postponed in case of moderate or severe febrile disease or acute disease.

## 4.4. Special warnings and precautions for use

Traceability

In order to improve the traceability of biological medicinal products, the name and the batch number of the administered product should be clearly recorded.

As with all injectable vaccines, appropriate medical treatment and supervision should always be readily available in case of an anaphylactic reaction following the administration of the vaccine.

VAXIGRIPTETRA 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 a bleeding disorder since bleeding may occur following an intramuscular administration to these subjects.

Syncope (fainting) can occur following, or even before, any vaccination as a psychogenic response to the needle injection. Procedures should be in place to prevent injury from fainting and manage syncopal reactions.

VAXIGRIPTETRA is intended to provide protection against those strains of influenza virus from which the vaccine is prepared.

As with any vaccine, vaccination with VAXIGRIPTETRA may not protect all vaccinees.

Regarding passive protection, not all infants less than 6 months of age born to women vaccinated during pregnancy may be protected (see section 5.1).

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

*Interference with serological testing*

See section 4.5.

**VAXIGRIPTETRA contains potassium and sodium**

This vaccine contains less than 1 mmol potassium (39 mg) and less than 1 mmol sodium (23 mg) per dose, that is to say it is essentially “potassium-free” and “sodium-free”.

## 4.5. Interaction with other medicinal products and other forms of interaction

No interaction studies have been performed with VAXIGRIPTETRA.

VAXIGRIPTETRA can be given at the same time as other vaccines, based on clinical experience with Vaxigrip. Separate injection sites and separate needles should be used in case of concomitant administration.

The immunological response may be reduced 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 results could be due to the IgM response by the vaccine.

## 4.6. Fertility, pregnancy and lactation

**Pregnancy**

Pregnant women are at high risk of influenza complications, including premature labour and delivery, hospitalisation, and death: pregnant women should receive an influenza vaccine.

VAXIGRIPTETRA can be used in all stages of pregnancy.

Larger datasets on safety of inactivated influenza vaccines are available for the second and third trimesters, than for the first trimester. Data from worldwide use of inactivated influenza vaccines, including VAXIGRIPTETRA and Vaxigrip (trivalent inactivated influenza vaccine), do not indicate any adverse foetal and maternal outcomes attributable to the vaccine. This is consistent with results observed in one clinical study where VAXIGRIPTETRA and Vaxigrip were administered in pregnant women during the second or third trimester (230 exposed pregnancies and 231 live births for VAXIGRIPTETRA and 116 exposed pregnancies and 119 live births for Vaxigrip).

Data from four clinical studies with the trivalent inactivated influenza vaccine (Vaxigrip) administered in pregnant women during the second or third trimester (more than 5,000 exposed pregnancies and more than 5,000 live births followed up to approximately 6 months post-partum) do not indicate any adverse foetal, newborn, infant and maternal outcomes attributable to the vaccine.

In clinical studies conducted in South Africa and Nepal, there were no significant differences between the Vaxigrip and placebo groups with regards to foetal, newborn, infant and maternal outcomes (including miscarriage, stillbirth, premature birth, low birth weight).

In a study conducted in Mali, there were no significant differences between the Vaxigrip and control vaccine (quadrivalent meningococcal conjugate vaccine) groups with regards to prematurity rate, stillbirth rate and low birth weight/small for gestational age rate.

For additional information, see Sections 4.8 and 5.1.

One animal study with VAXIGRIPTETRA did not indicate direct or indirect harmful effects with respect to pregnancy, embryo-foetal development or early post-natal development.

**Breastfeeding**

VAXIGRIPTETRA may be used during breastfeeding.

**Fertility**

There are no fertility data available in Humans. One animal study with VAXIGRIPTETRA did not indicate harmful effects on female fertility.

## 4.7. Effects on ability to drive and use machines

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

## 4.8. Undesirable effects

**Summary of the safety profile**

The safety of VAXIGRIPTETRA was assessed in six clinical trials in which 3,040 adults from 18 to 60 years of age, 1,392 elderly over 60 years of age and 429 children from 9 to 17 years of age received one dose of VAXIGRIPTETRA, 884 children from 3 to 8 years of age received one or two doses of VAXIGRIPTETRA depending on their influenza vaccination history and 1614 children from 6 to 35 months of age received two doses (0.5 ml) of VAXIGRIPTETRA.

Most reactions usually occurred within the first 3 days following vaccination, resolved spontaneously within 1 to 3 days after onset. The intensity of these reactions was mild.

The most frequently reported adverse reaction after vaccination, in all populations, including the whole group of children from 6 to 35 months of age, was injection site pain (between 52.8% and 56.5% in children from 3 to 17 years of age and in adults, 26.8% in children from 6 to 35 months of age and 25.8% in elderly). In subpopulation of children less than 24 months of age, irritability (32.3%) was the most frequently reported adverse reaction.
In subpopulation children from 24 to 35 months of age, malaise (26.8%) is the most frequently reported adverse reaction.

The other most frequently reported adverse reactions after vaccination were:

- In adults: headache (27.8%), myalgia (23%) and malaise (19.2%),
- In elderly: headache (15.6%) and myalgia (13.9%),
- In children from 9 to 17 years of age: myalgia (29.1%), headache (24.7%), malaise (20.3%) and injection site swelling (10.7%),
- In children from 3 to 8 years of age: malaise (30.7%), myalgia (28.5%), headache (25.7%), injection site swelling (20.5%), injection site erythema (20.4%), injection site induration (16.4%), shivering (11.2%).
- For all children from 6 to 35 months of age: fever (20.4%) and injection site erythema (17.2%),
- In children less than 24 months of age: appetite lost (28.9%), crying abnormal (27.1%), vomiting (16.1%) and drowsiness (13.9%),
- In children from 24 months to 35 months of age: headache (11.9%) and myalgia (11.6%).

Adverse reactions were generally less frequent in the elderly than in adults and children.

**Tabulated summary of adverse reactions**

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

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): adverse reactions have been spontaneously reported following commercial use of VAXIGRIPTETRA. Because these reactions are reported voluntarily from a population of uncertain size, it is not possible to reliably estimate their frequency.

Within each frequency grouping, the adverse reactions are presented in decreasing order of seriousness.

*Adults and elderly*

The safety profile presented below is based on:

- data from 3,040 adults from 18 to 60 years of age and 1,392 elderly over 60 years of age.
- data from worldwide post-marketing surveillance (*).

| ADVERSE REACTIONS | FREQUENCY |
|---|---|
| ***Blood and lymphatic system disorders*** | |
| Lymphadenopathy (1) | Uncommon |
| ***Immune system disorders*** | |
| Hypersensitivity (1), allergic reactions such as angioedema (1), dermatitis allergic (1), pruritus generalised (1), urticaria (1), pruritus (2), erythema | Rare |
| Anaphylactic reactions | Not known* |
| ***Nervous system disorders*** | |
| Headache | Very common |
| Dizziness (3) | Uncommon |
| Paraesthesia, somnolence | Rare |
| ***Vascular disorders*** | |
| Hot flush (4) | Uncommon |
| ***Respiratory, thoracic and mediastinal disorders*** | |
| Dyspnoea (1) | Rare |
| ***Gastrointestinal disorders*** | |
| Diarrhoea, nausea (5) | Uncommon |
| ***Skin and subcutaneous tissue disorders*** | |
| Hyperhidrosis | Rare |
| ***Musculoskeletal and connective tissue disorders*** | |
| Myalgia | Very common |
| Arthralgia (1) | Rare |
| ***General disorders and administration site conditions*** | |
| Malaise (6)<br>Injection site pain | Very common |
| Shivering, fever (2)<br>Injection site erythema, injection site swelling, injection site induration | Common |
| Fatigue<br>Injection site ecchymosis, injection site pruritus, injection site warmth | Uncommon |
| Asthenia, flu-like illness<br>Injection site discomfort (1) | Rare |

(1) In adults (2) Uncommon in elderly (3) Rare in adults
(4) In elderly (5) Rare in elderly (6) Common in elderly

*Paediatric population*

The safety profile presented below is based on:

- data from 429 children from 9 to 17 years of age who received one dose of VAXIGRIPTETRA and from 884 children from 3 to 8 years of age who received one or two doses of VAXIGRIPTETRA depending on their influenza vaccination history.
- data from worldwide post-marketing surveillance (*).

| ADVERSE REACTIONS | FREQUENCY |
|---|---|
| ***Blood and lymphatic system disorders*** | |
| Thrombocytopenia (1) | Uncommon |
| ***Immune system disorders*** | |
| Allergic including anaphylactic reactions | Not known* |
| ***Psychiatric disorders*** | |
| Moaning (2), restlessness (2) | Uncommon |
| ***Nervous system disorders*** | |
| Headache | Very common |
| Dizziness (2) | Uncommon |
| ***Gastrointestinal disorders*** | |
| Diarrhoea, vomiting (2), abdominal pain upper (2) | Uncommon |
| ***Musculoskeletal and connective tissue disorders*** | |
| Myalgia | Very common |
| Arthralgia (2) | Uncommon |
| ***General Disorders and administration site conditions*** | |
| Malaise, shivering (3)<br>Injection site pain, injection site swelling, injection site erythema (3), injection site induration (3) | Very common |
| Fever<br>Injection site ecchymosis | Common |
| Fatigue (2)<br>Injection site warmth (2), injection site pruritus (4) | Uncommon |

(1) Reported in one child of 3 years of age (2) Reported in children from 3 to 8 years of age
(3) Common in children from 9 to 17 years of age (4) Reported in children from 9 to 17 years of age

The safety profile presented below is based on:

- data from 1,614 children from 6 to 35 months of age who received two doses of VAXIGRIPTETRA.
- data from worldwide post-marketing surveillance (*).

| ADVERSE REACTIONS | FREQUENCY |
|---|---|
| ***Immune System Disorders*** | |
| Hypersensitivity | Uncommon |
| Allergic reactions such as pruritus generalised, rash papular | Rare |
| Anaphylactic reactions | Not known* |
| ***Nervous System Disorders*** | |
| Headache [(1)] | Very common |
| ***Gastrointestinal Disorders*** | |
| Vomiting [(2)] | Very common |
| Diarrhoea | Uncommon |
| ***Musculoskeletal and Connective Tissue Disorders*** | |
| Myalgia [(3)] | Very common |
| ***General Disorders and Administration Site Conditions*** | |
| Irritability [(4)], appetite lost [(4)], crying abnormal [(5)], malaise [(3)], fever, drowsiness [(5)]<br>Injection site pain/tenderness, injection site erythema | Very common |
| Shivering [(1)]<br>Injection site induration, injection site swelling, injection site ecchymosis | Common |
| Influenza like illness<br>Injection site rash, injection site pruritus | Rare |

[(1)] Reported in children ≥ 24 months of age
[(2)] Uncommon in children ≥ 24 months of age
[(3)] Rare in children < 24 months of age
[(4)] Rare in children ≥ 24 months of age
[(5)] Reported in children < 24 months of age

In children from 6 months to 8 years of age, the safety profile of VAXIGRIPTETRA was similar after the first and the second injections with a trend of lower incidence of adverse reactions after the second injection compared to the first one in children from 6 to 35 months of age.

**Adverse events**

The following adverse events were reported following commercial use of Vaxigrip. A causal relationship with VAXIGRIPTETRA has not been established.

- ***Blood and lymphatic system disorders***

Transient thrombocytopenia [(1)], lymphadenopathy [(1)].

- ***Nervous system disorders***

Paraesthesia [(1)], Guillain-Barré Syndrome (GBS), neuritis, neuralgia, convulsions, encephalomyelitis.

- ***Vascular disorders***

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

[(1)] These adverse events were reported during clinical trials only in some age groups (see Tabulated summary of adverse reactions).

**Other special populations**

The safety profile of VAXIGRIPTETRA observed in a limited number of subjects with co-morbidities enrolled in the clinical studies does not differ from the one observed in the overall population. In addition, studies conducted with Vaxigrip in renal transplant patients, and asthmatic patients showed no major differences in terms of safety profile of Vaxigrip in these populations.

*Pregnant women*

In clinical studies conducted in pregnant women in South Africa and Mali with Vaxigrip (see Sections 4.6 and 5.1), the frequencies of local and systemic solicited reactions reported within 7 days following administration of the vaccine were consistent with those reported for the adult population during clinical studies conducted with Vaxigrip. In the South Africa study, local reactions were more frequent in the Vaxigrip group than in the placebo group in both HIV-negative and HIV-positive cohorts. There were no other significant differences in solicited reactions between Vaxigrip and placebo groups in both cohorts.

In one clinical study conducted in pregnant women in Finland with VAXIGRIPTETRA (see sections 4.6 and 5.1), frequencies of local and systemic solicited reactions reported within 7 days following administration of VAXIGRIPTETRA were consistent with those reported for the adult population (with the exception of pregnant women) during clinical studies conducted with VAXIGRIPTETRA even though higher for some adverse reactions (injection site pain, malaise, shivering, headache, myalgia).

**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. Healthcare professionals are asked to report any suspected adverse reactions via the national reporting system: “Agence nationale de sécurité du médicament et des produits de santé (ANSM) et réseau des Centres Régionaux de Pharmacovigilance - Site internet : www.signalement-sante.gouv.fr.”

## 4.9. Overdose

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

# 5. PHARMACOLOGICAL PROPERTIES

## 5.1. Pharmacodynamic properties

**Pharmacotherapeutic group: INFLUENZA VACCINE, ATC code: J07BB02.**

**Mechanism of action**

VAXIGRIPTETRA provides active immunisation against four influenza virus strains (two A subtypes and two B types) contained in the vaccine.

VAXIGRIPTETRA induces humoral antibodies against the haemagglutinins within 2 to 3 weeks. These antibodies neutralise influenza viruses.

Specific levels of haemagglutination-inhibition (HAI) antibody titre post-vaccination with inactivated influenza virus vaccines have not been correlated with protection from influenza illness but the HAI antibody titres have been used as a measure of vaccine activity. In some human challenge studies, HAI antibody titres of ≥1:40 have been associated with protection from influenza illness in up to 50% of subjects.

Since influenza viruses constantly evolve, the virus strains selected in the vaccine are reviewed annually by the WHO.

Annual revaccination with VAXIGRIPTETRA has not been studied. However, based on clinical experience with the trivalent vaccine, annual influenza vaccination is recommended given the duration of immunity provided by the vaccine and because circulating strains of influenza virus change from year to year.

**Efficacy of VAXIGRIPTETRA**

*Paediatric population*

- Children from 6 to 35 months of age (active immunisation):

A randomized placebo controlled study was conducted in 4 regions (Africa, Asia, Latina America and Europe) over 4 influenza seasons, in more than 5,400 children from 6 to 35 months of age who received two doses (0.5 mL) of VAXIGRIPTETRA (N=2,722), or placebo (N=2,717) 28 days apart to assess VAXIGRIPTETRA efficacy for the prevention of laboratory-confirmed influenza illness caused by any strain A and/or B and caused by vaccine similar strains (as determined by sequencing).

Laboratory-confirmed influenza illness was defined as influenza like-illness (ILI) [occurrence of fever ≥ 38°C (that lasts at least 24 hours) concurrently with at least one of the following symptoms: cough, nasal congestion, rhinorrhoea, pharyngitis, otitis, vomiting, or diarrhoea], laboratory-confirmed by reverse transcriptase polymerase chain reaction (RT-PCR) and/or viral culture.

**Table 1: Influenza Attack Rates and VAXIGRIPTETRA Efficacy against laboratory-confirmed influenza illness in children from 6 to 35 months of age**

| | **VAXIGRIPTETRA (N=2,584)** | | **Placebo (N=2,591)** | | **Efficacy** |
|---|---|---|---|---|---|
| | **n** | **Influenza attack rate (%)** | **n** | **Influenza attack rate (%)** | **% (2-sided 95% CI)** |
| **Laboratory-confirmed influenza illness caused by:** | | | | | |
| **- Any influenza A or B type** | 122 | 4.72 | 255 | 9.84 | 52.03 (40.24; 61.66) |
| **- Viral strains similar to those contained in the vaccine** | 26 | 1.01 | 85 | 3.28 | 69.33 (51.93; 81.03) |

N: Number of children analysed (full set)
n: number of subjects fulfilling the item listed
CI: Confidence Interval

In addition, a predefined complementary analysis showed VAXIGRIPTETRA prevented 56.6% (95% CI: 37.0; 70.5) of severe laboratory-confirmed influenza illnesses due to any strain, and 71.7% (95% CI: 43.7; 86.9) of severe laboratory-confirmed influenza illnesses due to vaccine similar strains. Furthermore, subjects receiving VAXIGRIPTETRA were 59.2% (95% CI: 44.4; 70.4) less likely to experience a medically attended influenza illness than subjects receiving placebo.

Severe laboratory-confirmed influenza illnesses were defined as ILI laboratory-confirmed by RT-PCR and/or viral culture with at least one of the following items:

- fever > 39.5°C for subjects aged < 24 months or ≥ 39.0°C for subjects aged ≥ 24 months,
- and/or at least one significant ILI symptom which prevents daily activity (cough, nasal congestion, rhinorrhoea, pharyngitis, otitis, vomiting, diarrhoea),
- and/or one of the following events: acute otitis media, acute lower respiratory infection (pneumonia, bronchiolitis, bronchitis, croup), inpatient hospitalisation.

- Children from 3 to 8 years of age (active immunisation):

Based on immune responses observed in children from 3 to 8 years of age, the efficacy of VAXIGRIPTETRA in this population is expected to be at least similar to the efficacy observed in children from 6 to 35 months (see “Children from 6 to 35 months of age” above and “Immunogenicity of VAXIGRIPTETRA“ below).

- Infants less than 6 months of age born to women vaccinated during pregnancy (passive protection):

Infants less than 6 months of age are at high risk of influenza, resulting in high rates of hospitalisation; however, influenza vaccines are not indicated for active immunisation in this age group.

The efficacy in infants born to women who received a single 0.5 mL dose of VAXIGRIPTETRA during the second or third trimester of pregnancy has not been studied; however, the efficacy in infants born to women who received a single 0.5 mL dose of the trivalent inactivated influenza vaccine (Vaxigrip) during the second or third trimester of pregnancy has been demonstrated in clinical trials and can be extrapolated to VAXIGRIPTETRA.

The efficacy of the trivalent inactivated influenza vaccine (Vaxigrip) in infants born to women vaccinated during the first trimester of pregnancy has not been studied in these trials. If influenza vaccination is considered necessary during the first trimester of pregnancy, it should not be postponed (see section 4.6).

In randomised, controlled phase IV clinical studies conducted in Mali, Nepal and South Africa, approximately 5,000 pregnant women received Vaxigrip (trivalent influenza vaccine) and approximately 5,000 pregnant women received a placebo or control vaccine (quadrivalent meningococcal conjugate vaccine) during the second or third trimester of pregnancy. Vaccine efficacy against laboratory confirmed influenza illness in pregnant women was evaluated as a secondary endpoint in all three studies.

The studies conducted in Mali and South Africa demonstrated the efficacy of Vaxigrip for the prevention of influenza in pregnant women following vaccination during these trimesters of pregnancy (see table 2). In the study conducted in Nepal, the efficacy of Vaxigrip for the prevention of influenza in pregnant women following vaccination during these trimesters of pregnancy was not demonstrated.

**Table 2: Influenza Attack Rates and Vaxigrip Efficacy against laboratory-confirmed influenza Illness in pregnant women**

| | **Influenza Attack Rate (Any influenza A or B type) % (n/N)** | | **Vaxigrip Efficacy % (95% CI)** |
|---|---|---|---|
| | **Vaxigrip** | **Control*** | |
| **Mali** | 0.5 (11/2,108) | 1.9 (40/2,085) | 70.3 (42.2; 85.8) |
| | **Vaxigrip** | **Placebo** | |
| **South Africa** | 1.8 (19/1,062) | 3.6 (38/1,054) | 50.4 (14.5; 71.2) |

* Meningococcal vaccine
N: Number of pregnant women included in analysis
n: number of subjects with laboratory confirmed infuenza illness
CI: Confidence Interval

In the same randomised, controlled, phase IV clinical studies conducted in Mali, Nepal and South Africa, 4,530 of the 4,898 (92%) infants born to women who received Vaxigrip (trivalent influenza vaccine) during the second or third trimester of pregnancy, and 4,532 of the 4,868 (93%) infants born to pregnant women who received a placebo or control vaccine (quadrivalent meningococcal conjugate vaccine) during the second or third trimester of pregnancy (see table 3) were followed-up until approximately 6 months of age.

These studies confirmed the efficacy of Vaxigrip for the prevention of influenza in infants born to women vaccinated during these trimesters of pregnancy, from birth until approximately 6 months of age. Women in their first trimester of pregnancy were not included in these studies; the efficacy of Vaxigrip in infants born to women vaccinated during the first trimester of pregnancy could therefore not be evaluated.

**Table 3: Influenza Attack Rates and Vaxigrip Efficacy against Laboratory-confirmed influenza illness in infants born to women vaccinated during pregnancy**

| | Influenza Attack Rate (Any influenza A or B type) % (n/N) | | Vaxigrip Efficacy % (95% CI) |
|---|---|---|---|
| | **Vaxigrip** | **Control*** | |
| **Mali** | 2.4 (45/1,866) | 3.8 (71/1,869) | 37.3 (7.6; 57.8) |
| | **Vaxigrip** | **Placebo** | |
| **Nepal** | 4.1 (74/1,820) | 5.8 (105/1,826) | 30.0 (5; 48) |
| **South Africa** | 1.9 (19/1,026) | 3.6 (37/1,023) | 48.8 (11.6; 70.4) |

* Meningococcal vaccine
N: Number of infants included in the analysis
n: number of subjects with laboratory-confirmed influenza illness
CI: Confidence Interval

The efficacy data indicate a waning protection over time, after birth, of the infants born to women vaccinated during pregnancy.

In the trial conducted in South Africa, vaccine efficacy was higher in infants 8 weeks of age or younger (85.8% [95% CI: 38.3; 98.4]) and decreased over time; vaccine efficacy was 25.5% (95% CI: -67.9; 67.8) for infants from 8 to 16 weeks of age and 30.4% (95% CI: -154.9; 82.6) for infants from 16 to 24 weeks of age.

In the trial conducted in Mali, there is also a trend to higher efficacy of the trivalent inactivated influenza vaccine in infants during the first 4 months after birth, with lower efficacy within the 5$^{th}$ month and a marked fall during the 6$^{th}$ month where protection is no longer evident.

The prevention of influenza can only be expected if the infants are exposed to the strains included in the vaccine administered to the mother.

**Immunogenicity of VAXIGRIPTETRA**

Clinical studies performed in adults from 18 to 60 years of age, in elderly over 60 years of age, in children from 3 to 8 years of age and from 6 to 35 months assessed VAXIGRIPTETRA immune response for HAI Geometric mean antibody titre (GMT) at Day 21 (for adults) and at Day 28 (for children), HAI seroconversion rate (4-fold rise in reciprocal titre or change from undetectable [<10] to a reciprocal titre of ≥40), and HAI GMTR (post-/pre-vaccination titres).

One clinical study performed in adults from 18 to 60 years of age and in children from 9 to 17 years of age described the immune response of VAXIGRIPTETRA for HAI antibody GMT at Day 21. Another clinical study performed in children from 9 to 17 years of age described the immune response of VAXIGRIPTETRA.

One clinical study performed in pregnant women described the immune response of VAXIGRIPTETRA for HAI GMT at Day 21, HAI seroconversion rate, and HAI GMTR, after one dose administered during the second or third trimester of pregnancy. In this study, the transplacental transfer was evaluated using HAI GMTs of maternal blood, of cord blood and the ratio of cord blood/maternal blood, at delivery.

VAXIGRIPTETRA induced a significant immune response against the 4 influenza strains contained in the vaccine.

*Adults and elderly*

A total of 832 adults from 18 to 60 years of age and 831 elderly over 60 years of age were assessed in terms of immune response after one dose of VAXIGRIPTETRA.

Immunogenicity results are presented in the tables below:

**Table 4: Immunogenicity results in adults from 18 to 60 years of age and in elderly over 60 years of age**

| Antigen strain | 18 to 60 years of age<br>N=832 | Over 60 years of age<br>N=831 |
|---|---|---|
| **GMT (95% CI)** | | |
| **A (H1N1)** [a][b] | 608 (563; 657) | 219 (199; 241) |
| **A (H3N2)** | 498 (459; 541) | 359 (329; 391) |
| **B (Victoria)** | 708 (661; 760) | 287 (265; 311) |
| **B (Yamagata)** | 1715 (1607; 1830) | 655 (611; 701) |
| **SC % (95% CI)** [c] | | |
| **A (H1N1)** [a][b] | 64.1 (60.7; 67.4) | 45.6 (42.1; 49.0) |
| **A (H3N2)** | 66.2 (62.9; 69.4) | 47.5 (44.1; 51.0) |
| **B (Victoria)** | 70.9 (67.7; 74.0) | 45.2 (41.8; 48.7) |
| **B (Yamagata)** | 63.7 (60.3; 67.0) | 42.7 (39.3; 46.2) |
| **GMTR (95% CI)** [d] | | |
| **A (H1N1)** [a][b] | 9.77 (8.69; 11.0) | 4.94 (4.46; 5.47) |
| **A (H3N2)** | 10.3 (9.15; 11.5) | 5.60 (5.02; 6.24) |
| **B (Victoria)** | 11.6 (10.4; 12.9) | 4.61 (4.18; 5.09) |
| **B (Yamagata)** | 7.35 (6.66; 8.12) | 4.11 (3.73; 4.52) |

N= number of subjects with available data for the considered endpoint
GMT: Geometric Mean Titre; CI: Confidence Interval;
(a) N=833 for 18-60 years of age group
(b) N=832 for over 60 years of age group (c) SC: Seroconversion or significant increase: for subjects with a pre-vaccination titre <10 (1/dil), proportion of subjects with a post-vaccination titre ≥ 40 (1/dil) and for subjects with a pre-vaccination titre ≥10 (1/dil), proportion of subjects with a ≥four-fold increase from pre- to post-vaccination titre
(d) GMTR: Geometric mean of individual titre ratios (post-/pre-vaccination titres)

*Pregnant women and transplacental transfer*

A total of 230 pregnant women received VAXIGRIPTETRA during the second or third trimester of pregnancy (from 20 to 32 weeks of pregnancy).

Immunogenicity results by HAI method, in pregnant women 21 days after vaccination with VAXIGRIPTETRA are presented in table 5.

**Table 5: Immunogenicity results by HAI method in pregnant women, 21 days post-vaccination with VAXIGRIPTETRA**

| Antigen Strain | VAXIGRIPTETRA<br>N=216 |
|---|---|
| **GMT (95% CI)** | |
| **A (H1N1)*** | 525 (466; 592) |
| **A (H3N2)*** | 341 (286; 407) |
| **B1 (Victoria)*** | 568 (496; 651) |
| **B2 (Yamagata)*** | 993 (870; 1134) |

| Antigen Strain | VAXIGRIPTETRA<br>N=216 |
|---|---|
| **≥4-fold-rise n (%) [(a)]** | |
| **A (H1N1)*** | 38.0 (31.5; 44.8) |
| **A (H3N2)*** | 59.3 (52.4; 65.9) |
| **B1 (Victoria)*** | 61.1 (54.3; 67.7) |
| **B2 (Yamagata)*** | 59.7 (52.9; 66.3) |
| **GMTR (95% CI) [(b)]** | |
| **A (H1N1)*** | 3.81 (3.11; 4.66) |
| **A (H3N2)*** | 8.63 (6.85; 10.9) |
| **B1 (Victoria)*** | 8.48 (6.81; 10.6) |
| **B2 (Yamagata)*** | 6.26 (5.12; 7.65) |

* A/H1N1: A/Michigan/45/2015 (H1N1) pdm09-like virus;
A/H3N2: A/Hong Kong/4801/2014 (H3N2)-like virus;
B1: B/Brisbane/60/2008-like virus (B/Victoria lineage);
B2: B/Phuket/3073/2013-like virus (B/Yamagata lineage)
N= number of subjects with available data for the considered endpoint
GMT: Geometric Mean Titre; CI: Confidence Interval
(a) SC: Seroconversion or significant increase: for subjects with a pre-vaccination titre <10 (1/dil), proportion of subjects with a post-vaccination titre ≥40 (1/dil) and for subjects with a pre-vaccination titre ≥10 (1/dil), proportion of subjects with a ≥four-fold increase from pre- to post-vaccination titre
(b) GMTR: Geometric mean of individual titre ratios (post-/pre-vaccination titres)

Immunogenicity descriptive assessment by HAI method, at delivery, in blood sample of mother (BL03M) and in cord blood sample (BL03B) and of the transplacental transfer (BL03B/BL03M) are presented in table 6.

**Table 6: Immunogenicity descriptive assessment by HAI method of VAXIGRIPTETRA, at delivery**

| Antigen Strain | VAXIGRIPTETRA<br>N=178 |
|---|---|
| **BL03M (Maternal blood)<br>GMT (95% CI)** | |
| **A (H1N1)*** | 304 (265; 349) |
| **A (H3N2)*** | 178 (146; 218) |
| **B1 (Victoria)*** | 290 (247; 341) |
| **B2 (Yamagata)*** | 547 (463; 646) |
| **BL03B (Cord blood)<br>GMT (95% CI)** | |
| **A (H1N1)*** | 576 (492; 675) |
| **A (H3N2)*** | 305 (246; 379) |
| **B1 (Victoria)*** | 444 (372; 530) |
| **B2 (Yamagata)*** | 921 (772; 1099) |
| **Transplacental transfer: BL03B/BL03M§<br>GMT (95% CI)** | |
| **A (H1N1)*** | 1.89 (1.72; 2.08) |
| **A (H3N2)*** | 1.71 (1.56; 1.87) |
| **B1 (Victoria)*** | 1.53 (1.37; 1.71) |
| **B2 (Yamagata)*** | 1.69 (1.54; 1.85) |

N: number of subjects with available data for the considered endpoint: women who received VAXIGRIPTETRA, delivered at least 2 weeks after injection and with available cord blood and mother blood at the time of delivery.

* A/H1N1: A/Michigan/45/2015 (H1N1) pdm09-like virus;
A/H3N2: A/Hong Kong/4801/2014 (H3N2)-like virus;
B1: B/Brisbane/60/2008-like virus (B/Victoria lineage)
B2: B/Phuket/3073/2013-like virus (B/Yamagata lineage)
§ If a mother has X babies, her titres values is counted X times

At delivery, the higher level of antibodies in the cord sample compared to the maternal blood sample is consistent with transplacental antibody transfer from mother to the foetus following vaccination of women with VAXIGRIPTETRA during the second or third trimester of pregnancy.

These data are consistent with the passive protection demonstrated in infants from birth to approximately 6 months of age following vaccination of women during the second or third trimester of pregnancy with Vaxigrip in studies conducted in Mali, Nepal, and South Africa (see subsection Efficacy of VAXIGRIPTETRA).

*Paediatric population*

- Children from 9 to 17 years of age:

In a total of 429 children from 9 to 17 years of age who received one dose of VAXIGRIPTETRA, the immune response against the 4 strains contained in the vaccine was similar to the immune response induced in adults from 18 to 60 years of age.

- Children from 6 months to 8 years of age:

A total of 863 children from 3 to 8 years of age received either one or two doses of VAXIGRIPTETRA depending on their previous influenza vaccination history.

Children who received a one- or two-dose schedule of VAXIGRIPTETRA presented a similar immune response following the last dose of each schedule.

In addition to the VAXIGRIPTETRA efficacy, the immunogenicity of two 0.5 mL doses of VAXIGRIPTETRA was assessed 28 days after the last injection of VAXIGRIPTETRA by HAI method in 341 children from 6 to 35 months of age.

Immunogenicity results are presented in the table below:

**Table 7: Immunogenicity results in children from 6 months to 8 years of age**

| Antigen strain | 6-35 months of age<br>N=341 | 3-8 years of age<br>N=863 |
|---|---|---|
| **GMT (95% CI)** | | |
| **A (H1N1)** | 641 (547; 752) | 971 (896; 1052) |
| **A (H3N2)** | 1071 (925; 1241) | 1568 (1451; 1695) |
| **B (Victoria)** | 623 (550; 706) | 1050 (956; 1154) |
| **B (Yamagata)** [(a)] | 1010 (885; 1153) | 1173 (1,078; 1,276) |
| **SC % (95% CI)** [(b)] | | |
| **A (H1N1)** | 90.3 (86.7; 93.2) | 65.7 (62.4; 68.9) |
| **A (H3N2)** | 90.3 (86.7; 93.2) | 64.8 (61.5; 68.0) |
| **B (Victoria)** | 98.8 (97.0; 99.7) | 84.8 (82.3; 87.2) |
| **B (Yamagata)** [(a)] | 96.8 (94.3; 98.4) | 88.5 (86.2; 90.6) |
| **GMTR (95% CI)** [(c)] | | |
| **A (H1N1)** | 36.6 (30.8; 43.6) | 6.86 (6.24; 7.53) |
| **A (H3N2)** | 42.6 (35.1; 51.7) | 7.49 (6.72; 8.35) |
| **B (Victoria)** | 100 (88.9; 114) | 17.1 (15.5; 18.8) |
| **B (Yamagata)** [(a)] | 93.9 (79.5; 111) | 25.3 (22.8; 28.2) |

N=number of subjects with available data for the considered endpoint
GMT: Geometric Mean Titre; CI: Confidence Interval;
(a) N=862 for 3-8 years of age group
(b) SC: seroconversion or significant increase: for subjects with a pre-vaccination titre <10 (1/dil), proportion of subjects with a post-vaccination titre ≥40 (1/dil) and for subjects with a pre-vaccination titre ≥10 (1/dil), proportion of subjects with a ≥four-fold increase from pre- to post-vaccination titre
(c) GMTR: Geometric mean of individual titre ratios (post-/pre-vaccination titres)

These immunogenicity data provide supportive information in addition to vaccine efficacy data available in this population (see Efficacy of VAXIGRIPTETRA).

## 5.2. Pharmacokinetic properties

Not applicable.

## 5.3. Preclinical safety data

Non-clinical data revealed no special hazard for humans based on conventional studies of repeat dose and local toxicity, reproductive and developmental toxicity and safety pharmacology studies.

# 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 pre-filled syringe (type I glass) with attached needle, equipped with a plunger stopper (elastomer chlorobutyl or bromobutyl) – box of 1, 10 or 20.

0.5 mL of suspension in pre-filled syringe (type I glass) without needle, equipped with a plunger stopper (elastomer chlorobutyl or bromobutyl) – box of 1, 10 or 20.

Not all pack sizes may be marketed.

## 6.6. Special precautions for disposal and other handling

The vaccine should be allowed to reach room temperature before use.

Shake before use. Inspect visually prior to administration.

The vaccine should not be used if foreign particles are present in the suspension.

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

# 7. MARKETING AUTHORISATION HOLDER

**SANOFI PASTEUR**
14 ESPACE HENRY VALLÉE
69007 LYON

## 8. MARKETING AUTHORISATION NUMBER(S)

- 34009 300 677 2 7: 0.5 mL of suspension in pre-filled syringe (type I glass) with attached needle, equipped with a plunger stopper (elastomer chlorobutyl or bromobutyl) – box of 1.
- 34009 300 677 3 4: 0.5 mL of suspension in pre-filled syringe (type I glass) with attached needle, equipped with a plunger stopper (elastomer chlorobutyl or bromobutyl) – box of 10.
- 34009 300 677 4 1: 0.5 mL of suspension in pre-filled syringe (type I glass) with attached needle, equipped with a plunger stopper (elastomer chlorobutyl or bromobutyl) – box of 20.
- 34009 300 677 5 8: 0.5 mL of suspension in pre-filled syringe (type I glass) without needle, equipped with a plunger stopper (elastomer chlorobutyl or bromobutyl) – box of 1.
- 34009 300 677 7 2: 0.5 mL of suspension in pre-filled syringe (type I glass) without needle, equipped with a plunger stopper (elastomer chlorobutyl or bromobutyl) – box of 10.
- 34009 300 677 8 9: 0.5 mL of suspension in pre-filled syringe (type I glass) without needle, equipped with a plunger stopper (elastomer chlorobutyl or bromobutyl) – box of 20.

## 9. DATE OF FIRST AUTHORISATION/RENEWAL OF THE AUTHORISATION

- Date of first authorisation: 11 August 2016
- Renewal date of the authorisation: 21 June 2021

## 10. DATE OF REVISION OF THE TEXT

02 June 2022

## 11. DOSIMETRY

Not applicable.

## 12. INSTRUCTIONS FOR PREPARATION OF RADIOPHARMACEUTICALS

Not applicable.

## GENERAL CLASSIFICATION FOR SUPPLY

Medicinal product not subject to medical prescription.

# ANNEX II

## A. MANUFACTURER(S) OF THE BIOLOGICAL ACTIVE SUBSTANCE(S) AND MANUFACTURER(S) RESPONSIBLE FOR BATCH RELEASE

### A.1. Name and address of the manufacturer(s) of the biological active substance(s)

**SANOFI PASTEUR**
PARC INDUSTRIEL D'INCARVILLE
27100 VAL DE REUIL

### A.2. Name and address of the manufacturer(s) responsible for batch release

The printed package leaflet of the medicinal product must state the name and address of the manufacturer responsible for the release of the concerned batch.

**SANOFI PASTEUR**
1541 AVENUE MARCEL MERIEUX
69280 MARCY L'ETOILE

OR

**SANOFI PASTEUR**
PARC INDUSTRIEL D'INCARVILLE
27100 VAL DE REUIL

## B. CONDITIONS OR RESTRICTIONS REGARDING SUPPLY AND USE

Medicinal product not subject to medical prescription.

- Official batch release

In accordance with Article 114 of Directive 2001/83/EC, the official batch release will be undertaken by a state laboratory or a laboratory designated for that purpose.

## C. OTHER CONDITIONS AND REQUIREMENTS OF THE MARKETING AUTHORISATION

- **Periodic Safety Update Reports (PSUR)**

The requirements for submission of periodic safety update reports for this medicinal product are set out in the list of Union reference dates (EURD list) provided for under Article 107c (7) of Directive 2001/83/EC and any subsequent updates published on the European medicines web-portal.

## D. CONDITIONS OR RESTRICTIONS WITH REGARD TO THE SAFE AND EFFECTIVE USE OF THE MEDICINAL PRODUCT

- **Risk Management Plan (RMP)**

The Manufacturing Authorisation Holder shall perform the required pharmacovigilance activities and interventions detailed in the agreed RMP presented in Module 1.8.2 of the Marketing Authorisation and any agreed subsequent updates of the RMP.

An updated RMP should be submitted:

- At the request of competent authorities;
- Whenever the risk management system is modified, especially as the result of the new information being received that may lead to a significant change to the benefit/risk profile or as the result of an important (pharmacovigilance or risk minimisation) milestone being reached.

## E. SPECIFIC OBLIGATION TO COMPLETE POST-MARKETING AUTHORISATION MEASURES FOR THE MARKETING AUTHORISATION "UNDER EXCEPTIONAL CIRCUMSTANCES"

Not applicable.

## F. QUALITATIVE AND QUANTITATIVE COMPOSITION IN EXCIPIENTS

Saline buffer solution .....qs 0.5 mL

Formula of the saline solution buffered pH 7.2 (PBS)

Sodium chloride .....8 g

Potassium chloride ..... 0.20 g

Disodium phosphate dihydrate ..... 1.15 g

Potassium dihydrogen phosphate ..... 0.20 g

Water for injections .....qs 1000 mL

# ANNEXE IIIA

# LABELLING

## PARTICULARS TO APPEAR ON THE OUTER PACKAGING AND THE IMMEDIATE PACKAGING

## NATURE/TYPE OUTER PACKAGING OR IMMEDIATE PACKAGING

Outer packaging

## 1. NAME OF THE MEDICINAL PRODUCT

**VAXIGRIPTETRA, suspension for injection in pre-filled syringe**

**Quadrivalent influenza vaccine (split virion, inactivated)**

2023 season

## 2. STATEMENT OF ACTIVE SUBSTANCES

Influenza virus (inactivated, split) of the following strains*:

A/Sydney/5/2021 (H1N1)pdm09 - like strain

A/Darwin/9/2021 (H3N2) - like strain

B/Austria/1359417/2021 - like strain

B/Phuket/3073/2013 - like strain

15 microgram haemagglutinin per strain for one 0.5 mL dose

* propagated in eggs

## 3. LIST OF EXCIPIENTS

Sodium chloride, disodium phosphate dihydrate, potassium dihydrogen phosphate, potassium chloride, water for injections.

## 4. PHARMACEUTICAL FORM AND CONTENTS

Suspension for injection

1 pre-filled syringe (0.5 mL) with attached needle.

10 pre-filled syringes (0.5 mL) with attached needle.

20 pre-filled syringes (0.5 mL) with attached needle.

1 pre-filled syringe (0.5 mL) without needle.

10 pre-filled syringes (0.5 mL) without needle.

20 pre-filled syringes (0.5 mL) without needle.

## 5. METHOD AND ROUTE(S) OF ADMINISTRATION

**Intramuscular (IM) or subcutaneous (SC) use**

Read the package leaflet before use.

## 6. SPECIAL WARNING THAT THE MEDICINAL PRODUCT MUST BE STORED OUT OF THE SIGHT AND REACH OF CHILDREN

Keep out of the sight and reach of children.

## 7. OTHER SPECIAL WARNING(S), IF NECESSARY

Not applicable.

## 8. EXPIRY DATE

EXP {MM/YYYY}

## 9. SPECIAL STORAGE CONDITIONS

Store in a refrigerator. Do not freeze.

Keep the syringe in the outer carton in order to protect from light.

## 10. SPECIAL PRECAUTIONS FOR DISPOSAL OF UNUSED MEDICINAL PRODUCTS OR WASTE MATERIALS DERIVED FROM SUCH MEDICINAL PRODUCTS, IF APPROPRIATE

Not applicable.

## 11. NAME AND ADDRESS OF THE MARKETING AUTHORISATION HOLDER

### Holder

**SANOFI PASTEUR**
14 ESPACE HENRY VALLÉE
69007 LYON

### Distributor

**SANOFI PASTEUR EUROPE**
14 ESPACE HENRY VALLÉE
69007 LYON

## 12. MARKETING AUTHORISATION NUMBER(S)

Authorised medicinal product No:

## 13. BATCH NUMBER

Lot {number}

## 14. GENERAL CLASSIFICATION FOR SUPPLY

Medicinal product not subject to medical prescription.

## 15. INSTRUCTIONS ON USE

Indicated in the prevention of influenza.

## 16. INFORMATION IN BRAILLE

[Comply with the decision of May 7, 2008 taken pursuant to article R. 5121-138 of the Public Health Code, published in the OJ of May 22, 2008]

## 17. UNIQUE IDENTIFIER – 2D BARCODE

2D barcode carrying the unique identifier included.

## 18. UNIQUE IDENTIFIER - HUMAN READABLE DATA

PC: {number} [CIP code]

SN: {number} [serial number]

## PICTOGRAM TO APPEAR ON THE OUTER PACKAGING OR, WHERE THERE IS NO OUTER PACKAGING, ON THE IMMEDIATE PACKAGING

Pictogram on teratogenic or foetotoxic effects

Where applicable, the pictogram mentioned in section III of article R. 5121-139 of the Public Health Code (teratogenic or foetotoxic effects) must be affixed in compliance with the implementing decree provided for in the same article.

Pictogram on effects on the ability to drive

Not applicable.

## MINIMUM PARTICULARS TO APPEAR ON BLISTERS OR STRIPS

## NATURE/TYPE BLISTERS/STRIPS

Not applicable.

## 1. NAME OF THE MEDICINAL PRODUCT

Not applicable.

## 2. NAME OF THE MARKETING AUTHORISATION HOLDER

Not applicable.

## 3. EXPIRY DATE

Not applicable.

## 4. BATCH NUMBER

Not applicable.

## 5. OTHER

Not applicable.

## MINIMUM PARTICULARS TO APPEAR ON SMALL IMMEDIATE PACKAGING UNITS

## NATURE/TYPE SMALL PACKAGING UNITS

Pre-filled syringe

## 1. NAME OF THE MEDICINAL PRODUCT AND ROUTE(S) OF ADMINISTRATION

**VAXIGRIPTETRA**

<Suspension for injection>

<Quadrivalent influenza vaccine>

2023 <season>

IM - SC

## 2. METHOD OF ADMINISTRATION

Not applicable.

## 3. EXPIRY DATE

EXP {MM/YYYY}

## 4. BATCH NUMBER

Lot {number}

## 5. CONTENTS BY WEIGHT, BY VOLUME OR BY UNIT

0.5 mL

## 6. OTHER

Not applicable.

*<…> Optional information for multilingual labels in case of readability issues.*

# ANNEX IIIB

# PACKAGE LEAFLET: INFORMATION FOR THE USER

## Name of the medicinal product

**VAXIGRIPTETRA, suspension for injection in pre-filled syringe**

**Quadrivalent influenza vaccine (split virion, inactivated)**

## Boxed text

**Read all of this leaflet carefully before you or your child are vaccinated, because it contains important information for you.**

- Keep this leaflet. You may need to read it again.
- If you have any further questions, ask your doctor, pharmacist or nurse.
- This medicine has been prescribed for you or your child only. Do not pass it on to others.
- If you or your child get any side effects, talk to your doctor, pharmacist or nurse. This includes any possible side effects not listed in this leaflet. See section 4.

## What is in this leaflet



## 1. WHAT VAXIGRIPTETRA, suspension for injection in pre-filled syringe IS AND WHAT IT IS USED FOR

**Pharmacotherapeutic group: Influenza vaccines - ATC code: J07BB02.**

VAXIGRIPTETRA is a vaccine. This vaccine, administered to you or your child from 6 months of age, helps to protect you or your child against influenza (flu).

When a person is given VAXIGRIPTETRA, the immune system (the body's natural defence system) will produce its own protection (antibodies) against the disease. When administered during pregnancy, the vaccine helps to protect the pregnant woman but also helps to protect her baby(ies) from birth to almost 6 months of age through the transmission of protection from mother to baby during pregnancy (see also Sections 2 and 3).

None of the ingredients in the vaccine can cause flu.

The use of VAXIGRIPTETRA should be based on official recommendations.

Flu is a disease that can spread rapidly and is caused by different types of strains that can change every year. Due to this potential change in circulating strains on a yearly basis, as well as the duration of protection intended by the vaccine, vaccination is recommended every year. The greatest risk of catching flu is during the cold months. If you or your child were not vaccinated in the autumn, it is still sensible to be vaccinated up until the spring since you run the risk of catching flu until then. Your doctor will be able to recommend the best time to be vaccinated.

VAXIGRIPTETRA is intended to protect you or your child against the four strains of virus contained in the vaccine about 2 to 3 weeks after the injection. In addition, if you or your child are exposed to flu immediately before or after your vaccination, you or your child could still develop the illness as the incubation period for flu is a few days.

The vaccine will not protect you or your child against the common cold, even though some of the symptoms are similar to flu.

## 2. WHAT YOU NEED TO KNOW BEFORE YOU OR YOUR CHILD USE VAXIGRIPTETRA, suspension for injection in pre-filled syringe

To make sure that VAXIGRIPTETRA is suitable for you or your child, it is important to tell your doctor or pharmacist if any of the points below apply to you or your child. If there is anything you do not understand, ask your doctor or pharmacist to explain.

**Do not use VAXIGRIPTETRA, suspension for injection in pre-filled syringe**

- If you or your child are allergic to:
  - The active substances, or
  - Any of the other ingredients of this vaccine (listed in section 6), or
  - Any component that may be present in very small amounts such as eggs (ovalbumin, chicken proteins), neomycin, formaldehyde or octoxinol-9,
- If you or your child have an illness with a high or moderate temperature or an acute illness, the vaccination should be postponed until after you or your child have recovered.

**Warnings and precautions**

Talk to your doctor, your pharmacist or your nurse before using VAXIGRIPTETRA.

You should tell your doctor before vaccination if you or your child have:

- A poor immune response (immunodeficiency or taking medicines affecting the immune system),
- Bleeding problem or bruising easily.

Your doctor will decide if you or your child should receive the vaccine.

Fainting can occur (mostly in adolescents) following, or even before, any needle injection. Therefore, tell your doctor or nurse if you or your child fainted with a previous injection.

As with all vaccines, VAXIGRIPTETRA may not fully protect all persons who are vaccinated.

Not all babies less than 6 months of age born to pregnant women vaccinated during pregnancy may be protected.

If, for any reason, you or your child have a blood test within a few days following a flu vaccination, please tell your doctor. This is because false positive blood test results have been observed in a few patients who had recently been vaccinated.

**Children**

VAXIGRIPTETRA is not recommended for use in children below 6 months of age.

**Other medicines and VAXIGRIPTETRA, suspension for injection in pre-filled syringe**

Tell your doctor or pharmacist if you or your child are receiving, have recently received or might receive any other vaccines or any other medicines.

- VAXIGRIPTETRA can be given at the same time as other vaccines by using separate limbs.
- The immunological response may decrease in case of immunosuppressant treatment, such as corticosteroids, cytotoxic drugs or radiotherapy.

**VAXIGRIPTETRA, suspension for injection in pre-filled syringe with food, drink and alcohol**

Not applicable.

**Pregnancy and breast-feeding**

If you are pregnant or breast-feeding, think you may be pregnant, ask your doctor or pharmacist for advice before using this vaccine.

VAXIGRIPTETRA can be used in all stages of pregnancy.

VAXIGRIPTETRA may be used during breast-feeding.

Your doctor/pharmacist will be able to decide if you should receive VAXIGRIPTETRA.

**Driving and using machines**

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

**VAXIGRIPTETRA, suspension for injection in pre-filled syringe contains potassium and sodium**

This medicine contains less than 1 mmol potassium (39 mg) and less than 1 mmol sodium (23 mg) per dose, that is to say it is essentially “potassium-free” and “sodium-free”.

## 3. HOW TO USE VAXIGRIPTETRA, suspension for injection in pre-filled syringe

**Dosage**

Adults receive one 0.5 mL dose.

*Use in children*

Children from 6 months to 17 years of age receive one 0.5 mL dose.

If your child is less than 9 years old and has not been previously vaccinated against flu, a second dose of 0.5 mL should be given after an interval of at least 4 weeks.

If you are pregnant, the 0.5 mL dose administered to you during pregnancy may protect your baby from birth to almost 6 months of age. Ask your doctor or pharmacist for more information.

**How VAXIGRIPTETRA is given**

Your doctor or nurse will administer the recommended dose of the vaccine as an injection into the muscle or under the skin.

**If you or your child receive more VAXIGRIPTETRA, suspension for injection in pre-filled syringe than you should**

In some cases, more than the recommended dose has been inadvertently administered.

In these cases, when side effects were reported, they were in line with what is described following the administration of the recommended dose (see Section 4).

**If you or your child forget to use VAXIGRIPTETRA, suspension for injection in pre-filled syringe**

Not applicable.

**If you or your child stop using VAXIGRIPTETRA, suspension for injection in pre-filled syringe**

Not applicable.

If you have any further questions on the use of this product, ask your doctor or pharmacist.

## 4. POSSIBLE SIDE EFFECTS

Like all medicines, this vaccine can cause side effects, although not everybody gets them.

**Allergic reactions**

Contact your doctor or a healthcare professional immediately or go to the nearest hospital emergency room immediately if you or your child experience allergic reactions (reported as rare: may affect up to 1 in 1,000 people) that can be life threatening.

Symptoms may include rash, itching, hives, redness, difficulty breathing, shortness of breath, swelling of the face, lips, throat, or tongue, cold, clammy skin, palpitations, dizziness, weakness or fainting.

**Other side effects reported in adults and elderly**

*Very common (may affect more than 1 in 10 people):*

- Headache, muscular pain (myalgia), malaise [(1)], pain at the injection site.

[(1)] Common in elderly

*Common (may affect up to 1 in 10 people):*

- Fever [(2)], shivering, reactions at the injection site: redness (erythema), swelling, hardness (induration).

[(2)] Uncommon in elderly

*Uncommon (may affect up to 1 in 100 people):*

- Dizziness [(3)], diarrhoea, nausea [(4)], fatigue, reactions at the injection site: bruising (ecchymosis), itching (pruritus), and warmth.
- [(3)] Rare in adults [(4)] Rare in elderly
- Hot flush: only seen in the elderly.
- Swelling of the glands in the neck, armpit or groin (lymphadenopathy): only seen in adults.

*Rare (may affect up to 1 in 1,000 people):*

- Anomalies in the perception of touch, pain, heat and cold (paraesthesia), sleepiness, increased sweating (hyperhidrosis), unusual tiredness and weakness (asthenia), flu-like illness.
- Joint pain (arthralgia), discomfort at the injection site: only seen in adults.

**Other side effects reported in children from 3 to 17 years of age**

*Very common (may affect more than 1 in 10 people):*

- Headache, muscular pain (myalgia), malaise, shivering [(5)], reactions at the injection site: pain, swelling, redness (erythema) [(5)], hardness (induration) [(5)].
- [(5)] Common in children from 9 to 17 years of age

*Common (may affect up to 1 in 10 people):*

- Fever, bruising (ecchymosis) at the injection site.

*Uncommon (may affect up to 1 in 100 people) in children from 3 to 8 years of age:*

- Temporary reduction in the number of certain blood elements called platelets; a low number of these can result in excessive bruising or bleeding (transient thrombocytopenia): only seen in one child of 3 years of age.
- Moaning, restlessness.
- Dizziness, diarrhoea, vomiting, upper abdominal pain, joint pain (arthralgia), fatigue, warmth at the injection site.

*Uncommon (may affect up to 1 in 100 people) in children from 9 to 17 years of age:*

- Diarrhoea, itching (pruritus) at the injection site.

**Other side effects reported in children from 6 to 35 months of age**

*Very common (may affect more than 1 in 10 people):*

- Vomiting [(1)], muscular pain (myalgia) [(2)], irritability [(3)], appetite lost [(3)], generally feeling unwell (malaise) [(2)], fever.

[(1)] Uncommon in children from 24 to 35 months of age [(2)] Rare in children less than 24 months of age
[(3)] Rare in children from 24 to 35 months of age

- Reactions at the injection site: pain/tenderness, redness (erythema).
- Headache: only seen in children from 24 months of age.
- Drowsiness, unusual crying: only seen in children less than 24 months of age.

*Common (may affect up to 1 in 10 people):*

- Shivering: only seen in children 24 months and older.
- Reactions at the injection site: hardness (induration), swelling, bruising (ecchymosis).

*Uncommon (may affect up to 1 in 100 people):*

- Diarrhoea, hypersensitivity.

*Rare (may affect up to 1 in 1,000 people):*

- Flu-like illness, reactions at the injection site: rash, pruritus (itching).
-

In children from 6 months to 8 years of age who received 2 doses, side effects were similar after the first and after the second dose. Fewer side effects may happen after the second dose in children from 6 to 35 months of age.

When seen, side effects generally happen in the first 3 days after the vaccination and go away by themselves in 1 to 3 days after they start. The intensity of observed side effects was mild.

Side effects were generally less frequent in elderly than in adults and children.

The following side effects have been reported after administration of Vaxigrip. These side effects may occur with VAXIGRIPTETRA:

- pain situated on the nerve route (neuralgia), convulsions, neurological disorders that may result in stiff neck, confusion, numbness, pain and weakness of the limbs, loss of balance, loss of reflexes, paralysis of part or all the body (encephalomyelitis, neuritis, Guillain-Barré syndrome)
- blood vessel inflammation (vasculitis) which may result in skin rashes and in very rare cases in temporary kidney problems.
- Transient thrombocytopenia, lymphadenopathy, paraesthesia in other age groups than those described above for these side effects.

**Reporting of side effects**

If you or your child get any side effects, talk to your doctor, pharmacist or nurse. This includes any possible side effects not listed in this leaflet. You can also report side effects directly via the national reporting system: “Agence nationale de sécurité du médicament et des produits de santé (ANSM) et réseau des Centres Régionaux de Pharmacovigilance - Site internet : www.signalement-sante.gouv.fr”

By reporting side effects you can help provide more information on the safety of this medicine.

## 5. HOW TO STORE VAXIGRIPTETRA, suspension for injection in pre-filled syringe

Keep this vaccine out of the sight and reach of children.

Do not use this vaccine after the expiry date which is stated on the label and carton after EXP. The expiry date refers to the last day of that month.

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

Do not throw away any medicines via wastewater or household waste. Ask your pharmacist how to throw away medicines you no longer use. These measures will help protect the environment.

## 6. CONTENTS OF THE PACK AND OTHER INFORMATION

### What VAXIGRIPTETRA, suspension for injection in pre-filled syringe contains

- The active substances are: Influenza virus (inactivated, split) of the following strains*:

  A/Sydney/5/2021 (H1N1)pdm09 - like strain (A/Sydney/5/2021, SAN-013) .....
  .....15 micrograms HA**

  A/Darwin/9/2021 (H3N2) - like strain (A/Darwin/9/2021, IVR-228).....
  .....15 micrograms HA**

  B/Austria/1359417/2021 - like strain (B/Michigan/01/2021, wild type) .....
  .....15 micrograms HA**

  B/Phuket/3073/2013 - like strain (B/Phuket/3073/2013, wild type) .....
  .....15 micrograms HA**

  Per 0.5 mL dose

  * propagated in fertilised hens' eggs from healthy chicken flocks

  ** haemagglutinin

  This vaccine complies with the WHO (World Health Organisation) recommendations (Southern Hemisphere) for the 2023 season.

- The other ingredients are: a buffer solution containing sodium chloride, potassium chloride, disodium phosphate dihydrate, potassium dihydrogen phosphate, and water for injections.

  Some components such as eggs (ovalbumin, chicken proteins), neomycin, formaldehyde or octoxinol-9 may be present in very small amounts (see section 2).

### What VAXIGRIPTETRA, suspension for injection in pre-filled syringe is and contents of the pack

The vaccine, after shaking gently, is a colourless opalescent liquid.

VAXIGRIPTETRA is a suspension for injection presented in a pre-filled syringe of 0.5 mL, with attached needle or without needle, in box of 1, 10 or 20.

Not all pack sizes may be marketed.

### Marketing authorisation holder

**SANOFI PASTEUR**
14 ESPACE HENRY VALLÉE
69007 LYON

### Marketing authorisation distributor

**SANOFI PASTEUR EUROPE**
14 ESPACE HENRY VALLÉE
69007 LYON

### Manufacturer

**SANOFI PASTEUR**
14 ESPACE HENRY VALLÉE
69007 LYON

### Names of the medicinal product in the Member States of the European Economic Area

**This medicinal product is authorised in the Member States of the European Economic Area under the following names: In accordance with local requirements.**

Not applicable

## This leaflet was last revised in: **06/2022**

## Other

Detailed information on this medicine is available on the website of ANSM (France).

## The following information is intended for healthcare professionals only:

As with all injectable vaccines, appropriate medical treatment and supervision should always be readily available in case of an anaphylactic reaction following the administration of the vaccine.

The vaccine should be allowed to reach room temperature before use.

Shake before use. Inspect visually prior to administration.

The vaccine should not be used if foreign particles are present in the suspension.

It should not be mixed with other medicinal products in the same syringe.

This vaccine is not to be injected directly into a blood vessel.

See also section 3. How to use VAXIGRIPTETRA, suspension for injection in pre-filled syringe.