ANNEX I

SUMMARY OF PRODUCT CHARACTERISTICS

▼This medicinal product is subject to additional monitoring. This will allow quick identification of new safety information. Healthcare professionals are asked to report any suspected adverse reactions. See section 4.8 for how to report adverse reactions.

1. NAME OF THE MEDICINAL PRODUCT

Supemtek solution for injection in pre-filled syringe

Quadrivalent Influenza Vaccine (recombinant, prepared in cell culture)

2. QUALITATIVE AND QUANTITATIVE COMPOSITION

One dose (0.5 mL) contains:
Influenza virus haemagglutinin (HA) proteins, of the following strains*:

A/XXXXXX (H1N1)..... 45 micrograms HA

A/XXXXXX (H3N2)..... 45 micrograms HA

B/XXXXXX ..... 45 micrograms HA

B/XXXXXX ..... 45 micrograms HA

* produced by recombinant DNA technology using a baculovirus expression system in a continuous insect cell line that is derived from Sf9 cells of the fall armyworm, *Spodoptera frugiperda.*

This vaccine complies with the World Health Organization (WHO) recommendation (Northern Hemisphere) and EU recommendation for the XXXX/XXXX season.

Supemtek may contain traces of octylphenol ethoxylate.

For the full list of excipients, see section 6.1.

3. PHARMACEUTICAL FORM

Solution for injection in pre-filled syringe (injection).

Clear and colourless solution.

4. CLINICAL PARTICULARS

4.1 Therapeutic indications

Supemtek is indicated for active immunization for the prevention of influenza disease in adults.

Supemtek should be used in accordance with official recommendations.

4.2 Posology and method of administration

Posology:

One dose of 0.5 mL.

Paediatric population
Safety and efficacy of Supemtek have not yet been established in individuals below 18 years of age.

Method of administration:

For intramuscular injection only. The preferred site is in the deltoid muscle.
The vaccine must not be injected intravascularly and must not be mixed with other vaccines in the same syringe.

For instructions on the handling of the vaccine 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 trace residuals such as octylphenol ethoxylate.

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.

Hypersensitivity
Appropriate medical treatment and supervision should always be readily available in case of an anaphylactic event following the administration of the vaccine.

Intercurrent illness
Vaccination should be postponed in patients with acute febrile illness until the fever is resolved.

Immunodeficiency
Antibody response in patients with endogenous or iatrogenic immunosuppression may be insufficient to prevent influenza.

Thrombocytopenia and coagulation disorders
As with all injectable vaccines, Supemtek must be administered with caution to individuals with thrombocytopaenia or a bleeding disorder since bleeding may occur following an intramuscular administration to these subjects.

Syncope
Syncope can occur following or even before any vaccination as a psychogenic response to the needle injection.This can be accompanied by several neurological signs such as transient visual disturbance, paraesthesia and tonic-clonic limb movements during recovery. Procedures should be in place to prevent falling and injury and to manage syncope.

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

Sodium content

This medicinal product contains less than 1 mmol sodium (23 mg) per dose, that is to say is essentially “sodium free”.

4.5 Interaction with other medicinal products and other forms of interaction

No interaction studies have been performed, nor data to assess the concomitant administration of Supemtek with other vaccines.
If Supemtek is to be given at the same time as another injectable vaccine, the vaccines should always be administered at different injection sites.

4.6 Fertility, pregnancy and lactation

Pregnancy
There is a limited amount of data from the use of Supemtek in pregnant women.
One animal study performed with trivalent recombinant influenza vaccine did not indicate direct or indirect harmful effects with respect to pregnancy, embryo-foetal development or early post-natal development.
An assessment of the risks and benefits should be performed by a health care professional before administering Supemtek to a pregnant woman.

Breast-feeding
It is not known whether Supemtek vaccine is excreted in human milk.
An assessment of the risks and benefits should be performed by a health care professional before administering Supemtek to a breast-feeding woman.

Fertility
No human fertility data are available.
The animal study with trivalent recombinant influenza vaccine did not indicate harmful effects on female fertility.

4.7 Effects on ability to drive and use machines

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

4.8 Undesirable effects

Summary of the safety profile

Supemtek has been administered to and safety data collected from 998 adults 18-49 years of age (Study 1) and 4328 adults 50 years of age and older (Study 2).
The most common reactions occurring after vaccine administration were injection-site reactions (tenderness and pain) reported overall by 48% and 37% of study participants 18-49 years of age receiving Supemtek respectively. In study participants 50 years of age and older, injection site tenderness was reported by 34% and injection site pain reported by 19%.
The severity of the reactions was mild to moderate. Onset usually occurred within the first 3 days after vaccination. All resolved without sequelae.

Tabulated list of adverse reactions

The adverse reactions are listed by MedDRA system organ class 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);
Frequency not known (adverse reactions from post-marketing experience; cannot be estimated from the available data). Within each frequency grouping, adverse reactions are presented in the order of decreasing seriousness.

Table 1: Adverse reactions reported following vaccination in adults 18 years and older during clinical trials and post-marketing surveillance

MedDRA System Organ class	**Very common (≥1/10)**	**Common (≥1/100 to <1/10)**	**Uncommon (≥1/1,000 to <1/100)**	**Rare (≥1/10,000, <1/1,000)**	**Frequency not known**
Immune system disorders					Hypersensitivity including anaphylactic reaction
Nervous system disorders	Headache, Fatigue			Dizziness[4,6]	Guillain-Barré syndrome[7]
Respiratory, thoracic and mediastinal disorders			Cough, Oropharyngeal pain		
Gastrointestinal disorders		Nausea	Diarrhoea[4]		
Skin and subcutaneous tissue disorders			Pruritus[2,4] , Dermatitis[4,5], Rash[4,5]	Urticaria[4,6]	
Musculoskeletal and connective tissue disorders	Myalgia[1], Arthralgia[1]				
General disorders and administration site conditions	Local tenderness, Local pain	Firmness / Swelling, Redness, Fever [2,3], Shivering / Chills,	Flu-like symptoms[4,6], Injection site pruritus[4]		

[1] Common in adults 50 years of age and older.

[2] Rare (≥1/10,000 to <1/1,000) in adults 50 years of age and older.

[3] ≥38.0°C (100.4°F).

[4] Reported as unsolicited adverse reaction.

[5] Not reported in adults 50 years of age and older.

[6] Not reported in adults 18-49 years of age.

[7] Reported from post-marketing surveillance, no causal relationship established.

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 listed in Appendix V.

4.9 Overdose

No cases of overdose reported.

5. PHARMACOLOGICAL PROPERTIES

5.1 Pharmacodynamic properties

Pharmacotherapeutic group: Influenza vaccine, ATC code: J07BB02

Immunogenicity

Supemtek was evaluated in healthy adults of 18-49 years of age in a randomized, observer-blind, active controlled, non-inferiority immunogenicity, multi-center trial conducted during the 2014-2015 influenza season in the United States (study 1).

In the study 1, subjects received Supemtek (N=998) or an egg-based quadrivalent inactivated influenza vaccine (IIV4) (N=332). Immunogenicity was assessed before and 28 days after administration of a single dose of study vaccine.

Haemagglutination inhibition (HAI) geometric mean titers (GMTs) were determined for the two vaccine groups for each vaccine antigen. Immunogenicity was compared by calculating the difference in seroconversion rates (SCR) and the ratios of GMTs of Comparator to Supemtek.

Study 1 had two co-primary endpoints: GMTs and Day 28 HAI seroconversion rates for each of the four antigens contained in the study vaccines.

Supemtek met the success criterion for GMTs for three of the four antigens but did not meet the success criteria for the B/Victoria lineage antigen (Table 2). Antibody titres against the B/Victoria were low in both vaccine groups.

Table 2: Comparison of Day 28 Post-Vaccination Geometric Mean Titers (GMT) for Supemtek and Comparator in Adults 18-49 Years of Age, Study 1 (Immunogenicity Population) [1,2,3]

Antigen	Post-vaccination GMT Supemtek N=969	Post-vaccination GMT Comparator N=323	GMT Ratio Comparator/ Supemtek (95% CI)
A/H1N1	493	397	0.81 (0.71, 0.92)
A/H3N2	748	377	0.50 (0.44, 0.57)
B/Yamagata	156	134	0.86 (0.74, 0.99)
B/Victoria	43	64	1.49 (1.29, 1.71)

Abbreviations: CI, confidence interval; GMT, geometric mean titer.
[1] HI titers were assayed using egg-derived antigens.
[2] Comparator: egg-based quadrivalent inactivated influenza vaccine.
[3] Success in meeting the GMTs endpoint was pre-defined as an upper bound (UB) of the two-sided 95% CI of GMTComparator / GMT Supemtek ≤ 1.5.

Supemtek met the success criterion for SCRs for three of the four antigens (Table 3), but not for the B/Victoria lineage. The HAI response to the B/Victoria lineage antigen was low in both vaccine groups.

Table 3: Comparison of Day 28 Seroconversion Rates for Supemtek and Comparator in Adults 18-49 Years of Age, Study 1 (Immunogenicity Population) [1,2,3,4]

Antigen	SCR (%, 95% CI) Supemtek N=969	SCR (%, 95% CI) Comparator N=323	SCR Difference (%) Comparator - Supemtek [95% CI]
A/H1N1	66.7 (63.6, 69.6)	63.5 (58.0, 68.7)	-3.2 (-9.2, 2.8)
A/H3N2	72.1 (69.2, 74.9)	57.0 (51.4, 62.4)	-15.2 (-21.3, -9.1)
B/Yamagata	59.6 (56.5, 62.8)	60.4 (54.8, 65.7)	0.7 (-5.4, 6.9)
B/Victoria	40.6 (37.4, 43.7)	58.2 (52.6, 63.6)	17.6 (11.4, 23.9)

Abbreviations: CI, confidence interval; SCR, seroconversion rate

[1] HI titers were assayed using egg-derived antigens.

[2] Comparator was an egg-based quadrivalent inactivated influenza vaccine.

[3] Seroconversion was defined as either a pre-vaccination HAI titer of <1:10 and a post-vaccination HAI titer of ≥1:40, or a pre-vaccination HAI titer of ≥1:10 and a minimum 4- fold rise in post vaccination HAI titer, at Day 28.

[4] Success in meeting the seroconversion rate (SCR) endpoint was pre-defined as an upper bound (UB) of the two-sided 95% CI of SCR Comparator – SCR Supemtek ≤10%.

The study 1 in adults 18-49 years of age was conducted in parallel to the study 2 in adults of 50 years of age and older. These adults 18-49 years of age were vaccinated during the same influenza season (2014-2015 Northern Hemisphere influenza season) and received the same Supemtek formulation (same vaccine strain composition) as adults of 50 years of age and older in the study 2. The immune response induced by Supemtek was assessed by the same HAI assay and performed by the same laboratory for both studies. The immunogenicity results in adults 18-49 years of age (study 1) and adults 50 years of age and older (study 2) are presented in table 4.

Table 4: Summary of HAI Antibody Response to Supemtek for Each Strain in Adults 18-49 years (Study 1) and Adults≥50 years (Study 2) - Immunogenicity Analysis Set

	Adults 18-49 years N=969	Adults ≥50 years N=314
GMT post-vaccination (95% CI)		
A/California/7/2009 (H1N1)	493 (460; 527)	190 (164; 221)
A/Texas/50/2012 (H3N2)	748 (700; 800)	522(462; 589)
B/Massachusetts/02/2012 (Yamagata lineage)	156 (145; 168)	55 (48; 64)
B/Brisbane/60/2008 (Victoria lineage)	43 (40; 46)	29 (26; 33)
SCR % (95% CI)		
A/California/7/2009 (H1N1)	66.7 (63.6; 69.6)	44.9 (39.3; 50.6)
A/Texas/50/2012 (H3N2)	72.1 (69.2; 74.9)	54.5 (48.8; 60.1)
B/Massachusetts/02/2012 (Yamagata lineage)	59.6 (56.5; 62.8)	38.9 (33.4; 44.5)
B/Brisbane/60/2008 (Victoria lineage)	40.6 (37.4; 43.7)	21.0 (16.6; 25.9)
GMTR % (95% CI)		
A/California/7/2009 (H1N1)	8.35 (7.59; 9.19)	4.31 (3.71; 5.02)
A/Texas/50/2012 (H3N2)	10.1 (9.12; 11.1)	6.01 (5.03; 7.18)
B/Massachusetts/02/2012 (Yamagata lineage)	3.59 (3.35; 3.85)	2.16 (1.94; 2.40)
B/Brisbane/60/2008 (Victoria lineage)	5.89 (5.43; 6.40)	3.18 (2.81; 3.59)

N=number of subjects with available data for the considered endpoint

GMT: Geometric Mean Titer; CI: Confidence Interval; SCR: Seroconversion rate; GMTR: Geometric Mean Titer of individuals ratios (post dose / pre dose)

These immunogenicity data provide supportive information for the 18-49 years of age group in addition to vaccine efficacy data available in adults ≥ 50 years of age (see Clinical Efficacy).

Clinical efficacy

Supemtek efficacy in terms of prevention of laboratory-confirmed influenza-like illness (ILI) caused by any strain of influenza, was evaluated in adults ≥ 50 years of age and conducted during the 2014-2015 influenza season in the United States (study 2).

A total of 8963 healthy, medically stable adults were randomized in a 1:1 ratio to receive a single dose of Supemtek (n=4474) or an egg-based quadrivalent inactivated influenza vaccine (n=4489). A total of 5412 (60.4%) subjects were 50-64 years of age, 2532 (28.2%) were 65-74 years of age and 1019 (11.4 %) were ≥ 75 years of age.

The primary efficacy endpoint of Study 2 was reverse transcriptase polymerase chain reaction (rtPCR)-positive, protocol-defined ILI due to any strain of influenza.

Laboratory-confirmed protocol defined ILI was defined as having at least one symptom in each of two categories of respiratory and systemic symptoms, which could include sore throat, cough, sputum production, wheezing and difficulty breathing, or systemic symptoms such as fever > 99°F (>37°C) , chills, fatigue, headache and myalgia, laboratory-confirmed by rtPCR.
US epidemiological data for the 2014-2015 influenza season indicated that Influenza A (H3N2) viruses predominated and that most influenza A/H3N2 viruses were antigenically dissimilar while A/H1N1 and B viruses were antigenically similar to vaccine antigens. Supemtek met the pre-specified success criterion for non-inferiority to the comparator pre-defined as a lower bound of the two sided 95% CI >-20%.

Of the 4474 participants exposed to Supemtek in a phase 3 active-controlled study (Study 2), a total of 1761 were 65 years or older. Although no differences in safety or efficacy were observed between older and younger participants, the number of patients aged 65 and over in this study was not sufficient to determine statistically whether this age group will respond differently from younger individuals.

Table 5: Relative Vaccine Efficacy (rVE) of Supemtek versus Comparator against Laboratory-Confirmed Influenza, Regardless of Antigenic Similarity to Vaccine Antigens, Adults 50 Years of Age and Older, Study 2 (Efficacy Population)[1,2]

	Supemtek (N=4303)		Comparator (N=4301)		RR	rVE % (95% CI)
	n	Attack Rate % (n/N)	n	Attack Rate % (n/N)		
All rtPCR-positive Influenza[3]	96	2.2	138	3.2	0.70	30 (10^5, 47)
All rtPCR-positive Influenza A[3]	73	1.7	114	2.7	0.64	36 (14, 53)
All rtPCR-positive Influenza B[3]	23	0.5	24	0.6	0.96	4 (-72, 46)
All Culture-confirmed Protocol-defined ILI[3,4]	58	1.3	101	2.3	0.57	43 (21, 59)

Abbreviations: rtPCR=reverse transcriptase polymerase chain reaction; Comparator= an egg-based quadrivalent inactivated influenza vaccine; n=number of influenza cases; N=number of subjects in treatment group; RR=relative risk (Attack Rate Supemtek/Attack Rate IIV4); rVE = [(1-RR) x 100].

[1] Excluded subjects with protocol deviations that could adversely affect efficacy.

[2] Primary Analysis. All cases of rtPCR-confirmed influenza are included.

[3] *Post hoc* analyses. All cases of influenza A were A/H3N2. Cases of influenza B were not distinguished by lineage.

[4] Culture of rtPCR-positive samples was performed in MDCK cells.

[5] The lower bound (LB) of the 95% confidence interval met the pre-specified, exploratory criterion for superior relative vaccine efficacy, LB > 9%.

Efficacy of trivalent recombinant influenza vaccine (RIV3)

The efficacy of trivalent recombinant influenza vaccine (RIV3) is relevant to Supemtek because both vaccines are manufactured using the same process and have overlapping compositions.

The efficacy of trivalent recombinant influenza vaccine in protecting against influenza illness was evaluated in a randomized, observer-blind, placebo-controlled multicenter trial conducted in the United States during the 2007-2008 influenza season in adults 18-49 years of age (Study 3).

Study 3 enrolled and vaccinated 4648 healthy adults randomized in a 1:1 ratio to receive a single dose of RIV3 (n=2344) or saline placebo (n=2304).

The primary efficacy endpoint of Study 3 was defined as an influenza-like illness (ILI) with a positive culture for an influenza virus strain antigenically resembling a strain represented in RIV3. ILI is defined as fever of ≥100°F (37.8°C) oral accompanied by cough, sore throat, or both, on the same or consecutive days. Attack rates and vaccine efficacy (VE), defined as the reduction in the influenza rate for RIV3 relative to placebo, were calculated for the total vaccinated cohort (n=4648). Due to very small number of cultured confirmed influenza cases with matched strains, an exploratory analysis of VE of RIV3 against all strains, regardless of antigenic match, isolated from any subject with an ILI, not necessarily meeting ILI criteria was done, demonstrated an efficacy estimate of 44.8% (95% CI 24.4, 60.0). See Table 6 for VE by case definition.

Table 6: Vaccine Efficacy Against Culture-Confirmed Influenza in Healthy Adults 18-49 Years of Age, Study 3[1,3]

Case definition	RIV3 (N=2344)		Saline Placebo (N=2304)		RIV3 Vaccine Efficacy[4] %	95% Confidence Interval
	Cases, n	Rate, %	Cases, n	Rate, %		
Positive culture with a strain represented in the vaccine						
CDC-ILI[2], all matched strains[5]	1	0.04	4	0.2	75.4	(-148.0, 99.5)
Any ILI, all matched strains	2	0.1	6	0.3	67.2	(-83.2, 96.8)
Positive culture with any strain, regardless of match to the vaccine						
CDC-ILI[2], all strains	44	1.9	78	3.4	44.6	(18.8, 62.6)
Sub-Type A	26	1.1	56	2.4	54.4	(26.1, 72.5)
Type B	18	0.8	23	1.0	23.1	(-49.0, 60.9)
Any ILI, all strains	64	2.7	114	4.9	44.8	(24.4, 60.0)
Sub-Type A	41	1.7	79	3.4	49.0	(24.7, 65.9)
Type B	23	1.0	36	1.6	37.2	(-8.9, 64.5)

1 Vaccine efficacy (VE) = 1 minus the ratio of RIV3 /placebo infection rates (10).

[2] Centers for Disease Control and Prevention - defined influenza-like illness (CDC-ILI) defined as fever of ≥100ºF (37.8°C) oral accompanied by cough and/or sore throat, on the same day or on consecutive days.

[3] The pre-defined success criterion for the primary efficacy analysis was that the lower bound of the 95% confidence interval (CI) of VE should be at least 40%.

[4] Determined under the assumption of Poisson event rates, according to Breslow and Day, 1987.

[5] Primary endpoint of trial.

Paediatric population

The European Medicines Agency has waived the obligation to submit the results of studies with Supemtek in children from 6 months to 3 years of age for the prevention of influenza infection. The European Medicines Agency has deferred the obligation to submit the results of studies with Supemtek in children from 3 years to 17 years of age for the prevention of influenza infection (see section 4.2 for information on paediatric use).

5.2 Pharmacokinetic properties

Not applicable.

5.3 Preclinical safety data

Non-clinical safety data on the trivalent formulation revealed no special hazard for humans based on conventional studies of repeat dose and local toxicity, reproductive and developmental (including teratogenicity) toxicity and safety pharmacology studies.The results of these studies with trivalent recombinant influenza vaccine are relevant to Supemtek because both vaccines are manufactured using the same process and have overlapping compositions.

6. PHARMACEUTICAL PARTICULARS

6.1 List of excipients

Polysorbate 20 (E432)
Sodium chloride
Sodium phosphate monobasic, monohydrate
Sodium phosphate dibasic, dodecahydrate
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 pre-filled syringe in the outer carton in order to protect from light.

6.5 Nature and contents of container

0.5 mL solution in a pre-filled syringe (Type I borosilicate glass) with plunger stopper (grey butyl rubber), with separate needle or without needle.

Pack size:
10 pre-filled syringes, with separate needle or without needle.
5 pre-filled syringes, with separate needle or without needle.
1 pre-filled syringe, with separate needle or without needle.

Not all pack sizes may be marketed.

6.6 Special precautions for disposal and other handling

The vaccine should be inspected visually for particulate matter and/or discoloration prior to administration. If either of these conditions exists, the vaccine should be discarded.

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
France

8. MARKETING AUTHORISATION NUMBER(S)

EU/1/20/1484/001
EU/1/20/1484/002
EU/1/20/1484/003
EU/1/20/1484/004
EU/1/20/1484/005
EU/1/20/1484/006

9. DATE OF FIRST AUTHORISATION/RENEWAL OF THE AUTHORISATION

Date of first authorisation: {DD month YYYY}

10. DATE OF REVISION OF THE TEXT

Detailed information on this medicinal product is available on the website of the European Medicines Agency http://www.ema.europa.eu

ANNEX II

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

B. CONDITIONS OR RESTRICTIONS REGARDING SUPPLY AND USE

C. OTHER CONDITIONS AND REQUIREMENTS OF THE MARKETING AUTHORISATION

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

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

Name and address of the manufacturer(s) of the biological active substance(s)

Unigen Inc.
11 Azakamikasugo Miyaji Ikeda-cho
Ibi-gun Gifu, Japan

Name and address of the manufacturer(s) responsible for batch release

Sanofi Pasteur
Parc Industriel d'Incarville
27100 Val de Reuil
France

B. CONDITIONS OR RESTRICTIONS REGARDING SUPPLY AND USE

Medicinal product 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 (PSURs)**

The requirements for submission of PSURs 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.

The marketing authorisation holder (MAH) shall submit the first PSUR for this product within 6 months following authorisation.

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

- **Risk management plan (RMP)**

The marketing authorisation holder (MAH) 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 the European Medicines Agency;
- Whenever the risk management system is modified, especially as the result of 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.

ANNEX III

LABELLING AND PACKAGE LEAFLET

A. LABELLING

PARTICULARS TO APPEAR ON THE OUTER PACKAGING

Outer box, without needle or with separate needle – pack of 1, 5 and 10

1. NAME OF THE MEDICINAL PRODUCT

Supemtek solution for injection in pre-filled syringe
Quadrivalent Influenza Vaccine (recombinant, prepared in cell culture)
xxxx/xxxx season

2. STATEMENT OF ACTIVE SUBSTANCE(S)

Influenza virus haemagglutinin proteins of the following strains:
A/xxxxxx (H1N1) - like virus
A/xxxxxx (H3N2) - like virus
B/xxxxxx - like virus
B/xxxxxx - like virus

45 microgram haemagglutinin per strain per 0.5 mL dose.

3. LIST OF EXCIPIENTS

Polysorbate 20 (E432), sodium chloride, sodium phosphate monobasic monohydrate, sodium phosphate dibasic dodecahydrate, water for injections.

4. PHARMACEUTICAL FORM AND CONTENTS

Solution for injection in pre-filled syringe
1 pre-filled syringe (0.5 mL) without needle
10 pre-filled syringes (0.5 mL) without needle
5 pre-filled syringes (0.5 mL) without needle

1 pre-filled syringe (0.5 mL) with separate needle
10 pre-filled syringes (0.5 mL) with separate needle
5 pre-filled syringes (0.5 mL) with separate needle

5. METHOD AND ROUTE(S) OF ADMINISTRATION

Intramuscular use (IM).
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

8. EXPIRY DATE

EXP

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

11. NAME AND ADDRESS OF THE MARKETING AUTHORISATION HOLDER

Sanofi Pasteur
14 Espace Henry Vallée
69007 Lyon
France

12. MARKETING AUTHORISATION NUMBER(S)

EU/1/20/1484/001 1 pre-filled syringe without needle
EU/1/20/1484/002 1 pre-filled syringe with separate needle
EU/1/20/1484/003 5 pre-filled syringes without needle
EU/1/20/1484/004 5 pre-filled syringes with separate needle
EU/1/20/1484/005 10 pre-filled syringes without needle
EU/1/20/1484/006 10 pre-filled syringes with separate needle

13. BATCH NUMBER

Lot

14. GENERAL CLASSIFICATION FOR SUPPLY

15. INSTRUCTIONS ON USE

16. INFORMATION IN BRAILLE

Justification for not including braille accepted

17. UNIQUE IDENTIFIER – 2D BARCODE

2D barcode carrying the unique identifier included

18. UNIQUE IDENTIFIER – HUMAN READABLE DATA

<PC: {number}
SN: {number}>

MINIMUM PARTICULARS TO APPEAR ON SMALL IMMEDIATE PACKAGING UNITS

Pre-filled syringe

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

Supemtek
Injection
Quadrivalent Influenza Vaccine
xxxx/xxxx season

2. METHOD OF ADMINISTRATION

IM

3. EXPIRY DATE

EXP

4. BATCH NUMBER

Lot

5. CONTENTS BY WEIGHT, BY VOLUME OR BY UNIT

1 dose – 0.5 mL

6. OTHER

B. PACKAGE LEAFLET

Package Leaflet – Information for the User

Supemtek

Solution for injection

Quadrivalent Influenza Vaccine (recombinant, prepared in cell culture)

▼This medicine is subject to additional monitoring. This will allow quick identification of new safety information. You can help by reporting any side affects you may get. See the end of section 4 for how to report side effects.

Read all of this leaflet carefully before you receive this medicine 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, nurse or pharmacist.
- This vaccine has been prescribed for you only. Do not pass it on to others.
- If you 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 Supemtek is and what it is used for

Supemtek is a vaccine for adults who are 18 years of age and older. This vaccine helps to protect you against flu (influenza). Supemtek is egg-free because of the technology used to produce it.

How Supemtek works
When a person is given Supemtek, the body's natural defence (the immune system) produces protection against the influenza virus. None of the ingredients in the vaccine can cause flu.
As with all vaccines, Supemtek may not fully protect all persons who are vaccinated.

When to have a flu vaccine
Flu can spread very fast.

- It is caused by different types of flu virus that can change every year. This is why you might need to be vaccinated every year.
- The greatest risk of catching flu is during the cold months between October and March.
- If you 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.

2. What you need to know before you receive Supemtek

Do not use Supemtek if you are allergic to :
- the active ingredients or any of the other ingredients of this medicine (listed in section 6).
- octylphenol ethoxylate, a trace residual from the manufacturing process.

Warnings and precautions

Talk to your doctor, pharmacist or nurse before receiving Supemtek.

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

Before receiving the vaccine, tell your doctor, nurse or pharmacist if:
- you have a **short-term illness** with fever. Vaccination may need to be delayed until your fever has gone.
- you have a **weakened immune system** (immunodeficiency or you are taking medicines that affect the immune system such as cancer medicine (chemotherapy) or corticosteroid medicines).
- you have a **bleeding problem** or **bruise easily**.
- you have **fainted** with an injection before. Fainting can happen after, or even before an injection.

If any of the above apply to you (or you are not sure) talk to your doctor, pharmacist or nurse before receiving Supemtek.

Other medicines and Supemtek

Tell your doctor or nurse if you are using, have recently used or might use any other medicines, including medicines obtained without a prescription or if you have recently received any other vaccine.
Supemtek may be given at the same time as other vaccines by using separate limbs.

Pregnancy and breast-feeding

If you are pregnant or breast-feeding, think you may be pregnant or are planning to have a baby, ask your doctor or pharmacist for advice before using this vaccine. Your doctor or pharmacist will help you to decide if you should receive Supemtek.

Driving and using machines

Supemtek has no or negligible effect on your ability to drive and use machine.

Supemtek contains sodium

This vaccine contains less than 1 mmol sodium (23 mg) per dose, this means that it's essentially 'sodium free'.

3. How Supemtek is given

Supemtek is given to you by your doctor, nurse or pharmacist as an injection into the muscle at the top of the upper arm (deltoid muscle).

Adults from 18 years of age and older:

One dose of 0.5 mL.

4. Possible side effects

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

Severe allergic reactions
Contact your doctor or healthcare professional **immediately** or go to the nearest hospital emergency room right away if you have an allergic reaction. It can be life-threatening.
Symptoms include:
- difficulty breathing, shortness of breath
- swelling of the face, lips, throat or tongue
- cold, clammy skin
- palpitations
- feeling dizzy, feeling weak, fainting
- rash or itching

The following side effects have been reported with Supemtek:

Other side effects
Very common (may affect more than 1 in 10 people):
- pain at the injection site
- feeling tired (fatigue)
- headache
- muscle pain and joint pain

Muscle pain and joint pain are common in adults aged 50 years and older.

Common (may affect up to 1 in 10 people):
- feeling sick (nausea)
- redness, swelling, hardening around the area where the vaccine is injected
- fever, shivering

Fever is rare in adults aged 50 years and older.

Uncommon (may affect up to 1 in 100 people):
- diarrhoea
- itching, skin irritation, rash
- flu-like symptoms
- cough, mouth and throat pain
- itching where the vaccine is injected

Itching is rare in adults aged 50 years and older.
Skin irritation and rash have not been reported in adults aged 50 years and older.
Flu-like symptoms has not been reported in adults aged 18-49 years.

Rare (may affect up to 1 in 1000 people):
- feeling dizzy
- hives

Feeling dizzy and hives have not been reported in adults aged 18-49 years.

Not known (cannot be estimated from the available data):
- 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 (Guillain-Barré syndrome).

Reporting of side effects

If you 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 listed in Appendix V. By reporting side effects you can help provide more information on the safety of this medicine.

5. How to store Supemtek

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

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

Do not use this vaccine after the expiry date which is stated on the label and carton after EXP.

Do not throw away any medicines via wastewater or household waste. Ask you 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 Supemtek contains

One dose (0.5 mL) contains:
The active substances are influenza virus haemagglutinin (HA) proteins, of the following strains*:
A/xxxxxx (H1N1) -like virus.....45 micrograms HA
A/xxxxxx (H3N2) -like virus.....45 micrograms HA
B/xxxxxx- like virus.....45 micrograms HA
B/xxxxxx - like virus.....45 micrograms HA

* produced by recombinant DNA technology using a baculovirus expression system in a continuous insect cell line that is derived from Sf9 cells of the fall armyworm, *Spodoptera frugiperda*.

This vaccine complies with the World Health Organisation (WHO) recommendation (northern hemisphere) and EU recommendation for the {year/year} season.

The other ingredients are: polysorbate 20 (E432), sodium chloride, sodium phosphate monobasic monohydrate, sodium phosphate dibasic dodecahydrate, water for injections.

What Supemtek looks like and contents of the pack

Supemtek is a solution for injection in a pre-filled syringe (ready to use syringe).
Supemtek is a clear and colourless solution.
A single syringe contains 0.5 mL of solution for injection.

Supemtek is available in packs containing 1, 5 or 10 pre-filled syringes without needle or with separate needle.
Not all pack sizes may be marketed.

Marketing Authorisation Holder

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Manufacturer

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Other sources of information

Detailed information on this medicine is available on the European Medicines Agency web site: http://www.ema.europa.eu.

The following information is intended for healthcare professionals only:

Appropriate medical treatment and supervision should always be readily available in case of a rare anaphylactic event following the administration of the vaccine.

The vaccine should be visually inspected for particulate matter and discoloration prior to administration. In the event of any foreign particulate matter and/or variation of physical aspect being observed, do not administer the vaccine.