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

Vaxneuvance suspension for injection in pre-filled syringe
Pneumococcal polysaccharide conjugate vaccine (15-valent, adsorbed)

2. QUALITATIVE AND QUANTITATIVE COMPOSITION

1 dose (0.5 mL) contains:

Pneumococcal polysaccharide serotype 1[1,2]	2.0 micrograms
Pneumococcal polysaccharide serotype 3[1,2]	2.0 micrograms
Pneumococcal polysaccharide serotype 4[1,2]	2.0 micrograms
Pneumococcal polysaccharide serotype 5[1,2]	2.0 micrograms
Pneumococcal polysaccharide serotype 6A[1,2]	2.0 micrograms
Pneumococcal polysaccharide serotype 6B[1,2]	4.0 micrograms
Pneumococcal polysaccharide serotype 7F[1,2]	2.0 micrograms
Pneumococcal polysaccharide serotype 9V[1,2]	2.0 micrograms
Pneumococcal polysaccharide serotype 14[1,2]	2.0 micrograms
Pneumococcal polysaccharide serotype 18C[1,2]	2.0 micrograms
Pneumococcal polysaccharide serotype 19A[1,2]	2.0 micrograms
Pneumococcal polysaccharide serotype 19F[1,2]	2.0 micrograms
Pneumococcal polysaccharide serotype 22F[1,2]	2.0 micrograms
Pneumococcal polysaccharide serotype 23F[1,2]	2.0 micrograms
Pneumococcal polysaccharide serotype 33F[1,2]	2.0 micrograms

[1]Conjugated to CRM_{197} carrier protein. CRM_{197} is a nontoxic mutant of diphtheria toxin (originating from *Corynebacterium diphtheriae* C7) expressed recombinantly in *Pseudomonas fluorescens*.
[2]Adsorbed on aluminium phosphate adjuvant.

1 dose (0.5 mL) contains 125 micrograms aluminium (Al^{3+}) and approximately 30 micrograms CRM_{197} carrier protein.

For the full list of excipients, see section 6.1.

3. PHARMACEUTICAL FORM

Suspension for injection (injection).
The vaccine is an opalescent suspension.

4. CLINICAL PARTICULARS

4.1 Therapeutic indications

Vaxneuvance is indicated for active immunisation for the prevention of invasive disease and pneumonia caused by *Streptococcus pneumoniae* in individuals 18 years of age and older.

See sections 4.4 and 5.1 for information on protection against specific pneumococcal serotypes.

The use of Vaxneuvance should be in accordance with official recommendations.

4.2 Posology and method of administration

Posology

Individuals 18 years of age and older

1 dose (0.5 mL).

The need for revaccination with a subsequent dose of Vaxneuvance has not been established.

Paediatric population

The safety and efficacy of Vaxneuvance in children and adolescents less than 18 years of age have not been established.

Special populations

One dose of Vaxneuvance may be given to individuals who have one or more underlying conditions predisposing them to an increased risk of pneumococcal disease (e.g., adults living with human immunodeficiency virus (HIV) or immunocompetent adults 18 to 49 years of age with risk factors for pneumococcal disease; see section 5.1).

Method of administration

The vaccine should be administered by intramuscular injection. The preferred site is the deltoid muscle of the upper arm.

No data are available for administration via the subcutaneous or intradermal routes.

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 diphtheria toxoid-containing vaccine.

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.

Precaution related to route of administration

Vaxneuvance must not be administered intravascularly.

Anaphylaxis

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

Concurrent illness

Vaccination should be postponed in individuals suffering from acute severe febrile illness or acute infection. The presence of a minor infection and/or low-grade fever should not delay vaccination.

Thrombocytopenia and coagulation disorders

As with other intramuscular injections, the vaccine should be given with caution to individuals receiving anticoagulant therapy, or to those with thrombocytopenia or any coagulation disorder such as haemophilia. Bleeding or bruising may occur following an intramuscular administration in these individuals.

Immunocompromised individuals

Immunocompromised individuals, whether due to the use of immuno-suppressive therapy, a genetic defect, HIV infection, or other causes, may have reduced antibody response to active immunisation.

Safety and immunogenicity data for Vaxneuvance are available for individuals living with HIV infection (see section 5.1). Safety and immunogenicity data for Vaxneuvance are not available for individuals in other specific immunocompromised groups (e.g., haematopoietic stem cell transplant) and vaccination should be considered on an individual basis.

Protection

As with any vaccine, vaccination with Vaxneuvance may not protect all vaccine recipients. Vaxneuvance will only protect against *Streptococcus pneumoniae* serotypes included in the vaccine (see sections 2 and 5.1).

Sodium

This medicinal product contains less than 1 mmol sodium (23 milligrams) per dose, i.e. essentially 'sodium-free'.

4.5 Interaction with other medicinal products and other forms of interaction

Vaxneuvance can be administered concomitantly with seasonal quadrivalent influenza vaccine (split virion, inactivated).

There are no data on the concomitant administration of Vaxneuvance with other vaccines.

Different injectable vaccines should always be administered at different injection sites.

Immunosuppressive therapies may reduce the immune responses to vaccines.

4.6 Fertility, pregnancy, and lactation

Pregnancy

There is limited experience with the use of Vaxneuvance in pregnant women.

Animal studies do not indicate direct or indirect harmful effects with respect to pregnancy, embryo/foetal development, parturition or post-natal development (see section 5.3).

Administration of Vaxneuvance in pregnancy should only be considered when the potential benefits outweigh any potential risks for the mother and the foetus.

Breast-feeding

It is unknown whether Vaxneuvance is excreted in human milk.

Fertility

No human data on the effect of Vaxneuvance on fertility are available. Animal studies in female rats do not indicate harmful effects (see section 5.3).

4.7 Effects on ability to drive and use machines

Vaxneuvance has no or negligible influence on the ability to drive and use machines. However, some of the effects mentioned under section 4.8 “Undesirable effects” may temporarily affect the ability to drive or use machines.

4.8 Undesirable effects

Summary of the safety profile

The safety of Vaxneuvance in healthy and immunocompetent adults was assessed in 6 clinical studies in 7,136 adults ≥ 18 years of age. An additional clinical study assessed 302 adults ≥ 18 years of age living with HIV. Vaxneuvance was administered to 5,630 adults; 1,241 were 18 to 49 years of age, 1,911 were 50 to 64 years of age, and 2,478 were 65 years of age and older. Of those who received Vaxneuvance, 1,134 were immunocompetent adults 18 to 49 years of age who had no (n=285), 1 (n=620) or ≥ 2 (n=229) risk factors for pneumococcal disease and 152 were adults ≥ 18 years of age living with HIV. In addition, 5,253 adults were pneumococcal vaccine-naïve and 377 adults were previously vaccinated with 23-valent pneumococcal polysaccharide vaccine (PPV23) at least 1 year prior to enrolment.

The most frequently reported adverse reactions following vaccination with Vaxneuvance were solicited. In the pooled analysis of the 7 studies, the most frequent adverse reactions were injection-site pain (64.6%), fatigue (23.4%), myalgia (20.7%), headache (17.3%), injection-site swelling (16.1%), injection-site erythema (11.3%) and arthralgia (7.9%). The majority of solicited adverse reactions were mild (based on intensity or size) and of short duration (≤ 3 days); severe reactions (defined as an event that prevents normal daily activity or size > 10 cm) occurred in ≤ 1.5% of adults across the clinical program.

Older adults reported fewer adverse reactions than younger adults.

Tabulated list of adverse reactions

Local and systemic adverse reactions were solicited daily after vaccination for 5 and 14 days, respectively. Unsolicited adverse reactions were reported for 14 days after vaccination. The table presented below is based on safety data from 7 clinical studies in adults who received Vaxneuvance, of whom 4,389 were ≥ 50 years of age and 1,241 were 18 to 49 years of age.

Frequencies are reported as:
- 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 the available data).

Table 1: Tabulated list of adverse reactions

System Organ Class	Frequency	Adverse Reactions
Immune system disorders	Rare	Hypersensitivity reaction including urticaria, tongue oedema, flushing, and throat tightness
Nervous system disorders	Very Common	Headache
	Uncommon	Dizziness†
Skin and subcutaneous tissue disorders	Uncommon	Rash
Gastrointestinal disorders	Uncommon	Nausea† Vomiting
Musculoskeletal and connective tissue disorders	Very Common	Myalgia
	Common	Arthralgia*
General disorders and administration site conditions	Very Common	Injection-site pain Fatigue Injection-site swelling Injection-site erythema
	Common	Injection-site pruritus
	Uncommon	Pyrexia† Injection-site warmth Injection-site bruising/haematoma Chills†

*very common in adults 18 to 49 years of age
†common in adults 18 to 49 years of age

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

There are no data with regard to overdose.

5. PHARMACOLOGICAL PROPERTIES

5.1 Pharmacodynamic properties

Pharmacotherapeutic group: vaccines, pneumococcal vaccines, ATC code: J07AL02

Mechanism of action

Vaxneuvance contains 15 purified pneumococcal capsular polysaccharides from *Streptococcus pneumoniae* (1, 3, 4, 5, 6A, 6B, 7F, 9V, 14, 18C, 19A, 19F, 22F, 23F, 33F), each conjugated to a carrier protein (CRM_{197}). Vaxneuvance elicits a T-cell dependent immune response to induce antibodies that enhance opsonisation, phagocytosis, and killing of pneumococci to protect against pneumococcal disease.

Clinical immunogenicity in immunocompetent adults ≥ 18 years of age

Immune responses following natural exposure to *Streptococcus pneumoniae* or following pneumococcal vaccination can be determined by measuring opsonophagocytic activity (OPA) and immunoglobulin G (IgG) responses. OPA represents functional antibodies capable of opsonizing pneumococcal capsular polysaccharides for presentation to phagocytic cells for engulfment and subsequent killing, and are considered an important immunologic surrogate measure of protection

against pneumococcal disease in adults. OPA titres are expressed as the reciprocal of the highest serum dilution that reduces the survival of the pneumococci by at least 50%. A validated multiplex opsonophagocytic assay (MOPA) was used to measure serotype-specific OPA titres for each of the 15 serotypes in Vaxneuvance.

Five clinical studies (Protocol 007, Protocol 016, Protocol 017, Protocol 019, and Protocol 021) conducted in the Americas, Europe and Asia Pacific evaluated the immunogenicity of Vaxneuvance in healthy and immunocompetent adults across different age groups including individuals with or without previous pneumococcal vaccination. Each clinical study included adults with stable underlying medical conditions (e.g., diabetes mellitus, renal disorders, chronic heart disease, chronic liver disease, chronic lung disease including asthma) and/or behavioural risk factors (e.g., current tobacco use, increased alcohol consumption) that are known to increase the risk of pneumococcal disease.

In each study, immunogenicity was assessed by serotype-specific OPA and IgG responses at 30 days postvaccination. Study endpoints included OPA geometric mean titres (GMTs) and IgG geometric mean concentrations (GMCs). The pivotal study (Protocol 019) aimed to show noninferiority of the OPA GMTs for 12 of 13 serotypes that Vaxneuvance shares with the 13-valent pneumococcal polysaccharide conjugate vaccine, noninferiority and superiority for the shared serotype 3, and superiority for serotypes 22F and 33F, unique to Vaxneuvance. Superiority assessment of Vaxneuvance to the 13-valent pneumococcal polysaccharide conjugate vaccine was based on the between-group comparisons of OPA GMTs and the proportions of participants with a ≥ 4-fold rise in serotype-specific OPA titres from prevaccination to 30 days postvaccination.

Pneumococcal vaccine-naïve adults

In the pivotal, double-blind, active comparator-controlled study (Protocol 019), 1,205 immunocompetent pneumococcal vaccine-naïve subjects ≥ 50 years of age were randomised to receive Vaxneuvance or the 13-valent pneumococcal polysaccharide conjugate vaccine. The median age of participants was 66 years (range: 50 to 92 years), with approximately 69% over 65 years of age, and approximately 12% over 75 years of age. 57.3% were female and 87% reported history of at least one underlying medical condition.

The study demonstrated that Vaxneuvance is noninferior to the 13-valent pneumococcal polysaccharide conjugate vaccine for the 13 shared serotypes and superior for the 2 unique serotypes and for the shared serotype 3. Table 2 summarises the OPA GMTs at 30 days postvaccination. IgG GMCs were generally consistent with the results observed for the OPA GMTs.

Table 2: Serotype-specific OPA GMTs at 30 days Postvaccination in Pneumococcal Vaccine-Naïve Adults ≥ 50 Years of age (Protocol 019)

Pneumococcal Serotype	Vaxneuvance (N = 602)		13-valent PCV (N = 600)		GMT Ratio* (Vaxneuvance/13-valent PCV) (95% CI)*
	n	GMT*	n	GMT*	
13 Shared Serotypes[†]					
1	598	256.3	598	322.6	0.79 (0.66, 0.96)
3[‡]	598	216.2	598	135.1	1.60 (1.38, 1.85)
4	598	1125.6	598	1661.6	0.68 (0.57, 0.80)
5	598	447.3	598	563.5	0.79 (0.64, 0.98)
6A	596	5407.2	598	5424.5	1.00 (0.84, 1.19)
6B	598	4011.7	598	3258.2	1.23 (1.02, 1.48)
7F	597	4617.3	598	5880.6	0.79 (0.68, 0.90)
9V	598	1817.3	597	2232.9	0.81 (0.70, 0.94)
14	598	1999.3	598	2656.7	0.75 (0.64, 0.89)
18C	598	2757.7	598	2583.7	1.07 (0.91, 1.26)
19A	598	3194.3	598	3979.8	0.80 (0.70, 0.93)
19F	598	1695.1	598	1917.8	0.88 (0.76, 1.02)
23F	598	2045.4	598	1740.4	1.18 (0.96, 1.44)
2 Serotypes Unique to Vaxneuvance[§]					
22F	594	2375.2	586	74.6	31.83 (25.35, 39.97)
33F	598	7994.7	597	1124.9	7.11 (6.07, 8.32)

*GMTs, GMT ratio, and 95% CI are estimated from a cLDA model.

[†]A conclusion of non-inferiority for the 13 shared serotypes is based on the lower bound of the 95% CI for the estimated GMT ratio (Vaxneuvance/13-valent PCV) being > 0.5.

[‡]A conclusion of superiority for serotype 3 is based on the lower bound of the 95% CI for the estimated GMT ratio (Vaxneuvance/13-valent PCV) being > 1.2.

[§]A conclusion of superiority for the 2 unique serotypes is based on the lower bound of the 95% CI for the estimated GMT ratio (Vaxneuvance/13-valent PCV) being > 2.0.

N=Number of participants randomised and vaccinated; n=Number of participants contributing to the analysis.

CI=confidence interval; cLDA=constrained longitudinal data analysis; GMT=geometric mean titre (1/dil); OPA=opsonophagocytic activity; PCV=pneumococcal conjugate vaccine.

In a double-blind, descriptive study (Protocol 017), 1,515 immunocompetent subjects 18 to 49 years of age with or without risk factors for pneumococcal disease were randomised 3:1 and received Vaxneuvance or the 13-valent pneumococcal polysaccharide conjugate vaccine, followed by PPV23 6 months later. Risk factors for pneumococcal disease included the following: diabetes mellitus, chronic heart disease including heart failure, chronic liver disease with compensated cirrhosis, chronic lung disease including persistent asthma and chronic obstructive pulmonary disease (COPD), current tobacco use, and increased alcohol consumption. Overall, of those who received Vaxneuvance, 285 (25.2%) had no risk factor, 620 (54.7%) had 1 risk factor, and 228 (20.1%) had 2 or more risk factors.

Vaxneuvance elicited immune responses to all 15 serotypes contained in the vaccine as assessed by OPA GMTs (Table 3) and IgG GMCs. OPA GMTs and IgG GMCs were generally comparable between the two vaccination groups for the 13 shared serotypes and higher in the Vaxneuvance group for the 2 unique serotypes. Following vaccination with PPV23, OPA GMTs and IgG GMCs were generally comparable between the two vaccination groups for all 15 serotypes.

In a subgroup analysis based on the number of reported risk factors, Vaxneuvance elicited immune responses to all 15 serotypes contained in the vaccine as assessed by OPA GMTs and IgG GMCs at 30 days postvaccination in adults with no, 1, or 2 or more risk factors. The results in each subgroup were generally consistent with those observed in the overall study population. Sequential administration of Vaxneuvance followed 6 months later by PPV23 was also immunogenic for all 15 serotypes contained in Vaxneuvance.

Table 3: Serotype-specific OPA GMTs at 30 days Postvaccination in Pneumococcal Vaccine-Naïve Adults 18-49 Years of Age With or Without Risk Factors for Pneumococcal Disease (Protocol 017)

Pneumococcal Serotype	Vaxneuvance (N = 1,133)			13-valent PCV (N = 379)		
	n	Observed GMT	95% CI*	n	Observed GMT	95% CI*
13 Shared Serotypes						
1	1019	268.6	(243.7, 296.0)	341	267.2	(220.4, 323.9)
3	1004	199.3	(184.6, 215.2)	340	150.6	(130.6, 173.8)
4	1016	1416.0	(1308.9, 1531.8)	342	2576.1	(2278.0, 2913.2)
5	1018	564.8	(512.7, 622.2)	343	731.1	(613.6, 871.0)
6A	1006	12928.8	(11923.4, 14019.0)	335	11282.4	(9718.8, 13097.5)
6B	1014	10336.9	(9649.4, 11073.4)	342	6995.7	(6024.7, 8123.2)
7F	1019	5756.4	(5410.4, 6124.6)	342	7588.9	(6775.3, 8500.2)
9V	1015	3355.1	(3135.4, 3590.1)	343	3983.7	(3557.8, 4460.7)
14	1016	5228.9	(4847.6, 5640.2)	343	5889.8	(5218.2, 6647.8)
18C	1014	5709.0	(5331.1, 6113.6)	343	3063.2	(2699.8, 3475.5)
19A	1015	5369.9	(5017.7, 5746.8)	343	5888.0	(5228.2, 6631.0)
19F	1018	3266.3	(3064.4, 3481.4)	343	3272.7	(2948.2, 3632.9)
23F	1016	4853.5	(4469.8, 5270.2)	340	3887.3	(3335.8, 4530.0)
2 Serotypes Unique to Vaxneuvance						
22F	1005	3926.5	(3645.9, 4228.7)	320	291.6	(221.8, 383.6)
33F	1014	11627.8	(10824.6, 12490.7)	338	2180.6	(1828.7, 2600.2)

*The within-group 95% CIs are obtained by exponentiating the CIs of the mean of the natural log values based on the t-distribution.
N=Number of participants randomised and vaccinated; n=Number of participants contributing to the analysis.
CI=confidence interval; GMT=geometric mean titre (1/dil); OPA=opsonophagocytic activity; PCV=pneumococcal conjugate vaccine.

Sequential administration of pneumococcal vaccines in adults

The sequential administration of Vaxneuvance followed by PPV23 was assessed in Protocol 016, Protocol 017 (see section 5.1, *Pneumococcal vaccine-naïve adults*), and Protocol 018 (see section 5.1, *Adults living with HIV*).

In a double-blind, active comparator-controlled study (Protocol 016), 652 pneumococcal vaccine-naïve subjects ≥ 50 years of age were randomised to receive Vaxneuvance or the 13-valent pneumococcal polysaccharide conjugate vaccine, followed by PPV23 one year later.

Following vaccination with PPV23, OPA GMTs and IgG GMCs were comparable between the two vaccination groups for all 15 serotypes in Vaxneuvance.

Immune responses elicited by Vaxneuvance persisted up to 12 months postvaccination as assessed by OPA GMTs and IgG GMCs. Serotype-specific OPA GMTs declined over time, as they were lower at Month 12 than Day 30, but remained above baseline levels for all the serotypes contained in either Vaxneuvance or the 13-valent pneumococcal polysaccharide conjugate vaccine. OPA GMTs and IgG GMCs were generally comparable between the intervention groups at Month 12 for the 13 shared serotypes and higher for the 2 unique serotypes among recipients of Vaxneuvance.

Adults with prior pneumococcal vaccination

In a double-blind, descriptive study (Protocol 007), 253 subjects ≥ 65 years of age who were previously vaccinated with PPV23 at least one year prior to study entry were randomised to receive Vaxneuvance or the 13-valent pneumococcal polysaccharide conjugate vaccine.

IgG GMCs and OPA GMTs were generally comparable between the two vaccination groups for the 13 shared serotypes and higher in the Vaxneuvance group for the 2 unique serotypes.

In a clinical study, in which another PCV was administered ≤ 1 year after PPV23, reduced immune responses were observed for the common serotypes compared to immune responses observed when PCV was given either alone or before PPV23. The clinical significance of this is unknown.

Clinical immunogenicity in special populations

Adults living with HIV

In a double-blind, descriptive study (Protocol 018), 302 pneumococcal vaccine-naïve subjects ≥ 18 years of age living with HIV with CD4+ T-cell count ≥ 50 cells/µL and plasma HIV ribonucleic acid (RNA) < 50,000 copies/mL were randomised to receive Vaxneuvance or the 13-valent pneumococcal polysaccharide conjugate vaccine, followed by PPV23 2 months later. The majority of participants had a CD4+ T-cell count ≥ 200 cells/µL; 4 (1.3%) had a CD4+ T-cell count ≥ 50 to < 200 cells/µL, 152 (50.3%) had a CD4+ T-cell count ≥ 200 to < 500 cells/µL, and 146 (48.3%) had a CD4+ T-cell count ≥ 500 cells/µL.

Vaxneuvance elicited immune responses to all 15 serotypes contained in the vaccine as assessed by OPA GMTs and IgG GMCs at 30 days postvaccination. Immune responses seen in the HIV-infected participants were consistently lower compared to healthy participants but comparable for both vaccination groups, except for serotype 4. OPA GMT and IgG GMC for serotype 4 were lower for Vaxneuvance. After sequential administration with PPV23, OPA GMTs and IgG GMCs were generally comparable between the two vaccination groups for all 15 serotypes.

5.2 Pharmacokinetic properties

Not applicable.

5.3 Preclinical safety data

Non-clinical study data revealed no hazard for humans based on conventional studies of repeated dose toxicity and toxicity to reproduction and development.

Vaxneuvance administered to female rats had no effects on mating performance, fertility, embryonic/foetal development, or development of the offspring.

Vaxneuvance administered to pregnant female rats resulted in detectable antibodies to all 15 serotypes in offspring. This was attributable to the acquisition of maternal antibodies via placental transfer during gestation and possibly via lactation.

6. PHARMACEUTICAL PARTICULARS

6.1 List of excipients

Sodium chloride (NaCl)
L-histidine
Polysorbate 20
Water for injections

For adjuvant, see section 2.

6.2 Incompatibilities

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

6.3 Shelf life

2 years

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.

Vaxneuvance should be administered as soon as possible after being removed from the refrigerator.

In the event of temporary temperature excursions, stability data indicate that Vaxneuvance is stable at temperatures up to 25 °C for 48 hours.

6.5 Nature and contents of container

0.5 mL suspension in pre-filled syringe (Type I glass) with a plunger stopper (latex-free bromobutyl rubber) and a tip cap (latex-free styrene-butadiene rubber).

Pack sizes of 1 or 10 pre-filled syringes, either without needles, with 1 separate needle, or with 2 separate needles.

Not all pack sizes may be marketed.

6.6 Special precautions for disposal and other handling

- The vaccine should be used as supplied.
- Immediately prior to use, hold the pre-filled syringe horizontally and shake vigorously to obtain an opalescent suspension. Do not use the vaccine if it cannot be resuspended.
- Inspect the suspension visually for particulate matter and discolouration prior to administration. Discard the vaccine if particulates are present and/or if it appears discoloured.
- Attach a needle with Luer lock connection by twisting in a clockwise direction until the needle fits securely on the syringe.
- Inject immediately using the intramuscular (IM) route, preferably in the deltoid area of the upper arm.
- Exercise care to avoid harm from an accidental needle stick.

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

7. MARKETING AUTHORISATION HOLDER

Merck Sharp & Dohme B.V.
Waarderweg 39
2031 BN Haarlem
The Netherlands

8. MARKETING AUTHORISATION NUMBER(S)

EU/1/21/1591/001
EU/1/21/1591/002
EU/1/21/1591/003
EU/1/21/1591/004
EU/1/21/1591/005
EU/1/21/1591/006

9. DATE OF FIRST AUTHORISATION/RENEWAL OF THE AUTHORISATION

Date of first authorisation: {DD month YYYY}

10. DATE OF REVISION OF THE TEXT

<{MM/YYYY}>

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)

MSD International GmbH
Brinny, Innishannon
County Cork
Ireland

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

Merck Sharp & Dohme B.V.
Waarderweg 39
2031 BN Haarlem
The Netherlands

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 CARTON – Pre-filled syringe

1. NAME OF THE MEDICINAL PRODUCT

Vaxneuvance suspension for injection in pre-filled syringe
Pneumococcal polysaccharide conjugate vaccine (15-valent, adsorbed)

2. STATEMENT OF ACTIVE SUBSTANCE(S)

One dose (0.5 mL) contains 2 µg of pneumococcal polysaccharide of serotypes 1, 3, 4, 5, 6A, 7F, 9V, 14, 18C, 19A, 19F, 22F, 23F, 33F and 4 µg for serotype 6B conjugated to CRM_{197} carrier protein, adsorbed on aluminium phosphate adjuvant. One dose (0.5 mL) contains 125 µg Al^{3+}.

3. LIST OF EXCIPIENTS

Excipients: NaCl, L-histidine, polysorbate 20, water for injections

4. PHARMACEUTICAL FORM AND CONTENTS

Suspension for injection
1 pre-filled syringe (0.5 mL) without needle
10 pre-filled syringes (0.5 mL) without needle
1 pre-filled syringe (0.5 mL) + 1 separate needle
10 pre-filled syringes (0.5 mL) + 10 separate needles
1 pre-filled syringe (0.5 mL) + 2 separate needles
10 pre-filled syringes (0.5 mL) + 20 separate needles

5. METHOD AND ROUTE(S) OF ADMINISTRATION

Shake vigorously immediately before use.
Read the package leaflet before use.
Intramuscular 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

Merck Sharp & Dohme B.V.
Waarderweg 39
2031 BN Haarlem
The Netherlands

12. MARKETING AUTHORISATION NUMBER(S)

EU/1/21/1591/001 - pack of 1 without needle
EU/1/21/1591/002 - pack of 10 without needle
EU/1/21/1591/003 - pack of 1 + 1 separate needle
EU/1/21/1591/004 - pack of 10 + 10 separate needles
EU/1/21/1591/005 - pack of 1 + 2 separate needles
EU/1/21/1591/006 - pack of 10 + 20 separate needles

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
SN
NN

MINIMUM PARTICULARS TO APPEAR ON SMALL IMMEDIATE PACKAGING UNITS

LABEL – Pre-filled syringe

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

Vaxneuvance
Pneumococcal polysaccharide conjugate vaccine (15-valent, adsorbed)
Injection
IM

2. METHOD OF ADMINISTRATION

Shake vigorously before use.

3. EXPIRY DATE

EXP

4. BATCH NUMBER

Lot

5. CONTENTS BY WEIGHT, BY VOLUME OR BY UNIT

1 dose (0.5 mL)

6. OTHER

MSD

B. PACKAGE LEAFLET

Package leaflet: Information for the user

Vaxneuvance suspension for injection in pre-filled syringe
Pneumococcal polysaccharide conjugate vaccine (15-valent, adsorbed)

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

Read all of this leaflet carefully before you 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 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 Vaxneuvance is and what it is used for
2. What you need to know before you receive Vaxneuvance
3. How Vaxneuvance is given
4. Possible side effects
5. How to store Vaxneuvance
6. Contents of the pack and other information

1. What Vaxneuvance is and what it is used for

Vaxneuvance is a pneumococcal vaccine given to help protect against diseases caused by 15 types of bacteria called *Streptococcus pneumoniae* or pneumococcus in individuals 18 years of age and older.

These diseases include lung infection (pneumonia), inflammation of the coverings of the brain and spinal cord (meningitis), and a severe infection in the blood (bacteraemia).

2. What you need to know before you receive Vaxneuvance

Do not receive Vaxneuvance if:
- you are allergic to the active substances or to any of the ingredients of this vaccine (listed in section 6), or to any vaccine that contains diphtheria toxoid.

Warnings and precautions
Talk to your doctor, pharmacist, or nurse before you receive Vaxneuvance if:
- your immune system is weak (which means your body is less able to fight off infections) or if you are taking certain medicines that may make your immune system weak (for example, immunosuppressants or steroids).
- you have a high fever or severe infection. In these cases, the vaccination may have to be postponed until you have recovered. However, a mild fever or infection (for example having a cold) itself is not a reason to delay vaccination.
- you have any bleeding problems, bruise easily, or are taking medicines to prevent blood clots.

As with any vaccine, Vaxneuvance may not fully protect all persons who are vaccinated.

Children and adolescents
It has not been established whether Vaxneuvance can be used in children and adolescents younger than 18 years of age.

Other medicines/vaccines and Vaxneuvance
Vaxneuvance can be given at the same time as the flu (inactivated influenza) vaccine.

Tell your doctor, pharmacist, or nurse if:
- you are taking, have recently taken, or might take any prescription medicines (for example, immunosuppressants or steroids which may make your immune system weak) or any medicines obtained without a prescription.
- you have recently received or plan to receive any other vaccine.

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, pharmacist, or nurse for advice before you receive this vaccine.

Driving and using machines
Vaxneuvance has no or negligible influence on the ability to drive and use machines. However, some of the effects mentioned under section 4 "Possible side effects" may temporarily affect the ability to drive or use machines.

Vaxneuvance contains sodium
This medicine contains less than 1 mmol sodium (23 milligrams) per dose, that is to say essentially 'sodium-free'.

3. How Vaxneuvance is given

One injection of Vaxneuvance is given by your doctor, pharmacist or nurse into your muscle (preferably in your upper arm).

Tell your doctor, pharmacist, or nurse if you have been given a pneumococcal vaccine before.

Special populations

One injection of Vaxneuvance may be given to individuals who have one or more underlying conditions that increase their risk for pneumococcal disease (such as those living with human immunodeficiency virus [HIV]).

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

4. Possible side effects

Like all vaccines, Vaxneuvance can cause side effects, although not everybody gets them.

Get medical care right away if you have symptoms of an allergic reaction, which may include:
- Wheezing or trouble breathing
- Swelling of the face, lips, or tongue
- Hives
- Rash

The following side effects can be seen after the use of Vaxneuvance:

Very common (may affect more than 1 in 10 people):
- Pain, swelling, or redness at the injection site
- Feeling tired
- Muscle aches

- Headaches
- Joint pain (in those 18 to 49 years of age)

Common (may affect up to 1 in 10 people):
- Joint pain (in those 50 years of age and older)
- Nausea (in those 18 to 49 years of age)
- Fever (in those 18 to 49 years of age)
- Itchiness at the injection site
- Dizziness (in those 18 to 49 years of age)
- Chills (in those 18 to 49 years of age)

Uncommon (may affect up to 1 in 100 people):
- Fever (in those 50 years of age and older)
- Warmth at the injection site
- Bruising at the injection site
- Dizziness (in those 50 years of age and older)
- Nausea (in those 50 years of age and older)
- Vomiting
- Chills (in those 50 years of age and older)
- Rash

Rare (may affect up to 1 in 1,000 people):
- Allergic reaction such as hives, tongue swelling, flushing, and throat tightness

These side effects are generally mild and last a short time.

Tell your healthcare provider about these side effects or any other unusual symptoms that develop after you receive this vaccine.

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 Vaxneuvance

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 carton and syringe label 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 pre-filled syringe in the outer carton in order to protect from light.

Vaxneuvance should be administered as soon as possible after being removed from the refrigerator. However, in circumstances where Vaxneuvance is temporarily held outside of refrigeration, the vaccine is stable at temperatures up to 25 °C for 48 hours.

6. Contents of the pack and other information

What Vaxneuvance contains
The active substances are:
- bacterial sugars from pneumococcus types 1, 3, 4, 5, 6A, 7F, 9V, 14, 18C, 19A, 19F, 22F, 23F, and 33F (2.0 micrograms of each type);
- bacterial sugar from pneumococcus type 6B (4.0 micrograms).

Each bacterial sugar is linked to a carrier protein (CRM_{197}). The bacterial sugars and the carrier protein are not alive and do not cause disease.

One dose (0.5 mL) contains approximately 30 micrograms carrier protein, adsorbed on aluminium phosphate (125 micrograms aluminium [Al^{3+}]). Aluminium phosphate is included in the vaccine as an adjuvant. Adjuvants are included to improve the immune responses of vaccines.

The other ingredients are sodium chloride (NaCl), L-histidine, polysorbate 20, and water for injections.

What Vaxneuvance looks like and contents of the pack
Vaxneuvance is an opalescent suspension for injection, provided in a single-dose, pre-filled syringe (0.5 mL). Vaxneuvance is available in pack sizes of 1 or 10, either without needles, with 1 separate needle, or with 2 separate needles.

Not all pack sizes may be marketed.

Marketing Authorisation Holder and Manufacturer
Merck Sharp & Dohme B.V.
Waarderweg 39
2031 BN Haarlem
The Netherlands

For any information about this medicine, please contact the local representative of the Marketing Authorisation Holder:

België/Belgique/Belgien
MSD Belgium
Tél/Tel: +32 (0) 27766211
dpoc_belux@merck.com

България
Мерк Шарп и Доум България ЕООД,
тел.: + 359 2 819 3737
info-msdbg@merck.com

Česká republika
Merck Sharp & Dohme s.r.o.
Tel.: +420 233 010 111
dpoc_czechslovak@merck.com

Danmark
MSD Danmark ApS
Tlf: + 45 4482 4000
dkmail@merck.com

Deutschland
MSD Sharp & Dohme GmbH

Lietuva
UAB Merck Sharp & Dohme
Tel.: +370.5.2780.247
msd_lietuva@merck.com

Luxembourg/Luxemburg
MSD Belgium
Tél/Tel: +32 (0) 27766211
dpoc_belux@merck.com

Magyarország
MSD Pharma Hungary Kft.
Tel.: + 36.1.888.5300
hungary_msd@merck.com

Malta
Merck Sharp & Dohme Cyprus Limited.
Tel: 8007 4433 (+356 99917558)
malta_info@merck.com

Nederland
Merck Sharp & Dohme B.V.

Tel: 0800 673 673 673 (+49 (0) 89 4561 0)
e-mail@msd.de

Eesti
Merck Sharp & Dohme OÜ
Tel.: +372 6144 200
msdeesti@merck.com

Ελλάδα
MSD Α.Φ.Β.Ε.Ε.
Τηλ: +30 210 98 97 300
dpoc_greece@merck.com

España
Merck Sharp & Dohme de España, S.A.
Tel: +34 91 321 06 00
msd_info@merck.com

France
MSD VACCINS
Tél: +33 (0) 1 80 46 40 40
information.medicale@msd.com

Hrvatska
Merck Sharp & Dohme d.o.o.
Tel: +385 1 66 11 333
croatia_info@merck.com

Ireland
Merck Sharp & Dohme Ireland (Human Health) Limited
Tel: +353 (0)1 2998700
medinfo_ireland@merck.com

Ísland
Vistor hf.
Sími: + 354 535 7000

Italia
MSD Italia S.r.l.
Tel: +39 06 361911
medicalinformation.it@merck.com

Κύπρος
Merck Sharp & Dohme Cyprus Limited
Τηλ: 800 00 673 (+357 22866700)
cyprus_info@merck.com

Latvija
SIA Merck Sharp & Dohme Latvija
Tel: +371.67364.224
msd_lv@merck.com

Tel: 0800 9999000 (+31 23 5153153)
medicalinfo.nl@merck.com

Norge
MSD (Norge) AS
Tlf: +47 32 20 73 00
msdnorge@msd.no

Österreich
Merck Sharp & Dohme Ges.m.b.H.
Tel: +43 (0) 1 26 044
msd-medizin@merck.com

Polska
MSD Polska Sp. z o.o.
Tel.: +48.22.549.51.00
msdpolska@merck.com

Portugal
Merck Sharp & Dohme, Lda
Tel: +351 21 4465700
inform_pt@merck.com

România
Merck Sharp & Dohme Romania S.R.L
Tel: + 4021 529 29 00
msdromania@merck.com

Slovenija
Merck Sharp & Dohme, inovativna zdravila d.o.o.
Tel: +386.1.520.4201
msd.slovenia@merck.com

Slovenská republika
Merck Sharp & Dohme, s. r. o
Tel: +421 2 58282010
dpoc_czechslovak@merck.com

Suomi/Finland
MSD Finland Oy
Puh/Tel: +358 (0)9 804 650
info@msd.fi

Sverige
Merck Sharp & Dohme (Sweden) AB
Tel: +46 77 5700488
medicinskinfo@merck.com

United Kingdom (Northern Ireland)
Merck Sharp & Dohme Ireland (Human Health) Limited
Tel: +353 (0)1 2998700
medinfoNI@msd.com

This leaflet was last revised in {**MM/YYYY**}.

Other sources of information

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

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The following information is intended for healthcare professionals only:

Vaxneuvance must not be injected intravascularly.

- Immediately prior to use, hold the pre-filled syringe horizontally and shake vigorously to obtain an opalescent suspension. Do not use the vaccine if it cannot be resuspended.
- Inspect the suspension visually for particulate matter and discolouration prior to administration. Discard the vaccine if particulates are present and/or if it appears discoloured.
- Attach a needle with Luer lock connection by twisting in a clockwise direction until the needle fits securely on the syringe.
- Inject immediately using the intramuscular (IM) route, preferably in the deltoid area of the upper arm.
- Exercise care to avoid harm from an accidental needle stick.

No data are available for administration via the subcutaneous or intradermal routes.

Vaxneuvance must not be mixed with any other vaccines in the same syringe.

Vaxneuvance can be administered concomitantly with seasonal quadrivalent influenza vaccine (split virion, inactivated). Different injectable vaccines should always be administered at different injection sites.

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.

Vaxneuvance should be administered as soon as possible after being removed from the refrigerator.

In the event of temporary temperature excursions, stability data indicate that Vaxneuvance is stable at temperatures up to 25 °C for 48 hours.

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