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

CAPVAXIVE solution for injection in pre-filled syringe
Pneumococcal polysaccharide conjugate vaccine (21-valent)

2. QUALITATIVE AND QUANTITATIVE COMPOSITION

1 dose (0.5 mL) contains:

Pneumococcal polysaccharide serotype 3[1]	4 mcg
Pneumococcal polysaccharide serotype 6A[1]	4 mcg
Pneumococcal polysaccharide serotype 7F[1]	4 mcg
Pneumococcal polysaccharide serotype 8[1]	4 mcg
Pneumococcal polysaccharide serotype 9N[1]	4 mcg
Pneumococcal polysaccharide serotype 10A[1]	4 mcg
Pneumococcal polysaccharide serotype 11A[1]	4 mcg
Pneumococcal polysaccharide serotype 12F[1]	4 mcg
Pneumococcal polysaccharide serotype 15A[1]	4 mcg
Pneumococcal polysaccharide from deOAc15B (de-O-acetylated serotype 15B)[1]	4 mcg
Pneumococcal polysaccharide serotype 16F[1]	4 mcg
Pneumococcal polysaccharide serotype 17F[1]	4 mcg
Pneumococcal polysaccharide serotype 19A[1]	4 mcg
Pneumococcal polysaccharide serotype 20A[1]	4 mcg
Pneumococcal polysaccharide serotype 22F[1]	4 mcg
Pneumococcal polysaccharide serotype 23A[1]	4 mcg
Pneumococcal polysaccharide serotype 23B[1]	4 mcg
Pneumococcal polysaccharide serotype 24F[1]	4 mcg
Pneumococcal polysaccharide serotype 31[1]	4 mcg
Pneumococcal polysaccharide serotype 33F[1]	4 mcg
Pneumococcal polysaccharide serotype 35B[1]	4 mcg

[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*.

1 dose (0.5 mL) contains approximately 65 mcg CRM_{197} carrier protein.

Excipient(s) with known effect

1 dose (0.5 mL) contains 0.5 mg polysorbate 20.

For the full list of excipients, see section 6.1.

3. PHARMACEUTICAL FORM

Solution for injection (injection).
The vaccine is a colourless, clear to opalescent solution.

4. CLINICAL PARTICULARS

4.1 Therapeutic indications

CAPVAXIVE 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 CAPVAXIVE 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 CAPVAXIVE has not been established.

Paediatric population
The safety and efficacy of CAPVAXIVE in children younger than 18 years of age have not been established. No data are available.

Method of administration

CAPVAXIVE should be administered by intramuscular injection only. This vaccine should be administered preferably in the deltoid muscle of the upper arm in adults, with care to avoid injection into or near nerves and blood vessels.

For instructions on the handling of the vaccine before administration, see section 6.6.

4.3 Contraindications

Hypersensitivity to the active substances including diphtheria toxoid, or to any of the excipients listed in section 6.1.

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.

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 in individuals

receiving anticoagulant therapy or those with thrombocytopenia or any coagulation disorder (such as haemophilia) because bleeding or bruising may occur following an intramuscular administration in these individuals.

Anxiety-related reactions

Anxiety-related reactions, including vasovagal reactions (syncope), hyperventilation or stress-related reactions may occur in association with vaccination as a response to the needle injection. Stress-related reactions are temporary and resolve on their own. It is important that precautions are in place to avoid injury from fainting.

Immunocompromised individuals

Safety and immunogenicity data on CAPVAXIVE are not available for individuals in immunocompromised groups. Vaccination should be considered on an individual basis.

Based on experience with pneumococcal vaccines, immunocompromised individuals, including those receiving immunosuppressive therapy, may have a reduced immune response to CAPVAXIVE.

Protection

As with any vaccine, vaccination with CAPVAXIVE may not protect all vaccine recipients. This vaccine will only protect against *Streptococcus pneumoniae* serotypes included in the vaccine and to the cross-reactive serotype 15B (see sections 2 and 5.1).

Sodium

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

Polysorbate 20

This medicinal product contains 0.5 mg of polysorbate 20 in each dose. Polysorbates may cause allergic reactions.

4.5 Interaction with other medicinal products and other forms of interaction

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

CAPVAXIVE can be administered concomitantly with quadrivalent influenza vaccine (split virion, inactivated). There are no data on the concomitant administration of CAPVAXIVE with vaccines other than influenza vaccines.

4.6 Fertility, pregnancy and lactation

Pregnancy

There are no data on the use of CAPVAXIVE 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 CAPVAXIVE 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 CAPVAXIVE is excreted in human milk.

Fertility

No human data on the effect of CAPVAXIVE 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

CAPVAXIVE 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 most frequently reported adverse reactions following vaccination with CAPVAXIVE in individuals 18 years of age and older were solicited. Overall, the most frequently reported adverse reactions were injection-site pain (52.9%), fatigue (25.3%), headache (17.7%), and myalgia (10.4%).

The majority of local and systemic adverse reactions for individuals who received CAPVAXIVE were mild or moderate (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 ≤ 1.0% of adults (see Table 1).

Tabulated list of adverse reactions

Unless otherwise stated the frequency categories are based on the safety of CAPVAXIVE assessed in 6 clinical studies, conducted across the Americas, Europe, Asia Pacific and Africa which included 4 914 individuals >18 years of age; with or without stable underlying medical conditions.

Adverse reactions reported for all age groups are listed in this section per system organ class, in decreasing order of frequency and seriousness. The frequency is defined as follows:

- 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	Adverse Reactions	Frequency
Blood and lymphatic system disorders	Lymphadenopathy	Uncommon
Immune system disorders	Hypersensitivity reaction, including bronchospasm	Rare
Nervous system disorders	Headache	Very Common
	Dizziness	Uncommon
Gastrointestinal disorders	Nausea Diarrhoea Vomiting	Uncommon
Musculoskeletal and connective tissue disorders	Myalgia*	Common
	Arthralgia	Uncommon
General disorders and administration site conditions	Injection-site pain Fatigue	Very common
	Injection-site erythema* Injection-site swelling* Pyrexia	Common
	Injection-site pruritus Chills Injection-site bruising	Uncommon

* very common in individuals 18 to 49 years of age

Other special populations

Safety in individuals 65 years of age and older
A lower frequency of local injection-site reactions was observed in participants 75 years of age and older compared to participants 65 to 74 years of age. There were no clinically meaningful differences for other adverse events in participants 65 to 74 years of age and 75 years of age and older who received CAPVAXIVE.

Safety in adults living with HIV
The safety profile of CAPVAXIVE in adults living with HIV was generally comparable to the safety profile of pneumococcal 15-valent conjugate vaccine (PCV15) followed by pneumococcal 23-valent polysaccharide vaccine (PPSV23, see section 5.1).

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

Overdose with CAPVAXIVE is unlikely due to its presentation as a pre-filled syringe.

5. PHARMACOLOGICAL PROPERTIES

5.1 Pharmacodynamic properties

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

Mechanism of action

CAPVAXIVE contains 21 pneumococcal capsular polysaccharides from *Streptococcus pneumoniae* (3, 6A, 7F, 8, 9N, 10A, 11A, 12F, 15A, deOAc15B, 16F, 17F, 19A, 20A, 22F, 23A, 23B, 24F, 31, 33F, and 35B), which are known to contribute to the pathogenicity of pneumococci in adults. Each serotype of activated polysaccharide is individually conjugated to a carrier protein (CRM_{197}), and elicits antibodies that enhance opsonisation, phagocytosis, and killing of pneumococci to protect against pneumococcal disease. CAPVAXIVE elicits a T-cell dependent immune response. Carrier protein-specific helper T-cells support specificity, functionality, and maturation of serotype-specific B-cells.

Immune responses following natural exposure to *Streptococcus pneumoniae* or following pneumococcal vaccination can be determined through the assessments of opsonophagocytic activity (OPA) responses, to assess functional antibodies capable of opsonizing pneumococcal capsular polysaccharides for presentation to phagocytic cells for engulfment and subsequent killing. OPA responses are considered an important immunologic surrogate measure of protection against pneumococcal disease in adults. Specific threshold values that correlate with protection in adults have not been defined. There is a positive correlation between OPA responses and anti-capsular Immunoglobulin G (IgG) responses.

Serotype-specific immune responses (OPA and IgG) for the 21 serotypes contained in CAPVAXIVE and the cross-reactive serotype 15B were measured using a validated multiplexed opsonophagocytic assay (MOPA) and pneumococcal electrochemiluminescence (Pn ECL) assay. Serotype 15C represents the immune response to the deOAc15B polysaccharide as the molecular structure for deOAc15B and 15C are similar.

Clinical efficacy and safety

Clinical trials experience in individuals 18 years of age and older

Six Phase 3, clinical studies (Protocol 003, Protocol 004, Protocol 005, Protocol 006, Protocol 007, and Protocol 010) conducted across the Americas, Europe, Asia Pacific and Africa evaluated the immunogenicity of CAPVAXIVE in 8 369 individuals 18 years of age and older, of whom 5 450 received CAPVAXIVE. Participants enrolled in the Phase 3 studies included adults across different age groups; approximately 32% were 18 to 49 years of age, 32% were 50 to 64 years of age, 29% were 65 to 74 years of age, and 8% were 75 years of age and older. Of those vaccinated, 14% had received other prior pneumococcal vaccines, 33% had risk factors for pneumococcal disease (e.g., alcoholism, chronic heart disease, chronic liver disease, chronic lung disease including asthma, diabetes, renal disorders, smoking) and approximately 4% were adults living with HIV, which is associated with high risk of pneumococcal disease.

In each study, immunogenicity was assessed by serotype-specific OPA and IgG responses at 1-month postvaccination.

Clinical trials conducted in pneumococcal vaccine-naïve adults

CAPVAXIVE effectiveness in adults against invasive pneumococcal disease and pneumonia was assessed based on comparative immunogenicity to a licensed pneumococcal vaccine (pneumococcal 20-valent conjugate vaccine (PCV20) and PPSV23).

Protocol 003
In a double-blind study, 2 362 pneumococcal vaccine-naïve individuals 50 years of age and older were randomised to receive either CAPVAXIVE or PCV20. The immune response as assessed by the geometric mean titre (GMT) ratio (CAPVAXIVE/PCV20) is presented in Table 2.

CAPVAXIVE met the pre-defined statistical noninferiority criterion compared to PCV20 for the 10

serotypes included in both vaccines as assessed by the geometric mean titre (GMT) ratio (CAPVAXIVE/PCV20) where the noninferiority criterion was met if the lower bound of the 2-sided 95% Confidence Interval (CI) were > 0.5. CAPVAXIVE met the predefined superiority criterion compared to PCV20 for all but one (15C) of the 11 additional serotypes to CAPVAXIVE as assessed by the GMT ratio (CAPVAXIVE/PCV20) where the statistical superiority criterion was met if the lower bound of the 2 sided 95% CI were > 2.0 (see Table 2).

Table 2: Serotype-specific OPA GMTs in pneumococcal vaccine-naïve individuals ≥ 50 years of age (Protocol 003)

Pneumococcal Serotype	CAPVAXIVE (N=1 179)		PCV 20 (N=1 177)		GMT Ratio* (CAPVAXIVE/PCV20) (95% CI)*
	n	GMT*	n	GMT*	
10 Shared Serotypes†					
3	1 154	274.0	1 161	176.7	1.55 (1.40, 1.72)
6A	1 148	2 302.0	1 153	2 972.5	0.77 (0.68, 0.88)
7F	1 152	3 637.4	1 158	3 429.9	1.06 (0.95, 1.18)
8	1 155	2 501.3	1 158	1 811.1	1.38 (1.25, 1.53)
10A	1 161	3 893.4	1 159	4 678.0	0.83 (0.75, 0.93)
11A	1 145	3 232.6	1 150	2 092.8	1.54 (1.39, 1.72)
12F	1 160	2 641.2	1 161	2 499.6	1.06 (0.92, 1.21)
19A	1 159	2 136.1	1 162	2 871.8	0.76 (0.69, 0.84)
22F	1 147	3 874.5	1 154	4 770.1	0.81 (0.72, 0.92)
33F	1 154	13 558.9	1 157	11 742.1	1.15 (1.01, 1.32)
11 Additional Serotypes in CAPVAXIVE‡					
9N	1 147	7 470.7	1 150	1 640.4	4.55 (4.12, 5.04)
15A	1 107	5 237.2	1 102	1 589.0	3.30 (2.91, 3.74)
15C	1 153	4 216.2	1 158	2 072.3	2.03 (1.77, 2.34)
16F	1 151	4 868.2	1 153	846.3	5.75 (5.16, 6.41)
17F	1 148	7 764.9	1 156	460.4	16.86 (14.90, 19.09)
20A	1 161	6 099.2	1 155	631.1	9.66 (8.66, 10.79)
23A	1 132	3 737.2	1 104	461.5	8.10 (6.86, 9.55)
23B	1 160	1 082.5	1 160	107.3	10.09 (8.48, 12.00)
24F	1 153	2 728.6	1 130	70.5	38.71 (33.87, 44.25)
31	1 153	3 132.5	1 154	144.4	21.69 (18.68, 25.18)
35B	1 153	8 527.8	1 159	1 383.0	6.17 (5.59, 6.80)
Cross-reactive serotype					
15B	1 140	4 400.6	1 141	4 640.0	0.95 (0.84, 1.07)

* GMTs, GMT ratio, and 95% CI were estimated from a constrained Longitudinal Data Analysis model.

† The noninferiority criterion was met if the lower bound of the 2-sided 95% CI for the estimated GMT ratio (CAPVAXIVE/PCV20) was > 0.5.

‡ The superiority criterion was met if the lower bound of the 2-sided 95% CI for the estimated GMT ratio (CAPVAXIVE/PCV20) was > 2.0.

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

CAPVAXIVE met the superiority criterion compared to PCV20 for 10 of additional 11 serotypes (except 15C) in CAPVAXIVE as assessed by the proportion of individuals who achieved a ≥ 4-fold rise from prevaccination to 1-month postvaccination for OPA responses. The superiority criterion was defined as the difference between CAPVAXIVE and PCV20 being > 10 percentage points.

Immunobridging in pneumococcal vaccine-naïve individuals 18 to 49 years of age
In a double-blind study pneumococcal vaccine-naïve individuals 18 to 49 years of age were randomised in a 2:1 ratio to receive CAPVAXIVE (N=200) or PCV20 (N=100). The 18 to 49 year old group who received CAPVAXIVE (N=200) was compared to the 50 to 64 year old group (N=589) which also had received CAPVAXIVE to evaluate the OPA responses.

CAPVAXIVE successfully immunobridged serotype-specific immune responses to each of the 21 vaccine serotypes in individuals 18 to 49 years of age to individuals 50 to 64 years of age, as the lower bound of the 2-sided 95% CI for the GMT ratio for each serotype was > 0.5 (see Table 3).

Table 3: Comparison of serotype-specific OPA GMTs in pneumococcal vaccine-naïve individuals 18-49 years of age to 50-64 years of age who received CAPVAXIVE (Protocol 003)

Pneumococcal Serotype	18-49 years (N=200)		50-64 years (N=589)		GMT Ratio*† (18-49 years/50-64 years) (95% CI)*
	n	GMT	n	GMT	
3	194	308.6	572	282.7	1.09 (0.90, 1.33)
6A	196	5 289.6	569	2 572.9	2.06 (1.61, 2.62)
7F	198	6 447.2	571	4 278.8	1.51 (1.23, 1.84)
8	197	4 516.0	571	3 004.7	1.50 (1.26, 1.79)
9N	197	17 283.2	570	8 791.4	1.97 (1.59, 2.43)
10A	197	6 808.1	575	4 382.6	1.55 (1.26, 1.92)
11A	196	5 871.6	564	3 785.8	1.55 (1.26, 1.91)
12F	196	6 150.4	574	3 561.2	1.73 (1.37, 2.17)
15A	184	11 319.2	550	5 901.2	1.92 (1.55, 2.37)
15C	195	10 194.0	570	5 708.0	1.79 (1.36, 2.35)
16F	193	8 877.0	571	5 720.0	1.55 (1.26, 1.91)
17F	194	16 070.6	568	10 068.0	1.60 (1.26, 2.02)
19A	198	2 773.2	574	2 374.6	1.17 (0.97, 1.40)
20A	197	13 150.0	575	7 562.7	1.74 (1.39, 2.18)
22F	198	9 299.6	568	4 683.6	1.99 (1.58, 2.49)
23A	192	8 848.7	561	4 739.5	1.87 (1.43, 2.44)
23B	198	2 140.1	575	1 420.0	1.51 (1.11, 2.04)
24F	197	4 137.6	570	3 047.2	1.36 (1.10, 1.67)
31	195	8 005.6	570	3 820.7	2.10 (1.63, 2.69)
33F	197	34 805.5	570	17 607.4	1.98 (1.52, 2.57)
35B	198	13 933.4	573	9 053.9	1.54 (1.26, 1.87)

***** GMTs, GMT ratio, and 95% CI were estimated from a Longitudinal Data Analysis model.

† A conclusion of immunobridging was based on the lower bound of the 95% CI for the estimated GMT ratio (18-49 years / 50-64 years) being > 0.5.

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

Protocol 010
In a double-blind study, 1 484 pneumococcal vaccine-naïve individuals 50 years of age and older were randomised to receive either CAPVAXIVE or PPSV23; 46% of participants were 50 to 64 years of age, 54% were 65 years of age and older, and 10% were 75 years of age and older. The immune response as assessed by the GMT ratio (CAPVAXIVE/PPSV23) is presented in Table 4.

CAPVAXIVE met the pre-defined statistical noninferiority criterion compared to PPSV23 for the 12 serotypes included in both vaccines as assessed by the GMT ratio (CAPVAXIVE/PPSV23) where the noninferiority criterion was met if the lower bound of the 2-sided 95% Confidence Interval (CI) were > 0.5. CAPVAXIVE met the predefined superiority criterion compared to PPSV23 for the 9 additional serotypes to CAPVAXIVE as assessed by the GMT ratio (CAPVAXIVE/PPSV23) where the statistical superiority criterion was met if the lower bound of the 2 sided 95% CI were > 2.0 (see Table 4).

Table 4: Serotype specific OPA GMTs in pneumococcal vaccine-naïve individuals ≥ 50 years of age (Protocol 010)

Pneumococcal Serotype	CAPVAXIVE (N=739)		PPSV23 (N=741)		GMT Ratio* (CAPVAXIVE/PPSV23) (95% CI)*
	n	GMT*	n	GMT*	
12 Shared Serotypes†					
3	725	230.4	729	211.5	1.09 (0.96, 1.23)
7F	729	4 876.7	732	3 314.6	1.47 (1.29, 1.68)
8	730	3 379.6	733	2 882.1	1.17 (1.04, 1.32)
9N	728	7 346.6	729	6 545.9	1.12 (1.00, 1.26)
10A	725	4 382.9	726	2 818.7	1.55 (1.37, 1.77)
11A	728	3 711.1	729	1 809.7	2.05 (1.82, 2.31)
12F	728	3 031.8	732	1 854.9	1.63 (1.40, 1.90)
17F	722	8 215.7	730	4 060.5	2.02 (1.77, 2.31)
19A	731	2 670.0	732	1 879.9	1.42 (1.26, 1.60)
20A	730	6 966.1	733	4 208.4	1.66 (1.46, 1.88)
22F	725	4 724.1	728	3 084.9	1.53 (1.34, 1.75)
33F	727	15 497.3	731	17 483.0	0.89 (0.76, 1.04)
9 Additional Serotypes in CAPVAXIVE‡					
6A	729	3 193.9	730	964.0	3.31 (2.84, 3.87)
15A	715	6 746.5	703	1 462.1	4.61 (3.99, 5.33)
15C	729	7 604.8	730	2 605.0	2.92 (2.50, 3.42)
16F	726	6 675.4	723	1 482.2	4.50 (3.99, 5.09)
23A	711	4 804.2	690	837.2	5.74 (4.81, 6.85)
23B	730	2 252.6	726	137.2	16.42 (13.46, 20.03)
24F	723	4 568.0	705	1 346.7	3.39 (2.97, 3.87)
31	730	5 040.7	731	423.9	11.89 (10.16, 13.91)
35B	728	10 707.5	732	1 735.0	6.17 (5.54, 6.87)
Cross-reactive serotype					
15B	716	5 157.3	727	3 243.2	1.59 (1.37, 1.85)

***** GMTs, GMT ratio, and 95% CI were estimated from a constrained Longitudinal Data Analysis model.

† The noninferiority criterion was met if the lower bound of the 2-sided 95% CI for the estimated GMT ratio (CAPVAXIVE/PPSV23) was > 0.5.

‡ The superiority criterion was met if the lower bound of the 2-sided 95% CI for the estimated GMT ratio (CAPVAXIVE/PPSV23) was > 2.0.

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

CAPVAXIVE met the superiority criterion compared to PPSV23 for 8 of 9 additional serotypes (except 15C) in CAPVAXIVE as assessed by the proportion of individuals who achieved a ≥ 4-fold rise from prevaccination to 1-month postvaccination for OPA responses. The superiority criterion was defined as the difference between CAPVAXIVE and PPSV23 being > 10 percentage points.

Clinical trials conducted in adults with prior pneumococcal vaccination

Protocol 006

A descriptive Phase 3 study, enrolled individuals ≥ 50 years of age who were previously vaccinated with other pneumococcal vaccines at least 1 year prior to study entry. Subjects were randomised to receive CAPVAXIVE or another pneumococcal vaccine.

Across all 3 cohorts, CAPVAXIVE was immunogenic for all 21 serotypes contained in the vaccine as assessed by serotype-specific OPA GMTs. OPA GMTs were generally comparable between the two vaccination groups for the shared serotypes and higher in the CAPVAXIVE group for the additional serotypes included only in CAPVAXIVE.

Special populations

Adults living with HIV

Protocol 007
In a double-blind study, 313 adults living with HIV, with or without a history of prior pneumococcal vaccination, were randomised in a 1:1 ratio to receive either CAPVAXIVE followed by placebo 8 weeks later, or PCV15 followed by PPSV23 (PCV15+PPSV23) 8 weeks later. At screening, of the participants vaccinated 6.7% had a CD4+ T-cell counts ≥ 50 to < 350 cells/µL, 18.6% had CD4+ T-cell counts ≥ 350 to < 500 cells/µL and 74.7% had a CD4+ T-cell counts ≥ 500 cells/µL; 83% had an undetectable HIV viral load (< 20 copies/mL).

CAPVAXIVE was immunogenic for all 21 serotypes contained in the vaccine, as assessed by serotype specific OPA GMTs at 1-month postvaccination with CAPVAXIVE. CAPVAXIVE elicited immune responses that were generally comparable to PCV15+PPSV23 for the 13 common serotypes and higher for the 8 serotypes additional to CAPVAXIVE as assessed by OPA GMTs at 1-month postvaccination with CAPVAXIVE and 1-month postvaccination with PCV15+PPSV23.

Paediatric population

The European Medicines Agency has deferred the obligation to submit the results of studies with CAPVAXIVE in one or more subsets of the paediatric population in prevention of disease caused by *Streptococcus pneumoniae* (see section 4.2 for information on paediatric use).

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.

6. PHARMACEUTICAL PARTICULARS

6.1 List of excipients

Sodium chloride (NaCl)
Histidine
Polysorbate 20 (E432)
Hydrochloric acid (HCl; for pH adjustment)
Water for injections

6.2 Incompatibilities

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

6.3 Shelf life

30 months

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.

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

Stability data indicate that CAPVAXIVE is stable at temperatures up to 25° C for 96 hours. At the end of this time period CAPVAXIVE should be used or discarded. These data are intended to guide healthcare professionals in case of temporary temperature excursions only.

6.5 Nature and contents of container

0.5 mL solution in a single-dose pre-filled syringe (Type I glass) with a plunger stopper (bromobutyl rubber) and a tip cap (styrene butadiene or isoprene bromobutyl rubber).

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

Not all pack sizes may be marketed.

6.6 Special precautions for disposal and other handling

- The vaccine should be used as supplied.
- Inspect the solution 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.
- CAPVAXIVE should be administered by intramuscular injection only. This vaccine should be administered preferably in the deltoid muscle of the upper arm in adults, with care to avoid injection into or near nerves and blood vessels.

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/1/25/1913/001
EU/1/25/1913/002
EU/1/25/1913/003
EU/1/25/1913/004
EU/1/25/1913/005
EU/1/25/1913/006

9. DATE OF FIRST AUTHORISATION/RENEWAL OF THE AUTHORISATION

Date of first authorisation: 24 March 2025

10. DATE OF REVISION OF THE TEXT

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

ANNEX II

A. MANUFACTURER OF THE BIOLOGICAL ACTIVE SUBSTANCES AND MANUFACTURER 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 OF THE BIOLOGICAL ACTIVE SUBSTANCES AND MANUFACTURER RESPONSIBLE FOR BATCH RELEASE

Name and address of the manufacturer of the biological active substances

MSD International GmbH
Brinny, Innishannon
Cork,
T12 RD82
Ireland

Name and address of the manufacturer 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

CAPVAXIVE solution for injection in pre-filled syringe
Pneumococcal polysaccharide conjugate vaccine (21-valent)

2. STATEMENT OF ACTIVE SUBSTANCE(S)

1 dose (0.5 mL) contains 4 mcg of pneumococcal polysaccharide for serotypes 3, 6A, 7F, 8, 9N, 10A, 11A, 12F, 15A, de-O-acetylated type 15B, 16F, 17F, 19A, 20A, 22F, 23A, 23B, 24F, 31, 33F and 35B conjugated to CRM_{197} carrier protein.

3. LIST OF EXCIPIENTS

Excipients: NaCl, histidine, E432, HCl, water for injections.
See leaflet for further information.

4. PHARMACEUTICAL FORM AND CONTENTS

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

5. METHOD AND ROUTE(S) OF ADMINISTRATION

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/1/25/1913/001 - pack of 1 without needle
EU/1/25/1913/002 - pack of 1 + 1 needle
EU/1/25/1913/003 - pack of 1 + 2 needles
EU/1/25/1913/004 - pack of 10 without needles
EU/1/25/1913/005 - pack of 10 + 10 needles
EU/1/25/1913/006 - pack of 10 + 20 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

CAPVAXIVE
Solution for Injection
IM

2. METHOD OF ADMINISTRATION

Intramuscular 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

CAPVAXIVE solution for injection in pre-filled syringe
Pneumococcal polysaccharide conjugate vaccine (21-valent)

▼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 CAPVAXIVE is and what it is used for

CAPVAXIVE is a pneumococcal vaccine given to:
- **people aged 18 years and older** to help protect against illnesses caused by a bacterium called *Streptococcus pneumoniae* or pneumococcus. These diseases include: lung infection (pneumonia), inflammation of the brain and spinal cord (meningitis) and infection in the blood (bacteraemia).

The vaccine works by helping your body to make its own antibodies, which protect you against these diseases.

2. What you need to know before you receive CAPVAXIVE

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

Warnings and precautions
Talk to your doctor, pharmacist, or nurse before you receive CAPVAXIVE if:
- 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.
- you have anxiety related to injections or have ever fainted after any injection.
- your immune system is weakened (which means your body is less able to fight off infections) or if you are taking certain medicines that may weaken your immune system.

As with any vaccine, CAPVAXIVE may not fully protect all those who get the vaccine.

Children and adolescents
CAPVAXIVE has not been studied in children and adolescents younger than 18 years of age.

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

Tell your doctor, pharmacist, or nurse if:
- you are taking, have recently taken, or might take any other medicines.
- 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
CAPVAXIVE 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.

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

CAPVAXIVE contains polysorbate 20
This medicine contains 0.5 mg of polysorbate 20 in each 0.5 mL dose of solution for injection. Polysorbates may cause allergic reactions. Tell your doctor if you have any known allergies.

3. How CAPVAXIVE is given

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

Adults

You will receive 1 injection (1 dose of 0.5 mL).
Your doctor or nurse will give the vaccine into your upper arm muscle.

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

4. Possible side effects

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

Serious side effects
Rare (may affect up to 1 in 1 000 people):
CAPVAXIVE may cause allergic (hypersensitivity) reactions including excessive contraction of the airway muscles causing breathing difficulty (bronchospasm). 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

Other side effects
The following side effects have been seen after the use of CAPVAXIVE:

Very common (may affect more than 1 in 10 people):
- Headaches
- Pain at the injection site
- Feeling tired

Common (may affect up to 1 in 10 people):
- Muscle aches (very common in people 18 to 49 years of age)
- Redness or swelling at the injection site (very common in people 18 to 49 years of age)
- Fever

Uncommon (may affect up to 1 in 100 people):
- Swelling of lymph nodes
- Dizziness
- Feeling sick (nausea)
- Diarrhoea
- Vomiting
- Joint pain
- Itching at injection site
- Chills
- Bruising at injection site

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

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 CAPVAXIVE

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.

CAPVAXIVE should be administered as soon as possible after being removed from the refrigerator. However, in circumstances where CAPVAXIVE is temporarily held outside of refrigeration, the vaccine is stable at temperatures up to 25 °C for 96 hours. At the end of this time period CAPVAXIVE should be used or discarded. This information is intended to guide healthcare professionals in case of temporary temperature excursions only.

6. Contents of the pack and other information

What CAPVAXIVE contains
The active substances are:
- Polysaccharides from pneumococcus types 3, 6A, 7F, 8, 9N, 10A, 11A, 12F, 15A, de-O-acetylated type 15B, 16F, 17F, 19A, 20A, 22F, 23A, 23B, 24F, 31, 33F and 35B (4 micrograms of each type);

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

One dose (0.5 mL) contains approximately 65 micrograms carrier protein.

The other ingredients are sodium chloride (NaCl), histidine, polysorbate 20 (E432), hydrochloric acid (HCl; for pH adjustment) and water for injections. For more information on polysorbate 20 (E432), see Section 2.

What CAPVAXIVE looks like and contents of the pack
CAPVAXIVE is a colourless, clear to opalescent solution for injection (injection), provided in a single-dose, pre-filled syringe (0.5 mL). CAPVAXIVE is available in pack sizes of 1 or 10 pre-filled syringes, either without needles, with 1 separate needle or with 2 separate needles per pre-filled syringe.

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:

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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: https://www.ema.europa.eu.

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The following information is intended for healthcare professionals only:

- The vaccine should be used as supplied.
- Inspect the solution 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.
- CAPVAXIVE should be administered by intramuscular injection only. This vaccine should be administered preferably in the deltoid muscle of the upper arm in adults, with care to avoid injection into or near nerves and blood vessels.

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

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