

CAPVAXIVE

(Pneumococcal 21-valent Conjugate Vaccine)

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

¹Conjugated to CRM₁₉₇ carrier protein. CRM₁₉₇ 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 CRM₁₉₇ 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 $\leq 1.0\%$ 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 4914 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 ($\geq 1/10$)
- Common ($\geq 1/100$ to $< 1/10$)
- Uncommon ($\geq 1/1000$ to $< 1/100$)
- Rare ($\geq 1/10000$ to $< 1/1000$)
- Very rare ($< 1/10000$)
- 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).

Safety in adults with increased risk for pneumococcal disease

An additional study, Protocol 008, was conducted to evaluate CAPVAXIVE in pneumococcal vaccine-naïve adults 18 to 64 years of age with one or more prespecified chronic medical conditions known to increase the risk of pneumococcal disease (see section 5.1). The safety profile of CAPVAXIVE was generally comparable to PCV15 followed by PPSV23 and generally similar to the profile observed in the pivotal studies.

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. Please refer to the end of this leaflet for adverse effects reporting.

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 (CRM₁₉₇), 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 8369 individuals 18 years of age and older, of whom 5450 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, 2362 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=1179)		PCV 20 (N=1177)		GMT Ratio* (CAPVAXIVE/PCV20) (95% CI)*
	n	GMT*	n	GMT*	
10 Shared Serotypes†					
3	1154	274.0	1161	176.7	1.55 (1.40, 1.72)
6A	1148	2302.0	1153	2972.5	0.77 (0.68, 0.88)
7F	1152	3637.4	1158	3429.9	1.06 (0.95, 1.18)
8	1155	2501.3	1158	1811.1	1.38 (1.25, 1.53)
10A	1161	3893.4	1159	4678.0	0.83 (0.75, 0.93)
11A	1145	3232.6	1150	2092.8	1.54 (1.39, 1.72)
12F	1160	2641.2	1161	2499.6	1.06 (0.92, 1.21)
19A	1159	2136.1	1162	2817.8	0.76 (0.69, 0.84)
22F	1147	3874.5	1154	4770.1	0.81 (0.72, 0.92)
33F	1154	13558.9	1157	11742.1	1.15 (1.01, 1.32)
11 Additional Serotypes in CAPVAXIVE‡					
9N	1147	7470.7	1150	1640.4	4.55 (4.12, 5.04)
15A	1107	5237.2	1102	1589.0	3.30 (2.91, 3.74)
15C	1153	4216.2	1158	2072.3	2.03 (1.77, 2.34)
16F	1151	4868.2	1153	846.3	5.75 (5.16, 6.41)
17F	1148	7764.9	1156	460.4	16.86 (14.90, 19.09)
20A	1161	6099.2	1155	631.1	9.66 (8.66, 10.79)
23A	1132	3737.2	1104	461.5	8.10 (6.86, 9.55)
23B	1160	1082.5	1160	107.3	10.09 (8.48, 12.00)
24F	1153	2728.6	1130	70.5	38.71 (33.87, 44.25)
31	1153	3132.5	1154	144.4	21.69 (18.68, 25.18)
35B	1153	8527.8	1159	1383.0	6.17 (5.59, 6.80)
Cross-reactive serotype					
15B	1140	4400.6	1141	4640.0	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	5289.6	569	2572.9	2.06 (1.61, 2.62)
7F	198	6447.2	571	4278.8	1.51 (1.23, 1.84)
8	197	4516.0	571	3004.7	1.50 (1.26, 1.79)
9N	197	17283.2	570	8791.4	1.97 (1.59, 2.43)
10A	197	6808.1	575	4382.6	1.55 (1.26, 1.92)
11A	196	5871.6	564	3785.8	1.55 (1.26, 1.91)
12F	196	6150.4	574	3561.2	1.73 (1.37, 2.17)
15A	184	11319.2	550	5901.2	1.92 (1.55, 2.37)
15C	195	10194.0	570	5708.0	1.79 (1.36, 2.35)
16F	193	8877.0	571	5720.0	1.55 (1.26, 1.91)
17F	194	16070.6	568	10068.0	1.60 (1.26, 2.02)
19A	198	2773.2	574	2374.6	1.17 (0.97, 1.40)

20A	197	13150.0	575	7562.7	1.74 (1.39, 2.18)
22F	198	9299.6	568	4683.6	1.99 (1.58, 2.49)
23A	192	8848.7	561	4739.5	1.87 (1.43, 2.44)
23B	198	2140.1	575	1420.9	1.51 (1.11, 2.04)
24F	197	4137.6	570	3047.2	1.36 (1.10, 1.67)
31	195	8005.6	570	3820.7	2.10 (1.63, 2.69)
33F	197	34805.5	570	17607.4	1.98 (1.52, 2.57)
35B	198	13933.4	573	9053.9	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, 1484 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	4876.7	732	3314.6	1.47 (1.29, 1.68)
8	730	3379.6	733	2882.1	1.17 (1.04, 1.32)
9N	728	7346.6	729	6545.9	1.12 (1.00, 1.26)
10A	725	4382.9	726	2818.7	1.55 (1.37, 1.77)
11A	728	3711.1	729	1809.7	2.05 (1.82, 2.31)
12F	728	3031.8	732	1854.9	1.63 (1.40, 1.90)
17F	722	8215.7	730	4060.5	2.02 (1.77, 2.31)
19A	731	2670.0	732	1879.9	1.42 (1.26, 1.60)
20A	730	6966.1	733	4208.4	1.66 (1.46, 1.88)
22F	725	4724.1	728	3084.9	1.53 (1.34, 1.75)
33F	727	15497.3	731	17483.0	0.89 (0.76, 1.04)
9 Additional Serotypes in CAPVAXIVE‡					
6A	729	3193.9	730	964.0	3.31 (2.84, 3.87)
15A	715	6746.5	703	1462.1	4.61 (3.99, 5.33)
15C	729	7604.8	730	2605.0	2.92 (2.50, 3.42)
16F	726	6675.4	723	1482.2	4.50 (3.99, 5.09)
23A	711	4804.2	690	837.2	5.74 (4.81, 6.85)
23B	730	2252.6	726	137.2	16.42 (13.46, 20.03)
24F	723	4568.0	705	1346.7	3.39 (2.97, 3.87)
31	730	5040.7	731	423.9	11.89 (10.16, 13.91)
35B	728	10707.5	732	1735.0	6.17 (5.54, 6.87)
Cross-reactive serotype					
15B	716	5157.3	727	3243.2	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/ μ L, 18.6% had CD4+ T-cell counts ≥ 350 to < 500 cells/ μ L and 74.7% had a CD4+ T-cell counts ≥ 500 cells/ μ L; 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.

Adults with increased risk for pneumococcal disease

Protocol 008

In a double-blind study, 518 individuals 18 to 64 years of age with one or more prespecified chronic medical conditions known to increase the risk of pneumococcal disease (diabetes mellitus, chronic heart disease, chronic kidney disease, chronic liver disease, or chronic lung disease) were randomised in a 3:1 ratio to receive either CAPVAXIVE followed by placebo 8 weeks later, or PCV15 followed by PPSV23 (PCV15+PPSV23) 8 weeks later. The study participants had not previously received any pneumococcal vaccines other than routine childhood PCVs.

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 unique to CAPVAXIVE as assessed by OPA GMTs at 1-month postvaccination with CAPVAXIVE and 1-month postvaccination with PCV15+PPSV23.

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

36 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.

HARUS DENGAN RESEP DOKTER

No. Reg: DKIXXXXXXXXXXXXX

Manufactured and packed by:

MSD International GmbH

Carlow, Ireland

Released by:

MSD International GmbH (Singapore Branch)

70 Tuas West Drive, Singapore

Registered by:

PT Organon Pharma Indonesia Tbk

Indonesia

Distributed by:

PT Merck Sharp & Dohme Indonesia

Indonesia

PI Version 1.0

EU-SPC (2025), CCDS-V116-I-092024

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Pusat Farmakovigilans/ MESO Nasional

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Psikotropika, Prekursor dan Zat Adiktif

Badan Pengawas Obat dan Makanan Republik Indonesia

Melalui pos: Jl. Percetakan Negara No. 23, Jakarta Pusat, 10560

Email: pv-center@pom.go.id

Aplikasi pelaporan farmakovigilans Pusat Farmakovigilans/ MESO Nasional (e-meso)

dengan alamat: <https://e-meso.pom.go.id/>

Informasi untuk Pasien tentang CAPVAXIVE

CAPVAXIVE larutan untuk injeksi dalam jarum suntik yang sudah diisi

Vaksin konjugat polisakarida pneumokokus (21-valen)

Baca semua leaflet ini dengan cermat sebelum Anda divaksinasi karena mengandung informasi penting untuk Anda.

- Simpan leaflet ini. Anda mungkin perlu membacanya lagi.
- Jika Anda memiliki pertanyaan lebih lanjut, tanyakan kepada dokter, apoteker, atau perawat Anda.
- Vaksin ini hanya diresepkan untuk Anda. Jangan berikan kepada orang lain.
- Jika Anda mengalami efek samping, bicarakan dengan dokter, apoteker, atau perawat Anda. Ini termasuk kemungkinan efek samping yang tidak tercantum dalam leaflet ini. Lihat bagian 4.

Apa yang ada dalam leaflet ini

1. Apakah itu CAPVAXIVE dan untuk apa digunakan
2. Apa yang harus Anda ketahui sebelum vaksinasi dengan CAPVAXIVE
3. Bagaimana CAPVAXIVE diberikan
4. Kemungkinan efek samping
5. Cara menyimpan CAPVAXIVE
6. Isi kemasan dan informasi lainnya

1. Apakah itu CAPVAXIVE dan untuk apa digunakan

CAPVAXIVE adalah vaksin pneumokokus yang diberikan kepada:

- **Orang berusia 18 tahun ke atas** untuk membantu melindungi diri dari penyakit yang disebabkan oleh bakteri yang disebut *Streptococcus pneumoniae* atau pneumococcus. Penyakit-penyakit ini meliputi: infeksi paru-paru (*pneumonia*), radang pada otak dan sumsum tulang belakang (*meningitis*) dan infeksi dalam darah (bakteremia).

Vaksin ini bekerja dengan membantu tubuh Anda membuat antibodi sendiri, yang melindungi Anda dari penyakit-penyakit ini.

2. Apa yang harus Anda ketahui sebelum vaksinasi dengan CAPVAXIVE

Jangan menerima CAPVAXIVE:

- jika Anda alergi terhadap zat aktif, termasuk toksoid difteri, atau terhadap salah satu bahan dalam vaksin ini (tercantum dalam bagian 6).

Peringatan dan tindakan pencegahan

Bicaralah dengan dokter, apoteker, atau perawat sebelum Anda menerima CAPVAXIVE jika:

- Anda mengalami demam tinggi atau infeksi berat. Dalam kasus ini, vaksinasi mungkin harus ditunda hingga Anda pulih. Namun, demam ringan atau infeksi (misalnya pilek) sendiri bukan alasan untuk menunda vaksinasi.
- Anda mengalami masalah pendarahan, mudah memar, atau sedang mengonsumsi obat untuk mencegah pembekuan darah.
- Anda mengalami kecemasan terkait suntikan atau pernah pingsan setelah suntikan apa pun.
- sistem kekebalan tubuh Anda melemah (yang berarti tubuh Anda kurang mampu melawan infeksi) atau jika Anda mengonsumsi obat-obatan tertentu yang dapat melemahkan sistem kekebalan tubuh Anda.

Seperti halnya vaksin lainnya, CAPVAXIVE mungkin tidak sepenuhnya melindungi semua orang yang mendapatkan vaksin.

Anak-anak dan remaja

CAPVAXIVE belum dipelajari pada anak-anak dan remaja di bawah usia 18 tahun.

Obat/vaksin lain dan CAPVAXIVE

CAPVAXIVE dapat diberikan bersamaan dengan vaksin flu (influenza yang diinaktivasi).

Beri tahu dokter, apoteker, atau perawat Anda jika:

- Anda sedang mengonsumsi, baru saja mengonsumsi, atau mungkin akan mengonsumsi obat lain.
- Anda baru saja menerima atau berencana menerima vaksin lain.

Kehamilan dan menyusui

Jika Anda sedang hamil atau menyusui, merasa mungkin sedang hamil atau berencana untuk memiliki bayi, mintalah saran dari dokter, apoteker, atau perawat Anda sebelum Anda menerima vaksin ini.

Mengemudi dan menggunakan mesin

CAPVAXIVE tidak memiliki pengaruh atau pengaruh yang dapat diabaikan terhadap kemampuan mengemudi dan menggunakan mesin. Namun, beberapa efek yang disebutkan dalam bagian 4 "Kemungkinan efek samping" dapat memengaruhi kemampuan mengemudi atau menggunakan mesin untuk sementara.

CAPVAXIVE mengandung natrium

Obat ini mengandung kurang dari 1 mmol natrium (23 mg) per dosis, yang berarti pada dasarnya 'bebas natrium'.

CAPVAXIVE mengandung polisorbitat 20

Obat ini mengandung 0,5 mg polisorbitat 20 dalam setiap dosis 0,5 mL larutan injeksi. Polisorbitat dapat menyebabkan reaksi alergi. Beri tahu dokter jika Anda memiliki alergi yang diketahui.

3. Bagaimana CAPVAXIVE diberikan

Beri tahu dokter, apoteker, atau perawat Anda jika Anda pernah diberi vaksin pneumokokus sebelumnya.

Dewasa

Anda akan menerima 1 suntikan (1 dosis 0,5 mL).

Dokter atau perawat Anda akan memberikan vaksin ke otot lengan atas Anda.

Jika Anda memiliki pertanyaan lebih lanjut tentang penggunaan CAPVAXIVE, tanyakan kepada dokter, apoteker, atau perawat Anda.

4. Kemungkinan efek samping

Seperti semua vaksin, CAPVAXIVE dapat menimbulkan efek samping, meskipun tidak semua orang mengalaminya.

Efek samping serius

Jarang (dapat memengaruhi hingga 1 dari 1000 orang):

CAPVAXIVE dapat menyebabkan reaksi alergi (hipersensitivitas) termasuk kontraksi berlebihan pada otot saluran napas yang menyebabkan kesulitan bernapas (bronkospasme). Segera dapatkan perawatan medis jika Anda memiliki gejala reaksi alergi, yang dapat meliputi:

- Mengi atau kesulitan bernapas
- Pembengkakan wajah, bibir, atau lidah
- Biduran
- Ruam

Efek samping lainnya

Efek samping berikut telah terlihat setelah penggunaan CAPVAXIVE:

Sangat umum (dapat mempengaruhi lebih dari 1 dari 10 orang):

- Sakit kepala
- Nyeri di tempat suntikan
- Merasa lelah

Umum (dapat mempengaruhi hingga 1 dari 10 orang):

- Nyeri otot (sangat umum pada orang berusia 18 hingga 49 tahun)
- Kemerahan atau pembengkakan di tempat suntikan (sangat umum pada orang berusia 18 hingga 49 tahun)
- Demam

Tidak umum (dapat mempengaruhi hingga 1 dari 100 orang):

- Pembengkakan kelenjar getah bening
- Pusing
- Merasa sakit (Mual)
- Diare

- Muntah
- Nyeri sendi
- Gatal di tempat suntikan
- Menggigil
- Bengkak di tempat suntikan

Efek samping ini umumnya ringan atau sedang dan berlangsung dalam waktu singkat.

Pelaporan efek samping

Jika Anda mengalami efek samping, bicarakan dengan dokter, apoteker, atau perawat Anda. Ini termasuk kemungkinan efek samping yang tidak tercantum dalam leaflet ini. Silakan merujuk ke akhir leaflet ini untuk pelaporan efek samping.

Overdosis

Capvaxive tersedia dalam bentuk jarum suntik yang sudah diisi yang hanya berisi satu dosis tunggal, sehingga membantu memastikan bahwa jumlah dosis yang diberikan sudah tepat.

5. Cara menyimpan CAPVAXIVE

Jauhkan vaksin ini dari pandangan dan jangkauan anak-anak.

Jangan gunakan vaksin ini setelah tanggal kedaluwarsa yang tertera pada karton dan label spuit setelah EXP.

Tanggal kedaluwarsa mengacu pada hari terakhir bulan tersebut.

Simpan dalam pendingin (2°C – 8°C). Jangan dibekukan. Simpan spuit yang sudah diisi sebelumnya di karton luar untuk melindungi dari cahaya.

CAPVAXIVE harus diberikan sesegera mungkin setelah dikeluarkan dari pendingin. Namun, dalam keadaan di mana CAPVAXIVE disimpan sementara di luar pendingin, vaksin stabil pada suhu hingga 25°C selama 96 jam. Pada akhir periode waktu ini CAPVAXIVE harus digunakan atau dibuang. Informasi ini dimaksudkan untuk memandu profesional perawatan kesehatan jika terjadi perubahan suhu sementara saja.

6. Isi kemasan dan informasi lainnya

Apa yang terkandung dalam CAPVAXIVE

Zat aktifnya adalah:

- Polisakarida dari pneumococcus serotipe 3, 6A, 7F, 8, 9N, 10A, 11A, 12F, 15A, serotipe de-O-asetilasi 15B, 16F, 17F, 19A, 20A, 22F, 23A, 23B, 24F, 31, 33F dan 35B (4 mikrogram untuk setiap serotipe);

Setiap polisakarida dihubungkan dengan protein pembawa (CRM₁₉₇). Polisakarida dan protein pembawa tidak hidup dan tidak menyebabkan penyakit.

Satu dosis (0,5 mL) mengandung sekitar 65 mikrogram protein pembawa.

Bahan-bahan lainnya adalah natrium klorida (NaCl), histidin, polisorbitat 20 (E432), asam klorida (HCl; untuk penyesuaian pH) dan air untuk injeksi. Untuk informasi lebih lanjut tentang polisorbitat 20 (E432), lihat Bagian 2.

Bagaimana tampilan CAPVAXIVE dan isi kemasan

CAPVAXIVE adalah larutan injeksi (injeksi) yang tidak berwarna, bening hingga opalescent, tersedia dalam spuit dosis tunggal yang sudah diisi sebelumnya (0,5 mL). CAPVAXIVE tersedia dalam kemasan 1 atau 10 spuit yang sudah diisi sebelumnya, baik tanpa jarum, dengan 1 jarum terpisah atau dengan 2 jarum terpisah per spuit yang sudah diisi sebelumnya.

Tidak semua ukuran kemasan mungkin dipasarkan.

HARUS DENGAN RESEP DOKTER

No. Reg: DKIXXXXXXXXXXXXX

Diproduksi dan dikemas oleh:

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Carlow, Ireland

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Didaftarkan oleh:

PT Organon Pharma Indonesia Tbk

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Didistribusikan oleh:

PT Merck Sharp & Dohme Indonesia

Indonesia

PIL Version 1.0

EU-Package leaflet 2025, CCPPI-V116-I-092024

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