▼ This medicinal product is subject to additional monitoring in Australia. This will allow quick identification of new safety information. Healthcare professionals are asked to report any suspected adverse events at www.tga.gov.au/reporting-problems.

AUSTRALIAN PRODUCT INFORMATION – CAPVAXIVE® (Pneumococcal 21-valent Conjugate Vaccine)

1 NAME OF THE MEDICINE

Pneumococcal 21-valent Conjugate Vaccine

2 QUALITATIVE AND QUANTITATIVE COMPOSITION

Each 0.5 mL dose contains 84 micrograms of pneumococcal purified capsular polysaccharide antigen (4 micrograms each of polysaccharide serotypes 3, 6A, 7F, 8, 9N, 10A, 11A, 12F, 15A, deOAc15B, 16F, 17F, 19A, 20A, 22F, 23A, 23B, 24F, 31, 33F, and 35B) conjugated to approximately 65 mcg of diphtheria CRM197 protein.

CAPVAXIVE does not contain any preservatives.

For the full list of excipients, see Section 6.1 List of excipients.

3 PHARMACEUTICAL FORM

CAPVAXIVE is a solution for injection available in 0.5 mL single-dose prefilled syringes.

The vaccine is a colorless, clear to opalescent solution.

4 CLINICAL PARTICULARS

4.1 THERAPEUTIC INDICATIONS

CAPVAXIVE is indicated for active immunisation for the prevention of pneumococcal disease caused by *Streptococcus pneumoniae* serotypes (3, 6A, 7F, 8, 9N, 10A, 11A, 12F, 15A, 15B, 15C, 16F, 17F, 19A, 20A, 22F, 23A, 23B, 24F, 31, 33F, and 35B) in adults 18 years of age and older.

CAPVAXIVE may not prevent disease caused by *S. pneumoniae* serotypes that are not listed in the indications.

The use of CAPVAXIVE should be guided by official recommendations.

4.2 DOSE AND METHOD OF ADMINISTRATION

Dosage (dose and interval)

Administer a 0.5 mL dose of CAPVAXIVE intramuscularly.

Adults

One single dose.

For vaccination of individuals previously vaccinated with one or more doses of other pneumococcal vaccines, administer a single dose of CAPVAXIVE.

The dosing interval after the last dose of the prior pneumococcal vaccine should be guided by official recommendations.

Method of Administration

For intramuscular use only. Do not inject intravascularly.

Instructions For Use

CAPVAXIVE should not be diluted or mixed with other vaccines. The full recommended dose of the vaccine should be used.

When CAPVAXIVE is administered at the same time as another injectable vaccine(s), the vaccines should always be given at different injection sites [see Section 4.5 INTERACTIONS WITH OTHER MEDICINES AND OTHER FORMS OF INTERACTIONS].

The vaccine is a colourless, clear to opalescent solution. Parenteral drug products should be inspected visually for particulate matter and discoloration prior to administration. This product should not be used if particulate matter or discoloration is found.

The prefilled syringe is for single use only and should not be used for more than one individual. Discard the prefilled syringe after use. Attach a needle by twisting in a clockwise direction until the needle fits securely on the syringe. Inject the entire contents of the syringe.

4.3 CONTRAINDICATIONS

CAPVAXIVE is contraindicated in individuals with a history of a severe allergic reaction (e.g., anaphylaxis) to the active substances, diphtheria toxoid or to any of the excipients [see Sections 2 QUALITATIVE AND QUANTITATIVE COMPOSITION and 6.1 LIST OF EXCIPIENTS].

4.4 SPECIAL WARNINGS AND PRECAUTIONS FOR USE

Management of Allergic Reactions

Appropriate medical treatment to manage allergic reactions must be immediately available in the event an acute anaphylactic reaction occurs following administration of CAPVAXIVE.

Immunocompromised Individuals

No safety and immunogenicity data are available for CAPVAXIVE in immunocompromised individuals. Based on experience with pneumococcal vaccines, immunocompromised individuals, including those receiving immunosuppressive therapy, may have a reduced immune response to CAPVAXIVE.

Use in the Elderly

Across the Phase 3 clinical studies, approximately 34% of individuals were 65 years of age and older. Of those, 4,556 individuals received CAPVAXIVE; 1,487 (32.6%) were 65 years and older, and 339 (7.4%) were 75 years and older. Overall, there were no clinically meaningful differences in the safety profile observed in individuals 65 to 74 years and 75 years of age and older when compared to individuals less than 65 years of age.

Across all treatment groups, the opsonophagocytic activity (OPA) responses in individuals 65

years of age and older were generally lower than those observed in individuals less than 65 years of age [see Sections 4.8 ADVERSE EFFECTS (UNDESIRABLE EFFECTS) and 5.1 PHARMACODYNAMIC PROPERTIES – Clinical Trials].

Paediatric Use

The safety and effectiveness of CAPVAXIVE in children younger than 18 years of age have not been established.

Effects on laboratory tests

Not applicable.

4.5 INTERACTIONS WITH OTHER MEDICINES AND OTHER FORMS OF INTERACTIONS

Use with Other Vaccines

CAPVAXIVE can be administered concomitantly with inactivated influenza vaccine. Immune responses to CAPVAXIVE when administered concomitantly with inactivated influenza vaccine were non-inferior compared to when CAPVAXIVE was administered sequentially with inactivated influenza vaccine for 20 of 21 serotypes and 3 of 4 influenza strains. Concomitant vaccination with inactivated influenza vaccine demonstrated lower GMT responses to both vaccines compared to sequential vaccination. The clinical significance of this is unclear [see Sections 4.8 ADVERSE EFFECTS (UNDESIRABLE EFFECTS) and 5.1 PHARMACODYNAMIC PROPERTIES – Clinical Trials]. There are no data on the concomitant administration of CAPVAXIVE with other vaccines.

4.6 FERTILITY, PREGNANCY AND LACTATION

Effects on Fertility

CAPVAXIVE administered to female rats at one-half the full human dose providing an approximately 100-fold margin on a per kg basis had no effects on mating performance, fertility or embryonic/fetal survival.

Use in Pregnancy - Category B1

Animal Data

In a developmental and reproductive toxicity study, female rats were administered CAPVAXIVE by intramuscular injection 28 and 7 days prior to mating, on Gestation Day 6, and on Lactation Day 7. On each occasion, rats received 42 mcg/dose (one-half the full human dose) of CAPVAXIVE, providing a margin of approximately 100-fold on a per kg basis. There was no embryofetal lethality or fetal malformations and no adverse effects on pre-weaning development were observed. Antibodies to all 21 serotypes contained in CAPVAXIVE were detected in offspring, attributable to the acquisition of maternal antibodies via placental transfer during gestation and/or via lactation.

Human Data

There are no adequate and well-controlled studies of CAPVAXIVE in pregnant women, and human data available from clinical trials with CAPVAXIVE have not established the presence or absence of vaccine-associated risk during pregnancy. The decision to vaccinate a woman who is pregnant should consider the woman’s risk of pneumococcal disease; CAPVAXIVE should be administered only if clearly needed.

Use in Lactation

Human data are not available to assess the impact of CAPVAXIVE on milk production, its presence in breast milk, or its effects on the breastfed child. The developmental and health benefits of breastfeeding should be considered along with the mother's clinical need for CAPVAXIVE and any potential adverse effects on the breastfed child from CAPVAXIVE or from the underlying maternal condition. For preventive vaccines, the underlying condition is susceptibility to disease prevented by the vaccine.

4.7 EFFECTS ON ABILITY TO DRIVE AND USE MACHINES

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

4.8 ADVERSE EFFECTS (UNDESIRABLE EFFECTS)

Clinical Trials Experience

The safety of CAPVAXIVE was assessed in four clinical studies (Protocol 003, Protocol 004, Protocol 005, and Protocol 006) conducted across the Americas, Europe, and Asia Pacific, which included approximately 6,500 adults ranging in age from 18 to 97 years. Each study included adults with stable underlying medical conditions [see Section 5.1 PHARMACODYNAMIC PROPERTIES – Clinical Trials]. Across all 4 studies, approximately 4,500 adults received CAPVAXIVE, approximately 2,000 adults received an active comparator.

Safety was evaluated using an electronic Vaccination Report Card for 30 days postvaccination. Injection-site adverse events, systemic adverse events, and body temperature were solicited Day 1 through Day 5 postvaccination. Unsolicited adverse events were reported Day 1 through Day 30 postvaccination. Serious adverse events (SAEs) were reported through 6 months postvaccination with CAPVAXIVE in all studies.

The most commonly reported (>10%) solicited adverse reactions in individuals 18 to 49 years of age who received CAPVAXIVE were: injection-site pain (73.1%), fatigue (36.0%), headache (27.5%), myalgia (16.4%), injection-site erythema (13.8%), and injection-site swelling (13.3%).

The most commonly reported (>10%) solicited adverse reactions in individuals 50 years of age and older who received CAPVAXIVE were: injection-site pain (41.2%), fatigue (19.7%), and headache (11.0%).

Across the Phase 3 studies in individuals 18 years of age and older, the majority of local and systemic solicited adverse reactions for individuals who received CAPVAXIVE were mild (based on intensity or size) and of short duration (≤3 days); severe events (defined as an event that prevents normal daily activity or size >10 cm) occurred in ≤1.0% of adults.

<u>Pneumococcal Vaccine-Naïve Adults 18 years of Age and Older</u>

In Protocol 003, individuals 18 years of age and older who had not previously received a pneumococcal vaccine were enrolled and randomised to receive a single dose of CAPVAXIVE or Prevenar 20.

In Protocol 004, individuals 18 to 49 years of age who had not previously received a pneumococcal vaccine were enrolled and randomised to receive a single dose of CAPVAXIVE or PNEUMOVAX 23.

Adults 50 Years of Age and Older Who Previously Received Pneumococcal Vaccines

Protocol 006 enrolled individuals 50 years of age and older who previously received a pneumococcal vaccine at least 1 year prior to enrollment.

Adults who had previously received PNEUMOVAX 23 (double-blind; cohort 1) were randomised to receive a single dose of either CAPVAXIVE or VAXNEUVANCE.

Adults who had previously received Prevenar 13 (double-blind; cohort 2) were randomised to receive a single dose of either CAPVAXIVE or PNEUMOVAX 23.

Adults who had previously received other prior pneumococcal vaccines (Prevenar 13 + PNEUMOVAX 23, VAXNEUVANCE + PNEUMOVAX 23, PNEUMOVAX 23 + Prevenar 13, or VAXNEUVANCE) were allocated to receive a single dose of CAPVAXIVE (open label; cohort 3).

Solicited Adverse Events

Pneumococcal Vaccine-Naïve Adults 18 years of Age and Older

In Protocol 003, a comparable proportion of individuals within each age group (18 to 49 and 50 years of age and older) who received CAPVAXIVE or Prevenar 20, reported solicited adverse events. Pneumococcal vaccine naïve adults 50 years of age and older reported fewer solicited adverse events than adults 18 to 49 years of age, regardless of vaccination group (Table 1).

In Protocol 004, a comparable proportion of individuals 18 to 49 years of age who received CAPVAXIVE or PNEUMOVAX 23 reported solicited adverse events (Table 2).

Adults 50 Years of Age and Older Who Previously Received Pneumococcal Vaccines

In Protocol 006, within Cohort 1 and Cohort 2, a comparable proportion of pneumococcal vaccine experienced individuals who received CAPVAXIVE or active comparator reported solicited adverse events, regardless of the prior pneumococcal vaccines received. Across the 3 cohorts, comparable proportions of individuals who received CAPVAXIVE reported solicited adverse events, regardless of the prior pneumococcal vaccines received (Table 3).

Table 1: Individuals with Solicited Local and Systemic Adverse Events Within 5 Days Postvaccination in Pneumococcal Vaccine-naïve Adults 18-49 Years of Age and ≥50 Years of Age and Older – Protocol 003

	18-49 Years of Age		≥50 Years of Age	
	CAPVAXIVE n (%)	**Prevenar 20 n (%)**	**CAPVAXIVE n (%)**	**Prevenar 20 n (%)**
Individuals in population*	200	100	1,177	1,175
One or more solicited adverse events	161 (80.5)	78 (78.0)	600 (51.0)	708 (60.3)
No solicited adverse events	39 (19.5)	22 (22.0)	577 (49.0)	467 (39.7)
Local adverse event†				
Erythema	31 (15.5)	13 (13.0)	64 (5.4)	74 (6.3)
Pain	143 (71.5)	74 (74.0)	464 (39.4)	607 (51.7)
Swelling	28 (14.0)	14 (14.0)	71 (6.0)	98 (8.3)
Systemic adverse event†				
Fatigue	81 (40.5)	34 (34.0)	237 (20.1)	230 (19.6)
Headache	59 (29.5)	24 (24.0)	135 (11.5)	152 (12.9)
Myalgia	33 (16.5)	14 (14.0)	70 (5.9)	79 (6.7)
Pyrexia‡				
≥38.0°C to <38.5°C	3 (1.5)	0 (0.0)	7 (0.6)	7 (0.6)
≥38.5°C to <39.0°C	2 (1.0)	0 (0.0)	6 (0.5)	5 (0.4)
≥39.0°C	2 (1.0)	1 (1.0)	2 (0.2)	3 (0.3)

* Every individual is counted a single time for each applicable row and column.

† Injection-site erythema, injection site pain, injection site swelling, fatigue, headache, and myalgia were solicited from Day 1 through Day 5 postvaccination.

‡ Pyrexia was defined as temperature 38.0°C solicited from Day 1 through Day 5 postvaccination. Percentages are based on the number of individuals with temperature data.

Table 2: Individuals with Solicited Local and Systemic Adverse Events Within 5 Days Postvaccination in Pneumococcal Vaccine-naïve Adults 18-49 Years of Age – Protocol 004

	CAPVAXIVE	PNEUMOVAX 23
	n (%)	**n (%)**
Individuals in population*	1,616	541
One or more solicited adverse events	1,263 (78.2)	387 (71.5)
No solicited adverse events	353 (21.8)	154 (28.5)
Local adverse event†		
Erythema	219 (13.6)	41 (7.6)
Pain	1,184 (73.3)	328 (60.6)
Swelling	213 (13.2)	41 (7.6)
Systemic adverse event†		
Fatigue	573 (35.5)	184 (34.0)
Headache	440 (27.2)	116 (21.4)
Myalgia	264 (16.3)	47 (8.7)
Pyrexia‡		
≥38.0°C to <38.5°C	31 (1.9)	4 (0.7)
≥38.5°C to <39.0°C	11 (0.7)	2 (0.4)
≥39.0°C	6 (0.4)	6 (1.1)

* Every individual is counted a single time for each applicable row and column.

† Injection-site erythema, injection site pain, injection site swelling, fatigue, headache, and myalgia were solicited from Day 1 through Day 5 postvaccination.

‡ Pyrexia was defined as temperature 38.0°C solicited from Day 1 through Day 5 postvaccination. Percentages are based on the number of individuals with temperature data.

Table 3: Individuals with Solicited Local and Systemic Adverse Events Within 5 Days Postvaccination in Adults ≥50 Years of Age and Older with Prior Pneumococcal Vaccination – Protocol 006

	Cohort 1*		Cohort 2†		Cohort 3‡
	CAPVAXIVE n (%)	VAXNEUVANCE n (%)	CAPVAXIVE n (%)	PNEUMOVAX 23 n (%)	CAPVAXIVE n (%)
Individuals in population§	230	117	174	85	105
One or more solicited adverse events	107 (46.5)	65 (55.6)	86 (49.4)	52 (61.2)	51 (48.6)
No solicited adverse events	123 (53.5)	52 (44.4)	88 (50.6)	33 (38.8)	54 (51.4)
Local adverse event¶					
Erythema	17 (7.4)	9 (7.7)	13 (7.5)	8 (9.4)	8 (7.6)
Pain	82 (35.7)	51 (43.6)	72 (41.4)	40 (47.1)	46 (43.8)
Swelling	19 (8.3)	10 (8.5)	8 (4.6)	14 (16.5)	11 (10.5)
Systemic Events¶					
Fatigue	33 (14.3)	20 (17.1)	33 (19.0)	11 (12.9)	23 (21.9)
Headache	16 (7.0)	11 (9.4)	18 (10.3)	10 (11.8)	9 (8.6)
Myalgia	17 (7.4)	3 (2.6)	17 (9.8)	8 (9.4)	9 (8.6)
Pyrexia#					
≥38.0°C to <38.5°C	2 (0.9)	0 (0.0	1 (0.6)	0 (0.0)	0 (0.0)
≥38.5°C to <39.0°C	2 (0.9)	2 (1.7)	2 (1.1)	1 (1.2)	0 (0.0)
≥39.0°C	0 (0.0)	1 (0.9)	2 (1.1)	0 (0.0)	0 (0.0)

* Cohort 1 prior vaccination with PNEUMOVAX 23

† Cohort 2 prior vaccination with Prevenar 13

‡ Cohort 3 prior vaccination with Prevenar 13 + PNEUMOVAX 23 (n=45), or VAXNEUVANCE + PNEUMOVAX 23 (n=5), or PNEUMOVAX 23 + Prevenar 13 (n=54), or VAXNEUVANCE (n=1) or Prevenar 20 (n=0)

§ Every individual is counted a single time for each applicable row and column.

¶ Injection site erythema, injection site pain, injection site swelling, fatigue, headache, and myalgia were solicited from Day 1 through Day 5 postvaccination.

Pyrexia was defined as temperature 38.0°C solicited from Day 1 through Day 5 postvaccination. Percentages are based on the number of individuals with temperature data.

Safety with Concomitant Influenza Vaccine Administration

In Protocol 005, the safety profile of CAPVAXIVE when administered concomitantly with quadrivalent inactivated influenza vaccine (QIV) was generally consistent with the safety profile of CAPVAXIVE.

Unsolicited Adverse Events

Across the Phase 3 clinical studies, there were no notable patterns or imbalances between vaccine groups for unsolicited adverse events assessed to be related to study vaccine by the investigator that occurred within 1-month postvaccination.

Serious Adverse Events

Across the Phase 3 clinical studies, the proportion of individuals reporting 1 or more SAEs within 6 months postvaccination was comparable between individuals vaccinated with CAPVAXIVE (1.4%), and individuals vaccinated with an active comparator (2.0%). There were no notable patterns or imbalances between vaccine groups for SAEs. There were 2 SAEs (0.05%; bronchospasm, cellulitis) assessed by the investigator to be related to CAPVAXIVE.

Reporting Suspected Adverse Effects

Reporting suspected adverse reactions after registration 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 at http://www.tga.gov.au/reporting-problems.

4.9 OVERDOSE

There have been no reports of administration of higher than the recommended dose of CAPVAXIVE.

For information on the management of overdose, contact the Poison Information Centre on 131126 (Australia).

5 PHARMACOLOGICAL PROPERTIES

5.1 PHARMACODYNAMIC PROPERTIES

Mechanism of Action

CAPVAXIVE is a conjugated polysaccharide vaccine that protects against invasive disease and pneumonia caused by *S. pneumoniae*.

Pneumococcal conjugate vaccines have decreased the frequency of disease in populations vaccinated (direct impact), and in populations not vaccinated through reduction of colonisation and transmission (indirect impact). CAPVAXIVE contains serotype-specific pneumococcal purified capsular polysaccharides, which are known to contribute to the pathogenicity of pneumococci in adults. Each serotype of activated polysaccharide is individually conjugated to a carrier protein (diphtheria CRM197 protein), and elicits antibodies that enhance opsonization, 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 *S. pneumoniae* or following pneumococcal vaccination can be determined through the assessments of OPA responses, to assess functional antibodies capable of opsonizing pneumococcal purified 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 IgG responses.

Serotype-specific immune responses (OPA and IgG) for the 21 serotypes contained in CAPVAXIVE and 2 cross-reactive serotypes (15B and 6C) 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.

As with any vaccine, CAPVAXIVE may not protect all vaccine recipients.

Burden of Disease

Pneumococcal disease in adults is associated with significant morbidity and mortality worldwide, with disease incidence varying by age, region, and race. Mortality rates are elevated in older

adults, adults with comorbid conditions (e.g., diabetes mellitus, chronic lung disease, chronic liver disease), and immunocompromised individuals (e.g., HIV infection, cancer, transplant, immunosuppressive therapies). Adults with two or more comorbid conditions may have a risk of pneumococcal disease that is comparable to that of immunocompromised individuals. Furthermore, the incidence of invasive pneumococcal disease (IPD) in Aboriginal and Torres Straits Islanders (ATSI) adults is higher than non-ATSI adults.

Pneumococcal disease is classified as invasive pneumococcal disease (IPD) or noninvasive pneumococcal disease (non-IPD). IPD is defined by the isolation of S. pneumoniae in body fluids that are otherwise sterile and includes bacteraemic pneumonia, bacteraemia without focus, meningitis, pleuritis, and arthritis. Non-IPD mainly consists of nonbacteraemic pneumococcal pneumonia and acute otitis media. Community acquired pneumonia (CAP) remains one of the most important causes of death from infection in many countries, with S. pneumoniae being one of the most commonly identified bacterial pathogens.

Clinical Trials

Clinical Trials Experience in Adults 18 Years of Age and Older

Four Phase 3, clinical studies (Protocol 003, Protocol 004, Protocol 005, and Protocol 006) conducted across the Americas, Europe, and Asia Pacific evaluated the immunogenicity of CAPVAXIVE in approximately 6,500 adults 18 years of age and older, approximately 4,500 of whom received CAPVAXIVE. Of the 6,500 adults enrolled, approximately 1,000 had received other prior pneumococcal vaccines. Approximately 34% of enrolled adults had chronic medical conditions (e.g., diabetes, renal disorders, chronic heart disease, chronic liver disease, chronic lung disease including asthma, smoking, alcoholism) known to increase the risk of pneumococcal disease.

In each study, immunogenicity was assessed by serotype-specific OPA and immunoglobulin G (IgG) responses at 1-month postvaccination. The primary immunogenicity endpoints included OPA geometric mean titers (GMTs) and the proportion of individuals who achieved a ≥4 fold rise in OPA responses from prevaccination to 1-month postvaccination.

Table 4: Summary of Clinical trials for CAPVAXIVE for Immunogenicity and Safety

Study #	Study design	Dosage, route of administration and duration	Vaccinated Study subjects (n)	Mean age (years) (Range)	Sex
P003	Randomised, active comparator-controlled, parallel-group, multisite, double-blind study to evaluate the safety, tolerability, and immunogenicity of CAPVAXIVE in pneumococcal vaccine-naïve adults ≥18 years of age.	1 dose of 0.5mL of CAPVAXIVE or Prevenar 20 Intramuscular injection	N=2,656	60.7 (18 to 97 years)	Females: 1558 Males: 1098
P004	Randomised, active comparator-controlled, parallel-group, multisite, double-blind, lot-to-lot consistency study to evaluate the safety, tolerability, and immunogenicity of CAPVAXIVE in pneumococcal vaccine-naïve adults 18 to 49 years of age.	1 dose of 0.5mL of CAPVAXIVE or PNEUMOVAX 23 Intramuscular injection	N=2,157	34.6 (18 to 49 years)	Female: 1243 Male: 914
P005	Randomised, placebo-controlled, parallel-group, multisite, double-blind study of CAPVAXIVE to evaluate the safety, tolerability, and immunogenicity of CAPVAXIVE when administered concomitantly with quadrivalent influenza vaccine (QIV) in adults ≥50 years of age	1 dose of 0.5mL of CAPVAXIVE® + 1 dose of 0.5mL of QIV + 1 dose of 0.5mL of placebo (concomitant administration) OR 1 dose of 0.5mL of QIV + 1 dose of 0.5mL of placebo + 1 dose of 0.5ml of CAPVAXIVE (sequential administration) Intramuscular injection	N=1,072	64.2 (50 to 91 years)	Female: 584 Male: 488
P006	To evaluate the safety, tolerability and immunogenicity of CAPVAXIVE in participants ≥50 years of age who were pneumococcal vaccine-experienced (PNEUMOVAX 23, Prevenar 13, Prevenar 13 + PNEUMOVAX 23, VAXNEUVANCE + PNEUMOVAX 23, VAXNEUVANCE, Prevenar 20 or PNEUMOVAX 23 + Prevenar 13) Cohorts 1 and 2: Randomised, double-blind, parallel group, active comparator-controlled Cohort 3: Open-label, single group	Cohort 1: 1 dose of 0.5mL of CAPVAXIVE or VAXNEUVANCE Cohort 2: 1 dose of 0.5mL of CAPVAXIVE or PNEUMOVAX 23 Cohort 3: 1 dose of 0.5mL of CAPVAXIVE Intramuscular injection	N=712	67.9 (50 to 91 years)	Female: 381 Male: 331

Clinical Trials Conducted in Pneumococcal Vaccine-Naïve Adults

CAPVAXIVE effectiveness in adults against invasive pneumococcal disease and pneumonia was demonstrated based on comparative immunogenicity to a licensed pneumococcal vaccine (Prevenar 20).

Pneumococcal Vaccine-Naïve Individuals 50 Years of Age and Older

In a double-blind study (Protocol 003), 2,362 pneumococcal vaccine-naïve adults 50 years of age and older were randomised to receive either CAPVAXIVE or Prevenar 20. The study demonstrated that CAPVAXIVE was noninferior to Prevenar 20 for the 10 common serotypes as assessed by the GMT ratio (CAPVAXIVE/ Prevenar 20) where the noninferiority statistical criteria were met if the lower bound of the 2-sided 95% Confidence Interval (CI) was greater than 0.5. CAPVAXIVE was superior to Prevenar 20 for 10 of 11 serotypes unique to CAPVAXIVE as assessed by the GMT ratio (CAPVAXIVE/ Prevenar 20) where the superiority statistical criterion was met if the lower bound of the 2-sided 95% CI was greater than 2.0 (Table 5). The lower bound for serotype 15C was 1.77.

CAPVAXIVE was superior to Prevenar 20 for 10 of 11 unique serotypes 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 statistical criterion was defined as the difference between CAPVAXIVE and Prevenar 20 being greater than 10 percentage points (Table 6). For serotype 15C, 83.4% of individuals achieved a ≥4-fold rise in OPA responses from prevaccination to 1-month postvaccination; the lower bound of the 2 sided 95% CI of the difference (CAPVAXIVE - Prevenar 20) was 5.6 percentage points and did not meet the statistical criterion for superiority of >10 percentage points. The immune response to serotype 15C in the comparator group was likely attributed to cross-reactivity based on the presence of the 15B antigen.

Table 5: Serotype-Specific OPA GMTs in Pneumococcal Vaccine-Naïve Adults ≥50 Years of Age (Protocol 003)

Pneumococcal Serotype	CAPVAXIVE (N = 1,179)		Prevenar 20 (N = 1,177)		GMT Ratio* (CAPVAXIVE/Prevenar 20) (95% CI)*
	n	GMT*	n	GMT*	
10 Common 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 Serotypes Unique to 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)

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

† A conclusion of non-inferiority for the common serotypes was based on the lower bound of the 95% CI for the estimated GMT ratio (CAPVAXIVE/Prevenar 20) being >0.5.

‡ A conclusion of superiority for the unique serotypes in CAPVAXIVE compared to Prevenar 20 was based on the lower bound of the 95% CI for the estimated GMT ratio (CAPVAXIVE/Prevenar 20) being >2.0.

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

Table 6: Pneumococcal Vaccine Naïve Individuals ≥50 Years of Age With a ≥4-Fold Rise in OPA Responses for Serotypes Unique to CAPVAXIVE (Protocol 003)

Pneumococcal Serotype	CAPVAXIVE (N=1,179)	Prevenar 20 (N=1,177)	Percentage Point Difference (CAPVAXIVE – Prevenar 20)
	Observed Response Percentage (m/n)	Observed Response Percentage (m/n)	Estimate (95% CI)*,†
9N	64.7 (595/920)	19.9 (195/978)	44.7 (40.7, 48.6)
15A	66.7 (462/693)	35.8 (253/706)	30.9 (25.8, 35.8)
15C	83.4 (794/952)	74.2 (695/937)	9.2 (5.6, 12.9)
16F	71.9 (654/910)	20.8 (200/961)	51.1 (47.1, 54.9)
17F	75.8 (653/862)	9.5 (90/952	66.3 (62.8, 69.6)
20A	67.3 (675/1003)	9.6 (97/1011)	57.7 (54.2, 61.1)
23A	78.9 (598/758)	36.8 (270/734)	42.2 (37.6, 46.6)
23B	85.5 (873/1021)	49.6 (506/1021)	35.9 (32.1, 39.6)
24F	80.5 (745/925)	6.3 (55/872)	74.2 (71.1, 77.1)
31	76.5 (698/912)	17.9 (171/954)	58.6 (54.8, 62.1)
35B	60.0 (550/917)	6.8 (67/988)	53.2 (49.6, 56.6)

* Estimated difference and CI were based on the stratified Miettinen & Nurminen method.

† A conclusion of superiority was based on the lower bound of the 2-sided 95% CI of the differences (CAPVAXIVE – Prevenar 20) between the percentages of individuals with a ≥4-fold rise from prevaccination to 1-month postvaccination being >10 percentage points.

N=Number of individuals randomised and vaccinated; m=Number of individuals with the indicated response
n=Number of individuals contributing to the analysis

Pneumococcal Vaccine Naïve Adults 18 to 49 Years of Age

In a double-blind study (Protocol 003), pneumococcal vaccine-naïve individuals 18 to 49 years of age were randomised in a 2:1 ratio to receive CAPVAXIVE or Prevenar 20.

Effectiveness of CAPVAXIVE in individuals 18 to 49 years of age was assessed by a comparison of the OPA responses induced by CAPVAXIVE in this age group to the OPA responses of individuals 50 to 64 years of age. The OPA responses of individuals 18 to 49 years of age to each of 22 S. pneumoniae serotypes met the criteria for immunobridging as the lower bound of the 2-sided 95% CI for the GMT ratio for each serotype was >0.5 (see Table 7). The *S. pneumoniae* serotype 15B cross-reactive OPA GMT was 10,976.7 following administration of CAPVAXIVE in individuals 18 to 49 years of age and 5,438.9 following administration of CAPVAXIVE in individuals 50 to 64 years of age, with a GMT ratio of 2.02 (95% CI: 1.57, 2.60).

Table 7: Comparison of Serotype-Specific OPA GMTs in Pneumococcal Vaccine-Naïve Adults 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 (LDA).

† A conclusion of immunobridging was based on the lower bound of the 2-sided 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

In a double-blind study (Protocol 004), 2,162 pneumococcal vaccine naïve adults 18 to 49 years of age were randomised in a 1:1:1:1 ratio to receive 1 of 3 lots of CAPVAXIVE or PNEUMOVAX 23. The study demonstrated that all 3 lots were equivalent as the lower and upper limits of the 2 sided 95% CI of the serotype specific OPA GMT ratios between any 2 lots were within the equivalence margin (0.5 to 2.0) for all 21 serotypes. Immune responses following vaccination with CAPVAXIVE were comparable to PNEUMOVAX 23 for the 12 common serotypes and higher for 9 unique serotypes.

Clinical Trials Conducted in Adults with Prior Pneumococcal Vaccination

Protocol 006, a descriptive Phase 3 study, enrolled adults ≥50 years of age who were previously vaccinated with other pneumococcal vaccines at least 1 year prior to study entry (see Table 4).

Participants in cohort 1 were randomised to receive CAPVAXIVE (n=231) or VAXNEUVANCE (n=119), participants in cohort 2 were randomised to receive CAPVAXIVE (n=176) or PNEUMOVAX 23 (n=85), and participants in cohort 3 were allocated to receive CAPVAXIVE (n=106).

CAPVAXIVE was demonstrated to be immunogenic for all serotypes included in the vaccine, based on OPA GMTs and the proportion of individuals with ≥4-fold rise in OPA responses from baseline to 1-month postvaccination. In Cohort 1, CAPVAXIVE elicited OPA responses that were

comparable to VAXNEUVANCE for the 6 common serotypes, and higher for the 15 unique serotypes and serotype 15B. In Cohort 2, CAPVAXIVE elicited OPA responses comparable to PNEUMOVAX 23 for the 12 common serotypes and serotype 15B, and higher for the 9 unique serotypes. OPA responses to CAPVAXIVE were similar across the 3 cohorts of participants who previously received one or more pneumococcal vaccines.

Cross-Reactive Immune Responses to CAPVAXIVE

In the Phase 3 studies, CAPVAXIVE elicited an immune response to serotype 15B (cross reactive to serotype 15C) and serotype 6C (cross reactive to serotype 6A).

In Protocol 003, in individuals 50 years of age and older, CAPVAXIVE met the prespecified criterion for antibody response for serotype 15B (lower bound of the 2 sided 95% CI of the proportion of individuals with a ≥4-fold rise in OPA responses was >50%); 64.7% of individuals had ≥4 fold rise in OPA titers. CAPVAXIVE successfully immunobridged serotype-specific immune responses for serotype 15B 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. In individuals 50 years of age and older, CAPVAXIVE elicited a cross-reactive immune response to serotype 6C as assessed by OPA titers; 49.3% of individuals had a ≥4 fold rise in OPA responses, however the prespecified criterion for an acceptable response was not met. For the immune response to serotype 6C in individuals 18 to 49 years of age, as compared to individuals 50 to 64 years of age, the GMT ratio observed was 2.05 (95% CI: 1.52, 2.77).

Concomitant Vaccination

In a double-blind study (Protocol 005), 1,080 adults 50 years of age and older, with or without a history of prior pneumococcal vaccination, were randomised in a 1:1 ratio. One vaccination group received CAPVAXIVE and QIV concomitantly, followed by placebo 30 days later (concomitant group). A second vaccination group received QIV and placebo concomitantly, followed by CAPVAXIVE 30 days later (sequential group). Antibody responses were assessed 1-month postvaccination.

The OPA responses to CAPVAXIVE administered concomitantly with QIV were non inferior to the OPA responses to CAPVAXIVE administered sequentially after QIV for 20 of 21 serotypes [lower bound of the 2-sided 95% CI of the GMT ratio (concomitant group/sequential group) was >0.5]; the non-inferiority was not met for serotype 23B [lower bound of the 2-sided 95% CI of the GMT ratio (concomitant group/sequential group) was 0.44]. The OPA response to serotype 15B was not assessed for non-inferiority. In a descriptive analysis, the OPA GMT for serotype 15B in the concomitant group was 3,438.7 and in the sequential group was 4,440.5, with a GMT ratio of 0.77 (95% CI: 0.64, 0.94). The influenza strain-specific hemagglutination inhibition (HAI) responses to QIV administered concomitantly with CAPVAXIVE were non inferior to the HAI responses to QIV administered alone for 3 of 4 influenza strains [lower bound of the 2-sided 95% CIs for HAI GMT ratios (concomitant group/sequential group) was >0.67 (non-inferiority margin); the lower bound was 0.67 for the A/H3N2 influenza strain].

5.2 PHARMACOKINETIC PROPERTIES

Not applicable.

5.3 PRECLINICAL SAFETY DATA

Genotoxicity

CAPVAXIVE has not been evaluated for the potential to cause genotoxicity.

Carcinogenicity

CAPVAXIVE has not been evaluated for the potential to cause carcinogenicity.

6 PHARMACEUTICAL PARTICULARS

6.1 LIST OF EXCIPIENTS

Each 0.5 mL dose contains:
histidine
polysorbate 20
sodium chloride
water for injections

The product does not contain preservative.

6.2 INCOMPATIBILITIES

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

6.3 SHELF LIFE

In Australia, information on the shelf life can be found on the public summary of the Australian Register of Therapeutic Goods (ARTG). The expiry date can be found on the packaging.

6.4 SPECIAL PRECAUTIONS FOR STORAGE

Store refrigerated at 2°C to 8°C.
Do not freeze.
Protect from light.

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

In the event of temporary temperature excursions, stability data indicate that CAPVAXIVE is stable at temperatures up to 25°C for 96 hours.

6.5 NATURE AND CONTENTS OF CONTAINER

CAPVAXIVE is a solution for injection available in 0.5 mL single-dose pre-filled syringes (Type I glass) in packs of 1 and 10.

The tip cap and plunger stopper of the pre-filled syringe are not made with natural rubber latex.

6.6 SPECIAL PRECAUTIONS FOR DISPOSAL

In Australia, any unused medicine or waste material should be disposed of in accordance with local requirements.

6.7 PHYSICOCHEMICAL PROPERTIES

Chemical structure

Not applicable.

CAS number

Not applicable.

7 MEDICINE SCHEDULE (POISONS STANDARD)

Schedule 4 – Prescription Only Medicine

8 SPONSOR

Merck Sharp & Dohme (Australia) Pty Limited
Level 1, Building A, 26 Talavera Road
Macquarie Park NSW 2113
http://www.msd-australia.com.au
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9 DATE OF FIRST APPROVAL

05 February 2025

10 DATE OF REVISION

15 May 2025

Summary Table of Changes

Section changed	Summary of new information
4.1	Editorial correction

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