

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](http://www.tga.gov.au/reporting-problems).

## **AUSTRALIAN PRODUCT INFORMATION – VAXNEUVANCE® (Pneumococcal 15-valent Conjugate Vaccine [CRM<sub>197</sub> Protein], adsorbed)**

### **1 NAME OF THE MEDICINE**

VAXNEUVANCE (Pneumococcal 15-valent Conjugate Vaccine [CRM<sub>197</sub> Protein], adsorbed)

### **2 QUALITATIVE AND QUANTITATIVE COMPOSITION**

Each 0.5 mL dose contains 32 micrograms of total pneumococcal purified capsular polysaccharide (2.0 micrograms each of serotypes 1, 3, 4, 5, 6A, 7F, 9V, 14, 18C, 19A, 19F, 22F, 23F, and 33F, and 4.0 micrograms of serotype 6B) conjugated to 30 micrograms of non-toxic diphtheria CRM<sub>197</sub> protein, adsorbed on 125 micrograms of aluminium (as aluminium phosphate adjuvant).

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

### **3 PHARMACEUTICAL FORM**

VAXNEUVANCE is a suspension for injection available in 0.5 mL single-dose prefilled syringes.

The vaccine is an opalescent suspension.

### **4 CLINICAL PARTICULARS**

#### **4.1 THERAPEUTIC INDICATIONS**

VAXNEUVANCE is indicated for active immunisation for the prevention of pneumococcal disease caused by *Streptococcus pneumoniae* serotypes (1, 3, 4, 5, 6A, 6B, 7F, 9V, 14, 18C, 19A, 19F, 22F, 23F and 33F) in adults 18 years of age and older.

VAXNEUVANCE may not prevent disease caused by *S. pneumoniae* serotypes that are not contained in the vaccine.

The use of VAXNEUVANCE should be guided by official recommendations.

#### **4.2 DOSE AND METHOD OF ADMINISTRATION**

##### **Dosage (dose and interval)**

Administer a 0.5 mL dose of VAXNEUVANCE intramuscularly.

##### *Adults*

One single dose (0.5 mL).

##### *Special Populations*

The dosing schedule of VAXNEUVANCE in special populations should be guided by official recommendations.

##### **Method of administration**

For intramuscular use only. Do not inject intravascularly.

The preferred site for injection is the deltoid muscle of the upper arm in adults. The vaccine should not be injected in the gluteal area or areas where there may be a major nerve trunk and/or blood vessel.

### **Instruction for use**

VAXNEUVANCE should not be diluted or mixed with other vaccines.

The full recommended dose of the vaccine should be used.

When VAXNEUVANCE 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].

Because this product is a suspension containing an adjuvant, hold horizontally and shake vigorously immediately prior to use to obtain an opalescent suspension in the vaccine container. Do not use the vaccine if it cannot be resuspended. 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. Attach a needle by twisting in a clockwise direction until the needle fits securely on the syringe. Inject the entire contents of the syringe. Exercise caution to avoid harm from an accidental needle stick.

### **4.3 CONTRAINDICATIONS**

VAXNEUVANCE is contraindicated in individuals with a history of a severe allergic reaction (e.g., anaphylaxis) to any component of the vaccine or any diphtheria toxoid-containing vaccine [See Section 2 Qualitative and quantitative composition and Section 6.1 List of excipients].

### **4.4 SPECIAL WARNINGS AND PRECAUTIONS FOR USE**

Individuals with altered immunocompetence, including those receiving immunosuppressive therapy, may have a reduced immune response to VAXNEUVANCE [See Section 4.5 Interactions with other medicines and other forms of interactions].

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

#### **Use in the elderly**

Of the 4,344 individuals aged 50 years and older who received VAXNEUVANCE, 2,470 (56.9%) were 65 years and older, and 479 (11.0%) were 75 years and older [see Section 4.8 Adverse effects (Undesirable effects) and Section 5 Pharmacological properties – Clinical Trials].

#### **Paediatric use**

The safety and effectiveness of VAXNEUVANCE in individuals younger than 18 years of age have not yet been established.

#### **Effects on laboratory tests**

Not applicable.

### **4.5 INTERACTIONS WITH OTHER MEDICINES AND OTHER FORMS OF INTERACTIONS**

#### **Use with Other Vaccines**

VAXNEUVANCE can be administered concomitantly with inactivated influenza vaccine [see Section 4.8 Adverse effects (Undesirable effects) and Section 5 Pharmacological properties – Clinical Trials]. There are no data on the concomitant administration of VAXNEUVANCE with other vaccines.

#### **Use with Immunosuppressive Therapies**

Immunosuppressive therapies, including irradiation, antimetabolites, alkylating agents, cytotoxic drugs, corticosteroids, therapeutic proteins and targeted immunomodulators may reduce the immune responses to vaccines [see 4.4 Special warnings and precautions for use].

## 4.6 FERTILITY, PREGNANCY AND LACTATION

### Effects on fertility

VAXNEUVANCE administered to female rats at a dose approximately 200 times the adult human dose on a microgram/kg basis had no effects on mating performance, fertility or embryonic/fetal survival.

### Use in pregnancy - Category B1

#### *Animal Data*

Developmental and reproductive toxicity studies have been performed in female rats at a dose approximately 200 times the adult human dose on a microgram/kg basis. In these studies, female rats received VAXNEUVANCE (32 micrograms/rat/dose) by intramuscular injection 28 days and 7 days prior to mating, on gestation day 6 and on lactation day 7. There was no evidence of embryofetal lethality or fetal malformations and variations and no adverse effects on pre-weaning development were observed. Antibodies to all 15 serotypes contained in VAXNEUVANCE were detected in offspring, attributable to the acquisition of maternal antibodies via placental transfer during gestation and possibly via lactation.

#### *Human Data*

There are no adequate and well-controlled studies of VAXNEUVANCE in pregnant women, and human data available from clinical trials with VAXNEUVANCE 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 exposure to *S. pneumoniae*; VAXNEUVANCE should be administered only if clearly needed.

### Use in lactation

It is not known whether this vaccine is excreted in human milk.

Vaccine-specific antibodies were detected in rat offspring via maternal transfer from immunised female rats [see Use in pregnancy]. Evaluation of antibody levels in animal milk was not conducted.

## 4.7 EFFECTS ON ABILITY TO DRIVE AND USE MACHINES

VAXNEUVANCE 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 VAXNEUVANCE in healthy and immunocompetent adults was assessed in 6 randomized, double-blind clinical studies (Protocol 007, Protocol 016, Protocol 017, Protocol 019, Protocol 020 and Protocol 021) conducted across the Americas, Europe and Asia Pacific, which included 7,136 adults ranging in age from 18 to 98 years. Each study enrolled adults with stable underlying medical conditions and/or risk factors that are known to increase the risk of pneumococcal disease.

VAXNEUVANCE was administered to 5,478 adults; 1,134 were 18 to 49 years of age, 1,874 were 50 to 64 years of age, and 2,470 were 65 years of age and older. Of those who received VAXNEUVANCE, 5,101 adults were pneumococcal vaccine-naïve and 377 adults were previously vaccinated with PNEUMOVAX 23® [pneumococcal vaccine polyvalent] at least 1 year prior to enrollment.

The safety of VAXNEUVANCE in pneumococcal vaccine-naïve adults 50 years of age and older was evaluated in 3 active comparator-controlled clinical studies (Protocol 016, Protocol 019 and Protocol 020) in which 3,032 participants received VAXNEUVANCE and 1,154 participants received Prevenar 13® [Pneumococcal polysaccharide conjugate vaccine, 13-valent adsorbed] (PCV13). A descriptive study (Protocol 017) evaluated the safety of VAXNEUVANCE in pneumococcal vaccine-naïve adults 18 to 49 years of age.

The safety of VAXNEUVANCE in adults 65 years of age and older who were previously vaccinated with PNEUMOVAX 23 (at least 1 year prior to study entry) was evaluated in an additional descriptive study (Protocol 007).

The safety of concomitant administration of VAXNEUVANCE with seasonal inactivated influenza vaccine was evaluated in 1,196 adults 50 years of age and older, including those with or without a history of prior vaccination with PNEUMOVAX 23 (Protocol 021).

Safety was evaluated using a Vaccination Report Card for up to 14 days postvaccination. Oral body temperature and injection-site adverse events were solicited on Day 1 through Day 5 postvaccination. Systemic adverse events were solicited on Day 1 through Day 14 postvaccination. Unsolicited adverse events were reported on Day 1 through Day 14 postvaccination. The duration of the safety follow-up period postvaccination with VAXNEUVANCE was 1 month in Protocol 007, 6 months in Protocol 019, Protocol 020, Protocol 017 and Protocol 021 and 12 months in Protocol 016.

#### Solicited Adverse Reactions

The percentage of participants with solicited adverse reactions that occurred within 5 or 14 days following administration of VAXNEUVANCE or Prevenar 13 in 5 studies are shown in Tables 1-2. All solicited adverse reactions occurred in ≥5% of participants with VAXNEUVANCE; older adults reported fewer solicited adverse reactions than younger adults, regardless of vaccination group. The majority of solicited adverse reactions were mild (based on intensity or size) and of short duration (≤3 days); severe reactions (defined as an event that prevents normal daily activity or size >10 cm) occurred in ≤1.5% of adults.

**Table 1: Percentage of Participants with Solicited Local and Systemic Adverse Reactions Within 5 or 14 Days Postvaccination in Pneumococcal Vaccine-Naïve Adults**

Age in Years	Protocol 019		Protocol 020		Protocol 016		Protocol 017	
	≥50							
	VAXNEUVANC E (%) N=602	PCV1 3 (%) N=600	VAXNEUVANC E (%) N=2103	PCV1 3 (%) N=230	VAXNEUVANC E (%) N=327	PCV1 3 (%) N=324	VAXNEUVANC E (%) N=1134	PCV1 3 (%) N=378
<b>Local Reactions*</b>								
Pain	54.0	42.3	66.8	52.2	55.0	41.4	75.8	68.8
Erythema	9.0	11.3	10.9	9.6	9.8	5.6	15.1	14.0
Swelling	12.5	11.2	15.4	14.3	16.2	11.4	21.7	22.2
<b>Systemic Reactions†</b>								
Fatigue	17.4	17.3	21.5	22.2	23.5	13.9	34.3	36.8
Headache	11.6	13.0	18.9	18.7	14.1	12.7	26.5	24.9
Myalgia	15.4	12.0	26.9	21.7	17.7	11.1	28.8	26.5
Arthralgia	5.3	5.5	7.7	5.7	6.4	5.2	12.7	11.6
<b>Elevated Body Temperature*‡</b>								
≥38.0°C and <39.0°C	0.3	1.3	0.7	0.4	0.6	0.6	1.3	0.3
≥39.0°C	0.2	0.0	0.0	0.0	0.6	0.6	0.2	0.0

\* Solicited on Day 1 through Day 5 postvaccination

† Solicited on Day 1 through Day 14 postvaccination

‡ Percentages are based on the number of participants with temperature data

N=Number of participants vaccinated

**Table 2: Percentage of Participants with Solicited Local and Systemic Adverse Reactions Within 5 or 14 Days Postvaccination in Adults with Previous Pneumococcal Vaccination**

Protocol 007		
Age in Years	≥65	
	VAXNEUVANCE (%) N=127	PCV13 (%) N=126
<b>Local Reactions*</b>		
Pain	55.1	44.4
Erythema	7.9	7.1
Swelling	14.2	6.3
<b>Systemic Reactions†</b>		
Fatigue	18.1	19.0
Headache	13.4	15.9
Myalgia	15.7	11.1
Arthralgia	5.5	8.7
<b>Elevated Body Temperature*‡</b>		
≥38.0°C and <39.0°C	1.6	0.0
≥39.0°C	0.0	0.0

\* Solicited on Day 1 through Day 5 postvaccination

† Solicited on Day 1 through Day 14 postvaccination

‡ Percentages are based on the number of participants with temperature data

N=Number of participants vaccinated

#### *Unsolicited Adverse Reactions*

Injection-site pruritus occurred in 1.0% to 2.8% of pneumococcal vaccine-naïve adults vaccinated with VAXNEUVANCE.

#### *Additional Information in Special Populations*

##### Populations at Increased Risk for Pneumococcal Disease

##### Adults Living with HIV

In adults living with HIV (Protocol 018), the safety profile of VAXNEUVANCE was generally consistent with its safety profile in immunocompetent pneumococcal vaccine-naïve adults.

##### Adults with Chronic Conditions and Other Risk Factors

In adults 18 to 49 years of age with 1 risk factor or 2 or more risk factors for pneumococcal disease (Protocol 017), the safety profile of VAXNEUVANCE was generally consistent with its safety profile in the overall study population.

##### Safety with Concomitant Influenza Vaccine Administration

The safety profile of VAXNEUVANCE when administered concomitantly with inactivated influenza vaccine was generally consistent with the safety profile of VAXNEUVANCE.

#### **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 are no data with regard to overdose.

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

VAXNEUVANCE contains serotype-specific pneumococcal capsular polysaccharides each of which is conjugated to a carrier protein (CRM<sub>197</sub>), and elicits antibodies that enhance opsonisation, phagocytosis, and killing of pneumococci to protect against pneumococcal disease. VAXNEUVANCE is also expected to elicit 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 measurements of opsonophagocytic activity (OPA) and immunoglobulin G (IgG) responses. OPA represents functional antibodies capable of opsonising pneumococcal capsular polysaccharides for presentation to phagocytic cells for engulfment and subsequent killing and are considered an important immunologic surrogate measure of protection against pneumococcal disease in adults. OPA titers are expressed as the reciprocal of the highest serum dilution that reduces survival of the pneumococci by at least 50%. A validated multiplexed opsonophagocytic assay (MOPA) was used to measure serotype-specific OPA titers for each of the 15 serotypes contained in VAXNEUVANCE.

#### Burden of Disease

Pneumococcal disease is associated with significant morbidity and mortality in both children and adults worldwide. Although all age groups may be affected by pneumococcal disease, the highest rates of disease occur in young children <5 years of age and adults ≥65 years of age. Furthermore, the incidence of invasive pneumococcal disease (IPD) in Aboriginal and Torres Straits Islanders (ATSI) adults is approximately 3 times higher than non-ATSI adults. Mortality rates are elevated in older adults, adults with comorbid conditions (e.g., diabetes mellitus, chronic lung disease, chronic liver disease), and especially in immunocompromised individuals (e.g., HIV infection, cancer, transplant, immunosuppressive therapies). Adults with 2 or more comorbid conditions may have a risk of pneumococcal disease that is comparable to that of immunocompromised individuals.

Clinical syndromes include both IPD (i.e. sepsis, meningitis, and bacteraemic pneumonia) and noninvasive disease (e.g., non- bacteraemic pneumonia). Bacteraemic pneumococcal pneumonia represents approximately 80-90% of IPD cases in adults. 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

Six double-blind, clinical studies (Protocol 007, Protocol 016, Protocol 017, Protocol 019, Protocol 020 and Protocol 021) conducted across the Americas, Europe and Asia Pacific evaluated the immunogenicity of VAXNEUVANCE in healthy and immunocompetent adults across different age groups including individuals with or without previous pneumococcal vaccination. The clinical studies included adults with stable underlying medical conditions (e.g., diabetes mellitus, renal disorders, chronic heart disease, chronic liver disease, chronic lung disease including asthma) and/or behavioral risk factors (e.g., smoking, increased alcohol use) that are known to increase the risk of pneumococcal disease.

In each study, immunogenicity was assessed by serotype-specific opsonophagocytic activity (OPA) and immunoglobulin G (IgG) responses at 30 days postvaccination. Study endpoints included OPA geometric mean titers (GMTs) and IgG geometric mean concentrations (GMCs). The pivotal study (Protocol 19) was designed to show noninferiority of the OPA GMTs compared to Prevenar 13 for the 13 shared serotypes (in common between VAXNEUVANCE and Prevenar 13) and superiority for the 2 serotypes unique to VAXNEUVANCE (22F and 33F) and for shared serotype 3. Superiority assessment was based on the between-group comparisons of OPA GMTs and proportions of participants with a ≥4-fold rise in serotype-specific OPA titers from prevaccination to 30 days postvaccination.

#### Clinical Trials Conducted in Pneumococcal Vaccine-Naïve Adults

In the pivotal, double-blind, active comparator-controlled study (Protocol 019), 1,205 pneumococcal vaccine-naïve adults aged 50 years or older were randomized to receive either VAXNEUVANCE or Prevenar 13. The study demonstrated that VAXNEUVANCE is noninferior to Prevenar 13 for the 13 shared

serotypes and superior for the 2 unique serotypes and for shared serotype 3. Table 3 summarizes the OPA GMTs at 30 days postvaccination. Serotype-specific IgG GMCs were generally consistent with the results observed for the OPA GMTs.

**Table 3: Serotype-Specific OPA GMTs in Pneumococcal Vaccine-Naïve Adults ≥50 Years of Age (Protocol 019)**

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

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

<sup>†</sup> A conclusion of non-inferiority for the 13 shared serotypes is based on the lower bound of the 95% CI for the estimated GMT ratio (VAXNEUVANCE/Prevenar 13) being > 0.5.

<sup>‡</sup> A conclusion of superiority for serotype 3 is based on the lower bound of the 95% CI for the estimated GMT ratio (VAXNEUVANCE/Prevenar 13) being > 1.2.

<sup>§</sup> A conclusion of superiority for the 2 unique serotypes is based on the lower bound of the 95% CI for the estimated GMT ratio (VAXNEUVANCE/Prevenar 13) being > 2.0.

N=Number of participants randomized and vaccinated; n=Number of participants contributing to the analysis.  
CI=confidence interval; cLDA=constrained longitudinal data analysis; GMT=geometric mean titer (1/dil);  
OPA=opsonophagocytic activity

In a double-blind, lot consistency study (Protocol 020), 2,340 pneumococcal vaccine-naïve adults 50 years of age and older were randomized in a 3:3:3:1 ratio to receive 1 of 3 lots of VAXNEUVANCE or Prevenar 13. The study demonstrated that all 3 lots are equivalent as the lower and upper limits of the 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 15 serotypes. Immune responses following vaccination with VAXNEUVANCE were comparable to Prevenar 13 for the shared serotypes.

In a double-blind, descriptive study (Protocol 017), 1,515 immunocompetent adults 18 to 49 years of age with or without risk factors for pneumococcal disease were randomized 3:1 to receive either VAXNEUVANCE or Prevenar 13, followed by PNEUMOVAX 23 six months later. VAXNEUVANCE elicited immune responses to all 15 serotypes as assessed by OPA GMTs (Table 4) and IgG GMCs. OPA GMTs and IgG GMCs were generally comparable between the two vaccination groups for the 13 shared serotypes and higher in VAXNEUVANCE for the 2 unique serotypes. Following vaccination with PNEUMOVAX 23, OPA GMTs and IgG GMCs were generally comparable between the two vaccination groups for all 15 serotypes in VAXNEUVANCE.

Immune responses in adults with no risk factors (n=285; 25.2%) who received VAXNEUVANCE were generally consistent with those observed in the overall study population.

**Table 4: Serotype-Specific OPA GMTs in Pneumococcal Vaccine-Naïve Adults 18-49 Years of Age With or Without Risk Factors for Pneumococcal Disease (Protocol 017)**

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

\* The within-group 95% CIs are obtained by exponentiating the CIs of the mean of the natural log values based on the t-distribution.

N=Number of participants randomized and vaccinated; n=Number of participants contributing to the analysis.  
CI=confidence interval; GMT=geometric mean titer (1/dil); OPA=opsonophagocytic activity.

#### *Sequential Administration of Pneumococcal Vaccines in Adults*

In a double-blind, active, comparator-controlled study (Protocol 016), 652 pneumococcal vaccine-naïve adults 50 years of age and older were randomized to receive either VAXNEUVANCE or Prevenar 13, followed by PNEUMOVAX 23 one year later. Following vaccination with PNEUMOVAX 23, OPA GMTs and IgG GMCs were comparable between the two vaccination groups for all 15 serotypes in VAXNEUVANCE.

Immune responses elicited by VAXNEUVANCE persisted up to 12 months postvaccination as assessed by OPA GMTs and IgG GMCs. Immune responses at 30 days and 12 months postvaccination were comparable between the two vaccination groups for the 13 shared serotypes and higher in VAXNEUVANCE for the 2 unique serotypes.

The sequential administration of VAXNEUVANCE followed by PNEUMOVAX 23 was evaluated with an interval of 2 months in immunocompromised individuals (Protocol 018) and an interval of 6 months in immunocompetent individuals with or without risk factors for pneumococcal disease (Protocol 017) [See Clinical immunogenicity in special populations].

#### *Clinical Trials Conducted in Adults with Prior Pneumococcal Vaccination*

In a double-blind, descriptive study (Protocol 007), 253 adults 65 years of age and older who were previously vaccinated with PNEUMOVAX 23 at least 1 year prior to study entry were randomized to receive either VAXNEUVANCE or Prevenar 13. IgG GMCs and OPA GMTs were generally comparable between the vaccination groups for the 13 shared serotypes and higher in VAXNEUVANCE for the 2 unique serotypes.

#### *Clinical Immunogenicity in Special Populations*

##### *Populations at Increased Risk for Pneumococcal Disease*

##### *Adults with Chronic Conditions and Other Risk Factors*

In the double-blind, descriptive study (Protocol 017), the immunogenicity of VAXNEUVANCE was evaluated in a subset of immunocompetent adults 18 to 49 years of age with one or more of the following risk factors for pneumococcal disease: diabetes mellitus, chronic heart disease including heart failure, chronic liver disease with compensated cirrhosis, chronic lung disease including persistent asthma and chronic obstructive pulmonary disease (COPD), current tobacco use and increased alcohol consumption. Of those



who received VAXNEUVANCE, 54.7% (n=620) had 1 risk factor and 20.1% (n=228) had 2 or more risk factors. In both of these risk factor subgroups, VAXNEUVANCE elicited immune responses to all 15 serotypes contained in the vaccine as assessed by OPA GMTs and IgG GMCs at 30 days postvaccination, which were generally consistent with those observed in the overall study population. Sequential administration of VAXNEUVANCE followed by 6 months later by PNEUMOVAX 23 was also immunogenic for all 15 serotypes contained in the vaccine.

#### *Adults Living with HIV*

In a double-blind, descriptive study (Protocol 018), 302 pneumococcal vaccine-naïve adults ≥18 years of age living with HIV with CD4+ T-cell count ≥50 cells per microliter and plasma HIV ribonucleic acid (RNA) <50,000 copies/mL were randomized to receive either VAXNEUVANCE or Prevenar 13, followed by PNEUMOVAX 23 two months later. VAXNEUVANCE elicited immune responses to all 15 serotypes contained in the vaccine as assessed by OPA GMTs and IgG GMCs at 30 days postvaccination. After sequential administration with PNEUMOVAX 23, OPA GMTs and IgG GMCs were generally comparable between the two vaccination groups for all 15 serotypes.

#### *Clinical Trials Conducted in Adults with Prior Pneumococcal Vaccination*

In a double-blind, descriptive study (Protocol 007), 253 adults 65 years of age and older who were previously vaccinated with PNEUMOVAX 23 at least 1 year prior to study entry were randomized to receive either VAXNEUVANCE or Prevenar 13. IgG GMCs and OPA GMTs were generally comparable between the vaccination groups for the 13 shared serotypes and higher in VAXNEUVANCE for the 2 unique serotypes.

#### *Concomitant Vaccination*

In a double-blind, randomized study (Protocol 021), 1,200 adults 50 years of age and older, with or without a history of prior PNEUMOVAX 23 vaccination, were randomized to receive VAXNEUVANCE concomitantly or nonconcomitantly with seasonal inactivated quadrivalent influenza vaccine (QIV). One vaccination group received VAXNEUVANCE and QIV concomitantly, followed by placebo 30 days later. A second vaccination group received QIV and placebo concomitantly, followed by VAXNEUVANCE 30 days later.

VAXNEUVANCE administered concomitantly with QIV is noninferior to VAXNEUVANCE administered nonconcomitantly with QIV (based on a 2-fold noninferiority margin), as assessed by pneumococcal OPA GMTs at 30 days postvaccination with VAXNEUVANCE for all 15 serotypes contained in the vaccine. OPA GMTs were slightly lower for some serotypes when VAXNEUVANCE was administered concomitantly with QIV compared to VAXNEUVANCE administered alone. QIV administered concomitantly with VAXNEUVANCE is noninferior to QIV administered nonconcomitantly (based on a 2-fold noninferiority margin) as assessed by influenza strain-specific hemagglutination inhibition (HAI) GMTs at 30 days postvaccination with QIV for all 4 influenza strains.

## **5.2 PHARMACOKINETIC PROPERTIES**

Not applicable.

## **5.3 PRECLINICAL SAFETY DATA**

### **Genotoxicity**

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

### **Carcinogenicity**

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

## **6 PHARMACEUTICAL PARTICULARS**

### **6.1 LIST OF EXCIPIENTS**

Histidine  
Polysorbate 20  
Sodium chloride  
Water for injections

For adjuvant, see Section 2 Qualitative and quantitative composition.

The product does not contain antimicrobial 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.

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

## **6.5 NATURE AND CONTENTS OF CONTAINER**

VAXNEUVANCE is presented as a suspension 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

## **9 DATE OF FIRST APPROVAL**

XXXX

## **10 DATE OF REVISION**

Not applicable.

**Attachment 1: Product information for AusPAR - Vaxneuvance - pneumococcal 15-valent conjugate vaccine (CRM<sub>197</sub> protein), adsorbed - Merck Sharp & Dohme (Australia) Pty Ltd - PM-2020-06364-1-2 Final 12 October 2022. This is the Product Information that was approved with the submission described in this AusPAR. It may have been superseded. For the most recent PI, please refer to the TGA website at <<https://www.tga.gov.au/products/australian-register-therapeutic-goods-artg/product-information-one>>**

### Summary table of changes

Section changed	Summary of new information
New PI	New product

CCDS-V114-I-112020

RCN: 000014094-AU

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