1. NAME OF THE MEDICINAL PRODUCT

Prevenar 20 Suspension for Injection in Pre-filled Syringe
Pneumococcal polysaccharide conjugate vaccine (20-valent, adsorbed)

2. QUALITATIVE AND QUANTITATIVE COMPOSITION

One dose (0.5 mL) contains:

Pneumococcal polysaccharide serotype 1[1,2]	2.2 µg
Pneumococcal polysaccharide serotype 3[1,2]	2.2 µg
Pneumococcal polysaccharide serotype 4[1,2]	2.2 µg
Pneumococcal polysaccharide serotype 5[1,2]	2.2 µg
Pneumococcal polysaccharide serotype 6A[1,2]	2.2 µg
Pneumococcal polysaccharide serotype 6B[1,2]	4.4 µg
Pneumococcal polysaccharide serotype 7F[1,2]	2.2 µg
Pneumococcal polysaccharide serotype 8[1,2]	2.2 µg
Pneumococcal polysaccharide serotype 9V[1,2]	2.2 µg
Pneumococcal polysaccharide serotype 10A[1,2]	2.2 µg
Pneumococcal polysaccharide serotype 11A[1,2]	2.2 µg
Pneumococcal polysaccharide serotype 12F[1,2]	2.2 µg
Pneumococcal polysaccharide serotype 14[1,2]	2.2 µg
Pneumococcal polysaccharide serotype 15B[1,2]	2.2 µg
Pneumococcal polysaccharide serotype 18C[1,2]	2.2 µg
Pneumococcal polysaccharide serotype 19A[1,2]	2.2 µg
Pneumococcal polysaccharide serotype 19F[1,2]	2.2 µg
Pneumococcal polysaccharide serotype 22F[1,2]	2.2 µg
Pneumococcal polysaccharide serotype 23F[1,2]	2.2 µg
Pneumococcal polysaccharide serotype 33F[1,2]	2.2 µg

[1]Conjugated to CRM_{197} carrier protein (approximately 51 µg per dose)
[2]Adsorbed on aluminium phosphate (0.125 mg aluminium per dose)

For the full list of excipients, see section 6.1.

3. PHARMACEUTICAL FORM

Suspension for injection.
The vaccine is a homogeneous white suspension.

4. CLINICAL PARTICULARS

4.1. Therapeutic indications

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.

Prevenar 20 should be used in accordance with official recommendations.

4.2. Posology and method of administration

Posology

Individuals 18 years of age and older

Prevenar 20 is to be administered as a single dose to individuals 18 years of age and older.

The need for revaccination with a subsequent dose of Prevenar 20 has not been established.

No data on sequential vaccination with other pneumococcal vaccines or a booster dose are available for Prevenar 20. Based on the clinical experience with Prevenar 13 (a pneumococcal conjugate vaccine consisting of 13 polysaccharide conjugates that are also in Prevenar 20), if the use of 23-valent pneumococcal polysaccharide vaccine (Pneumovax 23 [PPSV23]) is considered appropriate, Prevenar 20 should be given first (see section 5.1).

Paediatric population

The safety and efficacy of Prevenar 20 in children and adolescents younger than 18 years of age have not been established. No data are available.

Special populations

There are no data with Prevenar 20 in special populations.

Limited experience from clinical studies with Prevenar 13 (a pneumococcal conjugate vaccine consisting of 13 polysaccharide conjugates that are also in Prevenar 20) are available in adults at higher risk of pneumococcal infection either immunocompromised individuals or following bone marrow transplantation (see sections 4.4 and 5.1).

Based on these data the following posology was recommended for Prevenar 13:

- Individuals at higher risk of pneumococcal infection (e.g., individuals with sickle cell disease or HIV infection), including those previously vaccinated with 1 or more doses of PPSV23, were recommended to receive at least 1 dose of Prevenar 13.
- In individuals with a hematopoietic stem cell transplant (HSCT), the recommended immunisation series with Prevenar 13 consisted of 4 doses of 0.5 mL each. The primary series consisted of 3 doses, with the first dose given 3 to 6 months after HSCT and with an interval of at least 1 month between doses. A booster dose was recommended 6 months after the third dose (see section 5.1).

Please also refer to sections 4.4. and 5.1.

Method of administration

For intramuscular use only.

One dose (0.5 mL) of Prevenar 20 should be administered intramuscularly, preferably in the deltoid muscle, 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, to any of the excipients listed in section 6.1, or to diphtheria toxoid.

4.4. Special warnings and precautions for use

Do not inject Prevenar 20 intravascularly.

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.

Hypersensitivity

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

Concurrent illness

Vaccination should be postponed in individuals suffering from acute severe febrile illness. However, the presence of a minor infection, such as a cold, should not result in the deferral of vaccination.

Thrombocytopenia and coagulation disorders

The vaccine must be administered with caution to individuals with thrombocytopenia or a bleeding disorder since bleeding may occur following an intramuscular administration.

The risk of bleeding in patients with coagulation disorders needs to be carefully evaluated before intramuscular administration of any vaccine, and subcutaneous administration should be considered if the potential benefit clearly outweighs the risks.

Protection against pneumococcal disease

Prevenar 20 will only protect against *Streptococcus pneumoniae* serotypes included in the vaccine, and will not protect against other microorganisms that cause invasive disease or pneumonia. As with any vaccine, Prevenar 20 may not protect all individuals receiving the vaccine from pneumococcal invasive disease or pneumonia. For most recent epidemiological information, you should consult with the relevant health authority.

Immunocompromised individuals

Safety and immunogenicity data on Prevenar 20 are not available for individuals in immunocompromised groups. Vaccination should be considered on an individual basis.

Based on experience with pneumococcal vaccines, some individuals with altered immunocompetence may have reduced immune responses to Prevenar 20.

Individuals with impaired immune response, whether due to the use of immunosuppressive therapy, a genetic defect, HIV infection, or other causes, may have reduced antibody response to active immunisation. The clinical relevance of this is unknown.

Safety and immunogenicity data with Prevenar 13 (a pneumococcal conjugate vaccine consisting of 13 polysaccharide conjugates that are also in Prevenar 20) are available for a limited number of individuals with HIV infection, or with a HSCT (see sections 4.8 and 5.1).

In adults across all studied age groups, formal non-inferiority criteria were met although numerically lower geometric mean titres were observed with Prevenar 20 for most of the serotypes compared to Prevenar 13 (see section 5.1), however the clinical relevance of this observation for immunocompromised individuals is unknown.

Excipient

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

4.5. Interaction with other medicinal products and other forms of interaction

Different injectable vaccines should always be given at different vaccination sites.

Do not mix Prevenar 20 with other vaccines/medicinal products in the same syringe.

Prevenar 20 can be administered concomitantly with influenza vaccine, adjuvanted (Fluad Quadrivalent [QIV]) and COVID 19 mRNA vaccine (nucleoside modified) (see section 5.1).

4.6. Fertility, pregnancy and lactation

Pregnancy

There are no data on the use of Prevenar 20 in pregnant women.

Animal studies do not indicate direct or indirect harmful effects with respect to reproductive toxicity.

Administration of Prevenar 20 in pregnancy should only be considered when the potential benefits outweigh any potential risks for the mother and foetus.

Breast-feeding

It is unknown whether Prevenar 20 is excreted in human milk.

Fertility

No human data on the effect of Prevenar 20 on fertility are available. Animal studies do not indicate direct or indirect harmful effects with respect to female fertility (see section 5.3).

4.7. Effects on ability to drive and use machines

Prevenar 20 has no or negligible influence on the ability to drive and use machines. However, some of the effects mentioned under section 4.8 may temporarily affect the ability to drive or use machines.

4.8. Undesirable effects

Summary of the safety profile

Participants 18 years of age and older

The safety of Prevenar 20 was evaluated in 4,552 participants 18 years of age and older in six clinical trials (two Phase 1, one Phase 2, and three Phase 3), and 2,496 participants in the control groups.

In the Phase 3 trials, 4,263 participants received Prevenar 20. This, included 1,798 participants 18 through 49 years of age, 334 participants 50 through 59 years of age, and 2,131 participants 60 years of age and older (1,138 were 65 years of age and older). Of the participants who received Prevenar 20 in the Phase 3 trials, 3,639 were naïve to pneumococcal vaccines, 253 had previously received Pneumovax 23 (pneumococcal polysaccharide vaccine [23-valent]; PPSV23) (≥ 1 to ≤ 5 years prior to enrollment), 246 had previously received Prevenar 13 only (≥ 6 months prior to enrollment), and 125 had previously received Prevenar 13 followed by PPSV23 (the dose of PPSV23 ≥ 1-year prior to enrollment).

Participants in the Phase 3 trial B7471007 (Pivotal Study 1007) were evaluated for adverse events for 1 month after vaccination, and serious adverse events through 6 months after vaccination. This study included 447 participants 18 to 49 years of age, 445 participants 50 to 59 years of age, 1,985 participants 60 to 64 years of age, 624 participants 65 to 69 years of age, 319 participants 70 to 79 years of age, and 69 participants ≥ 80 years of age.

In participants 18 to 49 years of age in Studies 1007 and a Phase 3 trial B7471008 (Lot Consistency Study 1008), the most frequently reported adverse reactions were pain at injection site (79.2%), muscle pain (62.9%), fatigue (46.7%), headache (36.7%), and joint pain (16.2%). In participants 50 to 59 years of age in Study 1007, the most frequently reported adverse reactions were pain at injection site (72.5%), muscle pain (49.8%), fatigue (39.3%), headache (32.3%), and joint pain (15.4%). In participants ≥ 60 years of age in Study 1007, the most frequently reported adverse reactions were pain at injection site (55.4%), muscle pain (39.1%), fatigue (30.2%), headache (21.5%), and joint pain (12.6%). These were usually mild or moderate in intensity and resolved within a few days after vaccination.

Phase 3 Study B7471006 (Study 1006) evaluated Prevenar 20 in participants ≥ 65 years of age with varying prior pneumococcal status (prior PPSV23, prior Prevenar 13 or prior Prevenar 13 followed by PPSV23). In this study, the most frequently reported adverse

reactions for participants were similar in frequency to those described for participants ≥ 60 years of age in Study 1007, with slightly higher injection site pain (61.2%) in participants with prior Prevenar 13, and joint pain (16.8%) in participants with prior Prevenar 13 followed by PPSV23.

Tabulated list of adverse reactions

Tabulated lists of adverse reactions from the Phase 3 clinical trials and postmarketing experience are presented below.

Adverse reactions from clinical trials

As Prevenar 20 contains the same 13 serotype-specific capsular polysaccharide conjugates and the same vaccine excipients as Prevenar 13, the adverse reactions already identified for Prevenar 13 have been adopted for Prevenar 20. Table 1 presents adverse reactions reported in Phase 3 trials of Prevenar 20, based on the highest frequency among adverse reactions, local reactions, or systemic events after vaccination in any Prevenar 20 group. In clinical trials, the safety profile of Prevenar 20 was similar to that of Prevenar 13. No new adverse reactions were identified as compared to Prevenar 13.

Adverse reactions are listed by system organ class in decreasing order of frequency and seriousness. The frequency is defined as follows: very common (≥ 1/10), common (≥ 1/100 to < 1/10), uncommon (≥ 1/1,000 to < 1/100), rare (≥ 1/10,000 to < 1/1,000), very rare (< 1/10,000), not known (cannot be estimated from available data).

Table 1. Adverse Drug Reactions From Prevenar 20 Clinical Trials

System Organ Class	Very Common	Common	Uncommon	Frequency Not Known
Immune system disorders			Hypersensitivity reaction, including face oedema, dyspnoea, bronchospasm	
Metabolism and nutrition disorders				Decreased appetite[a]
Nervous system disorders	Headache			
Gastrointestinal disorders			Diarrhoea[a] Nausea Vomiting[a]	
Skin and subcutaneous tissue disorders			Rash[a] Angioedema	
Musculoskeletal and connective tissue disorders	Joint pain Muscle pain			
General disorders and administration site conditions	Vaccination-site pain/tenderness Fatigue	Vaccination-site induration/swelling[a] Vaccination-site erythema[a] Pyrexia	Vaccination-site pruritus Lymphadenopathy Vaccination-site urticaria Chills[a]	Limitation of arm movement[a]

Table 1. Adverse Drug Reactions From Prevenar 20 Clinical Trials

System Organ Class	Very Common	Common	Uncommon	Frequency Not Known

a. Event reported in clinical trials with Prevenar 13 with very common frequency (≥ 1/10). Decreased appetite and limitation of arm movement were not reported in the adult Phase 3 trials of Prevenar 20; therefore, the frequency is not known.

Safety with concomitant vaccine administration in adults

The safety profile was similar when Prevenar 20 was administered with or without influenza vaccine, adjuvanted (Fluad Quadrivalent [QIV]).

Prevenar 20 administered together with COVID 19 mRNA vaccine (nucleoside modified) was observed to have a tolerability profile similar to COVID 19 mRNA vaccine (nucleoside modified) administered alone, and an overall safety profile consistent with Prevenar 20 or COVID-19 mRNA vaccine (nucleoside modified) given alone.

Adverse reactions from postmarketing experience

Table 2 includes adverse experiences that have been spontaneously reported during the postmarketing use of Prevenar 13, which may also occur with Prevenar 20. The postmarketing safety experience with Prevenar 13 is relevant to Prevenar 20, as Prevenar 20 contains all components (polysaccharide conjugates and excipients) of Prevenar 13. These events were reported voluntarily from a population of uncertain size. Therefore, it is not possible to reliably estimate their frequency or to establish, for all events, a causal relationship to vaccine exposure.

Table 2. Adverse Reactions From Prevenar 13 Postmarketing Experience

System Organ Class	Frequency Not Known
Immune system disorders	Anaphylactic/anaphylactoid reaction, including shock
Skin and subcutaneous tissue disorders	Erythema multiforme
General disorders and administration site conditions	Vaccination-site dermatitis

Events reported spontaneously in Prevenar 13 postmarketing experience; therefore, the frequencies could not be estimated from the available data and are considered as not known.

Additional information in special populations in studies with Prevenar 13

Participants ≥ 18 years of age with HIV infection have similar frequencies of adverse reactions in Table 1, except for pyrexia (5% to 18%) and vomiting (8% to 12%) which were very common and nausea (< 1% to 3%) which was common.

Participants ≥ 18 years of age with an HSCT have similar frequencies of adverse reactions in Table 1, except for pyrexia (4% to 15%), vomiting (6% to 21%), and diarrhoea (25% to 36%) which were very common.

4.9. Overdose

Overdose with Prevenar 20 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

Prevenar 20 contains 20 pneumococcal capsular polysaccharides all conjugated to a CRM_{197} carrier protein, which modifies the immune response to the polysaccharide from a T-cell independent response to a T-cell dependent response. The T-cell dependent response leads to both an enhanced antibody response and generation of memory B-cells, allowing for an anamnestic (booster) response on re-exposure to the bacterium.

Vaccination with Prevenar 20 induces serum antibody production and immunologic memory against the serotypes contained within the vaccine. In adults, the levels of circulating antibodies that correlate with protection against pneumococcal disease have not been clearly defined.

Clinical efficacy

No efficacy studies have been performed with Prevenar 20.

Immunogenicity data

Prevenar 20 clinical trials in adults

Three Phase 3 clinical trials, B7471006, B7471007 and B7471008 (Study 1006, Study 1007, and Study 1008), were conducted in the United States and Sweden evaluating the immunogenicity of Prevenar 20 in different adult age groups, and in participants who were either pneumococcal vaccine-naïve, or previously vaccinated with Prevenar 13, PPSV23, or both.

Each study included participants who were healthy or immunocompetent with stable underlying conditions, including chronic cardiovascular disease, chronic pulmonary disease, renal disorders, diabetes mellitus, chronic liver disease, and medical risk conditions and behaviours (e.g., smoking) that are known to increase the risk of serious pneumococcal pneumonia and IPD. In the pivotal study (Study 1007), these risk factors were identified in 34%, 32%, and 26% of participants 60 years of age and over, 50 to 59 years of age, and 18 to 49 years of age, respectively. A stable medical condition was defined as a medical condition not requiring significant change in therapy in the previous 6 weeks (i.e., change to new therapy category due to worsening disease), or any hospitalisation for worsening disease within 12 weeks before receiving the study vaccine.

In each study, immune responses elicited by Prevenar 20 and the control pneumococcal vaccines were measured by an opsonophagocytic activity (OPA) assay. OPA assays measure functional antibodies to *Streptococcus pneumoniae*.

Comparison of immune responses of Prevenar 20 to Prevenar 13 and PPSV23

In a randomised, active-controlled, double-blind, non-inferiority clinical trial (Pivotal Study 1007) of Prevenar 20 in the United States and Sweden, pneumococcal vaccine-naïve participants 18 years of age and older were enrolled into 1 of 3 cohorts based on their age at enrollment (18 to 49, 50 to 59, and ≥ 60 years of age), and randomised to receive Prevenar 20 or control. Participants 60 years of age and older were randomised in a 1:1 ratio to receive Prevenar 20 (n = 1,507) followed 1 month later with the administration of saline placebo or Prevenar 13 (n = 1,490), and with the administration of PPSV23 1 month later. Participants 18 to 49 years of age and 50 to 59 years of age were randomly assigned (3:1 ratio); they received a dose of Prevenar 20 (18 to 49 years of age: n = 335; 50 to 59 years of age: n = 334) or Prevenar 13 (18 to 49 years of age: n = 112; 50 to 59 years of age: n = 111).

Serotype-specific OPA geometric mean titres (GMTs) were measured before the first vaccination and 1 month after each vaccination. Non-inferiority of immune responses, OPA GMTs 1 month after vaccination, with Prevenar 20 to a control vaccine for a serotype was declared if the lower bound of the 2-sided 95% confidence interval (CI) for the GMT ratio (Prevenar 20/Prevenar 13; Prevenar 20/PPSV23) for that serotype was greater than 0.5.

In participants 60 years of age and older, the immune responses to all 13 matched serotypes elicited by Prevenar 20 were non-inferior to those elicited by Prevenar 13 for the same serotypes 1 month after vaccination. In general, numerically lower geometric mean titres were observed with Prevenar 20 in the matched serotypes compared to Prevenar 13 (Table 3), however the clinical relevance of these findings is unknown.

The immune responses induced by Prevenar 20 to 6/7 additional serotypes were non-inferior to those induced by PPSV23 to the same serotypes 1 month after vaccination. The response to serotype 8 missed the pre-specified statistical non-inferiority criterion (the lower bound of the 2-sided 95% CI for the GMT ratio is 0.49 instead of > 0.50) (Table 3). The clinical relevance of this observation is unknown. Supportive analyses for other serotype 8 endpoints in the Prevenar 20 group showed favourable outcomes. These include a geometric mean fold rise (GMFR) of 22.1 from before vaccination to 1 month post-vaccination, 77.8% of participants achieved a ≥ 4-fold rise in OPA titres from before vaccination to 1 month after vaccination, and 92.9% of participants achieved OPA titres ≥ LLOQ 1 month after vaccination.

Table 3. OPA GMTs 1 Month After Vaccination in Participants 60 Years of Age and Older Given Prevenar 20 Compared to Prevenar 13 for the 13 Matched Serotypes and to PPSV23 for the 7 Additional Serotypes (Study 1007)[a,b,c,d]

	Prevenar 20 (N = 1157–1430)	**Prevenar 13 (N = 1390–1419)**	**PPSV23 (N = 1201–1319)**	**Vaccine Comparison**	
	GMT[e]	**GMT[e]**	**GMT[e]**	**GMT Ratio[e]**	**95% CI[e]**
Serotype					
1	123	154		0.80	0.71, 0.90
3	41	48		0.85	0.78, 0.93
4	509	627		0.81	0.71, 0.93
5	92	110		0.83	0.74, 0.94
6A	889	1165		0.76	0.66, 0.88
6B	1115	1341		0.83	0.73, 0.95
7F	969	1129		0.86	0.77, 0.96
9V	1456	1568		0.93	0.82, 1.05
14	747	747		1.00	0.89, 1.13

Table 3. OPA GMTs 1 Month After Vaccination in Participants 60 Years of Age and Older Given Prevenar 20 Compared to Prevenar 13 for the 13 Matched Serotypes and to PPSV23 for the 7 Additional Serotypes (Study 1007)[a,b,c,d]

	Prevenar 20 (N = 1157–1430)	Prevenar 13 (N = 1390–1419)	PPSV23 (N = 1201–1319)	Vaccine Comparison	
	GMT[e]	GMT[e]	GMT[e]	GMT Ratio[e]	95% CI[e]
18C	1253	1482		0.85	0.74, 0.97
19A	518	645		0.80	0.71, 0.90
19F	266	333		0.80	0.70, 0.91
23F	277	335		0.83	0.70, 0.97
Additional Serotypes					
8	466		848	0.55	0.49, 0.62
10A	2008		1080	1.86	1.63, 2.12
11A	4427		2535	1.75	1.52, 2.01
12F	2539		1717	1.48	1.27, 1.72
15B	2398		769	3.12	2.62, 3.71
22F	3666		1846	1.99	1.70, 2.32
33F	5126		3721	1.38	1.21, 1.57

Abbreviations: CI = confidence interval; GMT = geometric mean titre; LLOQ = lower limit of quantitation; N = number of participants; OPA = opsonophagocytic activity; PPSV23 = pneumococcal polysaccharide vaccine (23-valent).

a. Study 1007 was conducted in the United States and in Sweden.
b. Non-inferiority for a serotype was met if the lower bound of the 2-sided 95% CI for the GMT ratio (ratio of Prevenar 20/comparator) was greater than 0.5 (2-fold criterion for non-inferiority).
c. Assay results below the LLOQ were set to 0.5 × LLOQ in the analysis.
d. Evaluable immunogenicity population.
e. GMTs and GMT ratios as well as the associated 2-sided CIs were based on analysis of log-transformed OPA titres using a regression model with vaccine group, sex, smoking status, age at vaccination in years, and baseline log transformed OPA titres.

Immunogenicity in participants 18 through 59 years of age

In Study 1007, participants 50 through 59 years of age and participants 18 through 49 years of age were randomly assigned (3:1 ratio) to receive 1 vaccination with Prevenar 20 or Prevenar 13. Serotype-specific OPA GMTs were measured before vaccination and 1 month after vaccination. With both vaccines, higher immune responses were observed in younger participants compared with older participants. A non-inferiority analysis of Prevenar 20 in the younger age group versus Prevenar 20 in participants 60 through 64 years of age per serotype was performed to support the indication in adults 18 through 49 years of age and 50 through 59 years of age. Non-inferiority was declared if the lower bound of the 2-sided 95% CI for the GMT ratio (Prevenar 20 in participants 18 through 49 years of age / 60 through 64 years of age and in 50 through 59 years of age / 60 through 64 years of age) for each of the 20 serotypes was > 0.5. Prevenar 20 elicited immune responses to all 20 vaccine serotypes in the two of the younger age groups that were non-inferior to responses in participants 60 through 64 years of age 1 month after vaccination (Table 4).

While not planned as an active control for immunogenicity evaluations in the study, a post hoc descriptive analysis showed generally numerically lower OPA geometric mean titres 1 month after Prevenar 20 for the matched serotypes compared to Prevenar 13 in participants 18 through 59 years of age, however the clinical relevance of these findings is unknown.

As noted above, individuals with risk factors were included in this study. Across all the age groups studied, in general, a numerically lower immune response was observed in participants with risk factors compared to participants without risk factors. The clinical relevance of this observation is unknown.

Table 4. Comparisons of OPA GMTs 1 Month After Prevenar 20 in Participants 18 Through 49 or 50 Through 59 Years of Age to Participants 60 Through 64 Years of Age (Study 1007)[a,b,c,d]

	18–49 Years (N = 251–317)	60–64 Years (N = 765–941)	18–49 Years Relative to 60–64 Years	50–59 Years (N = 266–320)	60–64 Years (N = 765–941)	50–59 Years Relative to 60–64 Years
	GMT[e]	GMT[e]	GMT Ratio[e] (95% CI)[e]	GMT[e]	GMT[e]	GMT Ratio[e] (95% CI)[e]
Serotype						
1	163	132	1.23 (1.01, 1.50)	136	132	1.03 (0.84, 1.26)
3	42	42	1.00 (0.87, 1.16)	43	41	1.06 (0.92, 1.22)
4	1967	594	3.31 (2.65, 4.13)	633	578	1.10 (0.87, 1.38)
5	108	97	1.11 (0.91, 1.36)	85	97	0.88 (0.72, 1.07)
6A	3931	1023	3.84 (3.06, 4.83)	1204	997	1.21 (0.95, 1.53)
6B	4260	1250	3.41 (2.73, 4.26)	1503	1199	1.25 (1.00, 1.56)
7F	1873	1187	1.58 (1.30, 1.91)	1047	1173	0.89 (0.74, 1.07)
9V	6041	1727	3.50 (2.83, 4.33)	1726	1688	1.02 (0.83, 1.26)
14	1848	773	2.39 (1.93, 2.96)	926	742	1.25 (1.01, 1.54)
18C	4460	1395	3.20 (2.53, 4.04)	1805	1355	1.33 (1.06, 1.68)
19A	1415	611	2.31 (1.91, 2.81)	618	600	1.03 (0.85, 1.25)
19F	655	301	2.17 (1.76, 2.68)	287	290	0.99 (0.80, 1.22)
23F	1559	325	4.80 (3.65, 6.32)	549	328	1.68 (1.27, 2.22)
Additional Serotypes						
8	867	508	1.71 (1.38, 2.12)	487	502	0.97 (0.78, 1.20)
10A	4157	2570	1.62 (1.31, 2.00)	2520	2437	1.03 (0.84, 1.28)
11A	7169	5420	1.32 (1.04, 1.68)	6417	5249	1.22 (0.96, 1.56)
12F	5875	3075	1.91 (1.51, 2.41)	3445	3105	1.11 (0.88, 1.39)
15B	4601	3019	1.52 (1.13, 2.05)	3356	2874	1.17 (0.88, 1.56)
22F	7568	4482	1.69 (1.30, 2.20)	3808	4228	0.90 (0.69, 1.17)
33F	7977	5693	1.40 (1.10, 1.79)	5571	5445	1.02 (0.81, 1.30)

Table 4. Comparisons of OPA GMTs 1 Month After Prevenar 20 in Participants 18 Through 49 or 50 Through 59 Years of Age to Participants 60 Through 64 Years of Age (Study 1007)[a,b,c,d]

	18–49 Years (N = 251–317)	60–64 Years (N = 765–941)	18–49 Years Relative to 60–64 Years	50–59 Years (N = 266–320)	60–64 Years (N = 765–941)	50–59 Years Relative to 60–64 Years
	GMT[e]	GMT[e]	GMT Ratio[e] (95% CI)[e]	GMT[e]	GMT[e]	GMT Ratio[e] (95% CI)[e]

Abbreviations: CI = confidence interval; GMT = geometric mean titre; LLOQ = lower limit of quantitation; N = number of participants; OPA = opsonophagocytic activity; PPSV23 = pneumococcal polysaccharide vaccine (23-valent).

a. Study 1007 was conducted in the United States and in Sweden.
b. Non-inferiority for a serotype was met if the lower bound of the 2-sided 95% CI for the GMT ratio (ratio of younger age group/60 through 64 years of age group) was greater than 0.5 (2-fold criterion for non-inferiority).
c. Assay results below the LLOQ were set to 0.5 × LLOQ in the analysis.
d. Evaluable immunogenicity population.
e. GMTs, GMT ratios, and the associated 2-sided CIs were based on analysis of log-transformed OPA titres using a regression model with age group, sex, smoking status, and baseline log transformed OPA titres. The comparisons between participants 18 through 49 years of age and participants 60 through 64 years of age and between participants 50 through 59 years of age and participants 60 through 64 years of age were based on separate regression models.

Immunogenicity of Prevenar 20 in adults previously vaccinated with pneumococcal vaccine

A Phase 3 randomised, open-label clinical trial (Study 1006) described immune responses to Prevenar 20 in participants 65 years of age and older previously vaccinated with PPSV23, with Prevenar 13, or with Prevenar 13 followed by PPSV23. Participants previously vaccinated with Prevenar 13 (Prevenar 13 only or followed by PPSV23) were enrolled at sites in the United States, whereas participants and previously vaccinated with PPSV23 only were also enrolled from Swedish sites (35.5% in that category).

Prevenar 20 elicited immune responses to all 20 vaccine serotypes in participants 65 years of age and older with prior pneumococcal vaccination (Table 5). Immune responses were lower in participants in both groups who received prior PPSV23 vaccinations.

Table 5. Pneumococcal OPA GMTs Before and 1 Month After Prevenar 20 in Participants 65 Years of Age and Older With Prior Pneumococcal Vaccination (Study 1006)[a,b,c,d]

	Prior PPSV23 only		Prior Prevenar 13 only		Prior Prevenar 13 and PPSV23	
	Before vaccination (N = 208–247)	After vaccination (N = 216–246)	Before vaccination (N = 210–243)	After vaccination (N = 201–243)	Before vaccination (N = 106–121)	After vaccination (N = 102–121)
	GMT (95% CI)[e]	GMT (95% CI)[e]	GMT (95% CI)[e]	GMT (95% CI)[e]	GMT (95% CI)[e]	GMT (95% CI)[e]
Serotype						
1	24 (20, 28)	51 (42, 62)	34 (28, 41)	115 (96, 138)	42 (32, 56)	82 (61, 110)
3	13 (11, 15)	31 (27, 36)	15 (13, 18)	54 (47, 63)	20 (17, 25)	39 (32, 48)
4	29 (23, 35)	150 (118, 190)	67 (53, 84)	335 (274, 410)	73 (53, 101)	194 (143, 262)
5	27 (24, 31)	63 (53, 75)	38 (32, 44)	87 (73, 104)	47 (37, 59)	83 (65, 108)
6A	57 (46, 70)	749 (577, 972)	125 (99, 158)	1081 (880, 1327)	161 (116, 224)	1085 (797, 1478)
6B	107 (86, 133)	727 (574, 922)	174 (138, 219)	1159 (951, 1414)	259 (191, 352)	1033 (755, 1415)

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	Prior PPSV23 only		Prior Prevenar 13 only		Prior Prevenar 13 and PPSV23	
	Before vaccination (N = 208–247)	After vaccination (N = 216–246)	Before vaccination (N = 210–243)	After vaccination (N = 201–243)	Before vaccination (N = 106–121)	After vaccination (N = 102–121)
	GMT (95% CI)[e]	GMT (95% CI)[e]	GMT (95% CI)[e]	GMT (95% CI)[e]	GMT (95% CI)[e]	GMT (95% CI)[e]
7F	156 (132, 184)	378 (316, 452)	210 (175, 251)	555 (467, 661)	206 (164, 258)	346 (277, 432)
9V	203 (171, 241)	550 (454, 667)	339 (282, 408)	1085 (893, 1318)	352 (270, 459)	723 (558, 938)
14	212 (166, 270)	391 (315, 486)	282 (224, 356)	665 (554, 798)	336 (238, 473)	581 (434, 777)
18C	173 (137, 218)	552 (445, 684)	219 (177, 272)	846 (693, 1033)	278 (209, 369)	621 (470, 821)
19A	82 (66, 100)	239 (197, 288)	124 (100, 153)	365 (303, 440)	182 (141, 235)	341 (264, 439)
19F	61 (52, 71)	159 (131, 192)	89 (74, 107)	242 (199, 294)	120 (94, 154)	218 (168, 282)
23F	23 (18, 28)	152 (115, 199)	48 (37, 62)	450 (358, 566)	66 (46, 94)	293 (204, 420)
Additional Serotypes						
8	55 (45, 67)	212 (172, 261)	28 (24, 33)	603 (483, 753)	139 (99, 195)	294 (220, 392)
10A	212 (166, 269)	1012 (807, 1270)	141 (113, 177)	2005 (1586, 2536)	400 (281, 568)	1580 (1176, 2124)
11A	510 (396, 656)	1473 (1192, 1820)	269 (211, 343)	1908 (1541, 2362)	550 (386, 785)	1567 (1141, 2151)
12F	147 (112, 193)	1054 (822, 1353)	53 (43, 65)	1763 (1372, 2267)	368 (236, 573)	1401 (1002, 1960)
15B	140 (104, 189)	647 (491, 853)	74 (56, 98)	1480 (1093, 2003)	190 (124, 291)	1067 (721, 1578)
22F	167 (122, 230)	1773 (1355, 2320)	60 (45, 82)	4157 (3244, 5326)	286 (180, 456)	2718 (1978, 3733)
33F	1129 (936, 1362)	2026 (1684, 2437)	606 (507, 723)	3175 (2579, 3908)	1353 (1037, 1765)	2183 (1639, 2908)

Abbreviations: CI = confidence interval; GMT = geometric mean titre; LLOQ = lower limit of quantitation; N = number of participants; OPA = opsonophagocytic activity; PPSV23 = pneumococcal polysaccharide vaccine (23-valent).

a. Study 1006 was conducted in the United States and in Sweden.
b. Assay results below the LLOQ were set to 0.5 × LLOQ in the analysis.
c. Evaluable immunogenicity population.
d. Open-label administration of Prevenar 20.
e. 2-sided CIs based on the Student t distribution.

Concomitant vaccine administration

Clinical trial in adults to assess Prevenar 20 given with influenza vaccine, adjuvanted (Fluad Quadrivalent [QIV])

In a double-blind, randomised study B7471004 (Study 1004), adults 65 years of age and older were randomised in a 1:1 ratio to receive Prevenar 20 concomitantly administered with an influenza vaccine, adjuvanted (Fluad Quadrivalent [QIV]) (Group 1, N = 898) or Prevenar 20 administered 1 month after receiving QIV (Group 2, N = 898). Pneumococcal

serotype-specific OPA GMTs were evaluated 1 month after Prevenar 20 and influenza vaccine strain hemagglutinin inhibition assay (HAI) GMTs were evaluated 1 month after QIV. The noninferiority criteria for the comparisons of OPA GMTs (lower limit of the 2-sided 95% CI of the GMT ratio [Group 1/Group 2] >0.5, 2-fold noninferiority criterion) were met for all 20 pneumococcal serotypes in Prevenar 20. The noninferiority criteria for the comparisons of HAI GMTs (lower limit of the 2-sided 95% CI for the GMT ratio [Group 1/Group 2] >0.67, 1.5-fold noninferiority criterion) were also met for all 4 influenza vaccine strains.

Clinical trial in adults to assess Prevenar 20 given with a third (booster) dose of COVID-19 mRNA vaccine (nucleoside modified)

In a double-blind, randomised descriptive study B7471026 (Study 1026), adults 65 years of age and older who had received 2 doses of COVID-19 mRNA vaccine (nucleoside modified) at least 6 months earlier, were randomized in a 1:1:1 ratio to receive Prevenar 20 concomitantly administered with a third (booster) dose of COVID-19 mRNA vaccine (nucleoside modified) (N = 190), Prevenar 20 administered alone (N = 191), or a third (booster) dose of COVID-19 mRNA vaccine (nucleoside modified) administered alone (N = 189).

Immune responses to both vaccines were observed after co-administration of Prevenar 20 and COVID-19 mRNA vaccine (nucleoside modified). OPA GMTs for the 20 pneumococcal serotypes were similar to Prevenar 20 administered alone and IgG GMCs for the full-length S-binding protein were similar to COVID-19 mRNA vaccine (nucleoside modified) administered alone. A post-hoc analysis found the immune responses to all 20 serotypes elicited by Prevenar 20 when co-administered with COVID-19 mRNA vaccine (nucleoside modified) would have met conventional 2-fold noninferiority criteria compared to Prevenar 20 alone. Additionally, the full-length S-binding IgG GMC and reference strain neutralizing GMT elicited by COVID-19 mRNA vaccine (nucleoside modified) would have met conventional 1.5-fold noninferiority criteria compared to COVID-19 mRNA vaccine (nucleoside modified) alone.

Immune responses in special populations

Individuals with the conditions described below have an increased risk of pneumococcal disease.

Studies in HIV and bone marrow transplant participants have not been conducted with Prevenar 20.

Limited experience from clinical studies with Prevenar 13 (a pneumococcal conjugate vaccine consisting of 13 polysaccharide conjugates that are also in Prevenar 20) are available in adults with HIV infection, and adults following a bone marrow transplant.

Participants who were healthy, or with stable non-immunocompromising chronic medical conditions, in all the age groups analysed had a lower immune response with Prevenar 20 compared with Prevenar 13 in spite of meeting the predefined non-inferiority margins. The clinical relevance of this observation is unknown.

HIV infection

Adults not previously vaccinated with a pneumococcal vaccine
In Study 6115A1-3002 (B1851021), 152 HIV-infected participants 18 years of age and older (CD4 ≥ 200 cells/µL, viral load < 50,000 copies/mL and free of active acquired immunodeficiency syndrome [AIDS]-related illness) not previously vaccinated with a pneumococcal vaccine were enrolled to receive 3 doses of Prevenar 13. As per the general recommendations, a single dose of PPSV23 was subsequently administered. The vaccines were administered at 1-month intervals. Immune responses were assessed in 131 to 137 evaluable participants approximately 1 month after each dose of the vaccine. After the first dose, Prevenar 13 elicited antibody levels, measured by immunoglobulin G (IgG) geometric mean concentrations (GMCs) and OPA GMTs, that were statistically significantly higher compared with levels prior to vaccination. After the second and third dose of Prevenar 13, immune responses were similar to or higher than those after the first dose.

Adults previously vaccinated with PPSV23
In Study 6115A1-3017 (B1851028), immune responses were assessed in 329 HIV-infected participants 18 years of age and older (CD4+ T-cell count ≥ 200 cells/µL and viral load < 50,000 copies/mL) previously vaccinated with PPSV23 administered at least 6 months prior to enrollment. Participants received 3 doses of Prevenar 13: at enrollment, 6 months, and 12 months after the first dose of Prevenar 13. After the first vaccination, Prevenar 13 elicited antibody levels measured by IgG GMCs and OPA GMTs that were statistically significantly higher compared with levels prior to vaccination. After the second and third dose of Prevenar 13, immune responses were comparable to or higher than those after the first dose. Participants who received previously 2 or more doses of PPSV23 showed a similar immune response compared to participants who previously received a single dose.

Hematopoietic stem cell transplant (HSCT)

In Study 6115A1-3003 (B1851022), 190 participants 18 years of age and older with an allogeneic HSCT were enrolled to receive 3 doses of Prevenar 13 with an interval of at least 1 month between doses. The first dose was administered at 3 to 6 months after HSCT. A fourth (booster) dose of Prevenar 13 was administered 6 months after the third dose. As per the general recommendations, a single dose of PPSV23 was administered 1 month after the fourth dose of Prevenar 13. Immune responses as measured by IgG GMCs were assessed in 130 to 159 evaluable participants approximately 1 month after vaccination. Prevenar 13 elicited increased antibody levels after each dose. Immune responses after the fourth dose of Prevenar 13 were significantly increased for all serotypes compared with those after the third dose.

This study demonstrated that 4 doses of Prevenar 13 elicited serum IgG concentrations similar to those induced by a single dose in healthy participants of the same age group.

Paediatric population

The safety and efficacy of Prevenar 20 in children and adolescents younger than 18 years of age have not been established. No data are available.

5.2. Pharmacokinetic properties

Not applicable.

5.3. Preclinical safety data

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

6. PHARMACEUTICAL PARTICULARS

6.1. List of excipients

Sodium chloride
Succinic acid
Polysorbate 80
Water for injections

For adjuvant, see section 2.

6.2. Incompatibilities

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

6.3. Shelf life

Refer to outer carton for expiration date.

6.4. Special precautions for storage

Store in a refrigerator (2 °C to 8 °C). Pre-filled syringes should be stored in the refrigerator horizontally to minimise the resuspension time.

Do not freeze. Discard if the vaccine has been frozen.

From a microbiological point of view, once removed from the refrigerator, the vaccine should be used immediately.

Stability data indicate that the vaccine is stable for 96 hours when stored at temperatures from 8 °C to 25 °C, or 72 hours when stored at temperatures from 0 °C to 2 °C. At the end of these time periods Prevenar 20 should be used or discarded. These data are intended to guide healthcare professionals in case of temporary temperature excursion only.

6.5. Nature and contents of container

0.5 mL suspension for injection in pre-filled syringe (Type I glass) with a tip cap (synthetic isoprene/bromobutyl blend rubber) and a plunger stopper (chlorobutyl rubber).

Pack size of 1 pre-filled syringe, with or without needle.

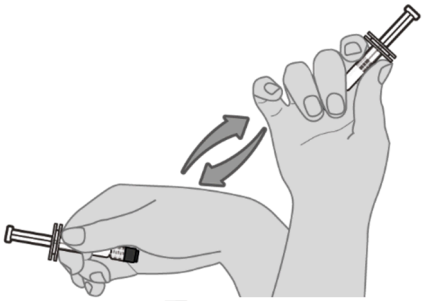
Not all presentations may be available locally.

6.6. Special precautions for disposal and other handling

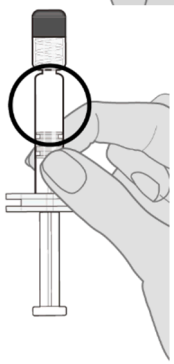
During storage, a white deposit and clear supernatant may be observed in the pre-filled syringe containing the suspension. Pre-filled syringes should be stored horizontally to minimise the resuspension time.

Preparation for administration

Step 1. Vaccine resuspension
Hold the pre-filled syringe horizontally between the thumb and the forefinger and shake vigorously until the contents of the syringe are a homogeneous white suspension. Do not use the vaccine if it cannot be resuspended.

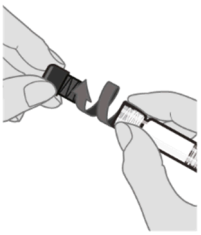


Step 2. Visual inspection
Visually inspect the vaccine for large particulate matter and discolouration prior to administration. Do not use if large particulate matter or discolouration is found. If the vaccine is not a homogenous white suspension, repeat steps 1 and 2.



Step 3. Remove syringe cap
Remove the syringe cap from the Luer lock adapter by slowly turning the cap counter-clockwise while holding the Luer lock adapter.

Note: Care should be taken to ensure that the extended plunger rod is not depressed while removing the syringe cap.



Step 4. Attach a sterile needle
Attach a needle appropriate for intramuscular administration to the pre-filled syringe by holding the Luer lock adapter and turning the needle clockwise.

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

7. PRODUCT OWNER

Pfizer Inc.
New York
United States