Prevenar 20

1. NAME OF THE MEDICINAL PRODUCT

Prevenar 20

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 pneumococcal disease caused by Streptococcus pneumoniae serotypes 1, 3, 4, 5, 6A, 6B, 7F, 8, 9V, 10A, 11A, 12F, 14, 15B, 18C, 19A, 19F, 22F, 23F, and 33F in individuals from 6 weeks of age and less than 18 years of age.

Active immunisation for the prevention of invasive disease and pneumonia caused by *Streptococcus pneumoniae* in individuals 18 years of age and older.

4.2 Posology and method of administration

Posology

Prevenar 20 should be used in accordance with official recommendations.

See sections 4.4 and 5.1 for information on protection against specific pneumococcal serotypes.

Paediatric population

The safety and efficacy of Prevenar 20 in infants below 6 weeks of age have not been established. No data are available.

No or only limited data are available for Prevenar 20 in preterm, older unvaccinated, or partially vaccinated infants and children (see sections 4.4, 4.8 and 5.1). The following dosing recommendations are predominantly based on experience with Prevenar 13.

Infants and children 6 weeks to less than 5 years of age

It is recommended that infants who receive a first dose of Prevenar 20 complete the vaccination course with Prevenar 20.

Vaccination schedule in infants and children 6 weeks to 15 months of age	
3-dose series (two-dose primary series followed by a booster dose)	The recommended immunisation series for Prevenar 20 given as part of a routine infant immunisation program, consists of three doses, each of 0.5 mL. The first dose is usually given at 2 months of age, with a second dose 2 months later. The first dose may be given as early as 6 weeks of age. The third (booster) dose is recommended between 11 and 15 months of age (see section 5.1).
4-dose series (three-dose primary series followed by a booster dose)	Prevenar 20 may be given as a 4-dose series, each of 0.5 mL. The primary infant series consists of three doses, with the first dose usually given at 2 months of age and with an interval of at least 4 weeks between doses. The first dose may be given as early as 6 weeks of age. The fourth (booster) dose is recommended between 11 and 15 months of age (see section 5.1).
Preterm infants (less than 37 weeks of gestation)[a]	The recommended immunisation series for Prevenar 20 consists of four doses, each of 0.5 mL. The primary infant series consists of three doses, with the first dose given at 2 months of age and with an interval of at least 4 weeks between doses. The first dose may be given as early as 6 weeks of age. The fourth (booster) dose is recommended between 11 and 15 months of age (see sections 4.4 and 5.1).
Vaccination schedule for infants and children less than 15 months of age transitioning from another pneumococcal conjugate vaccine[b]	
Prior vaccination with another pneumococcal conjugate vaccine	Infants and children who have begun immunisation with another pneumococcal conjugate vaccine may complete immunisation by transitioning to Prevenar 20 at any point in the schedule.
Catch-up vaccination schedule for infants and children 7 months to less than 18 years of age	

Unvaccinated infants 7 to less than 12 months of age[a]	Two doses, each of 0.5 mL, with an interval of at least 4 weeks between doses. A third dose is recommended in the second year of life.
Unvaccinated children 12 to less than 24 months of age[a]	Two doses, each of 0.5 mL, with an interval of at least 8 weeks between doses.
Unvaccinated children 2 to less than 5 years of age[a]	One single dose of 0.5 mL.
Children 15 months to less than 5 years of age previously vaccinated with a pneumococcal conjugate vaccine	1 dose (0.5 mL). If a previous pneumococcal conjugate vaccine was administered, at least 8 weeks should elapse before administering Prevenar 20 (see section 5.1).
Children 5 to less than 18 years of age regardless of prior pneumococcal conjugate vaccination	1 dose (0.5 mL). If a previous pneumococcal conjugate vaccine was administered, at least 8 weeks should elapse before administering Prevenar 20 (see section 5.1).

a. In preterm and unvaccinated infants and children 7 months to less than 5 years of age, Prevenar 20 is expected to perform similarly to Prevenar 13, a pneumococcal conjugate vaccine consisting of 13 polysaccharide conjugates that are also in Prevenar 20.

b. The safety and immunogenicity of Prevenar 20 administered to infants and children less than 15 months of age who have begun vaccination with another pneumococcal conjugate vaccine have not been established. However, safety and immunogenicity studies with a transition from a lower valent to higher valent pneumococcal conjugate vaccine are relevant to Prevenar 20. Based on clinical experience and relevant randomised controlled trials, the recommended transition from a lower to a higher valent pneumococcal conjugate vaccine may be considered in guiding vaccination with Prevenar 20 for infants and children who have not yet completed the infant vaccination series.

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).

Special populations

There are no data with Prevenar 20 in special populations.

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 children and adults at higher risk of pneumococcal infection including immunocompromised children and adults with human immunodeficiency virus (HIV) infection or haematopoietic stem cell transplant (HSCT), and children with sickle cell disease (SCD) (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 SCD 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 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 4 weeks between doses. A booster dose was recommended 6 months after the third dose (see section 5.1).

The recommended dosing of Prevenar 13 may be considered in guiding vaccination with Prevenar 20 in high-risk populations. For information on responses to pneumococcal vaccines in immunocompromised individuals, please also refer to sections 4.4. and 5.1.

Method of administration

For intramuscular use only.

The vaccine (0.5 mL) should be given by intramuscular injection. The preferred sites are the anterolateral aspect of the thigh (vastus lateralis muscle) in infants or the deltoid muscle of the upper arm in children and adults. Prevenar 20 should be administered, 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 may only protect against *Streptococcus pneumoniae* serotypes included in the vaccine, and will not protect against other microorganisms that cause invasive disease, pneumonia or otitis media (OM). As with any vaccine, Prevenar 20 may not protect all individuals receiving the vaccine from invasive pneumococcal disease (IPD), pneumonia or OM. For the most recent epidemiological information in your country, you should consult with the relevant national organisation.

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 individuals with HIV infection, SCD or with a HSCT (see sections 4.8 and 5.1). Prevenar 20 should be used in accordance with official recommendations.

In adults across all studied age groups, formal non-inferiority criteria were met although numerically lower geometric mean titres (GMTs) were observed with Prevenar 20 for most of the serotypes compared to Prevenar 13 (see section 5.1), , In children, numerically lower immunoglobulin G (IgG) geometric mean concentrations (GMCs) were observed for all shared serotypes compared with Prevenar 13 (see section 5.1). The clinical relevance of these observations for immunocompromised individuals are unknown.

Paediatric population

The potential risk of apnoea and the need for respiratory monitoring for 48 to 72 h should be considered when administering the primary immunisation series to very premature infants (born less than or equal to 28 weeks of gestation), and particularly for those with a previous history of respiratory immaturity. As the benefit of vaccination is high in this group of infants, vaccination should not be withheld or delayed.

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 administered at different vaccination sites.

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

Paediatric population

In infants and children 6 weeks to less than 5 years of age, Prevenar 20 can be administered concomitantly with any of the following vaccine antigens, either as monovalent or combination vaccines: diphtheria, tetanus, acellular pertussis, hepatitis B, *Haemophilus influenzae* type b, inactivated poliomyelitis, measles, mumps, rubella, and varicella vaccines. In clinical trials, rotavirus vaccines were permitted to be administered concomitantly with Prevenar 20 and no safety concerns were observed.

Individuals 18 years of age and older

Prevenar 20 may be administered concomitantly with seasonal influenza vaccine (QIV; surface antigen, inactivated, adjuvanted). In subjects with underlying conditions associated with a high risk of developing life-threatening pneumococcal disease, consideration may be given to separating administrations of QIV and Prevenar 20 (e.g., by approximately 4 weeks). In a double-blind, randomised study (B7471004) in adults 65 years of age and older, the immune response was formally non-inferior, however numerically lower titres were observed for all pneumococcal serotypes included in Prevenar 20 when given concomitantly with seasonal influenza vaccine (QIV, surface antigen, inactivated, adjuvanted) compared to when Prevenar 20 was given alone. The clinical relevance of this finding is unknown.

Prevenar 20 can be administered concomitantly with COVID-19 mRNA vaccine (nucleoside modified).

There are no data on the concomitant administration of Prevenar 20 with other vaccines.

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

Paediatric population

The safety of Prevenar 20 was evaluated in 5,987 participants, 6 weeks of age to less than 18 years of age, in five clinical trials (one Phase 2 and four Phase 3), four randomised, double-blind, active-controlled clinical trials and one single-arm clinical trial; 3,664 participants received at least 1 dose of Prevenar 20, and 2,323 participants received Prevenar 13 (control vaccine).

Participants 6 weeks to less than 15 months of age

Clinical trials were conducted in healthy infants 6 weeks to less than 15 months of age using a 3-dose schedule or a 4-dose schedule (see section 5.1). In these infant trials, 5,156 participants received at least 1 dose of vaccine: 2,833 received Prevenar 20, and 2,323 received Prevenar 13. Overall, approximately 90% of participants in each group received all doses through the study-specified toddler dose. In all studies, local reactions and systemic events were collected after each dose, and adverse events (AEs) were collected in all studies from the first dose through 1 month after the last infant vaccination and from the toddler dose through 1 month after the toddler dose. Serious adverse events were evaluated through 1 month after the last dose in the Phase 3 trial B7471012 (Study 1012) and through 6 months after the last dose in Phase 3 trials (Studies 1011, 1013) and Phase 2 trial (Study 1003).

Prevenar 20 was well tolerated, when administered in a 3-dose and a 4-dose series, in the infant study populations with low rates of severe local reactions and systemic events, and most reactions resolving within 1 to 3 days. The percentages of participants with local reactions and systemic events after Prevenar 20 were generally similar to those after Prevenar 13. The most frequently reported local reactions and systemic events after any dose of Prevenar 20 were irritability, drowsiness, and pain at injection site. In these studies, Prevenar 20 was co-administered or permitted to be administered with certain routine paediatric vaccines (see section 4.5).

Study 1012 was a pivotal, double-blind, randomised, active-controlled Phase 3 trial, in which 601 healthy infants received Prevenar 20 in a 3-dose series. The most frequently reported (> 10%) adverse reactions after any dose of Prevenar 20 were irritability (71.0% to 71.9%), drowsiness/increased sleep (50.9% to 61.2%), pain at injection site (22.8% to 42.4%), decreased appetite (24.7% to 39.3%), redness at the injection site (25.3% to 36.9%), swelling at the injection site (21.4% to 29.8%), and fever ≥ 38.0 °C (8.9% to 24.3%). Most adverse reactions occurred within 1 to 2 days following vaccination and were mild or moderate in severity and of short duration (1 to 2 days).

Studies 1011, 1013 and 1003, were double-blind, randomised, active-controlled trials that included 2,232 healthy infants, vaccinated with Prevenar 20 in a 4-dose series. The most frequently reported (> 10%) adverse reactions observed after any dose of Prevenar 20 in infants were irritability (58.5% to 70.6%), drowsiness/increased sleep (37.7% to 66.2%), pain at injection site (32.8% to 45.5%), decreased appetite (23.0% to 26.4%), redness at the injection site (22.6% to 24.5%), and swelling at the injection site (15.1% to 17.6%). Most adverse reactions were mild or moderate following vaccination and most reactions resolving within 1 to 3 days. Severe reactions were reported infrequently.

In Study 1013, the local reactions and systemic events in the preterm subgroup (111 infants born at 34 to less than 37 weeks of gestation) were similar to or lower than the term infants in the study. In the preterm subgroup, the frequency of any reported local reaction was 31.7% to 55.3% in the Prevenar 20 group, and any systemic event was 65.0% to 85.5% in the Prevenar 20 group.

Participants aged 15 months to less than 18 years of age

In the Phase 3 trial B7471014 (Study 1014), 831 participants 15 months to less than 18 years of age received a single dose of Prevenar 20 in four age groups (209 participants 15 to less than 24 months of age; 216 participants 2 years to less than 5 years of age; 201 participants 5 years to less than 10 years age; and 205 participants 10 years to less than 18 years of age). The participants less than 5 years of age had received at least 3 prior doses of Prevenar 13.

The most frequently reported (> 10%) adverse reactions observed after any dose of Prevenar 20 in participants less than 2 years of age were irritability (61.8%), pain at the injection site (52.5%), drowsiness/increased sleep (41.7%), redness at the injection site (37.7%), decreased appetite (25.0%), swelling at the injection site (22.1%), and fever ≥ 38.0 °C (11.8%). In participants aged 2 years and older, the most frequently reported adverse reactions were pain at the injection site (66.0% to 82.9%), muscle pain (26.5% to 48.3%), redness at the injection site (15.1% to 39.1%), fatigue (27.8% to 37.2%), headache (5.6% to 29.3%), and swelling at the injection site (15.6% to 27.1%).

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 infant Phase 2, Phase 3 clinical trials in paediatric and adult populations 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 the Phase 2 infant trial, and the Phase 3 trials in paediatric and adult populations, based on the highest frequency among adverse reactions, local reactions, or systemic events, after vaccination in an Prevenar 20 group or integrated dataset. The data from clinical trials in infants reflect Prevenar 20 administered simultaneously with other routine childhood vaccines.

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. Tabulated Adverse Reactions From Prevenar 20 Clinical Trials

System Organ Class	**Adverse Reactions**	**Frequency**		
		Infants/Children/Adolescents		**Adults**
		6 weeks to less than 5 years of age	**5 years to less than 18 years of age**	
Immune System Disorders	Hypersensitivity reaction including face oedema, dyspnoea, bronchospasm	Rare[a]	-	Uncommon
Metabolism and Nutrition Disorders	Decreased appetite	Very common	Very common[a]	Very common[a]
Psychiatric Disorders	Irritability	Very common	Very common[a]	-
	Crying	Uncommon[a]	-	-
Nervous System Disorders	Drowsiness/increased sleep	Very common	Very common[a]	-
	Seizures (including febrile seizures)	Uncommon	-	-
	Hypotonic-hyporesponsive episode	Rare[a]	-	-
	Restless sleep/decreased sleep	Very common[a]	Very common[a]	-
	Headache	-	Very common	Very common
Gastrointestinal Disorders	Diarrhoea	Common	Common[a]	Uncommon[b]
	Nausea	-	-	Uncommon
	Vomiting	Common	Common[a]	Uncommon[b]
Skin and Subcutaneous Tissue Disorders	Rash	Common	Common[a]	Uncommon[b]
	Angioedema	-	-	Uncommon
	Urticaria or urticaria-like rash	Uncommon	Uncommon	-

Table 1. Tabulated Adverse Reactions From Prevenar 20 Clinical Trials

System Organ Class	Adverse Reactions	Frequency		
		Infants/Children/Adolescents		Adults
		6 weeks to less than 5 years of age	5 years to less than 18 years of age	
Musculoskeletal and connective tissue Disorders	Muscle pain	-	Very common	Very common
	Joint pain	-	Common	Very common
General Disorders and Administration Site Conditions	Fever (pyrexia)	Very common	Uncommon	Common
	Fever greater than 38.9 °C	Common	-	-
	Fatigue	-	Very common	Very common
	Vaccination-site erythema	Very common	Very common	Common[b]
	Vaccination-site induration/swelling	Very common	Very common	Common[b]
	Vaccination-site erythema or induration/swelling (> 2.0-7.0 cm)	Very common (after toddler dose and in older children [age 2 to < 5 years])	-	-
		Common (after infant series)	-	-
	Vaccination-site erythema or induration/swelling (> 7.0 cm)	Uncommon	-	-
	Vaccination-site pain/tenderness	Very common	Very common	Very common
	Vaccination-site pain/tenderness causing limitation of limb movement	Common	Common	Very common[a]
	Vaccination-site pruritus	-	-	Uncommon
	Lymphadenopathy	-	-	Uncommon
	Vaccination-site urticaria	-	-	Uncommon
	Chills	-	-	Uncommon[b]
	Vaccination-site hypersensitivity	Rare[c]	-	-

a. These frequencies are based on adverse reactions (ARs) reported in clinical trials with Prevenar 13 as these ARs were not reported in Prevenar 20 trials of infants (Phase 2 and 3), children and adolescents less than 18 years of age, and adults 18 years and older (Phase 3); therefore, the frequency is not known.
b. Event reported from clinical trials in adults with Prevenar 13 with very common frequency (≥ 1/10).
c. AR not reported for Prevenar 13, although injection-site urticaria, injection-site pruritus, and injection-site dermatitis were reported in Prevenar 13 postmarketing experience.

Safety with concomitant vaccine administration in adults

When Prevenar 20 was administered to adults aged ≥ 65 years together with the third (booster) dose of a COVID-19 mRNA vaccine (nucleoside modified), the tolerability profile generally resembled that of the COVID-19 mRNA vaccine (nucleoside modified) administered alone. There were a few differences in the safety profile when compared to administration of Prevenar 20 alone. In the phase 3 trial B7471026 (Study 1026), pyrexia (13.0%) and chills (26.5%) were reported as "very common" with co-administration. There was also one report of dizziness (0.5%) in the co-administration group.

Adverse reactions from postmarketing experience

Table 2 includes adverse experiences that have been spontaneously reported during the postmarketing use of Prevenar 13 in paediatric and adult populations , 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
Blood and lymphatic system disorders	Lymphadenopathy localised to the region of the vaccination -site
Immune system disorders	Anaphylactic/anaphylactoid reaction, including shock
Skin and subcutaneous tissue disorders	Angioedema, Erythema multiforme
General disorders and administration site conditions	Vaccination-site dermatitis, Vaccination-site urticaria, Vaccination-site pruritus

Events reported spontaneously in Prevenar 13 postmarketing experience; therefore, the frequencies could not be estimated from the available Prevenar 20 data and are considered as not known.

Additional information in special populations in studies with Prevenar 13

Participants 6 to < 18 years of age with HIV infection have similar frequencies of adverse reactions in Table 1, except fever (11% to 19%), joint pain (24% to 42%), and vomiting (8% to 18%), which were very common. 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 2 to < 18 years of age with HSCT have similar frequencies of adverse reactions in Table 1, except vaccination-site pain causing limitation of limb movement (5% to 15%), vomiting (6% to 21%), diarrhoea (15% to 32%), and joint pain (25% to 32%), which were very 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.

Participants 6 to < 18 years of age with SCD have similar frequencies of adverse reactions in Table 1, except vaccination-site pain causing limitation of limb movement (11% to 16%), fever (21% to 22%), vomiting (13% to 15%), diarrhoea (13% to 25%), and joint pain (40% to 45%), which were very common.

Reporting of suspected adverse reactions

Reporting suspected adverse reactions after authorisation of the medicinal product is important. It allows continued monitoring of the benefit/risk balance of the medicinal product.

Any suspected adverse events should be reported to the Ministry of Health according to the National Regulation by using an online form https://sideeffects.health.gov.il/

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 bacteria.

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, and in paediatric populations the serotype-specific levels, that correlate with protection against pneumococcal disease have not been clearly defined.

Prevenar 20 effectiveness

No efficacy studies have been performed with Prevenar 20.

Approval of Prevenar 20 for the paediatric population is based on comparing the totality of the immune responses in infants after receiving Prevenar 20 to the immune responses after receiving Prevenar 13. The comparison, following the World Health Organization (WHO) guideline, included the percentage of participants with predefined IgG (immunoglobulin G) concentrations and IgG geometric mean concentrations (GMCs). This approach is largely based upon the observed relationship between immunogenicity and invasive pneumococcal disease (IPD) efficacy from 3 placebo-controlled trials with either Prevenar (7-valent pneumococcal conjugate vaccine) or the investigational 9-valent CRM_{197} conjugate polysaccharide vaccine conducted in Navajo and White Mountain Apache Indian infants (cluster randomised trial), infants in Soweto, South Africa, and infants in the Northern California Kaiser Permanente (NCKP) health organization in the United States (see Prevenar Efficacy and Prevenar 13 Effectiveness in Children below). The predefined IgG concentration corresponding to 0.35 µg/mL in the WHO enzyme-linked immunosorbent assay (ELISA) is only applicable at the population level and cannot be used to predict individual or serotype-specific protection against IPD.

Immunogenicity data

Prevenar 20 clinical trials in infants, children and adolescents

Two Phase 3 clinical trials (Study 1012, Study 1011) and one Phase 2 clinical trial (Study 1003) evaluated the immunogenicity of Prevenar 20 in a 3-dose and 4-dose series in infants. One Phase 3

trial (Study 1014) of children 15 months to less than 18 years of age evaluated a single dose of Prevenar 20.

Pneumococcal IgG immune responses following 3 doses of 3-dose vaccination series

In Study 1012, the immunogenicity of Prevenar 20 was evaluated in infants when administered in a series of 2 infant doses and 1 toddler dose in infants enrolled from Europe and Australia. The study enrolled infants 2 months (≥42 to ≤112 days) of age and born at >36 weeks of gestation. Participants were randomised (1:1) to receive either Prevenar 20 or Prevenar 13 with the first dose given at 42 to 112 days of age, a second dose given approximately 2 months later, and the third dose given at approximately 11 to 12 months of age. Participants received concomitant vaccines at these visits. Prevenar 20 elicited immune responses, as assessed by the percentage of participants with predefined IgG concentrations, IgG GMCs and OPA GMTs for all 20 serotypes contained in the vaccine. The observed IgG GMCs and percentage of participants with predefined IgG concentrations 1 month after the third (last) dose of Prevenar 20 were generally comparable to the Prevenar 13 group for the 13 matched serotypes and higher for the 7 additional serotypes (Table 3).
One month after the 2 infant doses the observed IgG GMCs were generally comparable for most serotypes to the Prevenar 13 group and the percentages of participants with predefined IgG concentrations for the 13 matched serotypes were generally lower in the Prevenar 20 group than the Prevenar 13 group (Table 4). The immune responses to the additional 7 serotypes were higher in the Prevenar 20 group than the Prevenar 13 group after the second dose.

Table 3. Percentages of Participants with Predefined Pneumococcal IgG Concentrations and Pneumococcal IgG GMCs (µg/mL) One Month after Dose 3 of a 3-Dose Series, Study 1012[a]

	Percentages of Participants with Predefined IgG Concentrations[b]			IgG GMCs		
	PREVENAR 20 N[c] = 493-495	Prevenar 13 N[c] = 501-502	Prevenar 20 – Prevenar 13	Prevenar 20 N[c] = 493-495	Prevenar 13 N[c] = 501-502	Prevenar 20/ Prevenar 13
	%	%	% (95% CI[d])	GMC[e]	GMC[e]	GMR[e] (95% CI[e])
Serotypes						
1	97.2	98.2	-1.0 (-3.1, 0.9)	1.71	2.53	0.67 (0.60, 0.75)
3	82.6	93.2	-10.6 (-14.7, -6.7)	0.72	1.09	0.66 (0.59, 0.73)
4	99.2	99.2	0 (-1.4, 1.3)	4.11	5.36	0.77 (0.68, 0.87)
5	98.4	98.0	0.4 (-1.4, 2.2)	1.74	2.41	0.72 (0.64, 0.81)
6A	98.8	98.8	0 (-1.6, 1.5)	7.75	11.82	0.66 (0.57, 0.75)
6B	98.4	97.6	0.8 (-1.1, 2.7)	2.64	4.63	0.57 (0.48, 0.67)
7F	99.6	100.0	-0.4 (-1.5, 0.4)	3.61	4.93	0.73 (0.67, 0.80)
9V	99.2	98.8	0.4 (-1.0, 1.9)	3.68	5.04	0.73 (0.66, 0.81)
14	96.6	98.0	-1.5 (-3.7, 0.6)	4.52	5.66	0.80 (0.69, 0.92)
18C	99.2	98.2	1.0 (-0.5, 2.7)	2.71	3.61	0.75 (0.67, 0.84)
19A	99.6	99.6	0 (-1.1, 1.1)	4.51	5.49	0.82 (0.72, 0.93)
19F	99.6	99.4	0.2 (-0.9, 1.4)	6.19	8.08	0.77 (0.68, 0.87)
23F	96.4	97.2	-0.9 (-3.2, 1.4)	2.64	4.40	0.60 (0.52, 0.69)
Additional Serotypes						
8	99.2	3.6	95.6 (93.4, 97.1)	3.57	0.03	113.37 (100.05, 128.46)
10A	97.8	1.6	96.2 (94.1, 97.6)	4.86	0.01	423.02 (372.25, 480.73)
11A	98.4	4.6	93.8 (91.3, 95.6)	3.74	0.02	229.66 (199.06, 264.96)
12F	96.6	0.2	96.4 (94.3, 97.7)	1.86	0.01	224.31 (204.73, 245.76)
15B	99.4	4.8	94.6 (92.3, 96.3)	13.09	0.02	527.47 (465.44, 597.77)
22F	99.2	1.4	97.8 (96.1, 98.8)	9.27	0.00	2193.09 (1908.27, 2520.41)

33F	98.6	1.8	96.8 (94.8, 98.0)	6.37	0.01	530.53 (470.15, 598.66)

Abbreviations: CI = confidence interval; GMC = geometric mean concentration; GMR = geometric mean ratio; IgG = immunoglobulin G; LLOQ = lower limit of quantitation.

Note: Noninferiority for a matched serotype was concluded if the lower bound of the 2-sided 95% CI for the percentage difference (Prevenar 20 - Prevenar 13) was > -10% or the lower bound of the 2-sided 95% CI for the GMR (Prevenar 20 to Prevenar 13) was >0.5 for that serotype.

Note: Assay results below the LLOQ were set to 0.5 × LLOQ in the analysis.

a. Study 1012 was conducted in Europe and Australia.

b. The predefined IgG concentration was ≥0.35 µg/mL for all serotypes except for serotypes 5, 6B and 19A which were ≥0.23 µg/mL, ≥0.10 µg/mL and ≥0.12 µg/mL respectively.

c. N = Number of participants with valid IgG concentrations.

d. Two-sided CI based on the Miettinen and Nurminen method.

e. GMCs, GMRs and the associated 2-sided CIs were calculated by exponentiating the means and the mean differences (Prevenar 20 – Prevenar 13) of logarithm of the concentrations and the corresponding CIs (based on the Student's t distribution).

Table 4. Percentage of Participants with Predefined Pneumococcal IgG Concentrations and Pneumococcal IgG GMCs (µg/mL) One Month after Dose 2 of a 3-Dose Series, Study 1012[a]

	Percentages of Participants With Predefined IgG Concentrations[b]			**IgG GMCs**		
	Prevenar 20 N[c] = 564-567	**Prevenar 13 N[c] = 561-562**	**Prevenar 20 – Prevenar 13**	**Prevenar 20 N[c] = 564-567**	**Prevenar 13 N[c] = 561-562**	**Prevenar20/ Prevenar 13**
	%	**%**	**% (95% CI[d])**	**GMC[e]**	**GMC[e]**	**GMR (95% CI[e])**
Serotypes						
1	70.7	84.2	-13.5 (-18.3, -8.7)	0.57	0.93	0.61 (0.54, 0.69)
3	58.0	75.8	-17.9 (-23.2, -12.4)	0.41	0.58	0.71 (0.64, 0.79)
4	68.6	79.5	-11.0 (-16.0, -5.9)	0.55	0.92	0.60 (0.52, 0.69)
5	63.4	76.0	-12.6 (-17.8, -7.2)	0.34	0.56	0.60 (0.52, 0.70)
6A	59.5	73.7	-14.1 (-19.5, -8.6)	0.45	0.84	0.54 0.45, 0.65)
6B	20.7	36.5	-15.8 (-21.0, -10.6)	0.03	0.06	0.51 (0.43, 0.61)
7F	87.6	90.2	-2.6 (-6.3, 1.1)	1.02	1.41	0.72 (0.64, 0.80)
9V	60.2	74.6	-14.3 (-19.7, -8.9)	0.45	0.77	0.59 (0.50, 0.69)
14	78.6	81.9	-3.3 (-7.9, 1.4)	1.05	1.28	0.82 (0.70, 0.96)
18C	71.0	76.5	-5.5 (-10.6, -0.4)	0.69	0.87	0.79 (0.67, 0.92)
19A	92.2	94.0	-1.7 (-4.8, 1.3)	0.67	1.13	0.59 (0.51, 0.69)
19F	94.3	95.7	-1.4 (-4.0, 1.2)	2.21	3.06	0.72 (0.64, 0.82)
23F	23.5	41.8	-18.3 (-23.6, -12.9)	0.13	0.25	0.52 (0.44, 0.62)
Additional Serotypes						
8	96.5	2.9	93.6 (91.2, 95.4)	1.62	0.02	91.19 (81.19, 102.43)
10A	28.9	2.7	26.3 (22.4, 30.3)	0.16	0.02	8.38 (7.20, 9.76)
11A	94.2	2.0	92.2 (89.7, 94.2)	1.62	0.02	74.53 (65.99, 84.17)
12F	30.3	0.2	30.2 (26.5, 34.1)	0.15	0.01	17.91 (15.66, 20.48)
15B	94.3	8.5	85.8 (82.5, 88.5)	3.33	0.04	83.56 (71.77, 97.28)
22F	94.4	2.0	92.4 (89.9, 94.3)	2.25	0.01	337.08 (287.86, 394.72)
33F	46.8	2.7	44.2 (39.8, 48.5)	0.31	0.03	12.19 (10.55, 14.09)

Abbreviations: CI = confidence interval; GMC = geometric mean concentration; GMR = geometric mean ratio; IgG = immunoglobulin G; LLOQ = lower limit of quantitation.

Note: Noninferiority for a matched serotype was concluded if the lower bound of the 2-sided 95% CI for the percentage difference (Prevenar 20 – Prevenar 13) was > -10% or the lower bound of the 2-sided 95% CI for the GMR (Pevenar 20 to Prevenar 13) was >0.5 for that serotype.

Note: Assay results below the LLOQ were set to 0.5 × LLOQ in the analysis.

a. Study 1012 was conducted in Europe and Australia.

b. The Predefined IgG concentration was ≥0.35 µg/mL for all serotypes except for serotypes 5, 6B and 19A which were ≥0.23 µg/mL, ≥0.10 µg/mL and ≥0.12 µg/mL respectively.

c. N = Number of participants with valid IgG concentrations.

d. Two-sided CI based on the Miettinen and Nurminen method.

e. GMCs, GMRs and the associated 2-sided CIs were calculated by exponentiating the means and the mean differences (Prevenar 20 – Prevenar 13) of the logarithm of the concentrations and the corresponding CIs (based on the Student's t distribution).

OPA responses after 2 and 3 doses in a 3-dose vaccination series of Prevenar 20

The OPA geometric mean titres (GMTs) for the 13 matched serotypes at 1 month after Dose 2 and 1 month after Dose 3 in the Prevenar 20 group were generally similar to the observed OPA GMTs in the Prevenar 13 group for most serotypes. The observed OPA GMTs were lower for serotype 6B after Dose 2 and serotype 1 after Dose 3 in the Pevenar 20 group. OPA GMTs were higher after Dose 3 than after Dose 2 for all serotypes. The observed OPA GMTs for the 7 additional serotypes, including serotypes 10A and 12F, both 1 month after the second dose and 1 month after the third dose were substantially higher in the Prevenar 20 group than those in the Prevenar 13 group (Table 5).

Table 5. Pneumococcal OPA GMTs One Month after Doses 2 and 3 in a 3-dose series, Study 1012[a]

	Prevenar 20 N[b] = 96-116 After Dose 2	**Prevenar 13 N[b] = 97-118 After Dose 2**	**Prevenar 20 N[b] = 72-106 After Dose 3**	**Prevenar 13 N[b] = 92-109 After Dose 3**
	GMT[c] (95% CI[c])	**GMT[c] (95% CI[c])**	**GMT[c] (95% CI[c])**	**GMT[c] (95% CI[c])**
Serotypes				
1	14 (12, 16)	23 (19, 28)	54 (43, 69)	101 (79, 129)
3	31 (26, 36)	40 (34, 47)	99 (84, 117)	129 (111, 150)
4	333 (270, 413)	391 (314, 486)	904 (752, 1086)	992 (777, 1266)
5	21 (18, 23)	27 (23, 31)	60 (50, 72)	82 (66, 101)
6A	347 (273, 441)	409 (318, 527)	1101 (897, 1350)	1304 (1018, 1671)
6B	54 (42, 71)	105 (76, 144)	537 (408, 706)	864 (664, 1125)
7F	858 (736, 1000)	895 (781, 1027)	1811 (1553, 2112)	2197 (1905, 2533)
9V	233 (182, 298)	285 (228, 358)	3254 (2596, 4079)	4544 (3681, 5610)
14	287 (215, 383)	360 (264, 489)	738 (606, 899)	926 (751, 1142)
18C	588 (467, 741)	719 (590, 876)	1296 (1048, 1602)	1870 (1489, 2348)
19A	57 (43, 75)	91 (69, 121)	754 (627, 907)	707 (558, 896)
19F	97 (81, 116)	117 (94, 146)	183 (140, 237)	258 (192, 347)
23F	59 (42, 84)	68 (48, 96)	697 (530, 917)	975 (734, 1296)
Additional Serotypes				
8	164 (133, 203)	17 (15, 18)	1398 (1088, 1796)	31 (25, 39)
10A	855 (610, 1199)	39 (34, 44)	3403 (2600, 4455)	69 (52, 91)
11A	327 (253, 423)	49 (47, 51)	2966 (2212, 3978)	66 (51, 85)
12F	4788 (3779, 6067)	26 (23, 28)	5501 (4499, 6725)	29 (25, 35)
15B	846 (605, 1183)	17 (15, 19)	2676 (1948, 3677)	23 (18, 30)
22F	4444 (3666, 5386)	10 (9, 11)	6523 (4848, 8777)	17 (13, 24)
33F	2373 (1759, 3202)	178 (163, 195)	11315 (8107, 15794)	708 (545, 920

Abbreviations: CI = confidence interval; GMT = geometric mean titre; LLOQ = lower limit of quantitation; OPA = opsonophagocytic activity.

Note: Assay results below the LLOQ were set to 0.5 × LLOQ in the analysis.

Note: OPA titres were determined on serum from randomly selected subsets of participants assuring equal representation of both vaccine groups.

a. Study 1012 was conducted in Europe and Australia.

b. N = Number of participants with valid OPA titres.

c. GMTs and 2-sided CIs were calculated by exponentiating the mean logarithm of the titres and the corresponding CIs (based on the Student's t distribution).

Booster responses after the last dose in a 3-dose infant vaccination series

Prevenar 20 immune responses show boosting in IgG GMCs and percentage of participants with a predefined IgG concentrations after Dose 3, that are higher than concentrations before Dose 3, and also increased relative to the levels after Dose 2, indicating that a memory response was elicited by the 2 infant doses (see Tables 3 and 4). For all serotypes, the OPA responses also show a generally similar pattern of boosting as observed with the IgG responses, with priming evidenced by the robust OPA responses (geometric mean fold rise (GMFRs) and the percentages of participants with a ≥4-fold rise in OPA titres) from before to one month after Dose 3. In summary, Prevenar 20 elicits immune responses that are comparable to Prevenar 13 for the 13 matched serotypes and the 7 additional serotypes after the third (toddler) dose.

The totality of data show that a 3-dose series of Prevenar 20 elicited immune responses expected to provide children protection against pneumococcal disease similar to that of Prevenar 13 for all 20 vaccine serotypes.

Immune responses following 3 and 4 doses in a 4-dose infant vaccination series

Clinical studies evaluating the immunogenicity of Prevenar 20 in infants with a 4-dose series (3 infant doses and a toddler dose) at 2, 4, 6, and 12 to 15 months of age have been conducted in 2 randomised Phase 2 (Study 1003) and Phase 3 studies (Study 1011) in United States/Puerto Rico.

In Study 1011, healthy infants 2 months (≥42 to ≤98 days) of age at the time of consent and born at >36 weeks of gestation, were enrolled. Participants were randomised (1:1) to receive either Prevenar 20 or Prevenar 13 at approximately 2, 4, 6, and 12 to 15 months of age. At one month after the fourth dose, the IgG GMCs for Prevenar 20 were noninferior to Prevenar 13 for all 13 matched serotypes, and 7 additional serotypes to the lowest IgG GMC among the vaccine serotypes (excluding serotype 3) in the Prevenar 13 group based on a 2-fold noninferiority criterion. This was also the case for the IgG GMCs for Prevenar 13, 1 month after the third dose. The percentages of participants with predefined serotype-specific IgG concentrations one month after the third dose was met for 8 of the 13 serotypes and missed by small margins for 4 serotypes (serotypes 1, 4, 9V, and 23F) with a 10% noninferiority criterion. Six of the 7 additional serotypes met the noninferiority criterion; serotype 12F missed the statistical noninferiority criterion. The IgG GMCs at both time points and percentages of participants with predefined IgG concentrations for all 7 additional serotypes, including serotype 12F, were much higher than the corresponding serotype responses in the Prevenar 13 group, consistent with statistically greater antibody levels based on the lower bounds of the nominal 2-sided 95% confidence limits (not adjusted for multiplicity).

OPA GMTs for the 13 matched serotypes 1 month after Dose 3 and Dose 4 in the Prevenar 20 group were generally numerically similar to the OPA GMTs in the Prevenar 13 group, and have similar distributions. The observed OPA GMTs were substantially higher for the 7 additional serotypes in the Prevenar 20 group than the Prevenar 13 group.

Prevenar 20 elicits IgG immune responses that are comparable to Prevenar 13 for the 13 matched serotypes and the 7 additional serotypes after 3 doses in infants and a fourth dose in toddlers. Prevenar 20 also elicits functional antibody to all 20 serotypes that was observed 1 month after Dose 3 and 1 month after Dose 4. Prevenar 20 immune responses also show boosting after Dose 4, indicating that a memory response was elicited by the 3 infant doses.

Children 15 months to less than 18 years of age (Study 1014)

In a multicenter, single-arm trial (Study 1014), participants were enrolled into the study by age group (approximately 200 participants per group) to receive a single dose Prevenar 20 as described below.

Children 15 months to less than 5 years of age previously vaccinated with Prevenar 13

In 15 to less than 24 months and 2 years to less than 5 years age groups, participants had been previously vaccinated with 3 or 4 doses of Prevenar 13. Increases in IgG concentrations from before to 1 month after Pevenar 20 were observed for all 20 vaccine serotypes in participants 15 months to less than 5 years of age with prior vaccination with Prevenar 13. The observed IgG GMFRs to the 7 additional serotypes ranged from 27.9 to 1847.7 and increases in IgG GMCs were observed in all 20 vaccine serotypes from before to 1 month after Prevenar 20 (Table 6). In children 15 months to less than 24 months of age 83.2% – 100.0% had predefined IgG concentrations to 6 of the 7 additional serotypes, serotype 12F was 40.0%.

Table 6: Pneumococcal IgG GMCs in Participants 15 Months to Less Than 5 Years of Age – Before and 1 Month after Vaccination – Evaluable Immunogenicity Population – Study 1014[a]

	≥15 to <24 Months N[b] = 186-190		≥2 to <5 Years N[b] = 179-183	
	Before Vaccination GMC[c] (95% CI[c])	**After Vaccination GMC[c] (95% CI[c])**	**Before Vaccination GMC[c] (95% CI[c])**	**After Vaccination GMC[c] (95% CI[c])**
Serotypes				
1	0.43 (0.37, 0.49)	1.46 (1.28, 1.67)	0.20 (0.17, 0.24)	4.21 (3.62, 4.90)
3	0.14 (0.12, 0.16)	0.54 (0.47, 0.61)	0.08 (0.06, 0.10)	1.21 (1.04, 1.42)
4	0.61 (0.52, 0.72)	2.59 (2.27, 2.96)	0.30 (0.25, 0.37)	8.37 (7.28, 9.62)
5	0.43 (0.36, 0.50)	1.53 (1.32, 1.77)	0.18 (0.15, 0.22)	5.09 (4.32, 5.99)
6A	1.61 (1.38, 1.88)	7.59 (6.67, 8.63)	0.71 (0.58, 0.88)	31.99 (27.85, 36.75)
6B	0.85 (0.71, 1.02)	4.27 (3.69, 4.94)	0.52 (0.42, 0.63)	17.78 (15.43, 20.48)
7F	1.17 (1.03, 1.33)	3.53 (3.16, 3.94)	0.51 (0.44, 0.60)	6.42 (5.69, 7.24)
9V	0.71 (0.61, 0.83)	2.70 (2.35, 3.09)	0.35 (0.28, 0.42)	7.94 (6.83, 9.24)
14	1.53 (1.31, 1.79)	4.42 (3.82, 5.12)	0.66 (0.53, 0.81)	14.60 (12.44, 17.13)
18C	0.65 (0.55, 0.76)	2.69 (2.32, 3.12)	0.26 (0.21, 0.32)	7.07 (6.01, 8.32)
19A	0.47 (0.38, 0.58)	3.29 (2.89, 3.76)	0.52 (0.40, 0.68)	12.48 (10.76, 14.48)
19F	0.80 (0.67, 0.94)	4.16 (3.61, 4.79)	0.56 (0.44, 0.71)	12.50 (10.48, 14.91)
23F	0.96 (0.79, 1.18)	5.35 (4.55, 6.30)	0.90 (0.71, 1.15)	16.18 (13.75, 19.04)
Additional Serotypes				
8	0.04 (0.03, 0.05)	4.66 (4.17, 5.22)	0.05 (0.04, 0.06)	5.08 (4.45, 5.80)
10A	0.01 (0.01, 0.02)	1.23 (1.02, 1.48)	0.03 (0.02, 0.03)	2.76 (2.28, 3.34)
11A	0.03 (0.02, 0.03)	1.61 (1.40, 1.86)	0.06 (0.04, 0.08)	2.64 (2.25, 3.09)
12F	0.01 (0.01, 0.01)	0.22 (0.18, 0.27)	0.01 (0.01, 0.01)	0.38 (0.31, 0.46)
15B	0.02 (0.02, 0.03)	1.17 (0.97, 1.40)	0.05 (0.04, 0.07)	3.96 (3.12, 5.03)
22F	0.01 (0.00, 0.01)	9.57 (8.12, 11.29)	0.02 (0.01, 0.02)	12.46 (10.82, 14.35)
33F	0.02 (0.01, 0.02)	1.91 (1.60, 2.27)	0.04 (0.03, 0.05)	3.16 (2.63, 3.79)

Abbreviations: CI = confidence interval; GMC = geometric mean concentration; IgG = immunoglobulin G; LLOQ = lower limit of quantitation.

Note: Assay results below the LLOQ were set to 0.5 × LLOQ in the analysis.

a. Study 1014 was conducted in the United States.

b. N = Number of participants with valid IgG concentrations at the given sampling time point.

c. GMCs and 2-sided CIs were calculated by exponentiating the mean logarithm of the concentrations and the corresponding CIs (based on the Student's t distribution).

Children and adolescents 5 years to less than 18 years of age previously unvaccinated or vaccinated with Prevenar 13 or Prevenar

In the study, age groups 5 to less than 10 years and 10 to less than 18 years, participants could be unvaccinated or previously vaccinated with Prevenar 13 or Prevenar. Prevenar 20 elicited robust IgG and OPA immune responses to the 20 vaccine serotypes after a single dose in participants 5 to less than 18 years of age. OPA GMFRs ranged from 11.5 to 499.0 to the 7 additional serotypes and increases in OPA GMTs were observed for all 20 vaccine serotypes (Table 7).
In summary, a single dose of Prevenar 20 administered to children and adolescents 15 months to less than 18 years of age is expected to generate protective responses against pneumococcal disease due to the 7 additional serotypes, and to the 13 matched serotypes.

Table 7: Pneumococcal OPA GMTs in Participants 5 to Less Than 18 Years of Age – Before and 1 Month after Vaccination – Evaluable Immunogenicity Population – Study 1014[a]

	≥5 to <10 Years N[b]=76-175		≥10 to <18 Years N[b]=86-187	
	Before Vaccination GMT[c] (95% CI[c])	**After Vaccination GMT[c] (95% CI[c])**	**Before Vaccination GMT[c] (95% CI[c])**	**After Vaccination GMT[c] (95% CI[c])**
Serotypes				
1	10 (9, 11)	548 (455, 660)	11 (9, 12)	396 (302, 519)
3	29 (22, 40)	155 (135, 178)	19 (14, 24)	105 (88, 124)
4	43 (27, 67)	2328 (1942, 2789)	34 (22, 51)	2290 (1822, 2878)
5	15 (15, 15)	385 (324, 458)	15 (15, 16)	216 (159, 294)
6A	74 (51, 106)	8268 (6617, 10331)	64 (44, 91)	9434 (7616, 11686)
6B	156 (99, 244)	6569 (5367, 8040)	237 (155, 363)	10085 (8263, 12309)
7F	541 (410, 713)	3981 (3446, 4598)	516 (381, 698)	3326 (2878, 3843)
9V	410 (289, 580)	11717 (9262, 14823)	469 (330, 667)	9627 (7492, 12369)
14	246 (172, 353)	4610 (3688, 5762)	97 (65, 145)	3925 (3153, 4885)
18C	152 (89, 261)	6766 (5585, 8197)	73 (45, 119)	3617 (2816, 4645)
19A	117 (76, 181)	2162 (1786, 2618)	66 (44, 100)	2212 (1801, 2717)
19F	91 (66, 125)	1095 (810, 1479)	57 (44, 73)	551 (401, 757)
23F	87 (53, 145)	2213 (1751, 2797)	46 (29, 73)	1842 (1391, 2439)
Additional Serotypes				
8	34 (28, 42)	3870 (3302, 4535)	35 (28, 43)	3125 (2680, 3642)
10A	745 (519, 1071)	21102 (17238, 25833)	554 (395, 777)	17417 (14301, 21214)
11A	1347 (962, 1887)	16882 (13650, 20880)	765 (543, 1076)	11677 (9751, 13982)
12F	48 (38, 60)	23860 (19002, 29959)	46 (36, 59)	20250 (16861, 24320)
15B	79 (54, 115)	25729 (19647, 33695)	45 (33, 61)	21496 (16697, 27672)
22F	259 (170, 394)	33615 (26198, 43130)	243 (161, 366)	27922 (22622, 34463)
33F	3334 (2847, 3905)	45921 (36768, 57353)	2895 (2448, 3424)	32363 (26219, 39946)

Abbreviations: CI = confidence interval; GMT = geometric mean titre; LLOQ = lower limit of quantitation; OPA = opsonophagocytic activity.

Note: OPA titres for all serotypes were determined on serum from randomly selected subsets of participants except for the 7 additional serotypes among participants ≥5 to <18 years of age, which were determined from all available samples.

Note: Assay results below the LLOQ were set to 0.5 × LLOQ in the analysis.

a. Study 1014 was conducted in the United States.

b n = Number of participants with valid OPA titres at the given sampling time point.

c. GMTs and 2-sided CIs were calculated by exponentiating the mean logarithm of the titres and the corresponding CIs (based on the Student's t distribution).

Preterm infants

The safety and tolerability of Prevenar 20 were evaluated in Study 1013, which included 111 late preterm infants (born at 34 to less than 37 weeks of gestational age) among the total study population. Participants were randomised to receive a 4-dose series of either Prevenar 20 (N=77) or Prevenar 13 (N=34). Studies have not been specifically conducted to describe the immunogenicity of Prevenar 20 in preterm infants. Based on experience with Prevenar and Prevenar 13, immune responses are elicited in preterm infants, although they may be lower than in term infants.

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 hospitalization 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 *S. 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 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% 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 8), 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 8). 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 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 8. 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
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 9).

While not planned as an active control for immunogenicity evaluations in the study, a post hoc descriptive analysis showed generally numerically lower OPA GMTs 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.

Table9. 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)

Table9. 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]
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)

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 10). Immune responses were lower in participants in both groups who received prior PPSV23 vaccinations.

Table 10. 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)

Table 10. 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]
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)
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

Paediatric population

In Study 1012, the concomitant administration of Infanrix hexa (containing DTaP, HBV, IPV, and Hib antigens) with all 3 doses of Prevenar 20 or Prevenar 13 and single doses of a vaccine containing MMR antigens and Varilrix (varicella antigens) were also administered with the third dose and evaluated 1 month after the third (toddler) dose of Prevenar 20 or Prevenar 13. Noninferiority was demonstrated for immune responses to diphtheria, tetanus, acellular pertussis, hepatitis B, poliovirus, Hib, MMR, and varicella vaccine antigens co-administered with Prevenar 20 compared with Prevenar 13. The results from Study 1012 support co-administration of Prevenar 20 with routine paediatric vaccines. No safety concerns were identified in this study.

In Study 1011, the concomitant administration of a vaccine containing DTaP, HBV, IPV antigens and Hiberix (Hib antigen) with each of the 3 infant doses of either Pevenar 20 or Prevenar 13 were evaluated 1 month after the third dose. Concomitant administration of single doses of M-M-R II (MMR antigens) and Varivax (varicella antigens) with the fourth dose of either Prevenar 20 or Prevenar 13 were evaluated 1 month following vaccination. Noninferiority was demonstrated for immune responses to the co-administered diphtheria, tetanus, acellular pertussis, hepatitis B virus, poliovirus, and Hib vaccine antigens 1 month after 3 infant doses and coadministered MMR, and varicella virus vaccine antigens after the fourth (toddler) dose of Prevenar 20 compared with Prevenar 13. The results from Study 1011 support co-administration of Prevenar 20 with routine paediatric vaccines. No safety concerns were identified in this study.

Influenza and rotavirus vaccines were permitted to be administered concomitantly at any time during these studies according to local or national recommendations.

Immune responses in special populations

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

Studies in individuals with SCD, HIV, and HSCT have not been conducted with Prevenar 20.

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 children and adults at higher risk of pneumococcal infection including immunocompromised children and adults with HIV infection or HSCT, and children with SCD.

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.

Sickle cell disease (SCD)

An open-label single-arm study with 2 doses of Prevenar 13 given 6 months apart was conducted in 158 children and adolescents 6 to < 18 years of age with SCD who were previously vaccinated with one or more doses of 23-valent pneumococcal polysaccharide vaccine at least 6 months prior to enrollment. After the first vaccination, Prevenar 13 elicited antibody levels measured by both IgG GMCs and OPA GMTs that were statistically significantly higher when compared with levels prior to vaccination. After the second dose, immune responses were comparable to those after the first dose. One year after the second dose, antibody levels measured by both IgG GMCs and OPA GMTs were

higher than levels prior to the first dose of Prevenar 13, except for the IgG GMCs for serotypes 3 and 5 that were numerically similar.

HIV infection

Children and adults not previously vaccinated with a pneumococcal vaccine
In Study 6115A1-3002 (B1851021), 151 participants 6 to < 18 years of age and 152 participants ≥ 18 years of age infected with HIV (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 128 to 133 evaluable participants 6 to < 18 years of age and in 131 to 137 evaluable participants ≥ 18 years of age approximately 1 month after each dose of the vaccine. After the first dose, 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 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 (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 enrolment. Participants received 3 doses of Prevenar 13: at enrolment, 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.

Haematopoietic stem cell transplant (HSCT)

In Study 6115A1-3003 (B1851022), 61 participants 2 to < 18 years of age and 190 participants ≥18 years of age 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 41 to 52 evaluable participants 2 to < 18 years of age and in 127 to 159 evaluable participants ≥ 18 years of age 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 with the exception of serotype 3 in the 2 to < 18 years age group. Overall, participants 2 to < 18 years of age had generally higher serotype specific immune responses compared with those ≥ 18 years of age.

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.

Invasive pneumococcal disease (IPD)

Vaccine effectiveness of Prevenar 13 against vaccine-serotype IPD was evaluated in the SpIDnet study, a multi-country enhanced IPD surveillance project in Europe. Based on data over a 6-year period (2012-2018) from 10 sites in 7 European countries using Prevenar 13, the effectiveness against IPD caused by serotypes in the vaccine among children < 5 years of age was 84.2% (95% CI,

79.0-88.1) and 88.7% (95% CI, 81.7-92.7) in children receiving ≥ 1 Prevenar 13 dose and a complete vaccination schedule, respectively.

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

The expiry date of the product is indicated on the packaging materials

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 sizes of 1, 10 pre-filled syringes, with or without needle.

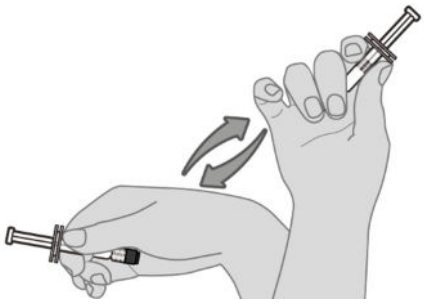
Not all pack sizes may be marketed.

6.6 Special precautions for disposal and other handling

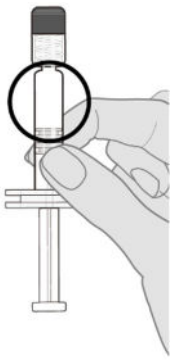
During storage, a white deposit and clear supernatant may be observed in the pre-filled syringe containing the suspension. Pre-filled syringes should be stored horizontally to minimise the resuspension time.

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.

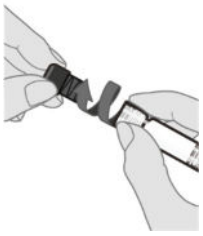


Step 2. Visual inspection
Visually inspect the vaccine for large particulate matter and discolouration prior to administration. Do not use if large particulate matter or discolouration is found. If the vaccine is not a homogenous white suspension, repeat steps 1 and 2.



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. LICENSE HOLDER

Pfizer Pharmaceuticals Ltd., 9 Shenkar St. Herzliya Pituach 46725.

8. LICENSE NUMBER

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