

**ANNEX I**  
**SUMMARY OF PRODUCT CHARACTERISTICS**

▼ This medicinal product is subject to additional monitoring. This will allow quick identification of new safety information. Healthcare professionals are asked to report any suspected adverse reactions. See section 4.8 for how to report adverse reactions.

## 1. NAME OF THE MEDICINAL PRODUCT

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

<sup>1</sup>Conjugated to CRM<sub>197</sub> carrier protein (approximately 51 µg per dose)

<sup>2</sup>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.

Apexxnar should be used in accordance with official recommendations.

## **4.2 Posology and method of administration**

### Posology

#### *Individuals 18 years of age and older*

Apexxnar 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 Apexxnar has not been established.

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

#### *Paediatric population*

The safety and efficacy of Apexxnar 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 Apexxnar in special populations.

Limited experience from clinical studies with Prevenar 13 (a pneumococcal conjugate vaccine consisting of 13 polysaccharide conjugates that are also in Apexxnar) 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 Apexxnar 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 Apexxnar 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

Apexxnar 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, Apexxnar may not protect all individuals receiving the vaccine from pneumococcal invasive disease or pneumonia. For the most recent epidemiological information in your country, you should consult with the relevant national organisation.

#### Immunocompromised individuals

Safety and immunogenicity data on Apexxnar 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 Apexxnar.

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 immunization. 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 Apexxnar) 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 Apexxnar 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**

Apexxnar 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 Apexxnar (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 Apexxnar when given concomitantly with seasonal influenza vaccine (QIV, surface antigen, inactivated, adjuvanted) compared to when Apexxnar was given alone. The clinical relevance of this finding is unknown.

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

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

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

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

### **4.6 Fertility, pregnancy and lactation**

#### Pregnancy

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

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

Administration of Apexxnar 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 Apexxnar is excreted in human milk.

#### Fertility

No human data on the effect of Apexxnar 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**

Apexxnar 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 Apexxnar 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 Apexxnar. 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 Apexxnar in the Phase 3 trials, 3,639 were naïve to pneumococcal vaccines, 253 had previously received Pneumovax 23 (pneumococcal polysaccharide vaccine [23-valent]; PPSV23) ( $\geq 1$  to  $\leq 5$  years prior to enrollment), 246 had previously received Prevenar 13 only ( $\geq 6$  months prior to enrollment), and 125 had previously received Prevenar 13 followed by PPSV23 (the dose of PPSV23  $\geq 1$ -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  $\geq 80$  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  $\geq 60$  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 Apexxnar in participants  $\geq 65$  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  $\geq 60$  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 Apexxnar 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 Apexxnar. Table 1 presents adverse reactions reported in Phase 3 trials of Apexxnar, based on the highest frequency among adverse reactions, local reactions, or systemic events after vaccination in any Apexxnar group. In clinical trials, the safety profile of Apexxnar 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 ( $\geq 1/10$ ), common ( $\geq 1/100$  to  $< 1/10$ ), uncommon ( $\geq 1/1,000$  to  $< 1/100$ ), rare ( $\geq 1/10,000$  to  $< 1/1,000$ ), very rare ( $< 1/10,000$ ), not known (cannot be estimated from available data).

**Table 1. Adverse Drug Reactions From Apexxnar 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 <sup>a</sup>
Nervous system disorders	Headache			
Gastrointestinal disorders			Diarrhoea <sup>a</sup> Nausea Vomiting <sup>a</sup>	
Skin and subcutaneous tissue disorders			Rash <sup>a</sup> 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 <sup>a</sup> Vaccination-site erythema <sup>a</sup> Pyrexia	Vaccination-site pruritus Lymphadenopathy Vaccination-site urticaria Chills <sup>a</sup>	Limitation of arm movement <sup>a</sup>

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

### *Safety with concomitant vaccine administration in adults*

When Apexxnar was administered to adults aged  $\geq 65$  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 Apexxnar 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, which may also occur with Apexxnar. The postmarketing safety experience with Prevenar 13 is relevant to Apexxnar, as Apexxnar 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  $\geq 18$  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  $\geq 18$  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.

#### Reporting of suspected adverse reactions

Reporting suspected adverse reactions after authorisation of the medicinal product is important. It allows continued monitoring of the benefit/risk balance of the medicinal product. Healthcare professionals are asked to report any suspected adverse reactions via the national reporting system listed in [Appendix V](#).

## **4.9 Overdose**

Overdose with Apexxnar 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

Apexxnar contains 20 pneumococcal capsular polysaccharides all conjugated to a CRM<sub>197</sub> 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 Apexxnar 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 Apexxnar.

### Immunogenicity data

#### *Apexxnar 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 Apexxnar 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 Apexxnar 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 Apexxnar to Prevenar 13 and PPSV23*

In a randomised, active-controlled, double-blind, non-inferiority clinical trial (Pivotal Study 1007) of Apexxnar 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  $\geq 60$  years of age), and randomised to receive Apexxnar or control. Participants 60 years of age and older were randomised in a 1:1 ratio to receive Apexxnar (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 Apexxnar (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 Apexxnar 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 (Apexxnar/Prevenar 13; Apexxnar/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 Apexxnar 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 Apexxnar in the matched serotypes compared to Prevenar 13 (Table 3), however the clinical relevance of these findings is unknown.

The immune responses induced by Apexxnar 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 Apexxnar 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  $\geq 4$ -fold rise in OPA titres from before vaccination to 1 month after vaccination, and 92.9% of participants achieved OPA titres  $\geq$  LLOQ 1 month after vaccination.

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

	Apexxnar (N = 1157–1430)	Prevenar 13 (N = 1390– 1419)	PPSV23 (N = 1201– 1319)	Vaccine Comparison	
				GMT Ratio <sup>e</sup>	95% CI <sup>e</sup>
	GMT <sup>e</sup>	GMT <sup>e</sup>	GMT <sup>e</sup>		
<b>Serotype</b>					
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
<b>Additional Serotypes</b>					
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).

- Study 1007 was conducted in the United States and in Sweden.
- Non-inferiority for a serotype was met if the lower bound of the 2-sided 95% CI for the GMT ratio (ratio of Apexxnar/comparator) was greater than 0.5 (2-fold criterion for non-inferiority).
- Assay results below the LLOQ were set to  $0.5 \times$  LLOQ in the analysis.
- Evaluable immunogenicity population.
- 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 Apexxnar 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 Apexxnar in the younger age group versus Apexxnar 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 (Apexxnar 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. Apexxnar 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 Apexxnar 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 Apexxnar in Participants 18 Through 49 or 50 Through 59 Years of Age to Participants 60 Through 64 Years of Age (Study 1007)<sup>a,b,c,d</sup>**

	18–49 Years (N = 251–317)	60–64 Years (N = 765–941)	18–49 Years Relative to 60–64 Years GMT Ratio <sup>e</sup> (95% CI) <sup>e</sup>	50–59 Years (N = 266–320)	60–64 Years (N = 765– 941)	50–59 Years Relative to 60–64 Years GMT Ratio <sup>e</sup> (95% CI) <sup>e</sup>
	GMT <sup>e</sup>	GMT <sup>e</sup>		GMT <sup>e</sup>	GMT <sup>e</sup>	
<b>Serotype</b>						
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)
<b>Additional Serotypes</b>						
8	867	508	1.71 (1.38, 2.12)	487	502	0.97 (0.78, 1.20)

**Table 4. Comparisons of OPA GMTs 1 Month After Apexxnar in Participants 18 Through 49 or 50 Through 59 Years of Age to Participants 60 Through 64 Years of Age (Study 1007)<sup>a,b,c,d</sup>**

	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 <sup>e</sup>	GMT <sup>e</sup>	GMT Ratio <sup>e</sup> (95% CI) <sup>e</sup>	GMT <sup>e</sup>	GMT <sup>e</sup>	GMT Ratio <sup>e</sup> (95% CI) <sup>e</sup>
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).

- Study 1007 was conducted in the United States and in Sweden.
- 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).
- Assay results below the LLOQ were set to  $0.5 \times$  LLOQ in the analysis.
- Evaluable immunogenicity population.
- 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 Apexxnar in adults previously vaccinated with pneumococcal vaccine*

A Phase 3 randomised, open-label clinical trial (Study 1006) described immune responses to Apexxnar 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).

Apexxnar 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 Apexxnar in Participants 65 Years of Age and Older With Prior Pneumococcal Vaccination (Study 1006)<sup>a,b,c,d</sup>**

	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) <sup>e</sup>	GMT (95% CI) <sup>e</sup>	GMT (95% CI) <sup>e</sup>	GMT (95% CI) <sup>e</sup>	GMT (95% CI) <sup>e</sup>	GMT (95% CI) <sup>e</sup>
<b>Serotype</b>						
1	24 (20, 28)	51 (42, 62)	34 (28, 41)	115 (96, 138)	42 (32, 56)	82 (61, 110)

**Table 5. Pneumococcal OPA GMTs Before and 1 Month After Apexxnar in Participants 65 Years of Age and Older With Prior Pneumococcal Vaccination (Study 1006)<sup>a,b,c,d</sup>**

	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) <sup>e</sup>	GMT (95% CI) <sup>e</sup>	GMT (95% CI) <sup>e</sup>	GMT (95% CI) <sup>e</sup>	GMT (95% CI) <sup>e</sup>	GMT (95% CI) <sup>e</sup>
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)
<b>Additional Serotypes</b>						
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).

- Study 1006 was conducted in the United States and in Sweden.
- Assay results below the LLOQ were set to  $0.5 \times$  LLOQ in the analysis.
- Evaluable immunogenicity population.
- Open-label administration of Apexxnar.
- 2-sided CIs based on the Student t distribution.

## 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 Apexxnar.

Limited experience from clinical studies with Prevenar 13 (a pneumococcal conjugate vaccine consisting of 13 polysaccharide conjugates that are also in Apexxnar) 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 Apexxnar 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  $\geq$  200 cells/ $\mu$ L, 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  $\geq$  200 cells/ $\mu$ L 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 European Medicines Agency has deferred the obligation to submit the results of studies with Apexxnar in one or more subsets of the paediatric population for the condition of prevention of disease caused by *Streptococcus pneumoniae* (see section 4.2 for information on paediatric use).

### **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**

24 months

### **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 Apexxnar 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, and 50 pre-filled syringes, with or without needle.

Not all pack sizes may be marketed.

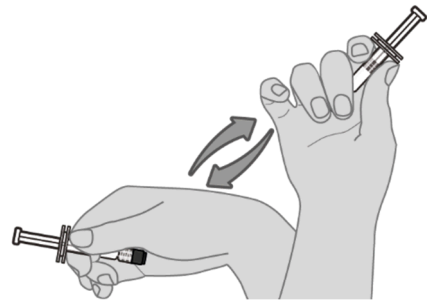
## 6.6 Special precautions for disposal and other handling

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

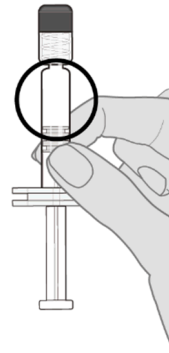
#### **Step 1. Vaccine resuspension**

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. MARKETING AUTHORISATION HOLDER**

Pfizer Europe MA EEIG  
Boulevard de la Plaine 17  
1050 Bruxelles  
Belgium

**8. MARKETING AUTHORISATION NUMBER(S)**

EU/1/21/1612/001  
EU/1/21/1612/002  
EU/1/21/1612/003  
EU/1/21/1612/004  
EU/1/21/1612/005  
EU/1/21/1612/006

**9. DATE OF FIRST AUTHORISATION/RENEWAL OF THE AUTHORISATION**

Date of first authorisation: 14 February 2022

**10. DATE OF REVISION OF THE TEXT**

Detailed information on this medicinal product is available on the website of the European Medicines Agency <http://www.ema.europa.eu>.

## **ANNEX II**

- A. MANUFACTURERS OF THE BIOLOGICAL ACTIVE SUBSTANCE(S) AND MANUFACTURER RESPONSIBLE FOR BATCH RELEASE**
- B. CONDITIONS OR RESTRICTIONS REGARDING SUPPLY AND USE**
- C. OTHER CONDITIONS AND REQUIREMENTS OF THE MARKETING AUTHORISATION**
- D. CONDITIONS OR RESTRICTIONS WITH REGARD TO THE SAFE AND EFFECTIVE USE OF THE MEDICINAL PRODUCT**

**A. MANUFACTURERS OF THE BIOLOGICAL ACTIVE SUBSTANCE(S) AND MANUFACTURER RESPONSIBLE FOR BATCH RELEASE**

Name and address of the manufacturers of the biological active substance

Wyeth BioPharma Division of Wyeth Pharmaceuticals LLC  
One Burtt Road  
Andover, MA 01810  
USA

Pfizer Ireland Pharmaceuticals  
Grange Castle Business Park  
Clondalkin  
Dublin 22  
Ireland

Wyeth Pharmaceutical Division of Wyeth Holdings LLC  
4300 Oak Park  
Sanford, NC 27330  
USA

Name and address of the manufacturer responsible for batch release

Pfizer Manufacturing Belgium NV  
Rijksweg 12  
2870 Puurs  
Belgium

**B. CONDITIONS OR RESTRICTIONS REGARDING SUPPLY AND USE**

Medicinal product subject to medical prescription.

- **Official batch release**

In accordance with Article 114 Directive 2001/83/EC, the official batch release will be undertaken by a state laboratory or a laboratory designated for that purpose.

**C. OTHER CONDITIONS AND REQUIREMENTS OF THE MARKETING AUTHORISATION**

- **Periodic safety update reports (PSURs)**

The requirements for submission of PSURs for this medicinal product are set out in the list of Union reference dates (EURD list) provided for under Article 107c(7) of Directive 2001/83/EC and any subsequent updates published on the European medicines web-portal.

## D. CONDITIONS OR RESTRICTIONS WITH REGARD TO THE SAFE AND EFFECTIVE USE OF THE MEDICINAL PRODUCT

### • Risk management plan (RMP)

The marketing authorisation holder (MAH) shall perform the required pharmacovigilance activities and interventions detailed in the agreed RMP presented in Module 1.8.2 of the marketing authorisation and any agreed subsequent updates of the RMP.

An updated RMP should be submitted:

- At the request of the European Medicines Agency;
- Whenever the risk management system is modified, especially as the result of new information being received that may lead to a significant change to the benefit/risk profile or as the result of an important (pharmacovigilance or risk minimisation) milestone being reached.

### • Obligation to conduct post-authorisation measures

The MAH shall complete, within the stated timeframe, the below measures:

Description	Due date
1. In order to further investigate the long-term effectiveness of Apexxnar for active immunisation for the prevention of pneumonia caused by <i>Streptococcus pneumoniae</i> , the MAH should conduct and submit the multi-country results of study B7471015, a Phase 4 study using a test-negative design to evaluate the effectiveness of Apexxnar against vaccine-type radiologically-confirmed community-acquired pneumonia in adults $\geq 65$ years of age.	CSR due 31/12/2027
2. In order to further investigate the long-term effectiveness of Apexxnar for active immunisation for the prevention of pneumonia caused by <i>Streptococcus pneumoniae</i> , the MAH should conduct and submit the European-specific analysis results of study B7471015, a Phase 4 study using a test-negative design to evaluate the effectiveness of Apexxnar against vaccine-type radiologically-confirmed community-acquired pneumonia in adults $\geq 65$ years of age.	CSR due 31/12/2030
3. In order to further investigate the long-term effectiveness of Apexxnar for active immunisation for the prevention of invasive disease caused by <i>Streptococcus pneumoniae</i> , the MAH should conduct and submit the results of a Phase 4 observational, real-world study to evaluate the effectiveness of Apexxnar against vaccine-type invasive pneumococcal disease in Europe according to an agreed protocol.	CSR due 31/12/2030

CSR: Clinical Study Report

**ANNEX III**  
**LABELLING AND PACKAGE LEAFLET**

## **A. LABELLING**

**PARTICULARS TO APPEAR ON THE OUTER PACKAGING**

**OUTER CARTON**

**Pack of 1, 10 and 50 pre-filled syringe, with or without needle – WITH BLUE BOX**

**1. NAME OF THE MEDICINAL PRODUCT**

Apexxnar suspension for injection  
pneumococcal polysaccharide conjugate vaccine (20-valent, adsorbed)

**2. STATEMENT OF ACTIVE SUBSTANCE(S)**

1 dose (0.5 mL) contains 2.2 µg of polysaccharide for serotypes 1, 3, 4, 5, 6A, 7F, 8, 9V, 10A, 11A, 12F, 14, 15B, 18C, 19A, 19F, 22F, 23F, 33F and 4.4 µg for serotype 6B conjugated to CRM<sub>197</sub> carrier protein, adsorbed on aluminium phosphate.

1 dose (0.5 mL) contains 0.125 mg aluminium.

**3. LIST OF EXCIPIENTS**

Sodium chloride, succinic acid, polysorbate 80 and water for injections.

**4. PHARMACEUTICAL FORM AND CONTENTS**

Suspension for injection

1 single-dose (0.5 mL) pre-filled syringe with separate needle

1 single-dose (0.5 mL) pre-filled syringe without needle

10 single-dose (0.5 mL) pre-filled syringes with separate needles

10 single-dose (0.5 mL) pre-filled syringes without needles

50 single-dose (0.5 ml) pre-filled syringes with separate needles

50 single-dose (0.5 ml) pre-filled syringes without needles

**5. METHOD AND ROUTE(S) OF ADMINISTRATION**

For intramuscular use only.

Shake well before use.

Read the package leaflet before use.

**6. SPECIAL WARNING THAT THE MEDICINAL PRODUCT MUST BE STORED OUT OF THE SIGHT AND REACH OF CHILDREN**

Keep out of the sight and reach of children.

**7. OTHER SPECIAL WARNING(S), IF NECESSARY**

**8. EXPIRY DATE**

EXP

**9. SPECIAL STORAGE CONDITIONS**

Store in a refrigerator.  
Do not freeze.  
Horizontal storage recommended.

**10. SPECIAL PRECAUTIONS FOR DISPOSAL OF UNUSED MEDICINAL PRODUCTS OR WASTE MATERIALS DERIVED FROM SUCH MEDICINAL PRODUCTS, IF APPROPRIATE****11. NAME AND ADDRESS OF THE MARKETING AUTHORISATION HOLDER**

Pfizer Europe MA EEIG  
Boulevard de la Plaine 17  
1050 Bruxelles  
Belgium

**12. MARKETING AUTHORISATION NUMBER(S)**

EU/1/21/1612/002 – pack of 1 with separate needle  
EU/1/21/1612/001 – pack of 1 without needle  
EU/1/21/1612/004 – pack of 10 with separate needles  
EU/1/21/1612/003 – pack of 10 without needles  
EU/1/21/1612/006 – pack of 50 with separate needles  
EU/1/21/1612/005 – pack of 50 without needles

**13. BATCH NUMBER**

Lot

**14. GENERAL CLASSIFICATION FOR SUPPLY****15. INSTRUCTIONS ON USE****16. INFORMATION IN BRAILLE**

Justification for not including Braille accepted.



**17. UNIQUE IDENTIFIER – 2D BARCODE**

2D barcode carrying the unique identifier included.

**18. UNIQUE IDENTIFIER - HUMAN READABLE DATA**

PC  
SN  
NN

**MINIMUM PARTICULARS TO APPEAR ON SMALL IMMEDIATE PACKAGING UNITS**

**Pre-filled syringes**

**1. NAME OF THE MEDICINAL PRODUCT**

Apexxnar suspension for injection  
IM

**2. METHOD OF ADMINISTRATION**

Shake well before use.

**3. EXPIRY DATE**

EXP

**4. BATCH NUMBER**

Lot

**5. CONTENT BY WEIGHT, BY VOLUME OR BY UNIT**

1 dose (0.5 mL)

**6. OTHER**

**B. PACKAGE LEAFLET**

## Package Leaflet: Information for the user

### Apexxnar suspension for injection

pneumococcal polysaccharide conjugate vaccine (20-valent, adsorbed)

▼ This medicine is subject to additional monitoring. This will allow quick identification of new safety information. You can help by reporting any side effects you may get. See the end of section 4 for how to report side effects.

**Read all of this leaflet carefully before you receive this vaccine because it contains important information for you.**

- Keep this leaflet. You may need to read it again.
- If you have any further questions, ask your doctor, pharmacist or nurse.
- This vaccine has been prescribed for you only. Do not pass it on to others.
- If you get any side effects, talk to your doctor, pharmacist or nurse. This includes any possible side effects not listed in this leaflet. See section 4.

#### What is in this leaflet

1. What Apexxnar is and what it is used for
2. What you need to know before you receive Apexxnar
3. How Apexxnar is given
4. Possible side effects
5. How to store Apexxnar
6. Contents of the pack and other information

#### 1. What Apexxnar is and what it is used for

Apexxnar is a pneumococcal vaccine given to:

- **individuals aged 18 years and older** to help prevent disease such as: pneumonia (lung infection), sepsis or bacteraemia (bacteria in the blood stream) and meningitis (inflammation around the brain) caused by 20 types of the bacteria *Streptococcus pneumoniae*.

Apexxnar provides protection against 20 types of *Streptococcus pneumoniae* bacteria.

The vaccine works by helping the body to make its own antibodies, which protect you against these diseases.

#### 2. What you need to know before you receive Apexxnar

##### Apexxnar should not be given

- if you are allergic (hypersensitive) to the active substances or to any of the other ingredients in this medicine (listed in section 6), or to any other vaccine that contains diphtheria toxoid.

#### Warnings and precautions

Talk to your doctor, pharmacist or nurse before the vaccination if you:

- have any present or past medical problems after any dose of Apexxnar such as an allergic reaction or problems with breathing,

- have a severe illness or high fever. However, a mild fever or upper respiratory infection (for example having a cold) itself is not a reason to delay vaccination,
- have any bleeding problems or bruise easily,
- have a weakened immune system (such as due to HIV infection); you may not get the full benefit from Apexxnar.

As with any vaccine, Apexxnar will not protect all persons who are vaccinated.

### **Other medicines/vaccines and Apexxnar**

Apexxnar may be given at the same time as the flu (inactivated influenza) vaccine at different injection sites. Depending on the individual risk assessment of your health care provider, separation of both vaccinations of e.g., 4 weeks might be advised.

Apexxnar can be given at the same time as the COVID-19 mRNA vaccine.

Tell your doctor, pharmacist or nurse if you are taking, have recently taken or might take any other medicines, or have recently received any other vaccine.

### **Pregnancy and breast-feeding**

If you are pregnant or breast-feeding, think you may be pregnant or are planning to have a baby, ask your doctor or pharmacist for advice before receiving this vaccine.

### **Driving and using machines**

Apexxnar has no or negligible influence on the ability to drive and use machines. However, some of the effects mentioned under section 4 “Possible side effects” may temporarily affect the ability to drive or use machines.

### **Apexxnar contains sodium**

This medicine contains less than 1 mmol sodium (23 mg) per dose, that is to say essentially ‘sodium-free’.

## **3. How Apexxnar is given**

The doctor or nurse will inject the recommended dose (0.5 mL) of the vaccine into your arm.

You should receive 1 injection.

Tell your doctor, pharmacist or nurse if you have been given a pneumococcal vaccine before.

If you have any further questions on the use of Apexxnar, ask your doctor, pharmacist or nurse.

#### 4. Possible side effects

Like all vaccines, Apexxnar can cause side effects, although not everybody gets them.

##### **Serious side effects**

Tell your doctor immediately if you notice signs of the following serious side effect (see also section 2):

swelling of the face, lips, mouth, tongue or throat (oedema), shortness of breath (dyspnoea), wheezing (bronchospasm) – these may be signs of a severe allergic reaction such as anaphylaxis, including shock.

##### **Other side effects**

**Very common:** may occur with more than 1 in 10 doses of the vaccine

- Headache.
- Joint pain and muscle pain.
- Pain/tenderness at injection site and tiredness.

**Common:** may occur up to 1 in 10 doses of the vaccine

- Swelling at injection site, redness at injection site and fever.

**Uncommon:** may occur up to 1 in 100 doses of the vaccine

- Diarrhoea, nausea, and vomiting.
- Rash and swelling of the face, lips, mouth, tongue or throat, which may cause difficulty in swallowing or breathing (angioedema).
- Itching at injection site, swollen glands in the neck, armpit or groin (lymphadenopathy), hives at the injection site (urticaria), and chills.

**The following side effects were seen with Prevenar 13 and may also be seen with Apexxnar:**

- A rash causing itchy red blotches (erythema multiforme).
- Irritation at injection site.
- Decreased appetite.
- Limitation of arm movement.

##### **Reporting of side effects**

If you get any side effects, talk to your doctor, pharmacist or nurse. This includes any possible side effects not listed in this leaflet. You can also report side effects directly via [the national reporting system](#) listed in [Appendix V](#). By reporting side effects you can help provide more information on the safety of this medicine.

## 5. How to store Apexxnar

Keep this medicine out of the sight and reach of children.

Do not use this medicine after the expiry date which is stated on the carton and label after EXP. The expiry date refers to the last day of that month.

Store in a refrigerator (2 °C to 8 °C).

Apexxnar should be used as soon as possible after being removed from refrigeration.

Do not freeze. Discard if vaccine has been frozen.

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 Apexxnar should be used or discarded. These data are intended to guide healthcare professionals in case of temporary temperature excursion only.

Pre-filled syringes should be stored in the refrigerator horizontally to minimise the resuspension time.

Do not throw away any medicines via wastewater or household waste. Ask your pharmacist how to throw away medicines you no longer use. These measures will help protect the environment.

## 6. Contents of the pack and other information

### What Apexxnar contains

The active substances are polysaccharide CRM<sub>197</sub> conjugates consisting of:

- 2.2 micrograms of polysaccharide for serotypes 1, 3, 4, 5, 6A, 7F, 8, 9V, 10A, 11A, 12F, 14, 15B, 18C, 19A, 19F, 22F, 23F and 33F
- 4.4 micrograms of polysaccharide for serotype 6B

One dose (0.5 mL) contains approximately 51 micrograms CRM<sub>197</sub> carrier protein, adsorbed on aluminium phosphate (0.125 mg aluminium).

The other ingredients are sodium chloride, succinic acid, polysorbate 80 and water for injections.

### What Apexxnar looks like and contents of the pack

The vaccine is a white suspension for injection, provided in a single-dose, pre-filled syringe (0.5 mL). It is provided in pack sizes of 1, 10 and 50, with or without needles. Not all pack sizes may be marketed.

### Marketing Authorisation Holder and Manufacturer

Marketing Authorisation Holder:  
Pfizer Europe MA EEIG  
Boulevard de la Plaine 17  
1050 Bruxelles  
Belgium

Manufacturer responsible for batch release:  
Pfizer Manufacturing Belgium N.V.  
Rijksweg 12  
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For any information about this medicine, please contact the local representative of the Marketing Authorisation Holder:

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This leaflet was last revised in <{MM/YYYY}>

**Other sources of information**

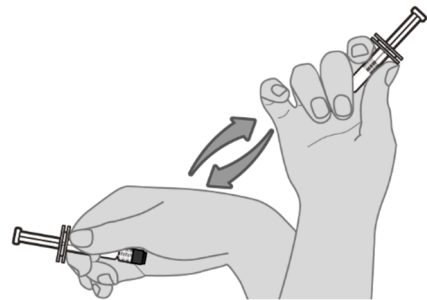
Detailed information on this product is available on the European Medicines Agency web site:  
<http://www.ema.europa.eu>.

**The following information is intended for healthcare professionals only:**

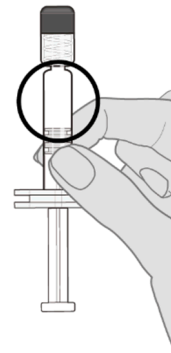
During storage, a white deposit and clear supernatant may be observed. This does not constitute a sign of deterioration. Pre-filled syringes should be stored horizontally to minimise the resuspension time.

**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 discoloration prior to administration. Do not use if large particulate matter or discoloration 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.

Administer the entire dose.

Apexxnar is for intramuscular use only.

Apexxnar must not be mixed with any other vaccines/medicinal products in the same syringe.

Apexxnar may be given to adults at the same time as the seasonal influenza vaccine (QIV; surface antigen, inactivated, adjuvanted). In individuals with underlying conditions associated with a high risk of developing life-threatening pneumococcal disease, consideration may be given to separating administrations of QIV and Apexxnar (e.g., by approximately 4 weeks). Different vaccination sites should be used.

Apexxnar can be given to adults at the same time as the COVID-19 mRNA vaccine (nucleoside modified).

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