ANNEX I

SUMMARY OF PRODUCT CHARACTERISTICS

1. NAME OF THE MEDICINAL PRODUCT

Prevenar suspension for injection
Pneumococcal saccharide conjugated vaccine, adsorbed

2. QUALITATIVE AND QUANTITATIVE COMPOSITION

Each 0.5 ml dose contains:

Pneumococcal polysaccharide serotype 4*	2 micrograms
Pneumococcal polysaccharide serotype 6B*	4 micrograms
Pneumococcal polysaccharide serotype 9V*	2 micrograms
Pneumococcal polysaccharide serotype 14*	2 micrograms
Pneumococcal polysaccharide serotype 18C*	2 micrograms
Pneumococcal polysaccharide serotype 19F*	2 micrograms
Pneumococcal polysaccharide serotype 23F*	2 micrograms

* Conjugated to the CRM_{197} carrier protein and adsorbed on aluminium phosphate (0.5 mg)

For a 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 against disease caused by *Streptococcus pneumoniae* serotypes 4, 6B, 9V, 14, 18C, 19F and 23F (including sepsis, meningitis, pneumonia, bacteraemia and acute otitis media) in infants and children from 2 months up to 5 years of age (see sections 4.2, 4.4 and 5.1).

For the number of doses to be administered in the different age groups, see section 4.2.

The use of Prevenar should be determined on the basis of official recommendations taking into consideration the impact of invasive disease in different age groups as well as variability of serotype epidemiology in different geographical areas (see sections 4.4, 4.8 and 5.1).

4.2 Posology and method of administration

Posology

The immunisation schedules for Prevenar should be based on official recommendations.

Infants aged 2 - 6 months:
The primary infant series consists of three doses, each of 0.5 ml, the first dose usually given at 2 months of age and with an interval of at least 1 month between doses. A fourth dose is recommended in the second year of life.

Alternatively, when Prevenar is given as part of a routine infant immunisation programme, a two-dose schedule may be considered. The first dose may be given from the age of 2 months with a second dose at least 2 months later and a third (booster) dose at 11-15 months of age (see section 5.1)

Previously unvaccinated older infants and children:
Infants aged 7 - 11 months: two doses, each of 0.5 ml, with an interval of at least 1 month between doses. A third dose is recommended in the second year of life.
Children aged 12 - 23 months: two doses, each of 0.5 ml, with an interval of at least 2 months between doses.
Children aged 24 months – 5 years: one single dose.

The need for a booster dose after these immunisation schedules has not been established.

Method of administration

The vaccine should be given by intramuscular injection. The preferred sites are anterolateral aspect of the thigh (vastus lateralis muscle) in infants or the deltoid muscle of the upper arm in young children.

4.3 Contraindications

Hypersensitivity to the active substances or to any of the excipients, or to diphtheria toxoid.

As with other vaccines, the administration of Prevenar should be postponed in subjects 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.

4.4 Special warnings and precautions for use

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

Do not administer Prevenar intravenously.

The potential risk of apnoea and the need for respiratory monitoring for 48-72h should be considered when administering the primary immunisation series to very premature infants (born ≤ 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.

Prevenar will not protect against other *Streptococcus pneumoniae* serotypes than those included in the vaccine nor other micro-organisms that cause invasive disease or otitis media.

This vaccine should not be given to infants or children with thrombocytopenia or any coagulation disorder that would contraindicate intramuscular injection unless the potential benefit clearly outweighs the risk of administration.

Although some antibody response to diphtheria toxoid may occur, immunisation with this vaccine does not substitute for routine diphtheria immunisation.

For children from 2 years through 5 years of age, a single dose immunisation schedule was used. A higher rate of local reactions has been observed in children older than 24 months of age compared with infants (see section 4.8).
Children with impaired immune responsiveness, whether due to the use of immunosuppressive therapy, a genetic defect, HIV infection, or other causes, may have reduced antibody response to active immunisation.

Limited data have demonstrated that Prevenar (three dose primary series) induces an acceptable immune response in infants with sickle cell disease with a safety profile similar to that observed in non-high-risk groups (see section 5.1). Safety and immunogenicity data are not yet available for children in other specific high-risk groups for invasive pneumococcal disease (e.g. children with another congenital or acquired splenic dysfunction, HIV-infected, malignancy, nephrotic syndrome). Vaccination in high-risk groups should be considered on an individual basis.

Children below 2 years old should receive the appropriate-for-age Prevenar vaccination series (see section 4.2). The use of pneumococcal conjugate vaccine does not replace the use of 23-valent pneumococcal polysaccharide vaccines in children ≥ 24 months of age with conditions (such as sickle cell disease, asplenia, HIV infection, chronic illness or who are immunocompromised) placing them at higher risk for invasive disease due to *Streptococcus pneumoniae*. Whenever recommended, children at risk who are ≥ 24 months of age and already primed with Prevenar should receive 23-valent pneumococcal polysaccharide vaccine. The interval between the pneumococcal conjugate vaccine (Prevenar) and the 23-valent pneumococcal polysaccharide vaccine should not be less than 8 weeks. There are no data available to indicate whether the administration of 23-valent pneumococcal polysaccharide vaccine to unprimed children or to children primed with Prevenar might result in hyporesponsiveness to further doses of Prevenar.

When Prevenar is co-administered with hexavalent vaccines (DTaP/Hib(PRP-T)/IPV/HepB), the physician should be aware that data from clinical studies indicate that the rate of febrile reactions was higher compared to that occurring following the administration of hexavalent vaccines alone. These reactions were mostly moderate (less than or equal to 39 °C) and transient (see section 4.8).

Antipyretic treatment should be initiated according to local treatment guidelines.

Prophylactic antipyretic medication is recommended:
- for all children receiving Prevenar simultaneously with vaccines containing whole cell pertussis because of higher rate of febrile reactions (see section 4.8).
- for children with seizure disorders or with a prior history of febrile seizures.

As with any vaccine, Prevenar may not protect all individuals receiving the vaccine from pneumococcal disease. Additionally, for vaccine serotypes, protection against otitis media is expected to be substantially lower than protection against invasive disease. As otitis media is caused by many organisms other than pneumococcal serotypes represented in the vaccine, protection against all otitis media is expected to be low (see section 5.1).

4.5 Interaction with other medicinal products and other forms of interaction

Prevenar can be administered simultaneously with other paediatric vaccines in accordance with the recommended immunisation schedules. Different injectable vaccines should always be given at different injection sites.

The immune response to routine paediatric vaccines co-administered with Prevenar at different injection sites was assessed in 7 controlled clinical studies. The antibody response to Hib tetanus protein conjugate (PRP-T), tetanus and Hepatitis B (HepB) vaccines was similar to controls. For CRM-based Hib conjugate vaccine, enhancement of antibody responses to Hib and diphtheria in the infant series was observed. At the booster, some suppression of Hib antibody level was observed but all children had protective levels. Inconsistent reduction in response to pertussis antigens as well as to inactivated polio vaccine (IPV) were observed. The clinical relevance of these interactions is unknown. Limited results from open label studies showed an acceptable response to MMR and varicella.

Data on concomitant administration of Prevenar with Infanrix hexa (DTaP/Hib(PRP-T)/IPV/HepB vaccine) have shown no clinically relevant interference in the antibody response to each of the individual antigens when given as a 3 dose primary vaccination.
Sufficient data regarding interference on the concomitant administration of other hexavalent vaccines with Prevenar are currently not available.

In a clinical trial that compared separate with concomitant administrations of Prevenar (three doses at 2, 3.5, 6 months and a booster dose at approximately 12 months) and Meningitec (meningococcal C conjugate vaccine; two doses at 2 and 6 months and a booster dose at approximately 12 months) there was no evidence of immune interference between the two conjugate vaccines after the primary series or after the booster doses.

4.6 Fertility, pregnancy and lactation

Prevenar is not intended for use in adults. Human data on the use during pregnancy or lactation and animal reproduction studies are not available.

4.7 Effects on ability to drive and use machines

Not relevant.

4.8 Undesirable effects

The safety of the vaccine was assessed in different controlled clinical studies in which more than 18,000 healthy infants (6 weeks to 18 months) were included. The majority of the safety experience comes from the efficacy trial in which 17,066 infants received 55,352 doses of Prevenar. Also safety in previously unvaccinated older children has been assessed.

In all studies, Prevenar was administered concurrently with the recommended childhood vaccines.

Amongst the most commonly reported adverse reactions were injection site reactions and fever.

No consistent increased local or systemic reactions within repeated doses were seen throughout the primary series or with the booster dose, the exceptions being a higher rate of transient tenderness (36.5 %) and tenderness that interfered with limb movement (18.5 %) were seen with the booster dose.

In older children receiving a single dose of vaccine, a higher rate of local reactions has been observed than that previously described in infancy. These reactions were primarily transient in nature. In a post licensure study involving 115 children between 2-5 years of age, tenderness was reported in up to 39.1 % of children; in 15.7 % of children the tenderness interfered with limb movement. Redness was reported in 40.0 % of children, and induration was reported in 32.2 % of subjects. Redness or induration $\geq$2cm in diameter was reported in 22.6 % and 13.9 % of children respectively.

When Prevenar is co-administered with hexavalent vaccines (DTaP/Hib(PRP-T)/IPV/HepB), fever $\geq$ 38 °C per dose was reported in 28.3 % to 48.3 % of infants in the group receiving Prevenar and the hexavalent vaccine at the same time as compared to 15.6 % to 23.4 % in the group receiving the hexavalent vaccine alone. Fever of greater than 39.5 °C per dose was observed in 0.6 to 2.8 % of infants receiving Prevenar and hexavalent vaccines (see section 4.4).

Reactogenicity was higher in children receiving whole cell pertussis vaccines concurrently. In a study, including 1,662 children, fever of $\geq$ 38 °C was reported in 41.2 % of children who received Prevenar simultaneously with DTP as compared to 27.9 % in the control group. Fever of > 39 °C was reported in 3.3 % of children compared to 1.2 % in the control group.

Adverse reactions reported in clinical trials or from the post-marketing experience are listed in the following table per system organ class and per frequency and this is for all age groups.

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)
Within each frequency grouping, undesirable effects are presented in order of decreasing seriousness.

Blood and lymphatic system disorders:
Very rare: Lymphadenopathy localised to the region of the injection site

Immune system disorders:
Rare: Hypersensitivity reactions such as anaphylactic/anaphylactoid reactions including shock, angioneurotic oedema, bronchospasm, dyspnoea, face oedema.

Nervous system disorders:
Rare: Seizures, including febrile seizures.

Gastrointestinal disorders:
Very common: Vomiting, diarrhoea, decreased appetite.

Skin and subcutaneous tissue disorders:
Uncommon: Rash/urticaria.
Very rare: Erythema multiforme.

General disorders and administration site conditions:
Very common: Injection site reactions (e.g. erythema, induration/swelling, pain/tenderness); fever ≥ 38 °C, irritability, crying, drowsiness, restless sleep.
Common: Injection site swelling/induration and erythema >2.4 cm, tenderness interfering with movement, fever > 39 °C.
Rare: Hypotonic hyporesponsive episode, injection site hypersensitivity reactions (eg., dermatitis, pruritus, urticaria), flushing.

Apnoea in very premature infants (≤ 28 weeks of gestation) (see section 4.4).

4.9 Overdose

There have been reports of overdose with Prevenar, including cases of administration of a higher than recommended dose and cases of subsequent doses administered closer than recommended to the previous dose. No undesirable effects were reported in the majority of individuals. In general, adverse reactions reported with overdose have also been reported with recommended single doses of Prevenar.

5. PHARMACOLOGICAL PROPERTIES

5.1 Pharmacodynamic properties

Pharmacotherapeutic group: pneumococcal vaccines, ATC code: J07AL02

Immunogenicity

Significant increases in antibody (measured by ELISA) were seen for all vaccine serotypes following a three-dose primary series of Prevenar in infants and following booster doses although geometric mean concentrations varied between the 7 serotypes. Prevenar has also been shown to elicit functional antibodies (measured by opsonophagocytosis) to all vaccine serotypes following the primary series. Long-term persistence of antibodies has not been investigated after administration of a primary series in infants plus booster or after administration of single priming doses to older children. Administration of unconjugated pneumococcal polysaccharides at 13 months following the primary series with Prevenar elicited an anamnestic antibody response for the 7 serotypes included in the vaccine, indicating that priming had occurred.

The immunogenicity of a two-dose primary series in infants plus a booster at about one year of age has been documented in several studies. Most of the data have indicated that smaller proportions of infants achieved antibody concentrations ≥0.35 µg/ml (the reference antibody concentration recommended by WHO)[1] against serotypes 6B and 23F after two-dose primary series when directly or indirectly compared with three-dose primary series. In addition, GMCs were lower for antibodies to most serotypes after a two-dose infant series than after a three-dose infant series. However, antibody response to booster doses in toddlers following two-dose or three-dose infant series were comparable for all 7 vaccine serotypes and indicated that both infant regimens had elicited adequate priming.

Significant increases in antibody (measured by ELISA) to all vaccine serotypes were seen after administration of single doses of Prevenar to children aged 2 to 5 years. Antibody concentrations were similar to those achieved following a three-dose infant series and a booster dose at less than 2 years of age. Efficacy trials in the 2- to 5-year-old population have not been conducted.

Clinical trial efficacy of the two-dose infant primary series plus a booster has not been established, and the clinical consequences of lower antibody concentrations against serotypes 6B and 23F after the two-dose infant series are not known.

Efficacy against invasive disease

Estimates of efficacy against invasive disease were obtained in the US population where vaccine serotype coverage ranged from 80 to 89 %. Epidemiological data between 1988 and 2003 indicated that in Europe coverage is lower and varies from country to country. Consequently, Prevenar should cover between 54 % and 84 % of isolates from invasive pneumococcal disease (IPD) in European children less than 2 years of age. In European children between 2 to 5 years of age, Prevenar should cover about 62 % to 83 % of the clinical isolates responsible for invasive pneumococcal disease. It is estimated that more than 80 % of the antimicrobial resistant strains would be covered by the serotypes included in the vaccine. The vaccine serotype coverage in the paediatric population decreases with increasing age. The decrease in the incidence of IPD seen in older children may be partly due to naturally acquired immunity.

Efficacy against invasive disease was assessed in a large-scale randomised, double-blind, clinical trial in a multiethnic population in Northern California (Kaiser Permanente trial). More than 37,816 infants were immunised with either Prevenar or a control vaccine (meningococcal conjugate group C vaccine), at 2, 4, 6 and 12-15 months of age. At the time of the study, the serotypes included in the vaccine accounted for 89 % of IPD.

A total of 52 cases of invasive disease caused by vaccine serotypes had accumulated in a blinded follow-up period through April 20, 1999. The estimate of vaccine serotype specific efficacy was 94 % (95 % CI: 81, 99) in the intent-to-treat population and 97 % (95 % CI: 85, 100) in the per protocol (fully immunized) population (40 cases). In Europe, the estimates of effectiveness in children less than 2 years of age range from 51 % to 79 % when considering vaccine coverage against serotypes causing invasive disease.

[1] WHO technical report No 927, 2005; Appendix serological criteria for calculation and licensure of new pneumococcal conjugate vaccine formulations for use in infants.

Efficacy against pneumonia

In the Kaiser Permanente trial, efficacy was 87.5 % (95 % CI: 7, 99) against bacteraemic pneumonia due to vaccine serotypes of *S. pneumoniae.*

Effectiveness (no microbiological confirmation of diagnosis was performed) against non-bacteraemic pneumonia was also assessed. As many pathogens other than pneumococcal serotypes represented in the vaccine may contribute to the burden of pneumonia in children, protection against all clinical pneumonia is expected to be lower than for invasive pneumococcal disease. In the per-protocol analysis, the estimated risk reduction for the first episode of clinical pneumonia with abnormal chest radiograph (defined as the presence of infiltrates, effusion or consolidation) was 35 % (95 % CI: 4, 56).

Efficacy against otitis media

Acute otitis media (AOM) is a common childhood disease with different aetiologies. Bacteria can be responsible for 60-70% of clinical episodes of AOM. The pneumococcus is responsible for 30-40% of all bacterial AOM and a greater fraction of severe AOM. Theoretically, Prevenar could prevent about 60-80% of serotypes causing pneumococcal AOM. It is estimated that Prevenar could prevent 6-13% of all clinical episodes of AOM.

Efficacy of Prevenar against acute otitis media (AOM) was assessed in a randomised, double blind, clinical trial of 1,662 Finnish infants immunised with either Prevenar or a control vaccine (Hepatitis B vaccine), at 2, 4, 6 and 12-15 months of age. The estimate for vaccine efficacy against vaccine-serotype AOM, the primary endpoint of the trial, was 57 % (95 % CI: 44, 67) in the per-protocol analysis and 54 % (95 % CI: 41, 64) in the intent-to-treat analysis. A 33 % (95 % CI: -1, 80) increase in AOM due to serogroups not included in the vaccine was observed in immunised subjects. However, the overall benefit was a 34 % (95 % CI: 21, 45) reduction in the incidence of all pneumococcal AOM. The impact of the vaccine on total number of episodes of otitis media regardless of etiology was a 6 % (95 % CI: -4, 16) reduction.

A subset of children in this study were followed until they reached 4 to 5 years of age. In this follow-up, vaccine efficacy for frequent OM (defined as at least 3 episodes within 6 months) was 18 % (95 % CI: 1, 32), for chronic otitis media with effusion, 50 % (95 % CI: 15, 71), and for tympanostomy tube placement, 39 % (95 % CI: 4, 61).

Efficacy of Prevenar against AOM was assessed as a secondary endpoint in the Kaiser Permanente trial. Children were followed until 3.5 years of age. The impact of the vaccine on total number of episodes of otitis media regardless of etiology was a 7 % reduction (95 % CI: 4, 10). The effect of the vaccine in the per-protocol analysis was a 9 % reduction (95 % CI: 3, 15) in recurrent AOM (defined as 3 episodes in six months or 4 episodes in one year) or a 23 % (95 % CI: 7, 36) reduction for recurrent AOM (5 episodes in six months or 6 episodes in one year). Tympanostomy tube placement was reduced by 24 % (95 % CI: 12, 35) in the per protocol analysis and by 23 % (95 % CI: 11, 34) in the intent-to-treat analysis.

Effectiveness

The effectiveness of Prevenar against IPD (i.e. comprising the protection afforded by vaccination and from herd immunity due to reduced transmission of vaccine serotypes in the population) has been evaluated in national immunisation programmes that employ three-dose or two-dose infant series, each with booster doses.

In the USA, generalised vaccination with Prevenar using a four-dose series in infants and a catch-up programme for children up to 5 years of age was introduced in 2000. Vaccine effectiveness against IPD caused by vaccine serotypes was evaluated in 3- to 59-month old children within the first four years of the

implementation of the programme. When compared with no vaccination, point estimates for the effectiveness of 2-, 3-, or 4-doses given on an infant schedule were similar: 96% (95% CI 88-99); 95% (95% CI 88-99); and 100% (95% CI 94-100), respectively. In the USA in the same time frame, there was a 94% reduction in vaccine type IPD in individuals under 5 years of age, compared to a pre-vaccine baseline (1998/99). In parallel, there was a 62% reduction in vaccine type IPD in individuals over 5 years of age. This indirect or herd effect is due to a reduction in transmission of vaccine serotypes from immunised young children to the rest of the population and coincides with decreased nasopharyngeal carriage of vaccine serotypes.

In Quebec, Canada Prevenar was introduced at 2, 4 and 12 months of age with a single dose catch-up programme in children up to 5 years of age. In the first two years of the programme, with over 90% coverage, the observed effectiveness against IPD caused by vaccine serotypes was 93% (95% CI 75-98) for the 2 dose infant series and 100% (95% CI 91-100) for the completed schedule.

Preliminary data from England and Wales reported less than 1 year following introduction of routine immunisation at 2, 4 and 13 months with a single dose catch-up programme for children 18 to 23 months of age have suggested that effectiveness of this schedule might be lower against serotype 6B than against the other serotypes in the vaccine.
The effectiveness of a two-dose primary series has not been established against pneumonia or acute otitis media.

Additional immunogenicity data

The immunogenicity of Prevenar has been investigated in an open label, multicenter study in 49 infants with sickle cell disease. Children were vaccinated with Prevenar (3 doses one month apart from the age of 2 months) and 46 of these children also received a 23-valent pneumococcal polysaccharide vaccine at the age of 15-18 months. After primary immunisation, 95.6% of the subjects had antibody levels of at least 0.35 µg/ml for all seven serotypes found in Prevenar. A significant increase was seen in the concentrations of antibodies against the seven serotypes after the polysaccharide vaccination, suggesting that immunological memory was well established.

5.2 Pharmacokinetic properties

Not applicable.

5.3 Preclinical safety data

A repeated dose intramuscular toxicity study (13 weeks, 5 injections, one every three weeks) of pneumococcal conjugate vaccine in rabbits revealed no evidence of any significant local or systemic toxic effects.

Repeated dose subcutaneous toxicity studies (13 weeks, 7 injections of the clinical dose, one every other week, followed by a 4-week recovery period) of Prevenar in rats and monkeys revealed no evidence of any significant local or systemic toxic effects.

6 PHARMACEUTICAL PARTICULARS

6.1 List of excipients

Sodium chloride
Water for injections

6.2 Incompatibilities

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

6.3 Shelf life

3 years

6.4 Special precautions for storage

Store in a refrigerator (2°C – 8°C).
Do not freeze.

6.5 Nature and contents of container

0.5 ml suspension for injection in vial (Type I glass) with a grey butyl rubber stopper.

Pack sizes:
1 or 10 vials without syringe/needles.

1 vial with syringe and 2 needles (1 for withdrawal, 1 for injection).

Not all pack sizes may be marketed.

6.6 Special precautions for disposal and other handling

Upon storage, a white deposit and clear supernatant can be observed.

The vaccine should be well shaken to obtain a homogeneous white suspension and be inspected visually for any particulate matter and/or variation of physical aspect prior to administration. Do not use if the content appears otherwise.

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

7. MARKETING AUTHORISATION HOLDER

Pfizer Limited
Ramsgate Road
Sandwich
Kent CT13 9NJ
United Kingdom

8. MARKETING AUTHORISATION NUMBER(S)

EU/1/00/167/001
EU/1/00/167/002
EU/1/00/167/005

9. DATE OF FIRST AUTHORISATION/RENEWAL OF THE AUTHORISATION

Date of first authorisation: 02/02/2001
Date of last renewal: 02/02/2011

10. DATE OF REVISION OF THE TEXT

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

1. NAME OF THE MEDICINAL PRODUCT

Prevenar suspension for injection in pre-filled syringe
Pneumococcal saccharide conjugated vaccine, adsorbed

2. QUALITATIVE AND QUANTITATIVE COMPOSITION

Each 0.5 ml dose contains:

Pneumococcal polysaccharide serotype 4*	2 micrograms
Pneumococcal polysaccharide serotype 6B*	4 micrograms
Pneumococcal polysaccharide serotype 9V*	2 micrograms
Pneumococcal polysaccharide serotype 14*	2 micrograms
Pneumococcal polysaccharide serotype 18C*	2 micrograms
Pneumococcal polysaccharide serotype 19F*	2 micrograms
Pneumococcal polysaccharide serotype 23F*	2 micrograms

* Conjugated to the CRM_{197} carrier protein and adsorbed on aluminium phosphate (0.5 mg)

For a full list of excipients, see section 6.1.

3. PHARMACEUTICAL FORM

Suspension for injection in pre-filled syringe.

The vaccine is a homogeneous white suspension.

4. CLINICAL PARTICULARS

4.1 Therapeutic indications

Active immunisation against disease caused by *Streptococcus pneumoniae* serotypes 4, 6B, 9V, 14, 18C, 19F and 23F (including sepsis, meningitis, pneumonia, bacteraemia and acute otitis media) in infants and children from 2 months up to 5 years of age (see sections 4.2, 4.4 and 5.1).

For the number of doses to be administered in the different age groups, see section 4.2.

The use of Prevenar should be determined on the basis of official recommendations taking into consideration the impact of invasive disease in different age groups as well as variability of serotype epidemiology in different geographical areas (see sections 4.4, 4.8 and 5.1).

4.2 Posology and method of administration

Posology
The immunisation schedules for Prevenar should be based on official recommendations.

Infants aged 2 - 6 months:
The primary infant series consists of three doses, each of 0.5 ml, the first dose usually given at 2 months of age and with an interval of at least 1 month between doses. A fourth dose is recommended in the second year of life.

Alternatively, when Prevenar is given as part of a routine infant immunisation programme, a two-dose schedule may be considered. The first dose may be given from the age of 2 months with a second dose at least 2 months later and a third (booster) dose at 11-15 months of age (see section 5.1)

Previously unvaccinated older infants and children:
Infants aged 7 - 11 months: two doses, each of 0.5 ml, with an interval of at least 1 month between doses. A third dose is recommended in the second year of life.
Children aged 12 - 23 months: two doses, each of 0.5 ml, with an interval of at least 2 months between doses.
Children aged 24 months – 5 years: one single dose.

The need for a booster dose after these immunisation schedules has not been established.

Method of administration

The vaccine should be given by intramuscular injection. The preferred sites are anterolateral aspect of the thigh (vastus lateralis muscle) in infants or the deltoid muscle of the upper arm in young children.

4.3 Contraindications

Hypersensitivity to the active substances or to any of the excipients, or to diphtheria toxoid.

As with other vaccines, the administration of Prevenar should be postponed in subjects 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.

4.4 Special warnings and precautions for use

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

Do not administer Prevenar intravenously.

The potential risk of apnoea and the need for respiratory monitoring for 48-72h should be considered when administering the primary immunisation series to very premature infants (born ≤ 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.

Prevenar will not protect against other *Streptococcus pneumoniae* serotypes than those included in the vaccine nor other micro-organisms that cause invasive disease or otitis media.

This vaccine should not be given to infants or children with thrombocytopenia or any coagulation disorder that would contraindicate intramuscular injection unless the potential benefit clearly outweighs the risk of administration.

Although some antibody response to diphtheria toxoid may occur, immunisation with this vaccine does not substitute for routine diphtheria immunisation.

For children from 2 years through 5 years of age, a single dose immunisation schedule was used. A higher rate of local reactions has been observed in children older than 24 months of age compared with infants (see section 4.8).

Children with impaired immune responsiveness, whether due to the use of immunosuppressive therapy, a genetic defect, HIV infection, or other causes, may have reduced antibody response to active immunisation.

Limited data have demonstrated that Prevenar (three dose primary series) induces an acceptable immune response in infants with sickle cell disease with a safety profile similar to that observed in non-high-risk groups (see section 5.1). Safety and immunogenicity data are not yet available for children in other specific high-risk groups for invasive pneumococcal disease (e.g. children with another congenital or acquired splenic dysfunction, HIV-infected, malignancy, nephrotic syndrome). Vaccination in high-risk groups should be considered on an individual basis.

Children below 2 years old should receive the appropriate-for-age Prevenar vaccination series (see section 4.2). The use of pneumococcal conjugate vaccine does not replace the use of 23-valent pneumococcal polysaccharide vaccines in children ≥ 24 months of age with conditions (such as sickle cell disease, asplenia, HIV infection, chronic illness or who are immunocompromised) placing them at higher risk for invasive disease due to *Streptococcus pneumoniae*. Whenever recommended, children at risk who are ≥ 24 months of age and already primed with Prevenar should receive 23-valent pneumococcal polysaccharide vaccine. The interval between the pneumococcal conjugate vaccine (Prevenar) and the 23-valent pneumococcal polysaccharide vaccine should not be less than 8 weeks. There are no data available to indicate whether the administration of 23-valent pneumococcal polysaccharide vaccine to unprimed children or to children primed with Prevenar might result in hyporesponsiveness to further doses of Prevenar.

When Prevenar is co-administered with hexavalent vaccines (DTaP/Hib(PRP-T)/IPV/HepB), the physician should be aware that data from clinical studies indicate that the rate of febrile reactions was higher compared to that occurring following the administration of hexavalent vaccines alone. These reactions were mostly moderate (less than or equal to 39 °C) and transient (see section 4.8).

Antipyretic treatment should be initiated according to local treatment guidelines.

Prophylactic antipyretic medication is recommended:
- for all children receiving Prevenar simultaneously with vaccines containing whole cell pertussis because of higher rate of febrile reactions (see section 4.8).
- for children with seizure disorders or with a prior history of febrile seizures.

As with any vaccine, Prevenar may not protect all individuals receiving the vaccine from pneumococcal disease. Additionally, for vaccine serotypes, protection against otitis media is expected to be substantially lower than protection against invasive disease. As otitis media is caused by many organisms other than pneumococcal serotypes represented in the vaccine, protection against all otitis media is expected to be low (see section 5.1).

4.5 Interaction with other medicinal products and other forms of interaction

Prevenar can be administered simultaneously with other paediatric vaccines in accordance with the recommended immunisation schedules. Different injectable vaccines should always be given at different injection sites.

The immune response to routine paediatric vaccines co-administered with Prevenar at different injection sites was assessed in 7 controlled clinical studies. The antibody response to Hib tetanus protein conjugate (PRP-T), tetanus and Hepatitis B (HepB) vaccines was similar to controls. For CRM-based Hib conjugate vaccine, enhancement of antibody responses to Hib and diphtheria in the infant series was observed. At the booster, some suppression of Hib antibody level was observed but all children had protective levels. Inconsistent reduction in response to pertussis antigens as well as to inactivated polio vaccine (IPV) were

observed. The clinical relevance of these interactions is unknown. Limited results from open label studies showed an acceptable response to MMR and varicella.

Data on concomitant administration of Prevenar with Infanrix hexa (DTaP/Hib(PRP-T)/IPV/HepB vaccine) have shown no clinically relevant interference in the antibody response to each of the individual antigens when given as a 3 dose primary vaccination.
Sufficient data regarding interference on the concomitant administration of other hexavalent vaccines with Prevenar are currently not available.

In a clinical trial that compared separate with concomitant administrations of Prevenar (three doses at 2, 3.5, 6 months and a booster dose at approximately 12 months) and Meningitec (meningococcal C conjugate vaccine; two doses at 2 and 6 months and a booster dose at approximately 12 months) there was no evidence of immune interference between the two conjugate vaccines after the primary series or after the booster doses.

4.6 Fertility, pregnancy and lactation

Prevenar is not intended for use in adults. Human data on the use during pregnancy or lactation and animal reproduction studies are not available.

4.7 Effects on ability to drive and use machines

Not relevant.

4.8 Undesirable effects

The safety of the vaccine was assessed in different controlled clinical studies in which more than 18,000 healthy infants (6 weeks to 18 months) were included. The majority of the safety experience comes from the efficacy trial in which 17,066 infants received 35,352 doses of Prevenar. Also safety in previously unvaccinated older children has been assessed.

In all studies, Prevenar was administered concurrently with the recommended childhood vaccines.

Amongst the most commonly reported adverse reactions were injection site reactions and fever.

No consistent increased local or systemic reactions within repeated doses were seen throughout the primary series or with the booster dose, the exceptions being a higher rate of transient tenderness (36.5 %) and tenderness that interfered with limb movement (18.5 %) were seen with the booster dose.

In older children receiving a single dose of vaccine, a higher rate of local reactions has been observed than that previously described in infancy. These reactions were primarily transient in nature. In a post licensure study involving 715 children between 2-5 years of age, tenderness was reported in 39.1 % of children; in 15.7 % of children the tenderness interfered with limb movement. Redness was reported in 40.0 % of children and induration was reported in 32.2 % of subjects. Redness or induration $\geq$2cm in diameter was reported in 22.6 % and 13.9% of children respectively.

When Prevenar is co-administered with hexavalent vaccines (DTaP/Hib(PRP-T)/IPV/HepB), fever $\geq$ 38 °C per dose was reported in 28.3 % to 48.3 % of infants in the group receiving Prevenar and the hexavalent vaccine at the same time as compared to 15.6 % to 23.4 % in the group receiving the hexavalent vaccine alone. Fever of greater than 39.5 °C per dose was observed in 0.6 to 2.8 % of infants receiving Prevenar and hexavalent vaccines (see section 4.4).

Reactogenicity was higher in children receiving whole cell pertussis vaccines concurrently. In a study, including 1,662 children, fever of $\geq$ 38 °C was reported in 41.2 % of children who received Prevenar

simultaneously with DTP as compared to 27.9 % in the control group. Fever of > 39 °C was reported in 3.3 % of children compared to 1.2 % in the control group.

Adverse reactions reported in clinical trials or from the post-marketing experience are listed in the following table per system organ class and per frequency and this is for all age groups.

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)

Within each frequency grouping, undesirable effects are presented in order of decreasing seriousness

Blood and lymphatic system disorders:
Very rare: Lymphadenopathy localised to the region of the injection site

Immune system disorders:
Rare: Hypersensitivity reactions such as, anaphylactic/anaphylactoid reactions including shock, angioneurotic oedema, bronchospasm, dyspnoea, face oedema.

Nervous system disorders:
Rare: Seizures, including febrile seizures.

Gastrointestinal disorders:
Very common: Vomiting, diarrhoea, decreased appetite.

Skin and subcutaneous tissue disorders:
Uncommon: Rash/urticaria.
Very rare: Erythema multiforme.

General disorders and administration site conditions:
Very common: Injection site reactions (e.g. erythema, induration/swelling, pain/tenderness); fever ≥ 38 °C, irritability, crying, drowsiness, restless sleep.
Common: Injection site swelling/induration and erythema >2.4 cm, tenderness interfering with movement, fever > 39 °C.
Rare: Hypotonic hyporesponsive episode, injection site hypersensitivity reactions (eg., dermatitis, pruritus, urticaria), flushing.

Apnoea in very premature infants (≤ 28 weeks of gestation) (see section 4.4).

4.9 Overdose

There have been reports of overdose with Prevenar, including cases of administration of a higher than recommended dose and cases of subsequent doses administered closer than recommended to the previous dose. No undesirable effects were reported in the majority of individuals. In general, adverse reactions reported with overdose have also been reported with recommended single doses of Prevenar.

5. PHARMACOLOGICAL PROPERTIES

5.1 Pharmacodynamic properties

Pharmacotherapeutic group: pneumococcal vaccines, ATC code: J07AL02

Immunogenicity

Significant increases in antibody (measured by ELISA) were seen for all vaccine serotypes following a three-dose primary series of Prevenar in infants and following booster doses although geometric mean concentrations varied between the 7 serotypes. Prevenar has also been shown to elicit functional antibodies (measured by opsonophagocytosis) to all vaccine serotypes following the primary series. Long-term persistence of antibodies has not been investigated after administration of a primary series in infants plus booster or after administration of single priming doses to older children. Administration of unconjugated pneumococcal polysaccharides at 13 months following the primary series with Prevenar elicited an anamnestic antibody response for the 7 serotypes included in the vaccine, indicating that priming had occurred.

The immunogenicity of a two-dose primary series in infants plus a booster at about one year of age has been documented in several studies. Most of the data have indicated that smaller proportions of infants achieved antibody concentrations ≥0.35 µg/ml (the reference antibody concentration recommended by WHO)[2] against serotypes 6B and 23F after two-dose primary series when directly or indirectly compared with three-dose primary series. In addition, GMCs were lower for antibodies to most serotypes after a two-dose infant series than after a three-dose infant series. However, antibody responses to booster doses in toddlers following two-dose or three-dose infant series were comparable for all 7 vaccine serotypes and indicated that both infant regimens had elicited adequate priming.
Significant increases in antibody (measured by ELISA) to all vaccine serotypes were seen after administration of single doses of Prevenar to children aged 2 to 5 years. Antibody concentrations were similar to those achieved following a three-dose infant series and a booster dose at less than 2 years of age. Efficacy trials in the 2- to 5-year-old population have not been conducted.

Clinical trial efficacy of the two-dose infant primary series plus a booster has not been established, and the clinical consequences of lower antibody concentrations against serotypes 6B and 23F after the two-dose infant series are not known.

Efficacy against invasive disease

Estimates of efficacy against invasive disease were obtained in the US population where vaccine serotype coverage ranged from 80 to 89 %. Epidemiological data between 1988 and 2003 indicated that in Europe coverage is lower and varies from country to country. Consequently, Prevenar should cover between 54 % and 84 % of isolates from invasive pneumococcal disease (IPD) in European children less than 2 years of age. In European children between 2 to 5 years of age, Prevenar should cover about 62 % to 83 % of the clinical isolates responsible for invasive pneumococcal disease. It is estimated that more than 80 % of the antimicrobial resistant strains would be covered by the serotypes included in the vaccine. The vaccine serotype coverage in the paediatric population decreases with increasing age. The decrease in the incidence of IPD seen in older children may be partly due to naturally acquired immunity.

Efficacy against invasive disease was assessed in a large-scale randomised, double-blind, clinical trial in a multiethnic population in Northern California (Kaiser Permanente trial). More than 37,816 infants were immunised with either Prevenar or a control vaccine (meningococcal conjugate group C vaccine), at 2, 4,

[2] WHO technical report No 927, 2005; Appendix serological criteria for calculation and licensure of new pneumococcal conjugate vaccine formulations for use in infants.

6 and 12-15 months of age. At the time of the study, the serotypes included in the vaccine accounted for 89 % of IPD.
A total of 52 cases of invasive disease caused by vaccine serotypes had accumulated in a blinded follow-up period through April 20, 1999. The estimate of vaccine serotype specific efficacy was 94 % (95 % CI: 81, 99) in the intent-to-treat population and 97 % (95 % CI: 85, 100) in the per protocol (fully immunised) population (40 cases). In Europe, the estimates of effectiveness in children less than 2 years of age range from 51 % to 79 % when considering vaccine coverage against serotypes causing invasive disease.

Efficacy against pneumonia

In the Kaiser Permanente trial, efficacy was 87.5 % (95 % CI: 7, 99) against bacteraemic pneumonia due to vaccine serotypes of *S. pneumoniae.*

Effectiveness (no microbiological confirmation of diagnosis was performed) against non-bacteraemic pneumonia was also assessed. As many pathogens other than pneumococcal serotypes represented in the vaccine may contribute to the burden of pneumonia in children, protection against all clinical pneumonia is expected to be lower than for invasive pneumococcal disease. In the per-protocol analysis, the estimated risk reduction for the first episode of clinical pneumonia with abnormal chest radiograph (defined as the presence of infiltrates, effusion or consolidation) was 35 % (95 % CI: 4, 56).

Efficacy against otitis media

Acute otitis media (AOM) is a common childhood disease with different aetiologies. Bacteria can be responsible for 60-70% of clinical episodes of AOM. The pneumococcus is responsible for 30-40% of all bacterial AOM and a greater fraction of severe AOM. Theoretically, Prevenar could prevent about 60-80% of serotypes causing pneumococcal AOM. It is estimated that Prevenar could prevent 6-13% of all clinical episodes of AOM.

Efficacy of Prevenar against acute otitis media (AOM) was assessed in a randomised, double blind, clinical trial of 1,662 Finnish infants immunised with either Prevenar or a control vaccine (Hepatitis B vaccine), at 2, 4, 6 and 12-15 months of age. The estimate for vaccine efficacy against vaccine-serotype AOM, the primary endpoint of the trial, was 57 % (95 % CI: 44, 67) in the per-protocol analysis and 54 % (95 % CI: 41, 64) in the intent-to-treat analysis. A 33 % (95 % CI: -1, 80) increase in AOM due to serogroups not included in the vaccine was observed in immunised subjects. However, the overall benefit was a 34 % (95 % CI: 21, 45) reduction in the incidence of all pneumococcal AOM. The impact of the vaccine on total number of episodes of otitis media regardless of etiology was a 6 % (95 % CI: -4, 16) reduction.

A subset of children in this study were followed until they reached 4 to 5 years of age. In this follow-up, vaccine efficacy for frequent OM (defined as at least 3 episodes within 6 months) was 18 % (95 % CI: 1, 32), for chronic otitis media with effusion, 50 % (95 % CI: 15, 71), and for tympanostomy tube placement, 39 % (95 % CI: 4, 61).

Efficacy of Prevenar against AOM was assessed as a secondary endpoint in the Kaiser Permanente trial. Children were followed until 3.5 years of age. The impact of the vaccine on total number of episodes of otitis media regardless of etiology was a 7 % reduction (95 % CI: 4, 10). The effect of the vaccine in the per-protocol analysis was a 9 % reduction (95 % CI: 3, 15) in recurrent AOM (defined as 3 episodes in six months or 4 episodes in one year) or a 23 % (95 % CI: 7,36) reduction for recurrent AOM (5 episodes in six months or 6 episodes in one year). Tympanostomy tube placement was reduced by 24 % (95 % CI: 12, 35) in the per-protocol analysis and by 23 % (95 % CI: 11, 34) in the intent-to-treat analysis.

Effectiveness

The effectiveness of Prevenar against IPD (i.e. comprising the protection afforded by vaccination and from herd immunity due to reduced transmission of vaccine serotypes in the population) has been evaluated in national immunisation programmes that employ three-dose or two-dose infant series, each with booster doses.

In the USA, generalised vaccination with Prevenar using a four-dose series in infants and a catch-up programme for children up to 5 years of age was introduced in 2000. Vaccine effectiveness against IPD caused by vaccine serotypes was evaluated in 3- to 59-month old children within the first four years of the implementation of the programme. When compared with no vaccination, point estimates for the effectiveness of 2-, 3-, or 4-doses given on an infant schedule were similar: 96% (95% CI 88-99); 95% (95% CI 88-99); and 100% (95% CI 94-100), respectively. In the USA in the same time frame, there was a 94% reduction in vaccine type IPD in individuals under 5 years of age, compared to a pre-vaccine baseline (1998/99). In parallel, there was a 62% reduction in vaccine type IPD in individuals over 5 years of age. This indirect or herd effect is due to a reduction in transmission of vaccine serotypes from immunised young children to the rest of the population and coincides with decreased nasopharyngeal carriage of vaccine serotypes.

In Quebec, Canada Prevenar was introduced at 2, 4 and 12 months of age with a single dose catch-up programme in children up to 5 years of age. In the first two years of the programme, with over 90% coverage, the observed effectiveness against IPD caused by vaccine serotypes was 93% (95% CI 75-98) for the 2 dose infant series and 100% (95% CI 91-100) for the completed schedule.

Preliminary data from England and Wales reported less than 1 year following introduction of routine immunisation at 2, 4 and 13 months with a single dose catch-up programme for children 13 to 23 months of age have suggested that effectiveness of this schedule might be lower against serotype 6B than against the other serotypes in the vaccine.

The effectiveness of a two-dose primary series has not been established against pneumonia or acute otitis media.

Additional immunogenicity data

The immunogenicity of Prevenar has been investigated in an open-label, multicenter study in 49 infants with sickle cell disease. Children were vaccinated with Prevenar (3 doses one month apart from the age of 2 months) and 46 of these children also received a 23-valent pneumococcal polysaccharide vaccine at the age of 15-18 months. After primary immunisation, 95.6% of the subjects had antibody levels of at least 0.35 µg/ml for all seven serotypes found in Prevenar. A significant increase was seen in the concentrations of antibodies against the seven serotypes after the polysaccharide vaccination, suggesting that immunological memory was well established.

5.2 Pharmacokinetic properties

Not applicable

5.3 Preclinical safety data

A repeated dose intramuscular toxicity study (13 weeks, 5 injections, one every three weeks) of pneumococcal conjugate vaccine in rabbits revealed no evidence of any significant local or systemic toxic effects.

Repeated dose subcutaneous toxicity studies (13 weeks, 7 injections of the clinical dose, one every other week, followed by a 4-week recovery period) of Prevenar in rats and monkeys revealed no evidence of any significant local or systemic toxic effects.

6. PHARMACEUTICAL PARTICULARS

6.1 List of excipients

Sodium chloride
Water for injections

6.2 Incompatibilities

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

6.3 Shelf life

4 years

6.4 Special precautions for storage

Store in a refrigerator (2°C – 8°C).
Do not freeze.

6.5 Nature and contents of container

0.5 ml suspension for injection in pre-filled syringe (Type I glass) with a plunger rod (polypropylene), a plunger stopper (latex free grey butyl rubber) and a protective-tip cap (latex free grey butyl rubber) -

Pack sizes:
1 or 10 pre- filled syringes with or without needle
Multi pack of 5 packs of 10 pre-filled syringes without needle.

Not all pack sizes may be marketed.

6.6 Special precautions for disposal and other handling

Upon storage, a white deposit and clear supernatant can be observed.

The vaccine should be well shaken to obtain a homogeneous white suspension and be inspected visually for any particulate matter and/or variation of physical aspect prior to administration. Do not use if the content appears otherwise.

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

7. MARKETING AUTHORISATION HOLDER

Pfizer Limited
Ramsgate Road
Sandwich
Kent CT13 9NJ
United Kingdom

8. MARKETING AUTHORISATION NUMBER(S)

EU/1/00/167/003
EU/1/00/167/004
EU/1/00/167/006
EU/1/00/167/007
EU/1/00/167/008

9. DATE OF FIRST AUTHORISATION/RENEWAL OF THE AUTHORISATION

Date of first authorisation: 02/02/2001
Date of last renewal: 02/02/2011

10. DATE OF REVISION OF THE TEXT

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

ANNEX II

A. MANUFACTURERS OF THE BIOLOGICAL ACTIVE SUBSTANCES AND MANUFACTURING AUTHORISATION HOLDER RESPONSIBLE FOR BATCH RELEASE

B. CONDITIONS OF THE MARKETING AUTHORISATION

A. MANUFACTURERS OF THE BIOLOGICAL ACTIVE SUBSTANCES AND MANUFACTURING AUTHORISATION HOLDER RESPONSIBLE FOR BATCH RELEASE

Name and address of the manufacturers of the biological active substances

CRM_{197}, Activated Saccharides, and Conjugates
Wyeth Pharmaceuticals, Division of Wyeth Holdings Corporation
4300 Oak Park
NC 27330, Sanford, USA

Pneumococcal Polysaccharides
Wyeth Pharmaceuticals, Division of Wyeth Holdings Corporation
401 North Middletown Road
NY 10965, Pearl River, USA

Name and address of the manufacturer responsible for batch release

John Wyeth & Brother Ltd.
Huntercombe Lane South
Taplow, Maidenhead
Berkshire, SL6 0PH
United Kingdom

B. CONDITIONS OF THE MARKETING AUTHORISATION

- **CONDITIONS OR RESTRICTIONS REGARDING SUPPLY AND USE IMPOSED ON THE MARKETING AUTHORISATION HOLDER**

Medicinal product subject to medical prescription.

- **CONDITIONS AND RESTRICTIONS WITH REGARD TO THE SAFE AND EFFECTIVE USE OF THE MEDICINAL PRODUCT**

Not applicable.

- **OTHER CONDITIONS**

Pharmacovigilance system
The marketing authorisation holder must ensure that the system of pharmacovigilance presented in Module 1.8.1. of the Marketing Authorisation, is in place and functioning before and whilst the product is on the market.

PSURs
The marketing authorisation holder shall submit periodic safety update reports for this product in accordance with the requirements set out in the list of Union reference dates (EURD list) provided for under Article 107c(7) of Directive 2001/83/EC and published on the European medicines web-portal.

Official batch release: in accordance with Article 114 of Council Directive 2001/83/EC as amended, the official batch release will be undertaken by a state laboratory or a laboratory designated for that purpose.

Official Medicines Control Laboratory (OMCL)
Agence Française de Sécurité Sanitaire des Produits de Santé
Direction des laboratoires et des contrôles
Avenue Jean Jaurès, 321
F - 69007 Lyon
France

ANNEX III

LABELLING AND PACKAGE LEAFLET

A. LABELLING

PARTICULARS TO APPEAR ON THE OUTER PACKAGING

OUTER CARTON TEXT – 1 vial pack

1. NAME OF THE MEDICINAL PRODUCT

Prevenar suspension for injection
Pneumococcal saccharide conjugated vaccine, adsorbed

2. STATEMENT OF ACTIVE SUBSTANCE(S)

Each 0.5 ml dose contains 2 micrograms of saccharide for serotypes 4, 9V, 14, 18C, 19F, and 23F, and 4 micrograms of serotype 6B per dose (16 micrograms total saccharide) conjugated to CRM_{197} carrier protein and adsorbed on aluminium phosphate (0.5 mg).

3. LIST OF EXCIPIENTS

Also contains sodium chloride and water for injections.

4. PHARMACEUTICAL FORM AND CONTENTS

Suspension for injection.
1 single-dose (0.5 ml) vial.

5. METHOD AND ROUTE(S) OF ADMINISTRATION

Intramuscular use.
Shake well before use.
Read the package leaflet before use.

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

Keep out of the reach and sight of children.

7. OTHER SPECIAL WARNING(S), IF NECESSARY

Do not inject intravenously.

8. EXPIRY DATE

EXP:

9. SPECIAL STORAGE CONDITIONS

Store in a refrigerator.
Do not freeze.

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 Limited
Ramsgate Road
Sandwich
Kent CT13 9NJ
United Kingdom

12. MARKETING AUTHORISATION NUMBER(S)

EU/1/00/167/001

13. BATCH NUMBER

Lot:

14. GENERAL CLASSIFICATION FOR SUPPLY

Medicinal product subject to medical prescription.

15. INSTRUCTIONS ON USE

16. INFORMATION IN BRAILLE

MINIMUM PARTICULARS TO APPEAR ON SMALL IMMEDIATE PACKAGING UNITS

VIAL LABEL

1. NAME OF THE MEDICINAL PRODUCT AND ROUTE(S) OF ADMINISTRATION

Prevenar suspension for injection
Pneumococcal saccharide conjugated vaccine, adsorbed
Intramuscular use.

2. METHOD OF ADMINISTRATION

Shake well before use.

3. EXPIRY DATE

EXP:

4. BATCH NUMBER

Lot:

5. CONTENTS BY WEIGHT, BY VOLUME OR BY UNIT

1 dose (0.5 ml)

6. OTHER

Pfizer Limited

PARTICULARS TO APPEAR ON THE OUTER PACKAGING

OUTER CARTON TEXT– 10 vials pack

1. NAME OF THE MEDICINAL PRODUCT

Prevenar suspension for injection
Pneumococcal saccharide conjugated vaccine, adsorbed

2. STATEMENT OF ACTIVE SUBSTANCE(S)

Each 0.5 ml dose contains 2 micrograms of saccharide for serotypes 4, 9V, 14, 18C, 19F, and 23F, and 4 micrograms of serotype 6B per dose (16 micrograms total saccharide) conjugated to CRM_{197} carrier protein and adsorbed on aluminium phosphate (0.5 mg).

3. LIST OF EXCIPIENTS

Also contains sodium chloride and water for injections.

4. PHARMACEUTICAL FORM AND CONTENTS

Suspension for injection.
10 single-dose (0.5 ml) vials.

5. METHOD AND ROUTE(S) OF ADMINISTRATION

Intramuscular use.
Shake well before use.
Read the package leaflet before use.

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

Keep out of the reach and sight of children.

7. OTHER SPECIAL WARNING(S), IF NECESSARY

Do not inject intravenously.

8. EXPIRY DATE

EXP:

9. SPECIAL STORAGE CONDITIONS

Store in a refrigerator.
Do not freeze.

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 Limited
Ramsgate Road
Sandwich
Kent CT13 9NJ
United Kingdom

12. MARKETING AUTHORISATION NUMBER(S)

EU/1/00/167/002

13. BATCH NUMBER

Lot:

14. GENERAL CLASSIFICATION FOR SUPPLY

Medicinal product subject to medical prescription.

15. INSTRUCTIONS ON USE

16. INFORMATION IN BRAILLE

PARTICULARS TO APPEAR ON THE OUTER PACKAGING

OUTER CARTON TEXT – 1 pre-filled syringe pack without needle

1. NAME OF THE MEDICINAL PRODUCT

Prevenar suspension for injection in pre-filled syringe
Pneumococcal saccharide conjugated vaccine, adsorbed

2. STATEMENT OF ACTIVE SUBSTANCE(S)

Each 0.5 ml dose contains 2 micrograms of saccharide for serotypes 4, 9V, 14, 18C, 19F, and 23F, and 4 micrograms of serotype 6B per dose (16 micrograms total saccharide) conjugated to CRM_{197} carrier protein and adsorbed on aluminium phosphate (0.5 mg).

3. LIST OF EXCIPIENTS

Also contains sodium chloride and water for injections.

4. PHARMACEUTICAL FORM AND CONTENTS

Suspension for injection in pre-filled syringe.
1 single-dose (0.5 ml) pre-filled syringe without needle.

5. METHOD AND ROUTE(S) OF ADMINISTRATION

Intramuscular use.
Shake well before use.
Read the package leaflet before use.

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

Keep out of the reach and sight of children.

7. OTHER SPECIAL WARNING(S), IF NECESSARY

Do not inject intravenously.

8. EXPIRY DATE

EXP:

9. SPECIAL STORAGE CONDITIONS

Store in a refrigerator.
Do not freeze.

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 Limited
Ramsgate Road
Sandwich
Kent CT13 9NJ
United Kingdom

12. MARKETING AUTHORISATION NUMBER(S)

EU/1/00/167/003

13. BATCH NUMBER

Lot:

14. GENERAL CLASSIFICATION FOR SUPPLY

Medicinal product subject to medical prescription.

15. INSTRUCTIONS ON USE

16. INFORMATION IN BRAILLE

MINIMUM PARTICULARS TO APPEAR ON SMALL IMMEDIATE PACKAGING UNITS

PRE-FILLED SYRINGE LABEL

1. NAME OF THE MEDICINAL PRODUCT AND ROUTE(S) OF ADMINISTRATION

Prevenar suspension for injection in pre-filled syringe
Pneumococcal saccharide conjugated vaccine, adsorbed.
Intramuscular use.

2. METHOD OF ADMINISTRATION

Shake well before use.

3. EXPIRY DATE

EXP:

4. BATCH NUMBER

Lot:

5. CONTENTS BY WEIGHT, BY VOLUME OR BY UNIT

1 dose (0.5 ml)

6. OTHER

Pfizer Limited

PARTICULARS TO APPEAR ON THE OUTER PACKAGING

OUTER CARTON TEXT – 10 pre-filled syringes pack without needle

1. NAME OF THE MEDICINAL PRODUCT

Prevenar suspension for injection in pre-filled syringe
Pneumococcal saccharide conjugated vaccine, adsorbed

2. STATEMENT OF ACTIVE SUBSTANCE(S)

Each 0.5 ml dose contains 2 micrograms of saccharide for serotypes 4, 9V, 14, 18C, 19F, and 23F, and 4 micrograms of serotype 6B per dose (16 micrograms total saccharide) conjugated to CRM_{197} carrier protein and adsorbed on aluminium phosphate (0.5 mg).

3. LIST OF EXCIPIENTS

Also contains sodium chloride and water for injections.

4. PHARMACEUTICAL FORM AND CONTENTS

Suspension for injection in pre-filled syringe.
10 single-dose (0.5 ml) pre-filled syringes without needle.

5. METHOD AND ROUTE(S) OF ADMINISTRATION

Intramuscular use.
Shake well before use.
Read the package leaflet before use.

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

Keep out of the reach and sight of children.

7. OTHER SPECIAL WARNING(S), IF NECESSARY

Do not inject intravenously.

8. EXPIRY DATE

EXP:

9. SPECIAL STORAGE CONDITIONS

Store in a refrigerator.
Do not freeze.

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 Limited
Ramsgate Road
Sandwich
Kent CT13 9NJ
United Kingdom

12. MARKETING AUTHORISATION NUMBER(S)

EU/1/00/167/004

13. BATCH NUMBER

Lot:

14. GENERAL CLASSIFICATION FOR SUPPLY

Medicinal product subject to medical prescription.

15. INSTRUCTIONS ON USE

16. INFORMATION IN BRAILLE

PARTICULARS TO APPEAR ON THE OUTER PACKAGING

OUTER CARTON TEXT – 1 vial pack with syringe/needles

1. NAME OF THE MEDICINAL PRODUCT

Prevenar suspension for injection
Pneumococcal saccharide conjugated vaccine, adsorbed

2. STATEMENT OF ACTIVE SUBSTANCE(S)

Each 0.5 ml dose contains 2 micrograms of saccharide for serotypes 4, 9V, 14, 18C, 19F, and 23F, and 4 micrograms of serotype 6B per dose (16 micrograms total saccharide) conjugated to CRM_{197} carrier protein and adsorbed on aluminium phosphate (0.5 mg).

3. LIST OF EXCIPIENTS

Also contains sodium chloride and water for injections.

4. PHARMACEUTICAL FORM AND CONTENTS

Suspension for injection.
1 single-dose (0.5 ml) vial.
1 separate syringe.
2 separate needles.

5. METHOD AND ROUTE(S) OF ADMINISTRATION

Intramuscular use.
Shake well before use.
Read the package leaflet before use.

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

Keep out of the reach and sight of children.

7. OTHER SPECIAL WARNING(S), IF NECESSARY

Do not inject intravenously.

8. EXPIRY DATE

EXP:

9. SPECIAL STORAGE CONDITIONS

Store in a refrigerator.
Do not freeze.

10. SPECIAL PRECAUTIONS FOR DISPOSAL OF UNUSED MEDICINAL PRODUCTS OR WASTE MATERIALS DERIVED FROM SUCH MEDICINAL PRODUCTS, (F APPROPRIATE

11. NAME AND ADDRESS OF THE MARKETING AUTHORISATION HOLDER

Pfizer Limited
Ramsgate Road
Sandwich
Kent CT13 9NJ
United Kingdom

12. MARKETING AUTHORISATION NUMBER(S)

EU/1/00/167/005

13. BATCH NUMBER

Lot:

14. GENERAL CLASSIFICATION FOR SUPPLY

Medicinal product subject to medical prescription

15. INSTRUCTIONS ON USE

16. INFORMATION IN BRAILLE

PARTICULARS TO APPEAR ON THE OUTER PACKAGING

OUTER CARTON TEXT – 1 pre-filled syringe pack with separate needle

1. NAME OF THE MEDICINAL PRODUCT

Prevenar suspension for injection in pre-filled syringe
Pneumococcal saccharide conjugated vaccine, adsorbed

2. STATEMENT OF ACTIVE SUBSTANCE(S)

Each 0.5 ml dose contains 2 micrograms of saccharide for serotypes 4, 9V, 14, 18C, 19F, and 23F, and 4 micrograms of serotype 6B per dose (16 micrograms total saccharide) conjugated to CRM_{197} carrier protein and adsorbed on aluminium phosphate (0.5 mg).

3. LIST OF EXCIPIENTS

Also contains sodium chloride and water for injections.

4. PHARMACEUTICAL FORM AND CONTENTS

Suspension for injection in pre-filled syringe.
1 single-dose (0.5 ml) pre-filled syringe with separate needle.

5. METHOD AND ROUTE(S) OF ADMINISTRATION

Intramuscular use.
Shake well before use. Read the package leaflet before use.

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

Keep out of the reach and sight of children.

7. OTHER SPECIAL WARNING(S), IF NECESSARY

Do not inject intravenously.

8. EXPIRY DATE

EXP:

9. SPECIAL STORAGE CONDITIONS

Store in a refrigerator.
Do not freeze.

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 Limited
Ramsgate Road
Sandwich
Kent CT13 9NJ
United Kingdom

12. MARKETING AUTHORISATION NUMBER(S)

EU/1/00/167/006

13. BATCH NUMBER

Lot:

14. GENERAL CLASSIFICATION FOR SUPPLY

Medicinal product subject to medical prescription.

15. INSTRUCTIONS ON USE

16. INFORMATION IN BRAILLE

PARTICULARS TO APPEAR ON THE OUTER PACKAGING

OUTER CARTON TEXT – 10 pre-filled syringes pack with separate needle

1. NAME OF THE MEDICINAL PRODUCT

Prevenar suspension for injection in pre-filled syringe
Pneumococcal saccharide conjugated vaccine, adsorbed

2. STATEMENT OF ACTIVE SUBSTANCE(S)

Each 0.5 ml dose contains 2 micrograms of saccharide for serotypes 4, 9V, 14, 18C, 19F, and 23F, and 4 micrograms of serotype 6B per dose (16 micrograms total saccharide) conjugated to CRM_{197} carrier protein and adsorbed on aluminium phosphate (0.5 mg).

3. LIST OF EXCIPIENTS

Also contains sodium chloride and water for injections.

4. PHARMACEUTICAL FORM AND CONTENTS

Suspension for injection in pre-filled syringe.
10 single-dose (0.5 ml) pre-filled syringes with separate needle.

5. METHOD AND ROUTE(S) OF ADMINISTRATION

Intramuscular use.
Shake well before use.
Read the package leaflet before use.

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

Keep out of the reach and sight of children.

7. OTHER SPECIAL WARNING(S), IF NECESSARY

Do not inject intravenously.

8. EXPIRY DATE

EXP:

9. SPECIAL STORAGE CONDITIONS

Store in a refrigerator.
Do not freeze.

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 Limited
Ramsgate Road
Sandwich
Kent CT13 9NJ
United Kingdom

12. MARKETING AUTHORISATION NUMBER(S)

EU/1/00/167/007

13. BATCH NUMBER

Lot:

14. GENERAL CLASSIFICATION FOR SUPPLY

Medicinal product subject to medical prescription.

15. INSTRUCTIONS ON USE

16. INFORMATION IN BRAILLE

PARTICULARS TO APPEAR ON THE OUTER PACKAGING

OUTER CARTON TEXT – 10 pre-filled syringes pack without needle: pack for multi pack presentation (5 x 10), without blue box

1. NAME OF THE MEDICINAL PRODUCT

Prevenar suspension for injection in pre-filled syringe
Pneumococcal saccharide conjugated vaccine, adsorbed

2. STATEMENT OF ACTIVE SUBSTANCE(S)

Each 0.5 ml dose contains 2 micrograms of saccharide for serotypes 4, 9V, 14, 18C, 19F, and 23F, and 4 micrograms of serotype 6B per dose (16 micrograms total saccharide) conjugated to CRM_{197} carrier protein and adsorbed on aluminium phosphate (0.5 mg).

3. LIST OF EXCIPIENTS

Also contains sodium chloride and water for injections.

4. PHARMACEUTICAL FORM AND CONTENTS

Suspension for injection in pre-filled syringe.
Component of a multipack comprising 5 packs, each containing 10 single-dose (0.5 ml) pre-filled syringes without needle.
Each individual pack cannot be sold separately.

5. METHOD AND ROUTE(S) OF ADMINISTRATION

Intramuscular use.
Shake well before use.
Read the package leaflet before use.

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

Keep out of the reach and sight of children.

7. OTHER SPECIAL WARNING(S), IF NECESSARY

Do not inject intravenously.

8. EXPIRY DATE

EXP:

9. SPECIAL STORAGE CONDITIONS

Store in a refrigerator.
Do not freeze.

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 Limited
Ramsgate Road
Sandwich
Kent CT13 9NJ
United Kingdom

12. MARKETING AUTHORISATION NUMBER(S)

EU/1/00/167/008

13. BATCH NUMBER

Lot:

14. GENERAL CLASSIFICATION FOR SUPPLY

Medicinal product subject to medical prescription.

15. INSTRUCTIONS ON USE

16. INFORMATION IN BRAILLE

PARTICULARS TO APPEAR ON THE OUTER PACKAGING

LABEL TEXT - Outer wrapper label to be applied on the transparent foil for multi pack presentation (5 x 10), including the blue box

1. NAME OF THE MEDICINAL PRODUCT

Prevenar suspension for injection in pre-filled syringe
Pneumococcal saccharide conjugated vaccine, adsorbed

2. STATEMENT OF ACTIVE SUBSTANCE(S)

Each 0.5 ml dose contains 2 micrograms of saccharide for serotypes 4, 9V, 14, 18C, 19F, and 23F, and 4 micrograms of serotype 6B per dose (16 micrograms total saccharide) conjugated to CRM_{197} carrier protein and adsorbed on aluminium phosphate (0.5 mg).

3. LIST OF EXCIPIENTS

Also contains sodium chloride and water for injections.

4. PHARMACEUTICAL FORM AND CONTENTS

Suspension for injection in pre-filled syringe.
Multipack comprising 5 packs, each containing 10 single-dose (0.5 ml) pre-filled syringes without needle.
Each individual pack cannot be sold separately.

5. METHOD AND ROUTE(S) OF ADMINISTRATION

Intramuscular use.
Shake well before use.
Read the package leaflet before use.

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

Keep out of the reach and sight of children.

7. OTHER SPECIAL WARNING(S), IF NECESSARY

Do not inject intravenously.

8. EXPIRY DATE

EXP:

9. SPECIAL STORAGE CONDITIONS

Store in a refrigerator.
Do not freeze.

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 Limited
Ramsgate Road
Sandwich
Kent CT13 9NJ
United Kingdom

12. MARKETING AUTHORISATION NUMBER(S)

EU/1/00/167/008

13. BATCH NUMBER

Lot:

14. GENERAL CLASSIFICATION FOR SUPPLY

Medicinal product subject to medical prescription.

15. INSTRUCTIONS ON USE

16. INFORMATION IN BRAILLE

B. PACKAGE LEAFLET

PACKAGE LEAFLET: INFORMATION FOR THE USER

Prevenar suspension for injection
Pneumococcal saccharide conjugated vaccine, adsorbed

Read all of this leaflet carefully before your child receives this vaccine.
- Keep this leaflet. You may need to read it again.
- If you have any further questions, ask your doctor, pharmacist or nurse.
- If any of the side effects gets serious, or if you notice any side effects not listed in this leaflet, please tell your doctor or pharmacist.

In this leaflet:

1. WHAT PREVENAR IS AND WHAT IT IS USED FOR

Prevenar is a pneumococcal vaccine. Prevenar is given to children from 2 months to 5 years to help protect against diseases such as: meningitis, sepsis or bacteraemia (bacteria in blood stream), pneumonia and ear infection caused by seven types of the bacteria *Streptococcus pneumoniae.*

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

2. BEFORE YOUR CHILD RECEIVES PREVENAR

Do not use Prevenar:
- if your child is allergic (hypersensitive) to the active substances, to any other ingredients or to diphtheria toxoid.
- if your child has a severe infection with a high temperature (over 38°C). If this applies to your child, then the vaccination will be postponed until your child is feeling better. A minor infection, such as a cold, should not be a problem. However, talk to your doctor, pharmacist, or nurse first.

Take special care with Prevenar:
- if your child has any present or past medical problems after any dose of Prevenar.
- if your child has any bleeding problems.

Prevenar will only protect against ear infections caused by the types of *Streptococcus pneumoniae* for which the vaccine has been developed. It will not protect against other infectious agents that can cause ear infections.

Using other medicines/vaccines:
Please tell your doctor, nurse or pharmacist if your child is taking or has recently taken any other medicines including medicines obtained without prescription or has recently received any other vaccine.

Important information about some of the ingredients of Prevenar:
This medicinal product contains less than 1 mmol sodium (23mg) per dose, i.e. essentially sodium-free

3. HOW PREVENAR IS GIVEN

The doctor or nurse will inject the recommended dose (0.5 ml) of the vaccine into your child's arm or leg muscle.
Prevenar can be given at the same time as other childhood vaccines; in this case different injection sites should be used.

Infants aged 6 weeks to 6 months of age

Typically, your child should receive an initial course of three injections followed by a booster dose
- The first injection may be given from 2 months of age
- Each injection will be given at least 1 month apart
- A fourth injection (booster) will be given between 11 and 15 months of age
- You will be told when your child should come back for the next injection

According to official recommendations in your country, an alternative schedule may be used by your health-care provider. Please speak to your doctor, pharmacist, or nurse for more information.

Unvaccinated infants and children over 7 months of age

Infants aged **7 to- 11 months** should receive two injections. Each injection will be given at least 1 month apart. A third injection will be given in the second year of life.
Children aged **12 to 23 months** should receive two injections. Each injection will be given at least 2 month apart.
Children aged **2 to 5 years** should receive one injection.

It is important to follow the instructions from the doctor, pharmacist, or nurse so that your child completes the course of injections.

If you forget to go back to the doctor or nurse at the scheduled time, ask the doctor or nurse for advice.

4. POSSIBLE SIDE EFFECTS

Like all vaccines, Prevenar can cause side effects, although not everybody gets them. The following side effects may happen with this vaccine.

The most common side effects (these may occur with more than 1 in 10 doses of the vaccine) are:
- Vomiting, diarrhoea, decreased appetite
- Pain, tenderness, redness, swelling, or hardness at the injection site; fever of 38 °C or higher, irritability, crying, drowsiness, restless sleep

Common side effects (these may occur with up to 1 in 10 doses of the vaccine) are:
- Redness, swelling, or hardness at the injection site greater than 2.4 cm; tenderness at the injection site interfering with movement
- Fever of 39°C or higher

Uncommon side effects (these may occur with up to 1 in 100 doses of the vaccine) are:
- Rash/hives (urticaria)

Rare side effects (these may occur with up to 1 in 1,000 doses of the vaccine) are:
- Seizures (or fits), including those caused by a high temperature
- Hypotonic-hyporesponsive episode (collapse or shock-like state)
- Hypersensitivity reaction, including swelling of the face and/or lips, difficulty in breathing, rash, urticaria or urticaria-like rash (hives)
- Flushing

Very rare side effects (these may occur with up to 1 in 10,000 doses of the vaccine) are:
- Enlarged lymph nodes or glands (lymphadenopathy) near the injection site, such as under the arm or in the groin
- Erythema multiforme (a rash causing itchy red blotches)

In babies born very prematurely (at or before 28 weeks of gestation) longer gaps than normal between breaths may occur for 2-3 days after vaccination.

Please speak with your doctor,pharmacist, or nurse should you have any questions or concerns. If any of the side effects gets serious or if you notice any side effects not listed in this leaflet, please tell your doctor or pharmacist.

5. HOW TO STORE PREVENAR

Keep out of the reach and sight of children

Store in a refrigerator (2°C – 8°C).
Do not freeze.

Do not use Prevenar after the expiry date stated on the carton and label. The expiry date refers to the last day of that month.

Medicines should not be disposed of via wastewater or household waste. Ask your pharmacist how to dispose of medicines no longer required. These measures will help to protect the environment.

6. FURTHER INFORMATION

What Prevenar contains

The active substances
Each 0.5 ml dose contains:

Pneumococcal polysaccharide serotype 4*	2 micrograms
Pneumococcal polysaccharide serotype 6B*	4 micrograms
Pneumococcal polysaccharide serotype 9V*	2 micrograms
Pneumococcal polysaccharide serotype 14*	2 micrograms
Pneumococcal polysaccharide serotype 18C*	2 micrograms
Pneumococcal polysaccharide serotype 19F*	2 micrograms
Pneumococcal polysaccharide serotype 23F*	2 micrograms

* Conjugated to the CRM_{197} carrier protein and adsorbed on aluminium phosphate (0.5 mg)

The other ingredients are sodium chloride and water for injections.

What Prevenar looks like and contents of the pack

The vaccine is a suspension for injection and provided in a single-dose vial (0.5 ml).
Pack sizes of 1 and 10 vials without syringe/needles.
Pack size of 1 vial with syringe and 2 needles (1 for withdrawal, 1 for injection).

Marketing Authorisation Holder and Manufacturer

Marketing Authorisation Holder:
Pfizer Limited
Ramsgate Road
Sandwich
Kent CT13 9NJ
United Kingdom

Manufacturing Authorisation Holder responsible for batch release:
John Wyeth & Brother Ltd.
Huntercombe Lane South
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United Kingdom

For any information about this medicinal product, please contact the local representative of the Marketing Authorisation Holder:

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Pfizer, podružnica za svetovanje s področja farmacevtske dejavnosti, Ljubljana
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United Kingdom
Pfizer Limited
Tel: +44 (0) 1304 616161

This leaflet was last approved in {MM/YYYY}.

Detailed information on this medicine is available on the European Medicines Agency website: http://www.ema.europa.eu

The following information is intended for medical or healthcare professionals only:

The vaccine should be well shaken to obtain a homogeneous white suspension and be inspected visually for any particulate matter and/or variation of physical aspect prior to administration. Do not use if the content appears otherwise.

Prevenar is for intramuscular use only. Do not administer intravenously.
This vaccine should not be given to infants or children with thrombocytopenia or any coagulation disorder that would contraindicate intramuscular injection unless the potential benefit clearly outweighs the risk of administration.

Infants age 2 - 6 months: the primary infant series consists of three doses, each of 0.5 ml, the first dose usually given at 2 months of age and with an interval of at least 1 month between doses.
A fourth dose is recommended in the second year of life.

Alternatively, when Prevenar is given as part of a routine infant immunisation programme, a two-dose schedule may be considered. The first dose may be given from the age of 2 months with a second dose at least 2 months later and a third (booster) dose at 11-15 months of age.

Infants aged 7 - 11 months: two doses, each of 0.5 ml, with an interval of at least 1 month between doses.
A third dose is recommended in the second year of life.
Children aged 12 - 23 months: two doses, each of 0.5 ml, with an interval of at least 2 months between doses.
Children aged 24 months - 5 years: one single dose.

The need for a booster dose after these immunisation schedules has not been established.

As with other vaccines, the administration of Prevenar should be postponed in subjects suffering from acute moderate or severe febrile illness.

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

Prevenar will not protect against other *Streptococcus pneumoniae* serotypes than those included in the vaccine or other micro-organisms that cause invasive disease or otitis media.

Although some antibody response to diphtheria toxoid may occur, immunisation with this vaccine does not substitute for routine diphtheria immunisation.

For children from 2 years through 5 years of age, a single dose immunisation schedule was used. A higher rate of local reactions has been observed in children older than 24 months of age compared with infants.

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

Limited data have demonstrated that Prevenar induces an acceptable immune response in infants with sickle cell disease with a safety profile similar to that observed in non-high-risk groups. Safety and immunogenicity data are not yet available for children in other specific high-risk groups for invasive pneumococcal disease (e.g. children with another congenital or acquired splenic dysfunction, HIV-infected, malignancy, nephrotic syndrome). Vaccination in high-risk groups should be considered on an individual basis.

Children below 2 years old (including those at high-risk) should receive the appropriate-for-age Prevenar vaccination series. The use of pneumococcal conjugate vaccine does not replace the use of 23-valent pneumococcal polysaccharide vaccines in children ≥ 24 months of age with conditions (such as sickle cell disease, asplenia, HIV infection, chronic illness or who are immunocompromised) placing them at higher risk for invasive disease due to *Streptococcus pneumoniae*. Whenever recommended, children at risk who are ≥ 24 months of age and already primed with Prevenar should receive 23-valent pneumococcal polysaccharide vaccine. The interval between the pneumococcal conjugate vaccine (Prevenar) and the 23-valent pneumococcal polysaccharide vaccine should not be less than 8 weeks. There are no data available to indicate whether the administration of 23-valent pneumococcal polysaccharide vaccine to unprimed children or to children primed with Prevenar might result in hyporesponsiveness to further doses of Prevenar.
Prophylactic antipyretic medication is recommended:
- for all children receiving Prevenar simultaneously with vaccines containing whole cell pertussis because of higher rate of febrile reactions
- for children with seizure disorders or with a prior history of febrile seizures.

Antipyretic treatment should be initiated whenever warranted or when the temperature rises above 39°C.

Children with impaired immune responsiveness, whether due to the use of immunosuppressive therapy, a genetic defect, HIV infection, or other causes, may have reduced antibody response to active immunisation.

As with any vaccine, Prevenar may not protect all individuals receiving the vaccine from pneumococcal disease. Additionally, for vaccine serotypes, protection against otitis media is expected to be substantially lower than protection against invasive disease. As otitis media is caused by many organisms other than pneumococcal serotypes represented in the vaccine, protection against all otitis media is expected to be low.

PACKAGE LEAFLET: INFORMATION FOR THE USER

Prevenar suspension for injection in pre-filled syringe
Pneumococcal saccharide conjugated vaccine, adsorbed

Read all of this leaflet carefully before your child receives this vaccine.
- Keep this leaflet. You may need to read it again.
- If you have any further questions, ask your doctor, pharmacist or nurse.
- If any of the side effects gets serious, or if you notice any side effects not listed in this leaflet, please tell your doctor or pharmacist.

In this leaflet:

1. WHAT PREVENAR IS AND WHAT IT IS USED FOR

Prevenar is a pneumococcal vaccine. Prevenar is given to children from 2 months to 5 years to help protect against diseases such as: meningitis, sepsis or bacteraemia (bacteria in blood stream), pneumonia and ear infection caused by seven types of the bacteria *Streptococcus pneumoniae.*

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

2. BEFORE YOUR CHILD RECEIVES PREVENAR

Do not use Prevenar:
- if your child is allergic (hypersensitive) to the active substances, to any other ingredients or to diphtheria toxoid.
- if your child has a severe infection with a high temperature (over 38°C). If this applies to your child, then the vaccination will be postponed until your child is feeling better. A minor infection, such as a cold, should not be a problem. However, talk to your doctor, pharmacist, or nurse first.

Take special care with Prevenar:
- if your child has any present or past medical problems after any dose of Prevenar.
- if your child has any bleeding problems.

Prevenar will only protect against ear infections caused by the types of *Streptococcus pneumoniae* for which the vaccine has been developed. It will not protect against other infectious agents that can cause ear infections.

Using other medicines/vaccines:
Please tell your doctor, nurse or pharmacist if your child is taking or has recently taken any other medicines including medicines obtained without prescription or has recently received any other vaccine

Important information about some of the ingredients of Prevenar:
This medicinal product contains less than 1 mmol sodium (23mg) per dose, i.e. essentially sodium-free.

3. HOW PREVENAR IS GIVEN

The doctor or nurse will inject the recommended dose (0.5 ml) of the vaccine into your child's arm or leg muscle.
Prevenar can be given at the same time as other childhood vaccines; in this case different injection sites should be used.

Infants aged 6 weeks to 6 months of age

Typically, your child should receive receive an initial course of three injections followed by a booster dose
- The first injection may be given from 2 months of age
- Each injection will be given at least 1 month apart
- A fourth injection (booster) will be given between 11 and 15 months of age
- You will be told when your child should come back for the next injection

According to official recommendations in your country, an alternative schedule may be used by your health-care provider. Please speak to your doctor, pharmacist, or nurse for more information.

Unvaccinated infants and children over 7 months of age

Infants aged **7 to 11 months** should receive two injections. Each injection will be given at least 1 month apart. A third injection will be given in the second year of life.
Children aged **12 to 23 months** should receive two injections. Each injection will be given at least 2 month apart.
Children aged **2 to 5 years** should receive one injection.

It is important to follow the instructions from the doctor, pharmacist, or nurse so that your child completes the course of injections.

If you forget to go back to the doctor or nurse at the scheduled time, ask the doctor or nurse for advice.

4. POSSIBLE SIDE EFFECTS

Like all vaccines, Prevenar can cause side effects, although not everybody gets them. The following side effects may happen with this vaccine.

The most common side effects (these may occur with more than 1 in 10 doses of the vaccine) are:
- Vomiting, diarrhoea, decreased appetite
- Pain, tenderness, redness, swelling, or hardness at the injection site; fever of 38 °C or higher, irritability, crying, drowsiness, restless sleep

Common side effects (these may occur with up to 1 in 10 doses of the vaccine) are:
- Redness, swelling, or hardness at the injection site greater than 2.4 cm; tenderness at the injection site interfering with movement
- Fever of 39°C or higher

Uncommon side effects (these may occur with up to 1 in 100 doses of the vaccine) are:
- Rash/hives (urticaria)

Rare side effects (these may occur with up to 1 in 1,000 doses of the vaccine) are:
- Seizures (or fits), including those caused by a high temperature
- Hypotonic-hyporesponsive episode (collapse or shock-like state)
- Hypersensitivity reaction, including swelling of the face and/or lips, difficulty in breathing, rash, urticaria or urticaria-like rash (hives)
- Flushing

Very rare side effects (these may occur with up to 1 in 10,000 doses of the vaccine) are:
- Enlarged lymph nodes or glands (lymphadenopathy) near the injection site, such as under the arm or in the groin
- Erythema multiforme (a rash causing itchy red blotches)

In babies born very prematurely (at or before 28 weeks of gestation) longer gaps than normal between breaths may occur for 2-3 days after vaccination.

Please speak with your doctor, pharmacist, or nurse should you have any questions or concerns. If any of the side effects gets serious or if you notice any side effects not listed in this leaflet, please tell your doctor or pharmacist.

5. HOW TO STORE PREVENAR

Keep out of the reach and sight of children

Store in a refrigerator (2°C – 8°C). Do not freeze.

Do not use Prevenar after the expiry date stated on the carton and label. The expiry date refers to the last day of that month.

Medicines should not be disposed of via wastewater or household waste. Ask your pharmacist how to dispose of medicines no longer required. These measures will help to protect the environment.

6. FURTHER INFORMATION

What Prevenar contains

The active substances
Each 0.5 ml dose contains:

Pneumococcal polysaccharide serotype 4*	2 micrograms
Pneumococcal polysaccharide serotype 6B*	4 micrograms
Pneumococcal polysaccharide serotype 9V*	2 micrograms
Pneumococcal polysaccharide serotype 14*	2 micrograms
Pneumococcal polysaccharide serotype 18C*	2 micrograms
Pneumococcal polysaccharide serotype 19F*	2 micrograms
Pneumococcal polysaccharide serotype 23F*	2 micrograms

* Conjugated to the CRM_{197} carrier protein and adsorbed on aluminium phosphate (0.5 mg)

The other ingredients are sodium chloride and water for injections.

What Prevenar looks like and contents of the pack

The vaccine is a suspension for injection and provided in a single-dose pre-filled syringe (0.5 ml). Pack sizes of 1 and 10 with or without needle.
Multipack presentation of 5 packs of 10 pre-filled syringes without needles.

Marketing Authorisation Holder and Manufacturer

Marketing Authorisation Holder:
Pfizer Limited
Ramsgate Road
Sandwich
Kent CT13 9NJ
United Kingdom

Manufacturing Authorisation Holder responsible for batch release:
John Wyeth & Brother Ltd.
Huntercombe Lane South
Taplow, Maidenhead
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United Kingdom

For any information about this medicinal product, please contact the local representative of the Marketing Authorisation Holder:

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This leaflet was last approved in {MM/YYYY}

Detailed information on this medicine is available on the European Medicines Agency website: http://www.ema.europa.eu

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The following information is intended for medical or healthcare professionals only:

The vaccine should be well shaken to obtain a homogeneous white suspension and be inspected visually for any particulate matter and/or variation of physical aspect prior to administration. Do not use if the content appears otherwise.

Prevenar is for intramuscular use only. Do not administer intravenously.
This vaccine should not be given to infants or children with thrombocytopenia or any coagulation disorder that would contraindicate intramuscular injection unless the potential benefit clearly outweighs the risk of administration.

Infants aged 2 - 6 months: the primary infant series consists of three doses, each of 0.5 ml, the first dose usually given at 2 months of age and with an interval of at least 1 month between doses.
A fourth dose is recommended in the second year of life.

Alternatively, when Prevenar is given as part of a routine infant immunisation programme, a two-dose schedule may be considered. The first dose may be given from the age of 2 months with a second dose at least 2 months later and a third (booster) dose at 11-15 months of age.

Infants aged 7 - 11 months: two doses, each of 0.5 ml, with an interval of at least 1 month between doses.
A third dose is recommended in the second year of life.
Children aged 12 - 23 months: two doses, each of 0.5 ml, with an interval of at least 2 months between doses.
Children aged 24 months - 5 years: one single dose.

The need for a booster dose after these immunisation schedules has not been established.

As with other vaccines, the administration of Prevenar should be postponed in subjects suffering from acute moderate or severe febrile illness.

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

Prevenar will not protect against other *Streptococcus pneumoniae* serotypes than those included in the vaccine or other micro-organisms that cause invasive disease or otitis media.

Although some antibody response to diphtheria toxoid may occur, immunisation with this vaccine does not substitute for routine diphtheria immunisation.

For children from 2 years through 5 years of age, a single dose immunisation schedule was used. A higher rate of local reactions has been observed in children older than 24 months of age compared with infants.

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

Limited data have demonstrated that Prevenar induces an acceptable immune response in infants with sickle cell disease with a safety profile similar to that observed in non-high-risk groups. Safety and immunogenicity data are not yet available for children in other specific high-risk groups for invasive pneumococcal disease (e.g. children with another congenital or acquired splenic dysfunction, HIV-infected, malignancy, nephrotic syndrome). Vaccination in high-risk groups should be considered on an individual basis.

Children below 2 years old (including those at high-risk) should receive the appropriate-for-age Prevenar vaccination series. The use of pneumococcal conjugate vaccine does not replace the use of 23-valent pneumococcal polysaccharide vaccines in children ≥ 24 months of age with conditions (such as sickle cell disease, asplenia, HIV infection, chronic illness or who are immunocompromised) placing them at higher risk for invasive disease due to *Streptococcus pneumoniae*. Whenever recommended, children at risk who are ≥ 24 months of age and already primed with Prevenar should receive 23-valent pneumococcal polysaccharide vaccine. The interval between the pneumococcal conjugate vaccine (Prevenar) and the 23-valent pneumococcal polysaccharide vaccine should not be less than 8 weeks. There are no data available to indicate whether the administration of 23-valent pneumococcal polysaccharide vaccine to unprimed

children or to children primed with Prevenar might result in hyporesponsiveness to further doses of Prevenar.

Prophylactic antipyretic medication is recommended:
- for all children receiving Prevenar simultaneously with vaccines containing whole cell pertussis because of higher rate of febrile reactions
- for children with seizure disorders or with a prior history of febrile seizures.
Antipyretic treatment should be initiated whenever warranted or when the temperature rises above 39°C.

Children with impaired immune responsiveness, whether due to the use of immunosuppressive therapy, a genetic defect, HIV infection, or other causes, may have reduced antibody response to active immunisation.

As with any vaccine, Prevenar may not protect all individuals receiving the vaccine from pneumococcal disease. Additionally, for vaccine serotypes, protection against otitis media is expected to be substantially lower than protection against invasive disease. As otitis media is caused by many organisms other than pneumococcal serotypes represented in the vaccine, protection against all otitis media is expected to be low.

ANNEX IV

SCIENTIFIC CONCLUSIONS AND GROUNDS FOR VARIATION TO THE TERMS OF THE MARKETING AUTHORISATIONS

Scientific conclusions and grounds for variation to the terms of the marketing authorisations

Due to the long-standing post marketing experience, the well characterised safety profile and the large exposure of the product the PRAC recommended to amend the PSUR frequency to 10-yearly and to amend Annex II accordingly to reflect the current QRD template sentence referring to the EURD list.

Therefore, in view of available data the PRAC considered that changes to the conditions of the marketing authorisation were warranted.