

DATA SHEET

Prevenar 13[®]

NAME OF THE MEDICINE

Prevenar 13

Pneumococcal polysaccharide conjugate vaccine, 13-valent adsorbed

DESCRIPTION

The vaccine is a ready to use homogeneous white suspension for intramuscular injection, supplied as a pre-filled syringe.

Active ingredients

Each 0.5 mL dose contains:

2.2 µg of pneumococcal purified capsular polysaccharides for serotypes 1, 3, 4, 5, 6A, 7F, 9V, 14, 18C, 19A, 19F and 23F

4.4 µg of pneumococcal purified capsular polysaccharides for serotype 6B.

Each serotype is individually conjugated to non-toxic diphtheria CRM₁₉₇ protein and adsorbed on aluminium phosphate (0.565 mg).

Excipients

Succinic acid, polysorbate 80, aluminium phosphate, sodium chloride in water for injections.

PHARMACOLOGY

Streptococcus pneumoniae is an important cause of morbidity and mortality in persons of all ages worldwide. It is a leading cause of death and illness in infants, among the elderly, and in persons who have certain underlying medical conditions. The organism causes invasive infections, including bacteraemia and meningitis, pneumonia and other lower respiratory tract infections, and upper respiratory tract infections including otitis media and sinusitis.

Based on serotype surveillance performed before the introduction of Prevenar, Prevenar 13 is estimated to cover 93.3% of serotypes causing IPD (Invasive Pneumococcal Disease) among children less than 5 years of age in Australia (Watson M. et al., *Communicable Disease Intelligence* 2004; 28(4): 455-464) and 92.8% in New Zealand (Heffernan H.M., et al., *Epidemiology of Infections* 2007; 1-8.)

Prevenar 13 is estimated to cover over 90% of serotypes causing antibiotic resistant IPD.

Pharmacodynamics

Pharmacotherapeutic group: pneumococcal vaccines.

Mode of action

Prevenar 13 contains the 7 pneumococcal capsular polysaccharides that are in Prevenar (7-valent) conjugate vaccine (4, 6B, 9V, 14, 18C, 19F, 23F) plus 6 additional polysaccharides (1, 3, 5, 6A, 7F, 19A) all conjugated to CRM₁₉₇ carrier protein. B-cells produce antibodies in response to antigenic stimulation via T-dependent and T-independent mechanisms. The immune response to most antigens is T-dependent and involves the collaboration of CD4⁺ T-cells and B-cells, recognising the antigen in a linked fashion. CD4⁺ T-cells (T-helper cells) provide signals to B-

cells directly through cell surface protein interactions, and indirectly through the release of cytokines. These signals result in proliferation and differentiation of the B-cells, and production of high-affinity antibodies. CD4+ T-cell signalling is a requisite for the generation of long-lived B-cells called plasma cells, which continuously produce antibodies of several isotypes (with an IgG component) and memory B-cells that rapidly mobilise and secrete antibodies upon re-exposure to the same antigen.

Bacterial capsular polysaccharides (PSs), while varied in chemical structure, share the common immunological property of being largely T-independent antigens. In the absence of T-cell help, PS-stimulated B-cells predominantly produce IgM antibodies; there is generally no affinity maturation of the antibodies, and no memory B-cells are generated. As vaccines, PSs are associated with poor or absent immunogenicity in infants less than 24 months of age and failure to induce immunological memory at any age. Conjugation of PSs to a protein carrier overcomes the T-cell-independent nature of PS antigens. Protein carrier-specific T-cells provide the signals needed for maturation of the B-cell response and generation of B-cell memory. Conversion of *Streptococcus pneumoniae* PSs to a T-cell-dependent antigen by covalent coupling to the immunogenic protein carrier CRM₁₉₇ enhances the antibody response and induces immune memory. This has been demonstrated to elicit booster responses on re-exposure in infants and young children to pneumococcal polysaccharides.

Pharmacokinetics

Evaluation of pharmacokinetic properties is not available for vaccines.

CLINICAL TRIALS

Prevenar 13 immunogenicity clinical trials

The World Health Organization (WHO) has recommended a serum anti-capsular polysaccharide IgG antibody concentration of 0.35 µg/mL using an enzyme-linked immunosorbent assay, measured one month after the primary infant series as a single antibody reference concentration to estimate the efficacy of new pneumococcal conjugate vaccines against IPD. This recommendation is largely based upon the observed correlation between immunogenicity and IPD efficacy from three placebo-controlled trials with either Prevenar or the investigational 9-valent CRM₁₉₇ conjugate polysaccharide vaccine. This reference concentration is only applicable on a population basis and cannot be used to predict protection against IPD on an individual basis.

Immune responses following a three-dose primary infant series

Clinical trials have been conducted in a number of European countries and the US using a range of primary vaccination schedules. The percentage of infants achieving pneumococcal anti-capsular polysaccharide IgG antibody concentrations ≥ 0.35 µg/mL and opsonophagocytic activity (OPA) antibody titers ≥ 1:8, one month after a three-dose primary series (at 2, 4 and 6 months) and after booster dosing, from representative studies are presented below (Table 1):

Table 1: Percentage of subjects with Pneumococcal Anti-capsular Polysaccharide IgG Antibody concentrations ≥ 0.35 µg/mL and OPA Antibody Titer ≥ 1:8 following Prevenar 13 administration in a 2, 4, 6 month primary schedule

Serotype	Primary Schedule (2, 4, 6 months)	Booster
----------	--------------------------------------	---------

		IgG (N=897-924) OPA (N=91-94)	IgG (N=458-479) OPA (N=88-92)
1	IgG \geq 0.35 μ g/mL	95.6-99.3%	98.7-100.0%
	OPA Antibody \geq 1:8	98.9%	98.9%
3	IgG \geq 0.35 μ g/mL	63.5-90.3%	90.5-92.2%
	OPA Antibody \geq 1:8	96.8%	97.8%
4	IgG \geq 0.35 μ g/mL	94.4-98.9%	99.1-99.2%
	OPA Antibody \geq 1:8	97.8%	98.9%
5	IgG \geq 0.35 μ g/mL	89.7-97.3%	99.1-99.6%
	OPA Antibody \geq 1:8	92.3%	98.9%
6A	IgG \geq 0.35 μ g/mL	96.0-98.2%	99.1-100.0%
	OPA Antibody \geq 1:8	100.0%	98.9%
6B	IgG \geq 0.35 μ g/mL	87.3-98.5%	99.6%
	OPA Antibody \geq 1:8	98.9%	98.9%
7F	IgG \geq 0.35 μ g/mL	98.4-100.0%	98.8-99.6%
	OPA Antibody \geq 1:8	100.0%	100.0%
9V	IgG \geq 0.35 μ g/mL	90.5-99.3%	99.1-100.0%
	OPA Antibody \geq 1:8	100.0%	98.9%
14	IgG \geq 0.35 μ g/mL	97.4-98.2%	98.7-100.0%
	OPA Antibody \geq 1:8	100.0%	100.0%
18C	IgG \geq 0.35 μ g/mL	96.8-98.1%	98.7-99.6%
	OPA Antibody \geq 1:8	100.0%	98.9%
19A	IgG \geq 0.35 μ g/mL	98.4-99.6%	100.0%
	OPA Antibody \geq 1:8	100.0%	97.8%
19F	IgG \geq 0.35 μ g/mL	98.0-99.3%	99.6-100.0%
	OPA Antibody \geq 1:8	90.4%	96.7%
23F	IgG \geq 0.35 μ g/mL	87.2-94.6%	99.1-99.6%
	OPA Antibody \geq 1:8	98.9%	98.9%

In Prevenar 13 recipients, antipolysaccharide binding antibody for each of the 13 serotypes has been demonstrated to be correlated with functional antibacterial opsonophagocytic activity (biologically active antibody).

Immune responses following a two-dose primary series

The immunogenicity after two doses in infants has been documented in four studies. The proportion of infants achieving a pneumococcal anti-capsular polysaccharide IgG concentration \geq 0.35 μ g/mL one month after the second dose ranged from 79.6% to 98.5% across 11 of the 13 vaccine serotypes. Smaller proportions of infants achieved this antibody concentration threshold for serotype 6B (27.9% to 58.4%) and 23F (55.8% to 68.6%). Compared to a three-dose infant series, pneumococcal anti-capsular polysaccharide IgG GMCs were lower after a two-dose infant series for most serotypes.

Booster responses following two-dose and three-dose primary series

Post-booster antibody concentrations were higher for 12 serotypes than those achieved after the infant primary series, which is consistent with adequate priming (the induction of immunologic memory). For serotype 3, antibody concentrations following the infant primary series and booster dose were similar. Antibody responses to booster doses following two-dose or three-dose infant primary series were comparable for all 13 vaccine serotypes.

For children aged from 7 months to 5 years, age appropriate catch-up immunisation schedules result in levels of anti-capsular polysaccharide IgG antibody responses to each of the 13 serotypes that are at least comparable to those of a three-dose primary series in infants.

Prevenar protective efficacy

The efficacy of Prevenar (7-valent) was evaluated in two major trials – the Northern California Kaiser Permanente (NCKP) trial and the Finnish Otitis Media trial (FinOM). Both trials were randomised, double-blind, active-control trials in which infants were randomised to receive either Prevenar (7-valent) or control vaccine (NCKP, meningococcal serogroup C CRM-conjugate [MnCC] vaccine; FinOM, hepatitis B vaccine) in a four-dose series at 2, 4, 6, and 12 - 15 months of age. The various efficacy results from these trials (for invasive pneumococcal disease, pneumonia, and acute otitis media) are presented below (Table 2).

Table 2: Summary of Efficacy of Prevenar (7-valent)

Test	Study	N	VE*	95% CI
Invasive Pneumococcal Disease (IPD)				
Per-protocol	NCKP	30,258	97%	85, 100
Intent-to-treat		37,866	94%	81, 99
Pneumonia (Per-protocol)				
<i>With bacteraemia</i>			87.5%	7, 99
<i>Clinical pneumonia with abnormal chest X-ray</i>			20.5%	4.4, 34.0
Acute Otitis Media (AOM)				
Per-protocol (reduction of)	NCKP	37,868		
<i>Total episodes</i>			7%	4, 10
<i>Recurrent AOM</i> <i>(3 episodes in 6 mo. or 4 episodes in 1 yr.)</i>			9%	3, 15
<i>Recurrent AOM</i> <i>(5 episodes in 6 mo. or 6 episodes in 1 yr.)</i>			23%	7, 36
<i>Tympanostomy tube placement</i>			20%	2, 35
Per-protocol (reduction of)	FinOM	1662		
<i>Total episodes</i>			6%	-4, 16
<i>All pneumococcal AOM</i>			34%	21, 45
<i>Vaccine-serotype AOM</i>			57%	44, 67
Intent-to-treat				
<i>Vaccine-serotype AOM</i>			54%	41, 64

* Vaccine efficacy

Prevenar effectiveness

The effectiveness of Prevenar (7-valent) against pneumococcal disease (comprising the protection afforded by vaccination and from herd immunity due to reduced transmission of vaccine serotypes in the population) has been evaluated in routine paediatric immunisation programmes that employ either three-dose or two-dose primary infant series, each with booster doses. This surveillance will continue with Prevenar 13.

Data from several countries is summarised in Table 3. It is important to note that as countries continually update the data from their surveillance systems, values included in this table may change over time.

Table 3. Summary of Effectiveness of Prevenar (7-valent) for Invasive Pneumococcal Disease				
Country	Year of Introduction	Recommended Schedule	Disease Reduction, %	95% CI
USA	2000	2, 4, 6, 12 - 15 months		
<i>Children <5^a</i>			Vaccine serotypes: 98% All serotypes: 77%	97, 99% 73, 79%
<i>Persons ≥65^b</i>			Vaccine serotypes: 76.2% All serotypes: 38.2%	NA
Canada (Quebec) ^c	2004	2, 4 and 12 months	All serotypes: 72.5%	NA
UK (England and Wales) ^d	2006	2, 4 and 13 months	Two doses under age 1: 85%	49, 95%
Australia ^e	2002	2, 4 and 6 months	Vaccine serotypes: 89.6%	NA

^a 2005 data.

^b 2004 data.

^c Children < 5 years of age. 2006 data.

^d Children <2 years of age. Calculated vaccine effectiveness as of May 2008 (Broome method). Complete effectiveness for routine 2+1 schedule not yet available.

^e Roche et al., *Communicable Disease Intelligence*. 2008; 32:18-30 (*incl in Mod 1.3.1*).

Effectiveness of Prevenar (7-valent) in a 3+1 schedule has also been observed against acute otitis media and pneumonia since its introduction in a national immunisation programme. In a retrospective evaluation of a large US insurance database, AOM visits were reduced by 42.7%, and prescriptions for AOM by 41.9%, in children younger than 2 years of age, compared with a pre-licensure baseline (2004 vs. 1997 - 99). In a similar analysis, hospitalisations and ambulatory visits for all-cause pneumonia were reduced by 52.4% and 41.1%, respectively. For those events specifically identified as pneumococcal pneumonia, the observed reductions in hospitalisations and ambulatory visits were 57.6% and 46.9%, respectively, in children younger than 2 years of age, compared with a pre-licensure baseline (2004 vs. 1997 - 99).

While direct cause-and-effect cannot be inferred from observational analyses of this type, these findings suggest that Prevenar (7-valent) plays an important role in reducing the burden of mucosal disease (AOM and pneumonia) in the target population.

Children with sickle cell disease

The immunogenicity of Prevenar (7-valent) has been investigated in an open-label, multicentre 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.

INDICATIONS

Active immunisation against disease caused by *Streptococcus pneumoniae* serotypes 1, 3, 4, 5, 6A, 6B, 7F, 9V, 14, 18C, 19A, 19F and 23F (including sepsis, meningitis, pneumonia, bacteraemia and acute otitis media) in infants and children from 6 weeks up to 5 years of age.

The use of Prevenar 13 should be determined on the basis of official recommendations, taking into consideration the impact of pneumococcal disease in different age groups as well as variability of serotype epidemiology in different geographical areas.

CONTRAINDICATIONS

- Hypersensitivity to the active substances or to any of the excipients, or to diphtheria toxoid
- Allergic reaction or anaphylactic reaction following prior administration of Prevenar.

PRECAUTIONS

Do not administer Prevenar 13 intravenously. Do not administer Prevenar 13 intravascularly. Take care to avoid injecting into or near nerves and blood vessels. The vaccine should not be injected in the gluteal area (see DOSGAGE AND ADMINISTRATION).

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.

As with other vaccines, the administration of Prevenar 13 should be postponed in subjects suffering from acute moderate or severe febrile illness.

Disease coverage

Prevenar 13 will not protect against *Streptococcus pneumoniae* serotypes other than those included in the vaccine nor other micro-organisms that cause invasive disease, pneumonia, or otitis media. As with any vaccine, Prevenar 13 may not protect all individuals receiving the vaccine from pneumococcal disease.

Children with blood disorders

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.

Children with impaired immune response

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.

Vaccination in high-risk groups

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. Safety and immunogenicity data for Prevenar 13 are not available for individuals in immunocompromised groups (e.g., congenital or acquired splenic dysfunction, HIV infected, malignancy, haematopoietic stem cell transplant, nephrotic syndrome) and vaccination should be considered on an individual basis.

Children below 2 years old should receive the appropriate-for-age Prevenar 13 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 13 should receive 23-valent pneumococcal polysaccharide vaccine. The interval between the 13-valent

pneumococcal conjugate vaccine (Prevenar 13) 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 13 might result in hyporesponsiveness to further doses of Prevenar 13.

Risk of apnoea

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 \leq 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.

Prophylactic antipyretics

Antipyretic treatment should be initiated according to local treatment guidelines.

Prophylactic antipyretic medication is recommended:

- for all children receiving Prevenar 13 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.

Carcinogenicity and mutagenicity

Prevenar 13 has not been evaluated for any carcinogenic or mutagenic potential, or impairment of fertility.

Preclinical safety data

Non-clinical data reveal no special hazard for humans based on conventional studies of safety pharmacology, repeated dose toxicity, and local tolerance studies.

Use in pregnancy

Category B2

Prevenar 13 is not indicated or recommended for use in pregnant women and has not been evaluated for potential harmful effects during pregnancy in animals or humans.

Use in lactation

Safety during lactation has not been established. It is not known whether vaccine antigens or antibodies are excreted in breast milk.

Geriatric use

The safety and effectiveness of Prevenar 13 in geriatric populations have not been established.

Interactions with other medicines

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

Prevenar 13 can be given with any of the following vaccine antigens, either as monovalent or combination vaccines: diphtheria, tetanus, acellular or whole cell pertussis, *Haemophilus influenzae* type b, inactivated poliomyelitis, hepatitis B, meningococcal serogroup C, measles, mumps, rubella and varicella. Clinical trials demonstrated that the immune responses and the safety profiles of the administered vaccines were unaffected.

Previously, trials with Prevenar and rotavirus vaccines have demonstrated that the immune responses of the seven pneumococcal serotypes in Prevenar and the rotavirus vaccine were unaffected. It is not expected that any differences in immune response for the six additional serotypes or the rotavirus vaccine will be observed if Prevenar 13 is used. In clinical trials, where there was concomitant administration of Prevenar 13 and rotavirus vaccine, no change in the safety profiles of these vaccines was observed.

Effects on ability to drive and operate machinery

Not relevant.

ADVERSE EFFECTS

Adverse reaction frequencies are listed below in CIOMS frequency categories:

Very common: $\geq 10\%$

Common: $\geq 1\%$ and $< 10\%$

Uncommon: $\geq 0.1\%$ and $< 1\%$

Rare: $\geq 0.01\%$ and $< 0.1\%$

Very rare: $< 0.01\%$

These data are from clinical trials in which Prevenar 13 was administered simultaneously with other routine childhood vaccines.

Body as a whole Very common:	Fever; any injection-site erythema, induration/swelling or pain/tenderness; Injection-site erythema or induration/swelling 2.5 cm –7.0 cm (after toddler dose and in older children [age 2 to 5 years]).
Common	Fever greater than 39°C; injection-site erythema or induration/swelling 2.5 cm - 7.0 cm (after infant series); injection-site pain/tenderness interfering with movement
Uncommon	Injection-site induration/swelling or erythema greater than 7.0 cm
Digestive system Common:	Diarrhoea; vomiting
Immune system disorders Rare:	Hypersensitivity reaction including face oedema, dyspnoea, bronchospasm
Metabolic and nutritional disorders Very common:	Decreased appetite
Nervous system Very common:	Drowsiness/increased sleep; restless sleep/decreased sleep
Uncommon:	Seizures (including febrile seizures)
Rare:	Hypotonic-hyporesponsive episode
Skin and appendages Common:	Rash
Uncommon:	Urticaria or urticaria-like rash
Psychiatric disorders Very common:	Irritability
Uncommon:	Crying

Table 4. Percentage of Infant and Toddler Subjects Reporting Solicited Local Reactions at the Prevenar 13 or Prevenar (7-valent) Injection Sites

	Dose 1 ^a		Dose 2 ^a		Dose 3 ^a		Dose 4 ^b	
Graded Local Reaction	Prevenar 13 (N ^c =3601-3878)	Prevenar 7 (N ^c =2025-2148)	Prevenar 13 (N ^c =3087-3388)	Prevenar 7 (N ^c =1699-1824)	Prevenar 13 (N ^c =2603-2809)	Prevenar 7 (N ^c =1245-1364)	Prevenar 13 (N ^c =1049-1198)	Prevenar 7 (N ^c =654-791)
Tenderness								
Any	46.8	44.9	44.7	43.9	41.0	39.5	52.1	56.0

Significant ^d	8.3	9.3	6.3	8.6*	6.0	5.9	6.2	8.1
Induration								
Any	23.0	21.9	28.0	28.9	30.1	30.3	32.6	33.5
Mild ^e	19.8	20.0	25.6	26.5	27.6	27.9	29.8	29.4
Moderate ^e	6.9*	4.7	7.0	6.1	8.0	7.2	12.0	10.5
Severe ^e	0	0	0.1	0	0	0	0	0
Erythema								
Any	26.3	27.8	35.3	35.1	38.3	37.0	43.6	43.7
Mild ^e	24.7	26.8	33.9	33.9	36.5	35.3	39.4	40.0
Moderate ^e	2.7*	1.8	3.0	3.1	5.0	5.3	11.8	11.7
Severe ^e	0	0	0.1	0	0	0	0.1	0.2

* Statistically significant difference $p < 0.05$

Follow-up time = 4 days following each dose for most studies. Two studies had a follow-up time of 7 days and one study had a follow-up time of 15 days for stage 1 and 8 days for stage 2.

- a. Infant dose data are included for 12 infant studies.
- b. Toddler dose data are included for the 6 infant studies with toddler dose data.
- c. Number of subjects reporting Yes for at least 1 day or No for all days.
- d. Significant = present and interfered with limb movement.
- e. Intensity of induration and erythema are rated by the diameter of the affected area: 0.5-2.0 cm = mild; 2.5-7.0 cm = moderate; >7.0 cm = severe.

Table 5. Percentage of Infant and Toddler Subjects Reporting Solicited Systemic Adverse Reactions, Fever and Antipyretic Medications after Each Vaccination

	Dose 1 ^a		Dose 2 ^a		Dose 3 ^a		Dose 4 ^b	
Graded Systemic Events	Prevenar 13 (N ^c =3594-4022)	Prevenar 7 (N ^c =1998-2215)	Prevenar 13 (N ^c =3110-3606)	Prevenar 7 (N ^c =1718-1969)	Prevenar 13 (N ^c =2580-3024)	Prevenar 7 (N ^c =1253-1480)	Prevenar 13 (N ^c =1073-1283)	Prevenar 7 (N ^c =666-873)
Decreased Appetite	38.4	37.2	37.8	41.0	36.6	38.1	42.2	50.2
Irritability	69.2	63.9	68.8	68.1	61.9	60.6	63.4	69.6
Increased Sleep	59.0	57.4	50.9	51.1	41.2	40.7	42.7	52.3
Decreased Sleep	36.4*	33.5	35.3	34.9	34.0	32.8	30.1	33.2
Fever^d								
Any	25.0*	24.4	32.2	38.4	27.8	32.4	43.0	49.8
Mild	24.1*	23.5	30.7	37.3	26.8	31.3	41.1	48.2
Moderate	1.5	1.2	3.0	2.9	2.9	2.6	6.6	8.3
Severe	0.0	0.2*	0.1	0.1	0.2	0.2	0.3	0.2
Antipyretic Medications								
Treat	45.9	45.9	49.8	55.3	46.1	51.9	43.0	50.4
Prevent	46.5	46.0	48.9	50.9	47.1	51.1	36.1	46.5

* Statistically significant difference $p < 0.05$

Follow-up time = 4 days following each dose for most studies. Two studies had a follow-up time of 7 days and one study had a follow-up time of 15 days for stage 1 and 8 days for stage 2.

- Infant dose data are included for 12 infant studies.
- Toddler dose data are included for the 6 infant studies with toddler dose data.
- Number of subjects reporting Yes for at least 1 day or No for all days.
- "Any" fever = subjects with any temperature $\geq 38^{\circ}\text{C}$; for subcategories of fever by grading, subjects may be included in more than 1 row. Fever grading: mild $\geq 38^{\circ}\text{C}$ but $\leq 39^{\circ}\text{C}$, moderate $> 39^{\circ}\text{C}$ but $\leq 40^{\circ}\text{C}$, severe $> 40^{\circ}\text{C}$.

Additional adverse reactions from Prevenar (7-valent)

Although the following adverse drug reactions were not observed in the clinical trials for Prevenar 13, they are considered adverse drug reactions for pneumococcal 7-valent conjugate vaccine and are considered adverse drug reactions for Prevenar 13 as well. These reactions are listed as follows with the frequency seen with pneumococcal 7-valent conjugate vaccine.

Adverse reactions from Prevenar (7-valent) post-marketing experience

These frequencies are based on spontaneous reporting rates for pneumococcal 7-valent conjugate vaccine and have been calculated using number of reports and number of doses distributed.

General disorders and administration site conditions

Very rare: Injection-site dermatitis; injection-site urticaria; injection-site pruritus

Blood and lymphatic system disorders

Very rare: Lymphadenopathy localized to the region of the injection-site

Immune system disorders

Very rare: Anaphylactic/anaphylactoid reaction including shock

Skin and subcutaneous tissue disorders

Very rare: Angioedema; erythema multiforme

DOSAGE AND ADMINISTRATION

The dose of Prevenar 13 is 0.5 mL given intramuscularly only, with care to avoid injection into or near nerves and blood vessels. 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.

Do not administer Prevenar 13 intravascularly or into the gluteal area. Do not administer Prevenar 13 intravenously, subcutaneously or intradermally, since the safety and immunogenicity of these routes have not been evaluated.

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. Prevenar 13 is a suspension containing an adjuvant. The vaccine must not be used if it cannot be uniformly suspended.

Prevenar 13 is not to be mixed with other vaccines or products in the same syringe. Prevenar 13 is for single-use in one patient only. The suspension contains no antimicrobial agent. Discard any residue.

Immunisation schedules

Data on the interchangeability of Prevenar or Prevenar 13 with other pneumococcal conjugate vaccines containing a protein carrier different from CRM₁₉₇ are not available.

It is recommended that infants who receive a first dose of Prevenar 13 complete the vaccination course with Prevenar 13.

The immunisation schedules for Prevenar 13 should be based on official recommendations.

Infants aged 6 weeks - 6 months

The primary infant series consists of three doses, each of 0.5 ml, with the first dose usually given at 6 weeks of age and with an interval of at least 1 month between doses. The first dose may be given as early as six weeks of age. A fourth (booster) dose is recommended after 12 months of age, and at least 2 months after the third dose.

Vaccination schedule for infants (6 weeks – 6 months of age)				
Dose:	Dose 1	Dose 2	Dose 3	Dose 4
Age at Dose:	6 weeks	4 months	6 months	12-15 months

Infants and children previously vaccinated with Prevenar

Prevenar 13 contains the same 7 serotypes contained in Prevenar and is manufactured based on the same conjugate technology using the same carrier protein CRM₁₉₇.

Infants and children who have begun immunisation with Prevenar may complete immunisation by switching to Prevenar 13 at any point in the schedule. In clinical trials, immunogenicity and safety profiles were comparable. Children up to 5 years of age who are considered completely immunised with Prevenar (7-valent) may receive one dose of Prevenar 13 to elicit immune responses to the six additional serotypes. This catch-up (supplemental) dose of Prevenar 13 should be administered with an interval of at least 8 weeks after the final dose of Prevenar (7-valent).

Vaccination schedule for previously unvaccinated children ≥7 months of age		
Age at first dose	Total number of 0.5 mL doses	Duration between doses
7-11 months of age	3	Between dose 1 and 2: At least 1 month Between dose 2 and 3: At least 2 months (3rd dose after 12 months of age)
12-23 months of age	2	At least 2 months
24 months to <72 months of age	1	N/A

Influence of foods, compatibility with drugs/fluids

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

OVERDOSAGE

Overdose with Prevenar 13 is unlikely due to its presentation as a pre-filled syringe. However, there have been reports of overdose with Prevenar 13 defined as subsequent doses administered closer than recommended to the previous dose. In general, adverse events reported with overdose are consistent with those that have been reported with doses given in the recommended schedules of Prevenar 13.

PRESENTATION

Prevenar 13 is presented as a suspension in 0.5 mL pre-filled syringes (Type I glass) in packs of 1 and 10. All syringe components are latex-free.

Storage

Store in a refrigerator (2°C – 8°C). Do not freeze. Discard if the vaccine has been frozen.

POISON SCHEDULE

Prescription Only Medicine (S4)

NAME AND ADDRESS

Pfizer New Zealand Ltd
P O Box 3998
Auckland, New Zealand, 1140.

Toll free telephone number: 0800 736 363 or email MedicalInformation.Australia@pfizer.com

Date of Preparation: 9 March 2011

® Registered Trade Mark