DATA SHEET

MENINGITEC® 0.5 mL

MENINGOCOCCAL SEROGROUP C CONJUGATE VACCINE

NAME OF MEDICINE

Meningococcal Serogroup C Conjugate Vaccine

DESCRIPTION

Meningitec is a sterile, ready to use suspension for intramuscular injection. It contains *Neisseria meningitidis* (meningococcal) Serogroup C oligosaccharide conjugated to *Corynebacterium diphtheriae* CRM_{197} protein.

CRM_{197} is a non-toxic variant of diphtheria toxin isolated from cultures of *Corynebacterium diphtheriae* strain C7 (β 197).

The manufacture of this product includes exposure to bovine derived materials. No evidence exists that any case of vCJD (considered to be the human form of bovine spongiform encephalopathy) has resulted from the administration of any vaccine product.

Active ingredients

Each 0.5 mL dose contains 10µg *Neisseria meningitidis* Serogroup C oligosaccharide (MnCO) conjugated to approximately 15µg *Corynebacterium diphtheriae* CRM_{197} carrier protein.

Excipients

Aluminium phosphate

Sodium chloride

Water for injections

PHARMACOLOGY

Neisseria meningitidis can cause severe systemic infections, including meningitis and septicaemia. The incidence of meningococcal disease in Australia is highest in infants under 4 years of age. The next highest risk group is young people aged 15-19 years. Whilst the incidence is greatest in the under 4's, mortality for Serogroup C disease is highest in the teenage years.

Vaccination with meningococcal polysaccharides induces the production of bactericidal antibodies that are serogroup specific. There are at least 13 serogroups known, of which Groups B and C are the most common. Infants below 2 years of age respond poorly to vaccination with unconjugated Serogroup C polysaccharide.

CLINICAL TRIALS

Immunogenicity

Primary series in infants

In four phase 2/3 studies conducted in the UK, 504 infants were administered 3 doses of 0.5 mL of Meningitec (10 µg of meningococcal Serogroup C polysaccharide, MnCC) intra-muscularly on a 2, 3, 4 month schedule. Of the total enrolled, 465 subjects were analysed for immunogenicity and of these, a subset of 288 was analysed for serum bactericidal antibody (SBA) titres. 98% to 100% of the subset of infants analysed for SBA titres developed SBA titres of at least 1/8, one month after the third dose.

In one randomised, double-blind phase 2 study (n=212) conducted in the US, 106 infants received 10 µg MnCC, and 30 of these subjects were analysed for SBA. 100% (30/30) developed SBA titres of at least,1:8 while 93% showed a four-fold increase in geometric mean titres (GMTs) after the third dose, compared to pre-vaccination titres.

Booster dose
Of 64 infants vaccinated with a booster dose of 10 µg MnCC in an earlier phase 2 US trial, 49 subjects were analysed for serum bactericidal antibodies, one month after the single booster dose. 100% (49/49) of infants analysed, developed SBA titres of at least 1/8 and 96% demonstrated a four-fold increase in post-vaccination GMTs compared to pre-vaccination levels.

Estimates of MnCC vaccine effectiveness from England's routine immunisation program (see Table 1 below) have demonstrated the need for a booster dose after the primary series, which is administered at 2, 3 and 4 months of age. At present, numbers of subjects are too small to make a recommendation regarding a booster dose for toddlers who have received a single priming dose. Effectiveness in all other age groups (up to 18 years) primed with a single dose has in four years of surveillance, remained approximately 90%, both within and more than one year after scheduled vaccination.

Table 1: Meningococcal Serogroup C conjugate vaccines#: effectiveness in immunised Cohorts, 4 years' surveillance data

Age at vaccination#	Doses scheduled*	Period of observation to Q1 2004, from:	Within 1 year of scheduled vaccination		More than 1 year after scheduled vaccination	
			Cases (vaccinated)	Vaccine effectiveness (95% CI)	Cases (vaccinated)	Vaccine effectiveness (95% CI)
2-4 months	3	Q1 2000	9 (3)	93% (67 to 99)	19 (18)	-81% (-7430 to 71)
5-11 months	2	Q3 2000	6 (2)	87% (11 to 99)	7 (3)	82% (-8 to 97)
1-2 years	1	Q3 2000	19 (6)	88% (65 to 96)	6 (4)	61% (-327 to 94)
3-4 years	1	Q3 2000	45 (1)	98 (90 to100)	19 (4)	93 (78 to 98)
11-16 years	1	Q2 2000	45 (4)	96% (89 to 99)	39 (8)	90% (77 to 96)
Total			124 (16)		90 (37)	

No data are available for subjects whose age at vaccination was 4-6, 7-10 years or 17-18 years.

* Vaccine effectiveness compares children eligible for complete vaccination who had received all scheduled doses versus no doses. Partly vaccinated children were excluded. All commercial vaccines in the UK market were included in the study.

Q= quarter. Ref: *Lancet* 2004; 364:365-7.

A bactericidal titre of ≥ 1:8 is considered a correlate of short-term protection based on effectiveness estimated from post-marketing surveillance.

Antibody persistence
In a double-blind, randomised study, of 212 infants enrolled, SBA titres were evaluated in 61 children administered Meningitec as a booster dose in the second year of life. SBA titres ≥ 1:8 were present in 79% of subjects (48/61) one year following the three-dose priming series, and prior to the administration of booster dose. The data indicate that antibodies persist for at least one year following the three-dose priming series.

Evidence of priming by conjugate vaccine
Seventeen subjects from an earlier phase 2 trial in UK infants were administered a challenge dose of one-fifth the adult volume of meningococcal polysaccharide vaccine, one year after the first dose of the primary series. 94% (16/17) of infants responded with SBA titres ≥ 1:8 and 88% demonstrated a four-fold increase in post-vaccination GMTs over pre-vaccination levels.

Immunogenicity of a single primary dose in toddlers and older children
Seventy five subjects who were 13 months old were administered a single dose of 10 µg MnCC in an open, single-group UK study. 91% (68/75) developed SBA titres ≥ 1:8 and 89% showed a four-fold increase over the pre-vaccination GMTs.

Immunogenicity of a single primary dose in adults

In a randomised, double-blind trial (n=30), healthy adult volunteers between 18 and 60 years of age were administered a single dose of 10 µg MnCC (n=15) or meningococcal polysaccharide vaccine (n=15). 100% of subjects (15/15) in the group receiving MnCC achieved SBA titres ≥ 1:8 and a four-fold rise in post-vaccination GMTs compared to pre-vaccination levels. In the group receiving the licensed polysaccharide vaccine, SBA titres ≥ 1:8 were achieved by all subjects, while only 87% of subjects (13/15) showed a four-fold rise in post-vaccination GMTs.

Evaluation of immune tolerance in young adults previously administered polysaccharide vaccine
In an open, partially-randomised study with two groups (n enrolled=242; analysed for Immunogenicity = 217), university students between 18 and 25 years of age, who had received polysaccharide vaccine 6 months previously, were administered either MnCC (n=83) or polysaccharide vaccine (n=85), and compared to non-randomised controls who received MnCC for the first time (n=49). SBA titres ≥ 1:8 were achieved by 99% of subjects (82/83) administered MnCC after polysaccharide, while 93% (79/85) achieved the same levels when given a second dose of polysaccharide. 100% (49/49) of naïve subjects achieved SBA titres ≥ 1:8.

Evaluation in immunocompromised patients
The safety and immunogenicity of Meningitec have not been studied in persons with functional or anatomic asplenia, or in persons with inherited defects of properidin or complement.

Protective efficacy
There have been no protective efficacy studies conducted with Meningitec. A post-marketing surveillance program conducted by the UK Health Protection Agency (Communicable Disease Surveillance Centre and Meningococcal Reference Unit) in England has analysed effectiveness in toddlers and 15-17 year olds, following the phased introduction of Meningitec followed by two other Serogroup C meningococcal conjugate vaccines into the UK.

Continued surveillance has disclosed that the combined meningococcal Serogroup C conjugate vaccines' effectiveness in the interval between one and four years after primary vaccination of infants had declined compared to the interval within a year after scheduled vaccination (see Table above), leading to the recommendation for a booster dose after routine infant vaccination. Evidence for waning effectiveness in toddlers (1 to 2 year olds) primed with a single dose was inconclusive and effectiveness in all other age groups (up to 18 years of age) primed with a single dose remained around 90% or more within and more than one year after vaccination.

Clinical studies with Prevenar and Meningitec
The concomitant administration of Prevenar and Meningitec at 2 and 6 months of age in different limbs gave immune responses that were similar to administration of either vaccine given alone. In this three-dose primary series clinical trial, the concomitant administration group was compared to a group given three doses of Prevenar or a group given two doses of Meningitec. (All infants also received three doses of Infanrix® hexa, DTPa-HBV-IPV / Hib, vaccine in the primary series.) There was no statistically significant difference in the proportion of infants who achieved a serotype-specific immune response ≥ 0.35 mcg/ml for each pneumococcal serotype, whether in the concomitant or the separate administration group. Likewise, there was no statistically significant difference in the percentage of infants with a MnC serum bactericidal activity titre ≥ 1:8 (concomitant 99.6% versus separate 98.0%) or ≥ 1:128 (concomitant 91.5% versus separate 84.6%). All children received a booster with the respective vaccine(s) given in the primary series.

Pharmacokinetic properties

No pharmacokinetic data are available, as they are not appropriate for vaccines.

INDICATIONS

Active immunisation of children from 6 weeks of age, adolescents and adults for the prevention of invasive disease caused by *Neisseria meningitidis* Serogroup C.

CONTRAINDICATIONS

Hypersensitivity to any component of the vaccine, including diphtheria toxoid.

Occurrence of significant neurological signs or symptoms, or an allergic or anaphylactoid/anaphylactic reaction

following a prior dose of Meningitec.

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

PRECAUTIONS

Meningitec may not protect 100% of the individuals receiving the vaccine. Meningitec will only confer protection against Serogroup C of *Neisseria meningitidis*. It will not protect against other groups of *Neisseria meningitidis* or other organisms that cause meningitis or septicaemia. Immunisation with Meningitec does not substitute for routine diphtheria vaccination.

The duration of antibody persistence (beyond 12 months) following vaccination with Meningitec and the duration of protection from invasive disease caused by *Neisseria meningitidis* are currently unknown. The need and appropriate time for revaccination are not currently known.

Although there is no evidence that the vaccine causes meningococcal C meningitis, symptoms of meningism, such as neck pain/stiffness or photophobia, have been reported. Clinical alertness to the possibility of co-incidental meningitis should, therefore, be maintained.

Meningitec must never be administered intravenously. Meningitec is for intramuscular use only.

Allergic reactions

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 Meningitec.

The vial stopper contains dry natural rubber. This product should be used with caution in patients with known or possible latex sensitivity and handled with caution by persons with latex sensitivity.

Patients with blood disorders

Meningitec should not be given to individuals with thrombocytopenia or any coagulation disorder that would contraindicate intramuscular injection unless the potential benefit clearly outweighs the risk of administration. If the decision is made to administer this vaccine to individuals with coagulation disorders, it should be given with caution.

Patients with impaired immune responsiveness

Individuals with impaired immune responsiveness, whether due to the use of immunosuppressive therapy, a genetic defect, HIV infection, or other causes, may have a reduced antibody response to active immunisation. (See Clinical Trials, *Evaluation in immunocompromised patients).*

Risk of apnoea

As with all injectable paediatric vaccines, the potential risk of apnoea should be considered when administering the primary immunisation series to premature infants. The need for monitoring for at least 48 hours after vaccination should be considered for very premature infants (born $\leq$ 30 weeks of gestation), who remain hospitalised at the time of the recommended administration. As the benefit of vaccination is high in this group of infants, vaccination should not be withheld or delayed.

Patients with minor illnesses

Minor illnesses, such as mild respiratory infection with or without low-grade fever, are not generally contraindications to vaccination. The decision to administer or delay vaccination because of a current or recent febrile illness depends largely on the severity of symptoms and their aetiology. The administration of meningococcal Serogroup C conjugate vaccine should be postponed in subjects suffering from acute severe febrile illness.

Carcinogenicity, mutagenicity, impairment of fertility

No carcinogenicity, mutagenicity or fertility studies have been conducted with Meningitec.

Use in pregnancy

Category B2

Meningitec is not recommended for use in pregnant women. There are no clinical study data on the use of this vaccine in pregnant women. The safety of the vaccine has not been established for pregnant women.

In pre-clinical studies, female mice were immunised intramuscularly with twice the clinical dose of meningococcal Serogroup C conjugate vaccine, either prior to mating or during the gestation period. Gross necropsy of viscera was performed on each mouse. All mice survived to either delivery or caesarean-section. No adverse clinical signs were present in any mouse and no parameters that were evaluated were affected by administration of the vaccine, in either the adult or foetal mice.

Use in lactation

Meningitec is not recommended for use in nursing mothers. Information on the safety of the vaccine during lactation is not available. It is not known whether vaccine antigens or antibodies are excreted in human milk.

Use in children

Meningitec has been shown to be usually well tolerated and immunogenic in infants from 6 weeks and in children up to 6 years. Safety and immunogenicity have not been established in children below the age of 6 weeks.

Use in the elderly

This vaccine is not recommended for use in any elderly populations.

Interactions with other vaccines

Simultaneous administration with other vaccines

Meningitec can be administered at the same time as Oral Polio Vaccine (OPV), Hepatitis-B Vaccine (HBV), *Haemophilus influenzae* type b (Hib) vaccine, Diphtheria Tetanus whole-cell Pertussis – Haemophilus b conjugate (DTP-Hib), Diphtheria Tetanus acellular Pertussis (DTPa), Diphtheria Tetanus (DT), Pneumococcal conjugate vaccine 7-valent, Tetanus low dose Diphtheria (Td) and Measles-Mumps-Rubella (MMR) vaccines if this fits conveniently in the immunisation scheme.

There are data from two studies supporting concomitant administration of meningococcal Serogroup C conjugate vaccine and an acellular pertussis vaccine or an inactivated poliovirus vaccine.

Lower levels of meningococcal Serogroup C antibodies have been observed in some studies of concomitant administration of meningococcal Serogroup C conjugates with combinations containing acellular pertussis as compared to those containing whole cell pertussis antigens. The clinical implications of these observations are unknown.

Meningitec must not be mixed with other vaccines in the same syringe. Different injectable vaccines should be given at separate injection sites.

Data on concomitant administration of Meningitec with Prevenar (pneumococcal conjugate vaccine 7-valent) have shown no clinically relevant interference in the antibody response to each of the individual antigens when given as primary series vaccinations (see Clinical Trials).

Effects on activities requiring concentration and performance

Dizziness and somnolence have been reported with meningococcal Serogroup C conjugate vaccine in clinical trials and post marketing reports in adults and children.

ADVERSE EFFECTS

Adverse events in clinical trials

The safety of Meningitec was assessed during clinical trials in which approximately 11,000 doses were administered to infants, 1,000 doses were administered to toddlers during the second year of life, and 200 doses were administered to older subjects (4 to 60 years). Table 2 displays the adverse events that occurred at a frequency of 1% or greater within any of those age groups. Both local and systemic reactions in infants and toddlers were ascertained by questioning of the parents. For older subjects, local and febrile reactions were ascertained by questioning, whereas all other events were spontaneously reported to the investigators.

Table 2. Adverse events reported at a frequency of ≥1% in at least one age group (all clinical trials)

Organ system	Adverse event	Incidence (Number with event/Number of doses evaluated)[a]		
		Infants[b] (first year of life)	Toddlers[b] (second year of life)	Older age groups[c] (4-60 years)
General disorders and administration site conditions	Injection site reaction: pain	20% (2058/10548)	21% (211/991)	63% (123/196)
	Significant[d]	5% (492/10548)	9% (83/919)	7% (1/15)
	Injection site reaction: redness	12% (1263/10724)	9% (94/992)	36% (72/202)
	≥2.5 cm	1% (126/10724)	1% (6/992)	13% (27/202)
	Injection site reaction: swelling	8% (849/10720)	7% (73/992)	16% (33/202)
	≥2.5 cm	1% (148/10720)	2% (15/992)	7% (15/202)
	Fever (at least 38.0° C)	25% (2786/10978)	30% (337/1136)	1% (3/202)
	≥39.1° C	2% (192/10978)	4% (41/1136)	0% (0/202)
	Increased crying	70% (376/537)	3% (2/73)	Not done
	Unusual high-pitched crying	2% (5/299)	Not done	Not done
Nervous system disorders	Irritability	62% (6822/11060)	55% (635/1165)	2% (5/237)
	Drowsiness/somnolence	36% (4026/11039)	20% (227/1163)	3% (6/237)
	Sleeping through feed	28% (97/349)	Not done	Not done
	Impaired sleeping	23% (2366/10387)	25% (270/1100)	Not done
	Headache	Not done	Not done	13% (31/237)
Gastrointestinal disorders	Anorexia/decreased appetite	22% (2423/11049)	23% (270/1162)	1% (2/237)
	Vomiting	14% (1468/10699)	6% (67/1164)	3% (7/237)
	Diarrhoea	10% (1037/10382)	11% (114/1026)	2% (5/237)
	Dyspepsia	Not done	Not done	2% (5/237)
	Abdominal pain	Not done	Not done	1% (3/237)
	Nausea	Not done	Not done	1% (2/237)
Respiratory, thoracic & mediastinal disorders	Shortness of breath/dyspnoea	<1% (29/10531)	<1% (1/1092)	1% (2/237)
Skin & subcutaneous tissue disorders	Urticaria	1% (130/10531)	1% (11/1092)	0% (0/237)
Musculoskeletal, connective tissue & bone disorders	Myalgia	Not done	Not done	3% (6/237)

[a]This is summary data derived from nine studies conducted in the United States and the United Kingdom. The recording of adverse events varied by age group.
[b]Events listed for infants and toddlers were the result of specific symptom inquiry by the clinical investigators within 4 days of injection.
[c]General disorders and administration site conditions listed for older age groups were the result of specific symptom inquiry by the clinical investigators within 4 days of injection. All other events listed for older age groups were spontaneously reported to the clinical investigators within 4 weeks of injection. The list excludes events that were reported at a frequency of 1-5% but were considered coincidental and not likely to be due to Meningitec, specifically malaise, trauma, infection, viral infection, otitis media, bronchospasm, pharynigitis, rhinitis, and upper respiratory tract infection.
[d]Interfered with limb movement.

The majority of the safety experience with Meningitec comes from a single study conducted in the United States (Kaiser Study D118 P8) in which Meningitec was compared with Prevenar® (pneumococcal conjugate vaccine, 7 valent [7VPnC]). Infants in this study received Meningitec or Prevenar on a 2, 4, 6 month schedule, along with routine immunisation with either DTP/Hib (Tetramune®) or DTPa (Acel-Imune®). The infants may also have received other routine childhood vaccines. When the immunised infants were 12 to 15 months old, each received a booster dose of Meningitec or Prevenar. Table 3 displays the local and systemic reactions that occurred at a frequency of 1% or greater following 1, 2, or 3 doses in infants and following the booster dose in toddlers. All adverse events in these subjects were obtained by questioning of the parents.

Table 3. Adverse events reported at a frequency of ≥1% in one comparative clinical trial in infants and toddlers (Kaiser Study D118 P8)

Organ system	Adverse event[a]	Incidence (Number with event/Number of doses evaluated)			
		Meningitec + DTP/Hib	Meningitec + DTPa	7VPnC + DTP/Hib	7VPnC + DTPa
Infants (2, 4, 6 months of age)					
General disorders & administration site conditions	Injection site reaction: pain	20% (1641/8087)	16% (242/1557)	26% (2146/8153)	18% (288/1641)
	Significant[b]	5% (424/8087)	2% (35/1557)	8% (628/8153)	3% (56/1641)
	Inj. site reaction: redness	12% (949/8087)	8% (117/1557)	14% (1134/8153)	11% (188/1641)
	≥2.5 cm	1% (94/8087)	1% (17/1557)	1% (113/8153)	1% (18/1641)
	Inj. site reaction: swelling	9% (696/8087)	5% (80/1557)	12% (975/8153)	11% (175/1641)
	≥2.5 cm	2% (128/8087)	<1% (6/1557)	3% (214/8153)	2% (28/1641)
	Fever (at least 38.0° C)	29% (2449/8322)	10% (171/1631)	36% (3019/8370)	19% (328/1726)
	≥39.1° C	2% (171/8322)	<1% (9/1631)	3% (260/8344)	2% (28/1726)
Nervous system disorders	Irritability	65% (5378/8328)	46% (758/1633)	70% (5862/8382)	52% (904/1729)
	Drowsiness	36% (3035/8317)	31% (505/1633)	36% (3046/8353)	30% (521/1727)
	Impaired sleeping	24% (1981/8317)	17% (284/1633)	26% (2163/8363)	20% (337/1727)
Gastrointestinal	Anorexia/decreased appetite	23% (1926/8329)	14% (221/1632)	25% (2094/8375)	18% (313/1729)

Table 3. Adverse events reported at a frequency of ≥1% in one comparative clinical trial in infants and toddlers (Kaiser Study D118 P8)

Organ system	Adverse event[a]	Incidence (Number with event/Number of doses evaluated)			
		Meningitec + DTP/Hib	**Meningitec + DTPa**	**7VPnC + DTP/Hib**	**7VPnC + DTPa**
disorders	Vomiting	14% (1171/8332)	14% (224/1631)	17% (1389/8376)	14% (245/1728)
	Diarrhoea	10% (861/8327)	9% (145/1626)	11% (960/8362)	10% (179/1727)
Skin and subcutaneous tissue disorders	Urticaria	<1% (69/8334)	<1% (11/1633)	<1% (79/8382)	1% (19/1730)
Toddlers (second year of life)					
General disorders & administration site conditions	Injection site reaction: pain Significant[b]	28% (172/618) 13% (79/618)	15% (27/178) 2% (3/178)	37% (219/599) 19% (111/599)	23% (38/165) 9% (15/165)
	Inj. site reaction: redness ≥2.5 cm	11% (68/618) <1% (5/618)	4% (8/178) 0% (0/178)	13% (76/599) 2% (10/599)	11% (18/165) 4% (6/165)
	Inj. site reaction: swelling ≥2.5 cm	9% (56/618) 2% (14/618)	4% (8/178) 0% (0/178)	11% (68/599) 3% (17/599)	12% (20/165) 6% (9/165)
	Fever (at least 38.0° C) ≥39.1° C	37% (270/732) 5% (33/732)	17% (39/230) 2% (4/230)	42% (297/709) 5% (32/709)	21% (47/224) 1% (3/224)
Nervous system disorders	Irritability	66% (482/733)	43% (98/230)	73% (516/709)	44% (99/224)
	Drowsiness	23% (166/731)	17% (38/230)	21% (150/706)	17% (38/223)
	Impaired sleeping	28% (205/731)	19% (44/230)	30% (211/706)	20% (45/223)
Gastrointestinal disorders	Anorexia/decreased appetite	27% (200/731)	23% (53/229)	33% (233/707)	21% (46/224)
	Vomiting	7% (50/732)	5% (11/230)	10% (68/708)	5% (11/224)
	Diarrhoea	11% (82/731)	9% (21/229)	12% (80/709)	12% (26/224)
Skin and subcutaneous tissue disorders	Urticaria	<1% (6/733)	2% (4/230)	1% (10/709)	<1% (1/224)

[a]Events listed were the result of specific symptom inquiry by the clinical investigators within 4 days of injection.
[b]Interfered with limb movement.
DTP/Hib was Tetramune®; DTPa was Acel-Imune®.

Children between the ages of 25 months and 47 months were not included as subjects in clinical trials, and therefore no safety information from clinical trials is available for this age group.

Of note, transient injection site tenderness was reported in 70% of adults (18-25 years of age) during clinical trials. Fever of at least 38.0°C was often observed, but did not usually exceed 39.1°C, particularly in older age groups. In infants and toddlers, there was no evidence that symptoms observed after vaccination (listed in Tables 2 and 3) were related to Meningitec rather than to the concomitantly administered vaccines, particularly DTP.

Additional adverse reactions from post marketing surveillance (for all age groups)

These frequencies are based on spontaneous reporting rates and have been calculated using number of reports and number of doses distributed.

Table 4

System organ class	Adverse reaction
Blood and lymphatic system disorders:	
Very rare (<0.01%):	Lymphadenopathy.
Immune system disorders:	
Very rare (<0.01%):	Anaphylactic/anaphylactoid reactions including shock; hypersensitivity reactions including bronchospasm, facial oedema, and angioedema.
Nervous system disorders:	
Very rare (<0.01%):	Dizziness; seizures (convulsions) including febrile seizures and seizures in patients with pre-existing seizure disorders; hypoaesthesia and/or paraesthesia; hypotonia, (including hypotonic-hyporesponsive episode [HHE]).
Gastrointestinal disorders:	
Very rare (<0.01%):	Nausea; abdominal pain.
Skin and subcutaneous tissue disorders:	
Very rare (<0.01%):	Rash; urticaria; pruritus; erythema multiforme; Stevens-Johnson syndrome.
Musculoskeletal, connective tissue and bone disorders:	
Very rare (<0.01%):	Arthralgia.
Renal and urinary disorders:	
	Relapse of nephrotic syndrome has been reported in association with Meningococcal Serogroup C conjugate vaccines.
General disorders and administration site conditions:	
Very rare (<0.01%):	Injection site vesicles; injection site dermatitis; injection site hypersensitivity, including urticaria; injection site induration; injection site inflammation; injection site mass; injection site pruritus.

There have been very rare spontaneous reports of hypotonia (including HHE) in temporal association with the administration of meningococcal Serogroup C conjugate vaccine. In most cases, meningococcal Serogroup C conjugate vaccine was administered concomitantly with other vaccines, the majority of which were pertussis-containing vaccines.

There have been spontaneous reports of very rare petechiae and/or purpura following immunisation in the post marketing experience. Since Meningitec may not protect against 100% of meningococcal Serogroup C disease or disease due to organisms other than *Neisseria meningitidis* Serogroup C, individuals who experience petechiae and/or purpura following vaccination should be thoroughly evaluated for the possibility of an infectious or other cause, unrelated to vaccination.

As with other paediatric vaccines, there have been spontaneous reports of apnoea in temporal association with the administration of meningococcal Serogroup C conjugate vaccine. In most cases meningococcal Serogroup C conjugate vaccine was administered concomitantly with other vaccines including diphtheria tetanus pertussis vaccine (DTP), inactivated polio vaccine (IPV), oral polio vaccine (OPV), Haemophilus influenzae type b vaccine (Hib), diphtheria tetanus pertussis – Haemophilus influenzae type b vaccine (DTP-Hib), and/or diphtheria tetanus acellular pertussis – hepatitis B vaccine (DTaP-HBV). In addition, in most of the reports existing medical conditions such as history of apnoea, infection, prematurity, and/or seizures were present.

DOSAGE AND ADMINISTRATION

Upon storage, a white deposit and clear supernatant can be observed. Before use, shake well to obtain a homogenous white suspension and visually inspect the vaccine for foreign particulate matter and/or discolouration prior to administration. The vaccine must not be used if it cannot be uniformly suspended, particulate matter is observed, or if it is discoloured. Meningitec is for single-use in one patient only. Discard

any residue.

The vaccine is not to be mixed with other vaccines/products in the same syringe.

For the vial presentation, the vaccine must be administered immediately after being drawn up into a syringe.

The vaccine should not be injected intradermally, subcutaneously or intravenously since the safety and immunogenicity of these routes have not been evaluated.

Meningitec is for intramuscular injection, preferably in the anterolateral thigh in infants and in the deltoid region in older children, adolescents and adults. Care should be taken to avoid injection into or near nerves and blood vessels.

The vaccine should not be injected in the gluteal area.

Infants under the age of 12 months: three doses, each of 0.5 mL, the first dose given not earlier than 6 weeks and with an interval of at least 1 month between doses.

Children over the age of 12 months, adolescents and adults: a single dose of 0.5 mL.

Booster dose

It is recommended that a booster dose should be given after completion of the primary immunisation series in infants. The booster dose should be administered at, or after, 12 months of age. The need for further boosters after this fourth dose, or for booster doses in other age groups who have been primed with a single MnCC dose, has not yet been established. See also in Clinical Trials, Booster dose and Protective Efficacy subsections.

OVERDOSAGE

There have been reports of overdose with Meningitec. Most cases have involved inadvertent revaccination at varying intervals following initial vaccination. Most individuals were asymptomatic. The majority of those events experienced have also occurred with recommended single doses of Meningitec.

PRESENTATION

Contents of container

Meningitec is presented as a suspension in single dose glass vials* or pre-filled glass syringes. Packs of 1 and 10.

* Not marketed

Storage

Store at 2° to 8°C (Refrigerate. Do not freeze). Discard if the vaccine has been frozen.

NAME AND ADDRESS OF SPONSOR

Pharmacy Retailing Pty Ltd
t/a Healthcare Logistics
58 Richard Pearse Drive
Airport Oaks
Auckland
New Zealand

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