# PRODUCT INFORMATION

## NAME OF THE DRUG

MENJUGATE® SYRINGE (Meningococcal Group C -CRM197 Conjugate Vaccine).

## DESCRIPTION

MENJUGATE® SYRINGE is a conjugated meningococcal oligosaccharide C vaccine supplied in a single-dose (0.5 mL) presentation consisting of a vial containing lyophilised powder (vaccine component) and a diluent syringe containing a suspension of aluminium hydroxide as the adjuvant.

Each 0.5 mL dose of the reconstituted vaccine contains:

| | |
|---|---|
| *Neisseria meningitidis* group C (strain C11) oligosaccharide | 10 micrograms |
| Conjugated to: | |
| *Corynebacterium diphtheriae* CRM-197 protein (a non-toxic mutant of diphtheria toxin) | 12.5 to 25 micrograms |
| Adsorbed on: | |
| Aluminium hydroxide | 1.0 mg |

Each 0.5 mL dose of the reconstituted vaccine contains the following excipients:

mannitol, sodium phosphate monobasic monohydrate, sodium phosphate dibasic heptahydrate, sodium chloride, water for Injections.

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 Encephalitis) has resulted from the administration of any vaccine product.

## PHARMACOLOGY

MENJUGATE® SYRINGE (Meningococcal Group C–CRM197 Conjugate Vaccine) is intended for the prevention of meningitis and/or septicemia caused by *Neisseria meningitidis* serogroup C in infants and older age groups. MENJUGATE® SYRINGE is composed of meningococcal group C oligosaccharides conjugated to a protein carrier, a non-toxic mutant of diphtheria toxin, CRM197. In the final vaccine, aluminium hydroxide is used as an adjuvant.

There are at least 13 serogroups of *N. meningitidis* known, of which Groups B and C are the most common. Vaccination with MENJUGATE® SYRINGE induces the production of bactericidal antibodies that are specific for *N. meningitidis* serogroup C.

Infants below 2 years of age respond poorly to vaccination with unconjugated group C polysaccharide.

Compared to licensed unconjugated polysaccharide vaccines, the primary immune response induced by MENJUGATE® SYRINGE is superior in toddlers, children and adolescents, and is comparable in adults. Additionally, unlike unconjugated polysaccharide vaccines, MENJUGATE® SYRINGE has been shown to induce immunological memory in infants, toddlers and older children

## Clinical Trials

The serum bactericidal assay (BCA) referenced in the text below used human serum as a source of complement (hBCA). Many laboratories use rabbit serum as a complement source. Serum bactericidal assay (BCA) results achieved with rabbit serum as a complement source have been found to be much higher than those achieved when human serum is used as a complement source. Therefore results from assays using different complement sources are not directly comparable.

In clinical trials, MENJUGATE® SYRINGE is shown to be highly immunogenic and to induce protective levels of bactericidal antibodies in a large number of subjects after vaccination. BCA titres of ≥ 1:4 have been shown to be protective when the BCA assay used human serum as the complement source. However the cut-off of hBCA titres ≥ 1:8 was chosen for the MENJUGATE® SYRINGE clinical studies as a conservative approach towards protection against invasive disease caused by *N. meningitidis* serogroup C.

Table 1 shows short term and longer term immunological data pooled from comparative clinical studies 30 days after vaccination with MENJUGATE® SYRINGE in infants (7 to 11 weeks of age), toddlers (1-2 years), children (3-5 years), adolescents (11-17 years) and adults (18-64 years).

All studies used plain meningococcal polysaccharide A + C (MenPS) as a comparator except the infant studies where this was inappropriate and HBV was used. The data in table 1 shows that vaccination with MENJUGATE® SYRINGE produces high immunological responses in all age groups. In comparison Men PS vaccine produced poor immunological responses in toddlers and young children. hBCA titres of ≥ 1:8 were seen in 68% (n=88; 95%CI 57%, 78%) of adolescents (11-17 years) vaccinated with Men PS. In adults the immunological responses were comparable as 90% of the adults vaccinated with MENJUGATE® SYRINGE (n=136; 95%CI 84%, 95%) and 88% of the adults vaccinated with MenPS (n=130; 95%CI 82%, 93%) achieved hBCA titres of ≥ 1:8. The infant control group vaccinated with HBV vaccine only achieved protective titres for MenC in less than 3% of infants.

**Table 1: Pooled immunogenicity data (30 days post-vaccination) from subjects vaccinated with MENJUGATE® SYRINGE in comparative randomised studies. (The BCA assay used human serum as a complement source)**

| Age Group | Infants Dose 2 | Infants Dose 3 | Toddlers Single dose | Children Single dose | Adolescent Single dose | Adults Single dose |
|---|---|---|---|---|---|---|
| **% hBCA ≥1:8** | 99% | 99.5% | 78% | 79% | 86% | 90% |
| **95% CI** | 98-100% | 98-100% | 72-83% | 68-87% | 77-93% | 84-95% |
| **N** | 417 | 409 | 237 | 80 | 88 | 136 |
| **IgG GMT (U/mL)** | 11 | 16 | 4.89 | 4.72 | 24 | 12 |
| **95% CI** | 10-12% | 15-17% | 4.06-5.9% | 3.47-6.41% | 17-33% | 9.15-16% |
| **N** | 419 | 409 | 252 | 94 | 86 | 136 |
| **Fold increase in GMT from baseline** | 51 | 74 | 23.3 | 22.5 | 92.3 | 40 |

Subsequent to the trials described above data on the use of a 2-dose primary immunisation series was generated from a clinical trial that compared a 2, 3, 4 month vaccination schedule to a 2, 4 month vaccination schedule in 241 infants. One month after completion of the primary series nearly all subjects had attained hBCA titres≥ 1:8 ( 100% and 98% in respective groups). At 28 days after a challenge dose of unconjugated MenC vaccine at 12 months of age, all of 50 subjects primed with three doses and 54/56 (96%) primed with two doses achieved hBCA titres ≥ 1:8.

**Immunological Memory**

Unlike unconjugated polysaccharide vaccine, MENJUGATE® SYRINGE induces immunological memory after vaccination.

In a subset (n=56) of MENJUGATE® SYRINGE-primed infants (i.e. infants given three primary injections of MENJUGATE® SYRINGE at 2, 3, and 4 months of age) and HBV-primed infants (n=28) given a dose of MenPS at 12 months of age, 96.5% of the MENJUGATE® SYRINGE-primed infants achieved hBCA titres ≥ 1:8 (and a 16-fold increase in GMTs from 12-month pre-booster levels) compared to only 11% of the HBV-primed infants (p<0.001). Similarly 100% of MENJUGATE® SYRINGE-treated infants given booster doses at 12 months of age (n=52) achieved hBCA titres ≥ 1:8 and a 40-fold increase in GMTs from 12-month pre-booster levels.

In MENJUGATE® SYRINGE-treated toddlers 100% (n=59; 95%CI 94%, 100%) of toddlers given a booster dose of MenPS 12 months after a series of 2 MENJUGATE® SYRINGE vaccinations achieved hBCA titres ≥ 1:8 and a 46-fold increase in GMTs from 12-month pre-booster levels.

Similarly 100% of toddlers (n=54; 95%CI 93%,100%) given a MENJUGATE® SYRINGE-booster dose 6 months after a single MENJUGATE® SYRINGE vaccination achieved hBCA titres of ≥ 1:8 and a 30-fold increase in GMTs from 6-month pre-booster levels.

Similarly an anamnestic response was demonstrated in a small subset of MENJUGATE® SYRINGE-treated children (3-5 years) given a 1/50th dose MenPS 12 months after first immunisation with MENJUGATE® SYRINGE.

**Protective Efficacy**

No company-sponsored protective efficacy studies have been conducted with MENJUGATE® SYRINGE, however the Public Health Laboratories Services (PHLS), UK assessed the immunogenicity and safety of MenC conjugate vaccines (including MENJUGATE® SYRINGE) in a series of studies in toddlers (12-17 months), children (3.5 to <6years), adolescents (14-17 years) and the school-aged population (4-18 years). These studies confirmed that:

- Meningococcal C conjugate vaccines are highly immunogenic,
- Concomitant administration of diphtheria/tetanus vaccine and Meningococcal C conjugate vaccine to children and adolescents does not interfere with the immunogenicity or reactogenicity of either vaccine; and
- Meningococcal C conjugate vaccines are well tolerated in toddlers and the school-aged population.

**Post-marketing surveillance following an immunisation campaign in the UK**

Estimates of vaccine effectiveness from the UK's routine immunisation programme (using various quantities of three meningococcal serogroup C conjugate vaccines) covering the period from introduction at the end of 1999 to March 2004 (see Table 2 below) have demonstrated the need for a booster dose after completion of the primary series (three doses administered at 2, 3 and 4 months). Within one year of completion of the primary series, vaccine effectiveness in the infant cohort was estimated at 93% (95% confidence intervals 67, 99). However, more than one year after completion of the primary series, there was clear evidence of waning protection. Estimates of effectiveness based on a small number of cases to date indicate that there may also be waning protection in children who received a single priming dose as toddlers. 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 so far remained around 90% or more within and more than one year after vaccination.

**Table 2: Meningococcal 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 to 100) | 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, 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.

## 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.

Persons who have shown signs of hypersensitivity after previous administration of MENJUGATE® SYRINGE.

As with other vaccines, administration of MENJUGATE® SYRINGE should be postponed in subjects presenting with an acute severe febrile illness.

## PRECAUTIONS

MENJUGATE® SYRINGE is intended for intramuscular use only.

Before the injection of any biological, the person responsible for administration should take all precautions known for the prevention of allergic or any other reactions. As with all injectable vaccines, appropriate medical treatment and supervision should always be readily available in case of a rare anaphylactic event following administration of the vaccine.

Prior to administration of any dose of MENJUGATE® SYRINGE, the parent or guardian should be asked about the personal history, family history, and recent health status of the vaccine recipient,

including immunisation history, current health status and any adverse event after previous immunisations.

Although MENJUGATE® SYRINGE induces immunological memory after vaccination, the duration of protection from invasive disease caused by *Neisseria meningitidis* serogroup C has not been established. The need and appropriate time for revaccination are not currently known.

MENJUGATE® SYRINGE will not protect against meningococcal diseases caused by any of the other serogroups of meningococcal bacteria (A, B, 29-E, H, I, K, L, W-135, X, Y, or Z, including non-typed). Complete protection against meningococcal serogroup C infection cannot be guaranteed.

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

Conjugate vaccines containing Cross Reacting Material 197 (CRM197) should not be considered as immunising agents against diphtheria. No changes in the schedule for administering vaccines containing Diphtheria Toxoid are recommended.

While HIV infection is not a contraindication, MENJUGATE® SYRINGE has not been specifically evaluated in the immunocompromised.

Any acute infection or febrile illness is reason for delaying the use of MENJUGATE® SYRINGE except when, in the opinion of the physician, withholding the vaccine entails a greater risk. A minor febrile illness, such as a mild upper respiratory infection, is not usually reason to defer immunisation.

The potential risk of apnoea and the need for respiratory monitoring for 48-72 hours 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.

MENJUGATE® SYRINGE has not been evaluated in persons with thrombocytopenia or bleeding disorders. The risk versus benefit for persons at risk of haemorrhage following intramuscular injection must be evaluated.

Parents should be informed of the immunisation schedule for this vaccine. Precautions such as useful antipyretic measures for this vaccine should be relayed to the parent or guardian and the need to report any adverse event should be stressed.

The tip cap of the syringe contains 10% Dry Natural Rubber. Although the risk for developing allergic latex reactions is very small, healthcare professionals are encouraged to consider the benefit risk prior to administering this vaccine to patients with known history of hypersensitivity to latex.

**Carcinogenicity, Mutagenicity and Impairment of Fertility**

No carcinogenicity, mutagenicity or fertility studies have been conducted with MENJUGATE® SYRINGE.

**Use in Pregnancy (Category B2)**

MENJUGATE® SYRINGE vaccine is not recommended for use in pregnant women. No information is available on administration of MENJUGATE® SYRINGE to pregnant women.

Female rabbits were immunised repeatedly by the intramuscular route with twice the clinical dose of meningococcal group C conjugate vaccine, either prior to mating or during the gestation period. High titres of anti-Men C antibodies were demonstrated in maternal blood 3 weeks prior to and during gestation. There were no signs of maternal or fetal toxicity or fetal malformations.

**Use in Lactation**
Safety in lactation has not been established. MENJUGATE® SYRINGE vaccine is not recommended for use in lactating women.

**Interactions with other Vaccines**
MENJUGATE® SYRINGE must not be mixed with other vaccines in the same syringe. Separate injection sites should be used if more than one vaccine is being administered.

Inactivated vaccines and live vaccines, particularly those in the childhood schedule, can be given during the same visit but in different limbs.

Administration of MENJUGATE® SYRINGE at the same time as the following vaccines does not reduce the immunological response to any of these other antigens:

- Polio (inactivated polio vaccine [IPV] and oral polio vaccine);
- Diphtheria (D) and Tetanus (T) toxoids alone or in combination with whole cell or acellular Pertussis (aP);
- Haemophilus Influenzae type B (Hib) conjugate vaccine;
- Hepatitis B (HBV) vaccine administered alone or at the same time as combined vaccine containing diphtheria, tetanus, Hib, inactivated polio and acellular pertussis;
- Combined measles, mumps and rubella; or
- 7-valent pneumococcal conjugate vaccine (Prevenar). The effect of concomitant administration of Menjugate with 7-valent pneumococcal conjugate vaccine (Prevenar) and a hexavalent vaccine (DTaP-HBV-IPV-Hib) on immune responses was assessed in infants vaccinated at median ages of approximately 2, 4.5 and 6.5 months. The potential for immune interference has not been assessed at other primary immunisation schedules.

Minor variations in GMT antibody titres were observed between studies; however, the clinical significance, if any, of these observations is not established.

## ADVERSE REACTIONS

### Clinical Trial Data

In controlled clinical studies performed in all age groups, signs and symptoms were actively monitored and recorded on diary cards following administration of the vaccine.

Of the local solicited symptoms, the most frequently reported were injection-site pain, erythema and swelling, which were normally mild and resolved within 24-72 hours following vaccination.

The general symptoms that have been solicited and reported were predominantly mild and resolved spontaneously. These include headache, malaise and myalgia in adolescents and adults; and irritability, change in appetite, diarrhoea and fever in younger children. These solicited general symptoms were also reported in the control groups and have been reported when MENJUGATE® SYRINGE was administered concomitantly with other vaccines.

In infants and toddlers symptoms including crying, irritability, drowsiness, impaired sleeping, anorexia, diarrhoea and vomiting were common after vaccination but there was no evidence that these were related to MENJUGATE® SYRINGE rather than concomitant vaccines, particularly DTP.

**Toddlers Through Adults**

Table 3 presents an analysis of local and systemic reactions occurring within 7 days after one immunisation with MENJUGATE® SYRINGE. Data are pooled from 11 studies, representing approximately 1400 subjects. Most local and systemic reactions occurred by day 1 following immunisation. In general, lower percentages of local and systemic reactions were present on days 2 through 6 following the first immunisation.

**Table 3: Summary of Local and Systemic Post-immunisation Reactions Within 7 Days Following One Immunisation of MENJUGATE® SYRINGE, by Age Group at Enrolment***

| | **Percentage of Subjects** | | |
|---|---|---|---|
| | **1-2 years** (N=942) | **3-5 years** (N=198) | **11-64 years** (N=269) |
| **Injection Site** | | | |
| Pain (Any) | 22% | 25% | 81% |
| Severe | <1% | 0 | 2% |
| Temperature (Any) | 15% | 5% | 47% |
| Hot | <1% | 1% | 8% |
| Erythema (Any) | 28% | 16% | 19% |
| >50 mm | <1% | 0 | 1% |
| Induration (Any) | 16% | 7% | 24% |
| >50 mm | <1% | 0 | 1% |
| **Systemic** | | | |
| Change in Eating Habits | 16% | 6% | - |
| Sleepiness | 19% | 9% | - |
| Unusual Crying | 4% | 1% | - |
| Persistent Crying | 1% | 0% | - |
| Irritability | 30% | 10% | - |
| Vomiting | 9% | 5% | - |
| Diarrhoea | 18% | 8% | - |
| Rash | 9% | 4% | - |
| Chills | - | - | 13% |
| Nausea | - | - | 16% |
| Malaise | - | - | 25% |
| Myalgia | - | - | 29% |
| Arthralgia | - | - | 16% |
| Headache | - | - | 34% |
| Temp ≥38°C | 9% | 4% | 2% |
| Stayed Home Due to Reaction | - | - | 7% |
| Analgesic/ Antipyretic Medication used | 25% | 9% | 18% |

*This is a summary of data derived from a meta-analysis of 11 studies conducted in the

United States, United Kingdom, Netherlands, and Canada. The recording of systemic reactions varied by age group, not all reactions were collected in all studies.

In clinical studies where subjects received MENJUGATE® SYRINGE or a meningococcal polysaccharide vaccine, the rates of local pain and warmth were significantly lower with MENJUGATE® SYRINGE in toddlers and children 3 to 5 years of age; no differences were seen in the older subjects. In children 3 to 5 years of age, severe pain was seen in 9% of subjects with the polysaccharide vaccine and no subjects with MENJUGATE® SYRINGE. The systemic reactions that were significantly less common in MENJUGATE® SYRINGE subjects were fever, change in eating habits, irritability, and analgesic/antipyretic use in toddlers, and irritability and analgesic/antipyretic use in children 3 to 5 years of age.

In adolescents and adults, the rates of all post-immunisation reactions were similar after MENJUGATE® SYRINGE or polysaccharide vaccine administration. The only difference seen in this age group was a tendency for injection-site pain to persist somewhat longer in MENJUGATE® SYRINGE recipients (72 hours) than in polysaccharide vaccine recipients (48 hours).

**Infants**

Table 4 presents a summary of clinical safety data from two clinical studies in infants who received up to three immunisations with MENJUGATE® SYRINGE, beginning at the age of two months.

**Table 4: Summary of Local and Systemic Post-immunisation Reactions Within 7 Days Following 1, 2 or 3 Injections of MENJUGATE® SYRINGE**

| | **Percentage of Subjects** | |
|---|---|---|
| | **UK (Multicentre)*** (N=467) | **Canada (Multicentre)**** (N=175) |
| **Age at First Immunisation** | 2 months | 2 months |
| **Schedule** | 3 doses 1 month apart | 3 doses 2 months apart |
| **Concomitant Vaccine Regimen** | DTP, HIB, OPV | DTaP, HIB, IPV# |
| **Local Reactions:** | | |
| Tenderness | 31% | 22% |
| Erythema>25 mm | 7% | 0% |
| Induration>25 mm | 4% | 0% |
| **Systemic Reactions:** | | |
| Irritability | 81% | 68% |
| Sleepiness | 69% | 54% |
| Change in Eating Habits | 46% | 39% |
| Diarrhoea | 43% | 28% |
| Vomiting | 34% | 19% |
| Rash | 16% | --*** |
| Temp>=38°C | 4% | 21% |
| High-pitched crying | 38% | --*** |
| Persistent crying | 16% | 4% |

* MacLennan, et. al. data on file
** Halperin, et al. data on file
*** Data not collected
# PENTACELTM - combination vaccine available in Canada

In a randomised, controlled clinical study performed in infants at three centres in Canada, the profile for MENJUGATE® SYRINGE administered at 2, 4, and 6 months of age with concomitant PENTACEL (DTaP/Hib/IPV) was similar to that observed in earlier infant studies. (See Tables 5 and 6.) The frequency of two local adverse events, induration and erythema, was higher in MENJUGATE® SYRINGE recipients than in the control HBV vaccine subjects, however the incidence of these reactions was lower among MENJUGATE® SYRINGE or HBV subjects than following the routine vaccine (DTaP/Hib/IPV) in these same subjects. The most frequently reported systemic reactions were irritability, analgesic/antipyretic medication use, sleepiness and change in eating habits, which were reported with similar frequency in MENJUGATE® SYRINGE and HBV vaccine subjects.

**Table 5: Local Reactogenicity Within 7 Days Following Any Immunisation Infant Study - Canada (Multicentre)**

| | **MENJUGATE® SYRINGE group N=175** | | **HBV group N=176** | | ***P*-value MenC vs HBV group** | |
|---|---|---|---|---|---|---|
| **Local Reactions** | MENJUGATE® SYRINGE | PENTACEL | HBV | PENTACEL | Study Vaccine | PENTACEL |
| Tenderness (Any)<br>(Cried when injected leg moved) | 38 (22%)<br>0 | 53 (30%)<br>3 (2%) | 31 (18%)<br>0 | 35 (20%)<br>0 | .33 | .025 |
| Erythema (Any)<br>>25 mm | 55 (31%)<br>0 | 67 (38%)<br>5 (3%) | 33 (19%)<br>0 | 63 (36%)<br>4 (3%) | .006 | .63 |
| Induration (Any)<br>>25 mm | 42 (24%)<br>0 | 65 (37%)<br>6 (3%) | 19 (11%)<br>1 (1%) | 70 (40%)<br>2 (1%) | .001 | .61 |

**Table 6: Systemic Reactogenicity Within 7 Days Following Any Immunisation Infant Study - Canada (Multicentre)**

| **Systemic Reactions** | **MENJUGATE® SYRINGE group N=175** | **HBV group N=176** | ***P*-value** |
|---|---|---|---|
| Change in Eating Habits | 68 (39%) | 63 (36%) | .55 |
| Sleepiness | 94 (54%) | 98 (56%) | .71 |
| Persistent Crying | 7 (4%) | 4 (2%) | .35 |
| Irritability | 119 (68%) | 124 (70%) | .62 |
| Vomiting | 34 (19%) | 39 (22%) | .53 |
| Diarrhoea | 49 (28%) | 44 (25%) | .52 |
| Rectal temp $\geq$ 38°C | 37 (21%) | 47 (27%) | .22 |
| Analgesic/antipyretic medication required | 96 (55%) | 105 (60%) | .36 |

In clinical trials of MENJUGATE® SYRINGE, approximately 6700 infants through adults were evaluated monitored for the occurrence of serious adverse experiences (SAEs). There were four SAEs which were considered to be at least possibly related to vaccine. These were one report each of: hypotonia, screaming syndrome, maculopapular rash and agitation, all of which occurred in an open label infant study conducted in the United Kingdom (UK), in which MENJUGATE® SYRINGE was administered concomitantly with DTP, Hib and OPV vaccines. Because these reactions have been reported previously in conjunction with DTP vaccines alone, a causal

relationship between these experiences and MENJUGATE® SYRINGE administration cannot be established.

### Post Marketing Data (for all age groups)

The most commonly reported suspected reactions in post marketing surveillance include dizziness, pyrexia, headache, nausea, vomiting and faints.

The frequencies given below are based on spontaneous reporting rates, for this and other Meningococcal C Conjugate vaccines and have been calculated using the number of reports received as the numerator and the total number of doses distributed as the denominator.

Immune System Disorders:
*Very rare (<0.01%)*: lymphadenopathy, anaphylaxis including anaphylactic shock, hypersensitivity reactions including bronchospasm, facial oedema and angioedema.

Nervous System Disorders:
*Very rare (<0.01%)*: dizziness, convulsions including febrile convulsions, faints, hypoaesthesia and paraesthesia, hypotonia.

There have been very rare reports of seizures following MENJUGATE® SYRINGE vaccination; individuals have usually rapidly recovered. Some of the reported seizures may have been faints. The reporting rate of seizures was below the background rate of epilepsy in children. In infants seizures were usually associated with fever and were likely to be febrile convulsions.

There have been very rare reports of visual disturbances and photophobia following vaccination with Meningococcal group C conjugate vaccines, usually in conjunction with other neurological symptoms like headache and dizziness.

Respiratory, thoracic and mediastinal disorders:
Apnoea in very premature infants (≤ 28 weeks of gestation) (see Precautions section)

Gastrointestinal Disorders:
*Very rare (<0.01%)*: vomiting, nausea and diarrhoea.

Skin and Subcutaneous Tissue Disorders:
*Very rare (<0.01%)*: rash, urticaria, pruritus, purpura, erythema multiforme and Stevens-Johnson Syndrome

Musculoskeletal, connective tissue and bone disorders:
*Very rare (<0.01%)*: myalgia and arthralgia

Renal and urinary disorders:
Relapse of nephrotic syndrome has been reported in association with Meningococcal group C conjugate vaccines.

## DOSAGE AND ADMINISTRATION

There are no data on the use of different Meningococcal group C conjugate vaccines within the primary series or for boosting. Whenever possible, the same vaccine should be used throughout.

### Dosage

The recommended dose for vaccines are:

**Primary immunisation**
Infants from 2 months up to 12 months - two doses, each of 0.5 mL, should be given with an interval of at least 2 months.

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

**Booster doses**
It is recommended that a booster dose should be given after completion of the primary immunisation series in infants. The timing of this dose should be in accordance with available official recommendations. Information on responses to booster doses and on co-administration with other childhood vaccines is given in the sections titled “Immunological memory” and “Interactions with other vaccines” respectively.

The need for booster doses in subjects primed with a single dose (i.e. aged 12 months or more when first immunised) has not yet been established.

## Method of Administration

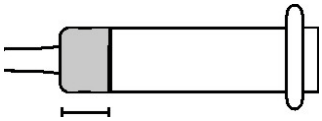
The reconstituted vaccine (0.5 mL) is intended for deep intramuscular injection, preferably in the anterolateral thigh in infants and in the deltoid region in older children, adolescents and adults.

Care must be taken to ensure the vaccine is not injected into a blood vessel. Do not inject intravenously or intradermally.

The lyophilised vaccine should be reconstituted only with the liquid aluminium hydroxide diluent supplied.

Gently agitate the syringe containing the aluminium hydroxide diluent. Remove the tip cap from the syringe and attach a suitable needle. Use the whole content of the syringe (0.6 mL of suspension) to reconstitute the Meningococcal C-CRM197 conjugate vial.

Gently shake the reconstituted vial until the vaccine is dissolved (this will ensure the antigen is bound to the adjuvant). Taking care not to withdraw the plunger completely out of the barrel of the syringe, withdraw the full contents of the vial into the syringe. Note that it is normal for a small residual amount of liquid to remain in the vial following withdrawal of the dose.
The amount of reconstituted vaccine in the syringe can be compared to the scale in the drawing below, to confirm that a sufficient dose of vaccine has been withdrawn.



**recommended dose (0.5 mL)**

A new needle with a gauge and length suitable for intramuscular injection should be used to administer the product. Ensure that no air bubbles are present in the syringe before injecting the vaccine.

Following reconstitution the vaccine is a slightly opaque homogeneous suspension, free from foreign particles.

MENJUGATE® SYRINGE should not be mixed with other vaccines in the same syringe. Separate injection sites should be used if more than one vaccine is being administered.

MENJUGATE® SYRINGE is for single use in one patient only. Discard any residue.

## OVERDOSAGE

There is no experience of overdosage with MENJUGATE® SYRINGE. Contact the Poisons Information Centre on 131 126 for further advice on overdosage management.

## PRESENTATION

MENJUGATE® SYRINGE is presented as a Type I glass vial with a bromobutyl rubber stopper containing the lyophilised vaccine and a Type I glass syringe of aluminium hydroxide with a Type I rubber plunger stopper and tip cap (either chlorobutyl rubber or styrene butadiene rubber) containing the diluent/adjuvant. Packs of single 0.5 mL dosage unit; 5 x 0.5 mL single dosage units or 10 x 0.5 mL single dosage units.

**Storage:** Store in a refrigerator at +2°C to +8°C. Do not freeze. Protect from light.

**Shelf life:** 36 months

Following reconstitution, the product should be used immediately.

The two components of the product may have different expiry dates. The outer carton bears the earlier of the two dates and this date must be respected. The carton and ALL its contents should be discarded on reaching this outer carton expiry date.

## NAME AND ADDRESS OF SPONSOR

CSL Limited
45 Poplar Road
Parkville, Vic, 3052
AUSTRALIA

AUST R 93942

**Date of TGA approval:** 4 March 2010

**Date of most recent amendment**: 8 April 2013

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