

# 13 Meningococcal disease

## Key information

Mode of transmission	By respiratory droplets or direct contact with nasopharyngeal secretions from a carrier or case.
Incubation period	2–10 days, commonly 3–4 days.
Period of communicability	Commonly 3–4 days without treatment, range 2–10 days. Antibiotic therapy eradicates <i>N. meningitidis</i> from mucosal surfaces within 24 hours, and the case is no longer considered infectious.
Funded vaccines	<ul style="list-style-type: none"> <li>• Quadrivalent meningococcal conjugate conjugated to diphtheria toxoid (MenACWY-D): Menactra.</li> <li>• Meningococcal group C conjugate (MenC): NeisVac-C.</li> </ul>
Other available vaccines	<ul style="list-style-type: none"> <li>• Quadrivalent meningococcal conjugate conjugated to tetanus toxoid (MenACWY-T): Nimenrix.</li> <li>• Meningococcal B recombinant (4CMenB): Bexsero.</li> </ul>
Dose, presentation, route	<p>0.5 mL per dose.</p> <p>Presentation:</p> <ul style="list-style-type: none"> <li>• MenACWY-D: vial</li> <li>• MenACWY-T: vial and pre-filled syringe; must be reconstituted before use</li> <li>• MenC: pre-filled syringe</li> <li>• 4CMenB: pre-filled syringe.</li> </ul> <p>Intramuscular injection.</p>
Funded vaccine indications	<p>MenACWY-D (Menactra) or MenC (NeisVac-C) for:</p> <ul style="list-style-type: none"> <li>• patients pre- or post-splenectomy or with functional asplenia</li> <li>• patients with HIV, complement deficiency (acquired, including monoclonal antibody therapy against C5, or inherited) or pre- or post-solid organ transplant</li> <li>• HSCT (bone marrow transplant) patients</li> <li>• patients prior to planned or following immunosuppression</li> <li>• close contacts of meningococcal cases (of relevant serotype)</li> <li>• adolescents and young adults aged 13–25 years inclusive who will be living or are currently living in a boarding school hostel or university hall of residence, military barracks or prison.</li> </ul>
Recommended, unfunded	<p>Laboratory workers handling bacterial cultures</p> <p>Health care professionals in very close contact with cases.</p>

Vaccine effectiveness	<p>MenACWY: effectiveness of 80–85%; effectiveness wanes to 50–60% within 2–5 years after vaccination.</p> <p>MenC: effectiveness of 83–100%; group C incidence reduce by 90% in post population-wide programmes; persistence of protection may be partially due to herd effects as antibody wanes within 2–3 years.</p> <p>4CMenB: based on bactericidal antibody levels and circulating meningococcal B strains, protection is estimated as 63–100% in under 2-year olds, 72–100% in 2–3-year olds and 91–100% in older children and adults. UK data over 3 years post programme implementation observed a 75% reduction in group B cases in infants.</p>
Potential responses to vaccines	<p>MenC and MenACWY: localised pain, irritability, headache and fatigue, mild fever.</p> <p>4CMenB: increased risk of fever and fever-related events in children &lt;2 years (prophylactic paracetamol advised). Older age groups: localised pain, nausea, myalgia, malaise, mild fever and headache.</p>
Contraindications	No specific contraindications or precautions, except prior anaphylaxis to vaccine components.
Public health measures	<p>All cases must be notified if clinically suspected.</p> <p>Parenteral antibiotics should be administered as soon as possible before admission to hospital or in hospital if delays of longer than 30 minutes are likely.</p>
Post-exposure prophylaxis	For chemoprophylaxis of contacts see section 13.8.2.

## 13.1 Bacteriology

Meningococcal disease is caused by *Neisseria meningitidis*, a gram-negative bacterium, causing sepsis, meningitis and some less common clinical syndromes. Groups B, W and C are currently the most important types in New Zealand. Increasingly, group W and Y organisms are the cause of bacteraemia and pneumonia in the elderly. Predominant groups differ between countries; group A is an important epidemic strain, particularly in Africa and the Middle East. Meningococci are spread from person to person by respiratory droplets or direct contact with nasopharyngeal secretions from a carrier or case.

## 13.2 Clinical features

Table 13.1 below describes the symptoms and signs of meningococcal disease – individuals may present with some or all of these. Meningococcal septicaemia is more common than meningitis, and presentation varies from a mild non-specific illness to rapid progression with fatal outcome. Symptoms and signs in infants are frequently non-specific. The classical rapidly progressing petechial or purpuric rash may not be present or may initially appear maculopapular. Atypical initial presentations, including gastrointestinal symptoms, septic arthritis and epiglottitis, are more frequently reported with meningococcal W disease, and may contribute to delayed diagnosis and increased case-fatality.<sup>1,2</sup> Pneumonia is more frequently reported with group Y.

**Table 13.1: Symptoms and signs of meningococcal disease**

Adolescents and adults	Young infants and children
<ul style="list-style-type: none"> <li>• Sepsis syndrome, including poor peripheral perfusion and tachycardia</li> <li>• Nausea/vomiting</li> <li>• Meningeal signs</li> <li>• Rash – petechial/purpuric, but may be maculopapular; rash may not be present early and absent in about one-third of cases</li> <li>• Sleepy, difficult to rouse</li> <li>• Occasionally in young adults, irrational behaviour</li> <li>• Arthralgia, myalgia, leg pain</li> <li>• Atypical presentation (particularly group W) may include pneumonia, septic arthritis, myocarditis or diarrhoea</li> </ul>	<p>As for adolescents and adults, plus the following:</p> <ul style="list-style-type: none"> <li>• bulging fontanelle</li> <li>• tachycardia</li> <li>• altered responsiveness</li> <li>• irritability and/or floppiness</li> <li>• refusing drinks or feeds</li> <li>• poor peripheral perfusion</li> <li>• atypical presentation may include epiglottitis, diarrhoea or septic arthritis</li> </ul>

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Notify all suspected cases urgently to local medical officer of health, including out-of-hours.

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Meningococcal disease covers a spectrum, from persistent fever with or without rash and arthritis to rapidly progressive purpuric rash and shock. Meningitis can occur with and without signs of sepsis. In fulminant cases, coma and death can occur within a few hours despite appropriate treatment.

Because of the potential for rapid progression, antibiotics should be administered (Table 13.2) as soon as possible before hospital admission. Antibiotics given prior to transfer should be clearly noted on information accompanying the patient to hospital.

**Table 13.2: Recommended antibiotics for suspected cases**

Antibiotic	Children <30kg	Children >30kg and Adults (max dose)
Ceftriaxone <sup>a</sup> (first line treatment)	50 mg/kg when given by GP/primary care 100 mg/kg IV (or IM) up to 2g when given in ED	2 g IV (or IM)
Benzylpenicillin <sup>b</sup> (second choice)	50 mg/kg IV (or IM)	2.4 g IV (or IM)

- Patients allergic to penicillin who do not have a documented history of anaphylaxis to penicillin can be given ceftriaxone.
- Patients with a documented history of anaphylaxis to penicillin and who are suspected of suffering from meningococcal disease should be sent immediately to hospital without pre-admission antibiotics.

## 13.3 Epidemiology

### 13.3.1 Global burden of disease

#### Incidence and serotypes

The prevalence of meningococcal groups varies geographically. The highest burden of disease occurs in sub-Saharan Africa, where despite a dramatic fall in Group A disease following introduction of a Group A conjugate vaccine this 'meningitis belt', epidemics continue with around 30,000 cases reported annually, now including Group W.

The incidence in Canada, the US and Europe varies substantially from 0.2 to 3 per 100,000 persons per year.<sup>3</sup> Group B has become the predominant capsular group in Europe, Americas and Australia, with incidence typically highest in children aged under 2 years.<sup>4</sup> Group C disease has almost disappeared in countries with universal immunisation programmes, but outbreaks have been observed in men who have sex with men in the US and Europe.

Since 2009 there has been an emerging global incidence of Group W disease, initially in the United Kingdom and South America. Australia has experienced a rapid increase in Group W cases since 2013 with New Zealand also seeing a rapid increase in cases since 2017. Like group C clonal complex ST11 strains, group W ST11 strains have enhanced virulence. Higher rates of carriage of these ST11 strains has been noted within age groups where invasive group W disease is more prevalent (infants and the elderly).<sup>5</sup>

Some parts of the world, particularly in Scandinavia, have reported an increase in group Y disease. In other regions, there is evidence of colonisation, but disease caused by group Y is rare. Patients with group Y strain disease are more likely to develop pneumonia and to be elderly than other strains.<sup>3,4</sup>

This emergence of group W and Y strains has led to meningococcal C vaccines being replaced by quadrivalent (group A, C, W, Y) meningococcal conjugate vaccines (MenACWY).

## Risk groups

The highest incidence of meningococcal disease occurs in children aged under 5 years (especially under 2 years) with a secondary peak in older adolescents (15–19 years). The age distribution for groups W and Y is more likely to include older people than for B and C. A pooled overall case-fatality rate of 8.3 percent (range 4.1–20 percent) is reported internationally, varying by group and age.<sup>6</sup>

Most infection occurs in healthy people, but those with certain rare immune deficiencies (terminal components of complement (C5–9) or properdin) or asplenia are at much higher risk, particularly of recurrent meningococcal disease. Individuals with infection caused by groups other than A, B, C, W, Y and untypeable strains or who experience recurrent disease should be investigated.

Close contacts of primary cases of meningococcal infection are at increased risk of developing infection, such as the case's household,<sup>7</sup> early childhood education services, semi-closed communities, schools, correctional facilities and military recruit camps. Students living in hostel accommodation may also be at higher risk.<sup>8, 9, 10</sup> In health care settings, only those with close exposure to oropharyngeal secretions of patients with meningococcal disease (as may occur during intubation or resuscitation) and microbiology laboratory workers are considered to be at increased risk.

It is not possible to calculate the incubation period for meningococcal disease for sporadic cases. Secondary cases (ie, in contacts of known cases of meningococcal disease) usually occur within four days, but it can be up to 10 days. The infectivity of patients with meningococcal disease is markedly reduced after 24 hours of antibiotic therapy, although treatment with cefotaxime, ceftriaxone, rifampicin or ciprofloxacin is necessary to reliably eradicate nasopharyngeal carriage and hence relax infection prevention and control precautions (see section 13.8.2).

In high-income countries in the absence of immunisation, nasopharyngeal carriage of *N. meningitidis* occurs in approximately 10 percent of the overall population, rising from 2 percent in children aged under 4 years to a peak of 24.5 percent to 32 percent among 15–24-year-olds, then declining with increasing age.<sup>3, 11</sup> In adolescents and young adults, the overall and capsular group carriage vary between regions and age groups.<sup>12</sup> The relationship between risk factors for disease and those associated with carriage is incompletely understood.<sup>3</sup> Carriage prevalence does not predict the disease incidence nor the occurrence or severity of outbreaks, as most of the carried strains are non-encapsulated and do not cause disease.<sup>3</sup> Smoking, passive smoking, household crowding and upper respiratory tract infections increase carriage.

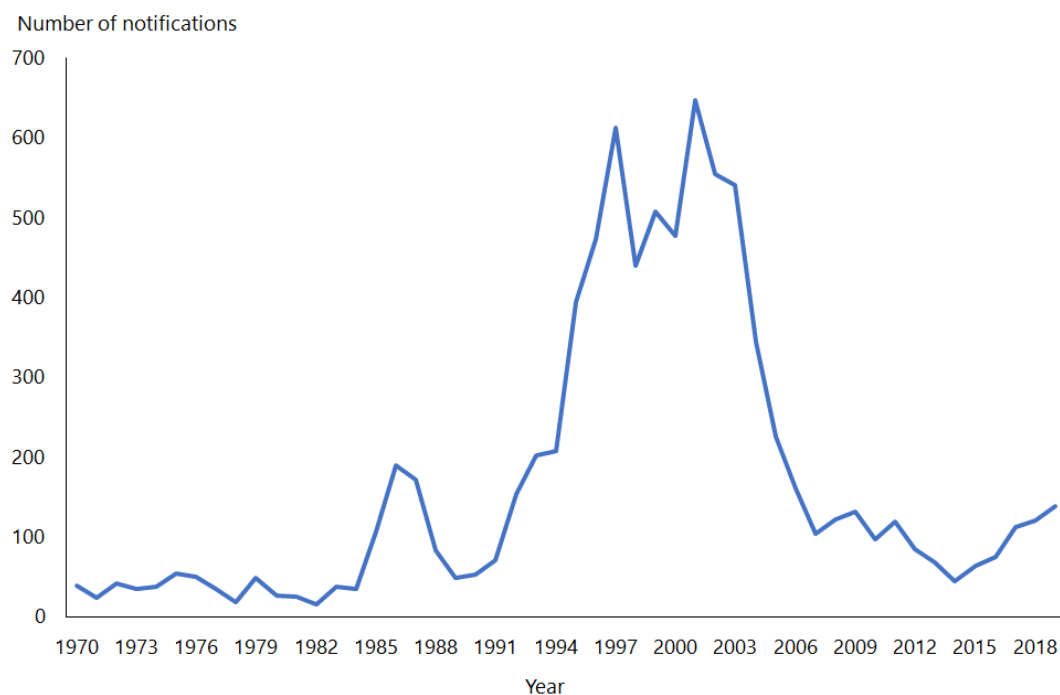
## 13.3.2 New Zealand epidemiology

### Incidence and mortality

In 2019 the notification rate for meningococcal disease was 2.8 cases per 100,000 population, with a total of 139 cases notified (134 laboratory-confirmed; ESR, 8 June 2020). Cases have increased since 2014, but remain significantly lower than the peak annual incidence rate of 16.7 per 100,000 for all ages and 200 per 100,000 in children under 12 months as experienced in 2001 during the meningococcal epidemic from 1991 to 2007. The epidemic was largely due to a single Group B subtype (B:4:P1.7b,4). The annual number of notified cases of meningococcal disease in New Zealand since 1970 is shown in Figure 13.1.

For further details and reports of meningococcal disease in New Zealand refer to the ESR surveillance reports (available at [surv.esr.cri.nz/surveillance/surveillance.php](http://surv.esr.cri.nz/surveillance/surveillance.php)).

**Figure 13.1: Notified cases of meningococcal disease, 1970–2019**



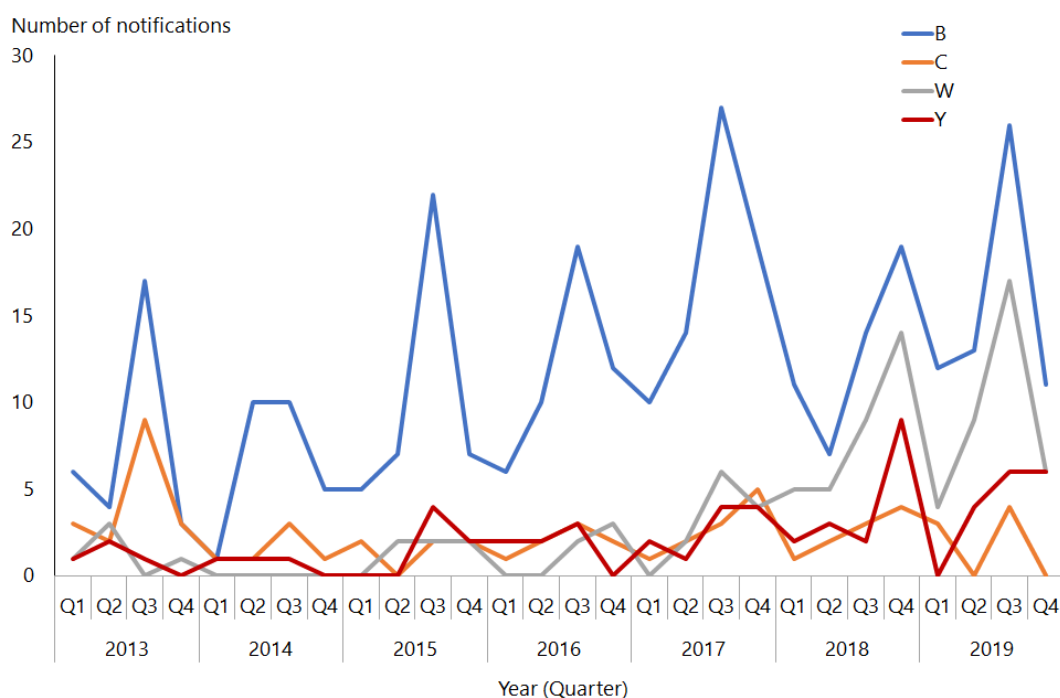
Source: ESR

Meningococcal disease incidence is about three-fold higher in Pacific people (9.2 per 100,000, 29 cases in 2019) and two-fold higher in Māori (6.1 per 100,000, 47 cases) compared with the total population. Household crowding is an important risk factor for meningococcal disease, independent of ethnicity.<sup>13</sup> In 2019, the highest age-specific disease rates were among those aged under 1 year (52.0 per 100,000, 31 cases) decreasing in ages 1–4 years (8.5 per 100,000, 21 cases). Ten deaths occurred in 2019, giving a case fatality rate of 7.2 percent (ESR, 8 June 2020).

## Strain types

Strain type was determined for 122 of the 134 laboratory-confirmed cases in 2019. Group B strains were the most prevalent, causing 51 percent of the confirmed cases (Figure 13.2). The group B strain (B:4:P1.7b,4) responsible for the epidemic caused 16 percent of all meningococcal disease in 2019 (19 of the 122 typed cases). Cases of meningococcal disease caused by group C strains decreased since 2011 (Figure 13.2), while group W increased from five cases in 2016 to 36 in 2019.

**Figure 13.2: Meningococcal disease notifications by group, 2013–2019**



Source: ESR

## 13.4 Vaccines

### 13.4.1 Introduction

Internationally, meningococcal vaccination programmes were revolutionised by the development of conjugate vaccines, which allow vaccination in younger children and induced herd immunity when used in population-wide programmes due to reduced nasopharyngeal carriage (see section 1.4.3).

The monovalent (C) and quadrivalent (ACWY) conjugate vaccines are conjugated to a protein, either CRM<sub>197</sub> (diphtheria toxin-derived), diphtheria toxoid or tetanus toxoid. Previously used, polysaccharide-only vaccines provided three to five years' protection in adults, but they are generally regarded as inferior to conjugate vaccines and are no longer available or registered in New Zealand. Those travelling to Africa, the Middle East and other areas with wide serogroup prevalence, including group A, require

MenACWY vaccine for broad protection. In 2018, a multicomponent meningococcal group B recombinant vaccine (4CMenB) was registered in New Zealand to protect against group B disease.

With the current New Zealand epidemiology, neither MenACWY nor 4CMenB give protection across all prevailing meningococcal groups and both types of vaccine are recommended. The meningococcal vaccines registered and available are summarised in Table 13.3 below.

**Table 13.3: Meningococcal vaccines registered and available in New Zealand**

Name (manufacturer)	Vaccine type
Menactra (Sanofi)	Quadrivalent meningococcal conjugate (MenACWY-D): contains group A, C, W and Y polysaccharides conjugated to diphtheria toxoid
Nimenrix (Pfizer NZ Ltd)	Quadrivalent meningococcal conjugate (MenACWY-T): contains group A, C, W and Y polysaccharides conjugated to tetanus toxoid
NeisVac-C (Pfizer NZ Ltd)	Meningococcal group C conjugate (MenC): contains group C polysaccharide conjugated to tetanus toxoid
Bexsero (GSK)	Meningococcal group B four-component recombinant (4CMenB)

## Funded vaccines

No meningococcal vaccines are on the routine Schedule but group C conjugate and quadrivalent meningococcal conjugate vaccines are recommended and funded for certain individuals (see section 13.5).

Two meningococcal conjugate vaccines are funded for certain at-risk groups.

- Meningococcal group C conjugate vaccine MenC (NeisVac-C, Pfizer NZ Ltd) contains 10 µg of polysaccharide derived from the group C capsule, conjugated to 10–20 µg of tetanus toxoid. Other components include aluminium hydroxide and sodium chloride.
- Quadrivalent meningococcal conjugate vaccine MenACWY-D (Menactra, Sanofi) contains 4 µg of each polysaccharide derived from the capsules of group A, C, W and Y *N. meningitidis* strains, each conjugated to diphtheria toxoid. Other components include sodium chloride and sodium phosphate.

## Other vaccines

### Quadrivalent meningococcal conjugate vaccines

A second quadrivalent meningococcal conjugate vaccine MenACWY-T (Nimenrix, Pfizer NZ Ltd) is registered and available in New Zealand for individuals from age 6 weeks. MenACWY-T contains 5 µg of each polysaccharide derived from the capsules of group A, C, W and Y *N. meningitidis* strains, conjugated to 44 µg of tetanus toxoid carrier



protein. Other components and excipients include sodium chloride, trometamol and sucrose.

Another quadrivalent meningococcal vaccine, MenACWY-CRM<sub>197</sub> (Menveo, GSK) is licensed from 2 months of age elsewhere, including Australia, Europe, UK and the US, which is conjugated to a diphtheria-toxin derived CRM<sub>197</sub> protein (as used in PCV13). It is not available in New Zealand.

### Group B meningococcal vaccines

The 4CMenB recombinant vaccine (Bexsero, GSK) is available in New Zealand from age 6 weeks (not funded). Based on bactericidal antibody titres, it is expected to provide protection against more than 75 percent of the circulating group B strains, including the former epidemic strain B:4:P1.7b,4 (NZ 98/254). This vaccine contains four components from the group B meningococci: three recombinant group B surface proteins associated with bacterial adhesion and survival plus detoxified outer membrane vesicles containing antigen used in the MenNZB epidemic vaccine.

The UK funded 4CMenB vaccine for infants from September 2015.<sup>14</sup> Doses are given at age 8 weeks and 16 weeks, with a booster at 12 months.<sup>15</sup>

A two-component meningococcal group B recombinant vaccine (2CMenB; Trumenba, Pfizer Ltd) is licensed from 10 years of age in the US, Europe and Australia. It is not registered in New Zealand.<sup>16</sup>

In February 2015 the US Advisory Committee on Immunization Practices recommended that individuals aged 10 years or older at increased risk for meningococcal disease should receive a meningococcal B vaccine (either 4CMenB or 2CMenB).<sup>17</sup> In June 2015, this recommendation was extended to include all aged 16–23 years (with a preferred age of 16–18 years), to provide short-term protection against most circulating strains of serogroup B meningococcal disease.<sup>18</sup>

### Historic MeNZB vaccine

A strain-specific group B meningococcal vaccine (MeNZB, Chiron/Novartis) containing outer membrane vesicles derived from the epidemic strain B:4:P1.7b,4 (NZ 98/254) was developed for epidemic control in New Zealand and used between 2004 and 2008. The programme ceased in 2008 because of a decline in incidence of group B disease (see previous editions of the *Handbook*).

Since the immune response to MeNZB was short-lived, previous recipients who wish to be protected against meningococcal B disease will need to be fully immunised with 4CMenB.

## 13.4.2 Efficacy and effectiveness

### Meningococcal conjugate vaccines

#### Quadrivalent meningococcal conjugate vaccines

Clinical trial data use immunogenicity and bactericidal antibody titres as a proxy for efficacy. Effectiveness of conjugate meningococcal vaccination against laboratory-confirmed disease is difficult to assess due to the low incidence of cases, even during localised epidemics, such that data is limited around the effectiveness of the MenACWY vaccines. With the emergence of group W and Y strains, more countries have implemented mass campaigns and routine immunisation programmes to control outbreaks with MenACWY vaccines and can assess impact through disease incidence and carriage studies.

The overall effectiveness of a single dose of diphtheria conjugate quadrivalent meningococcal vaccine (MenACWY-D, Menactra) given at age 11–12 years was estimated to be 69 percent up to eight years post-vaccination (from 79 percent in year one to 61 percent up to eight years post-vaccination).<sup>19</sup> These findings cannot be extrapolated across all MenACWY vaccines due to differences in immunogenicity.

Following a mass vaccination campaign in children aged 9 months to 4 years in Chile with MenACWY (MenACWY-D or MenACWY-CRM, depending on age), there was a 92.3 percent reduction in group W disease and the case-fatality rate declined from 23 percent in 2012 to 0 percent in 2016 in children aged 1–4 years. However, there was no impact in infants aged under 12 months or adults aged 80 years or older.<sup>20</sup>

The MenACWY-D vaccine was poorly immunogenic in infants aged under 6 months,<sup>21</sup> and it is currently registered in New Zealand for individuals aged 9 months to 55 years.

The MenACWY-T vaccine (Nimenrix) is registered in New Zealand for individuals from aged 6 weeks. Clinical trials showed that the vaccine elicited bactericidal antibodies against all four groups from age 2 months with acceptable reactogenicity and safety profile.<sup>22</sup>

The conjugate quadrivalent meningococcal vaccines are available in New Zealand. There is no published data on effectiveness in older adults.

#### Meningococcal group C conjugate vaccines

Meningococcal C conjugate vaccines were used successfully in national immunisation and mass vaccination programmes from 1999 in the UK, resulting in almost complete elimination of group C disease.<sup>15</sup> A targeted immunisation campaign during an epidemic in Salvador, Brazil demonstrated MenC vaccination to be 98 percent effective against group C disease in young children.<sup>23</sup>

Data from the UK programme indicated that a booster dose in the second year of life was important for sustained protection following infant vaccination.<sup>24</sup> Protective efficacy against carriage by adolescents of group C one year after the UK immunisation campaign was estimated at 69 percent.<sup>25</sup> Countries that included catch-up vaccinations for older children and adolescents, including the UK and Australia, have observed the greatest impact from meningococcal immunisation campaigns through herd immunity

and a reduction in transmission across all age groups. There was a 67 percent reduction in group C disease among unvaccinated children within the target age groups and a reduction of 35 percent of cases in unvaccinated adults older than age 25 years.<sup>26</sup> At the same time there was no evidence of capsular switching or an increase in disease caused by group B strains.<sup>27</sup>

With the emergence of group W and now group Y meningococci, MenC has generally been replaced by MenACWY vaccines on national programmes in infants and adolescents.

### Meningococcal group B recombinant vaccine

Three years after initiation of the introduction of 4CMenB to the national immunisation schedule in the UK, a 75 percent reduction in group B disease was reported in the vaccine-eligible age groups compared with a historical cohort.<sup>28</sup> With 88 percent coverage but a low number of cases (25), adjusted vaccine effectiveness for all group B strains was 59.1 percent (95% CI: -31.1–87.2) following two primary doses and one booster dose, with an estimated 277 cases prevented.<sup>28</sup> This research is ongoing.

As has been observed during college outbreaks in the US,<sup>29, 30</sup> in South Australia where 4CMenB is administered in a school-based programme at age 15–18 years, 4CMenB had no effect on disease-causing meningococci carriage suggesting that vaccination of adolescents is unlikely to generate herd immunity.<sup>31</sup> A 4CMenB vaccination campaign used during an isolated outbreak in a region of Québec, Canada outbreak demonstrated direct protection of 79 percent against outbreak strain group B disease and an overall impact of 86 percent in target groups with no herd effects.<sup>32</sup>

The safety and efficacy of 4CMenB in adults above 50 years of age have not been established. There is limited data on its use in patients with chronic medical conditions and immunocompromised by medication or disease, such as HIV infection or hereditary immune system defects.

## 13.4.3 Transport, storage and handling

Transport according to the *National Standards for Vaccine Storage and Transportation for Immunisation Providers 2017 (2nd edition)* (available at [www.health.govt.nz/publication/national-standards-vaccine-storage-and-transportation-immunisation-providers-2017](http://www.health.govt.nz/publication/national-standards-vaccine-storage-and-transportation-immunisation-providers-2017)).

Store at +2°C to +8°C. MenACWY-D, MenACWY-T and 4CMenB should be protected from light. Do not freeze.

### Reconstitution

MenACWY-T (Nimenrix) must be reconstituted with the supplied diluent and used as soon as possible.

## 13.4.4 Dosage and administration

### Quadrivalent meningococcal conjugate vaccines (MenACWY)

Each MenACWY dose is 0.5 mL, administered by intramuscular injection (see section 2.2.3).

#### Menactra (MenACWY-D)

MenACWY-D (Menactra) is registered in New Zealand for individuals aged 9 months to 55 years. For children aged 9–23 months, two doses are given at least three months apart. For individuals aged 2–55 years, one dose is given. See Table 13.5 for schedules for at-risk individuals.

MenACWY-D can be concurrently administered with other vaccines in separate syringes and at separate sites,<sup>33, 34, 35, 36</sup> except for PCV13. MenACWY-D should preferably be administered at least four weeks after PCV13. This is because, when administered concurrently, there is possible blunting of the immune response to some of the pneumococcal serotypes.<sup>37, 38</sup> (see section 13.5.2 for recommendations in regard to high-risk children age under 12 months and section 4.3.3).

#### Nimenrix (MenACWY-T)

MenACWY-T (Nimenrix) is registered in New Zealand for individuals from age 6 weeks. For infants aged under 12 months, two doses are given eight weeks apart, with a booster from age 12 months at least six months after second dose. For adults and children from age 12 months, one dose is given. A booster dose may be indicated in some individuals.

MenACWY-T can be concurrently administered with other vaccines in separate syringes and at separate sites; there is no data on concurrent administration of MenACWY-T and PCV13, however, interference is unlikely.

### Meningococcal group C conjugate vaccine (MenC)

Each MenC (NeisVac-C) dose is 0.5 mL, administered by intramuscular injection (see section 2.2.3).

For infants aged under 9 months, two doses are given at least eight weeks apart, with the first dose given not earlier than age 6 weeks. One dose of MenACWY is recommended in the second year of life from age 12 months. See Table 13.5 for schedules for at-risk individuals. MenC can be administered concurrently with other scheduled vaccines, in separate syringes and at separate sites.

In view of the New Zealand epidemiology, a quadrivalent (MenACWY) vaccine would be preferable, to obtain broader meningococcal protection.

## Meningococcal group B recombinant vaccine (4CMenB)

Each 4CMenB (Bexsero) dose is 0.5 ml, administered by intramuscular injection (see section 2.2.3).

For infants aged 6 weeks to  $\leq 11$  months, two doses are given with a minimum of eight weeks between doses, with a booster given from 12 months at least six months after the second dose.

For children aged 12 months to under 11 years, two doses are given at least eight weeks apart. No booster dose is required. For children and adults aged 11 years to 50 years, two doses are given one month apart. No booster dose is required. (Note: the safety and efficacy in individuals aged over 50 years have not been established.)

4CMenB can be administered concurrently with other scheduled vaccines, in separate syringes and at separate sites.

Note: 4CMenB elicits a robust immune response, sometimes with high fevers in some infants. Routine use of paracetamol with every dose of 4CMenB in children aged under 2 years, whether given alone or with other vaccines, is recommended to reduce the risk of high fever and injection-site pain. Some infants will still develop a fever and/or injection-site pain even though they have received paracetamol doses.

Prophylactic paracetamol is recommended to be given 30 minutes prior to and six-hourly for up to 48 hours following vaccination for children aged under 2 years. For children and infants aged from 2 months, ibuprofen may be given as an alternative to paracetamol.

# 13.5 Recommended immunisation schedule

## 13.5.1 Individuals at increased risk

Meningococcal vaccines are not on the Schedule but are funded in special circumstances, as described in the shaded section of Table 13.4; Table 13.5 shows the recommended dosing schedules.

See sections 4.3, 4.4 and 4.5 for more information about vaccination of special groups, including recommended immunisation schedules for high-risk individuals with certain medical conditions.

The meningococcal vaccines are recommended (but not funded) for other individuals at risk, as described in Table 13.4.

## Before travel

There are areas of the world where the risk of meningococcal disease is increased. Nevertheless, the risk to travellers to the developing world has been estimated as being less than one in a million per month. Recurrent epidemics of meningococcal disease occur in the sub-Saharan 'meningitis belt', from Senegal in the west to Ethiopia in the east, usually during the dry season (December to June). Epidemics are occasionally identified in other parts of the world, including in Europe and the Americas. Generally, countries outside of Africa experience smaller outbreaks, but case-fatality rates can be high.

The preferred vaccines (MenACWY and/or 4CMenB) for travel would be based on the epidemiology of the country. For website sources for information about meningococcal vaccines for travellers, see the WHO website ([www.who.int/ith/en](http://www.who.int/ith/en)). Quadrivalent meningococcal vaccine is a requirement for pilgrims to the Hajj.

## Before moving into communal living situations

MenACWY-D is recommended and funded from age 13–25 years inclusively for individuals who will be living in communal accommodation within the next three months, or who are in their first year of living in communal accommodation (specifically, boarding school hostels, tertiary education halls of residence, military barracks or prisons) as they are likely to be at higher risk of acquiring meningococcal infection.

A catch-up dose of MenACWY-D is also funded for individuals who are currently living in boarding school hostels, tertiary education halls of residence, military barracks, or prisons, from 1 December 2019 to 30 November 2021.

## Table 13.4: Meningococcal vaccine recommendations

Note: **Funded circumstances are in the shaded rows.**

See the Pharmaceutical Schedule ([www.pharmac.govt.nz](http://www.pharmac.govt.nz)) for any changes to the funding decisions.

<b>Recommended and funded</b>
MenC and MenACWY-D are recommended and funded for: <ul style="list-style-type: none"><li>• patients pre- or post-splenectomy or with functional asplenia<sup>a,b</sup></li><li>• patients with HIV, complement deficiency (acquired, including monoclonal antibody therapy against C5, or inherited) or who are pre- or post-solid organ transplant<sup>b</sup></li><li>• HSCT (bone marrow transplant) patients<sup>b</sup></li><li>• patients prior to planned immunosuppression<sup>b,c</sup></li><li>• patients following immunosuppression<sup>b,c</sup></li><li>• close contacts of meningococcal cases<sup>d</sup></li><li>• individuals aged 13–25 years inclusively who are entering within three months or are in their first year of living in boarding school hostels, tertiary education halls of residence, military barracks or prisons.</li></ul>
<b>Recommended but not funded</b>
<b>Priority groups</b> <p>MenACWY-D or MenACWY-T and 4CMenB are recommended, but not funded, for:</p> <ul style="list-style-type: none"><li>• individuals are laboratory workers regularly handling meningococcal cultures</li><li>• adolescents and young adults living in communal or overcrowded accommodation not covered by funded vaccine</li><li>• individuals who are travelling to high-risk countries (see <a href="http://www.who.int/ith/en">www.who.int/ith/en</a>) or before the Hajj.</li></ul> <p>MenACWY-T is recommended but not funded for high-risk infants age under 9 months in place of MenC.</p> <p>4CMenB is recommended but not funded for all the above high-risk groups.</p>
<b>Other groups</b> <p>MenACWY and 4CMenB are recommended but not funded for all infants, young children, adolescents and young adults.</p>

a. Pneumococcal, Hib, influenza and varicella vaccines are also recommended for individuals pre- or post-splenectomy or with functional asplenia. See section 4.3.4.

b. See section 4.3.4 for more information.

c. The period of immunosuppression due to steroid or other immunosuppressive therapy must be longer than 28 days.

d. Only one dose is funded for close contacts of meningococcal cases.

**Table 13.5: Recommended meningococcal vaccine schedule for high-risk individuals (funded)**

Note: See the Pharmaceutical Schedule ([www.pharmac.govt.nz](http://www.pharmac.govt.nz)) for any changes to funding decisions.

Age at diagnosis	Vaccine (trade name)	Recommended vaccine schedule
Infants aged 6 weeks to under 12 months	MenC (NeisVac-C) and MenACWY-D (Menactra)	<ul style="list-style-type: none"> <li>If aged under 9 months, give 2 doses of MenC 8 weeks apart, followed by MenACWY-D<sup>a</sup> at ages 9 and 13 months. Administer one MenACWY-D booster dose after 3 years, then 5-yearly. (See alternative unfunded MenACWY-T (Nimenrix) option in Table 13.6.)</li> <li>If aged 9–11 months, give 2 doses of MenACWY-D<sup>a</sup> at least 3 months apart, followed by a booster dose after 3 years, then 5-yearly.</li> </ul>
Children aged 12 months to under 18 years	MenACWY-D (Menactra)	<ul style="list-style-type: none"> <li>If aged 12 months – under 8 years at diagnosis, give 2 doses of MenACWY-D<sup>a</sup> at least 3 months apart followed by a booster dose after 3 years, then 5-yearly.</li> <li>If aged 8 years or older give 2 doses of MenACWY-D 8 weeks apart followed by a booster dose 5-yearly.<sup>a</sup></li> </ul>
Adults aged 18 years and older	MenACWY-D (Menactra)	Give 2 doses 8 weeks apart, then 1 dose every 5 years. <sup>a,b</sup>
Individuals aged between 13 and 25 years, in certain communal living situations <sup>c</sup>	MenACWY-D (Menactra)	1 dose, no booster required

a. Give MenACWY-D at least 4 weeks before or after PCV13<sup>37, 38</sup> (see below).

b. MenACWY-D is registered for individuals aged 9 months to 55 years, but there are not expected to be any safety concerns when administered to adults older than 55 years.

c. Funded for individuals aged 13–25 years inclusively who either: are entering within three months or who are in their first year of living in boarding school hostels, tertiary education halls of residence, military barracks or prisons; or to 30 November 2021 who are currently living in boarding school hostels, tertiary education halls of residence, military barracks or prisons.

There is a possibility of blunting of some PCV serotype antibody responses when MenACWY-D (Menactra) is given concurrently with the PCV13 series because both vaccines contain diphtheria-derived proteins as conjugates. The clinical significance of this blunting, observed in a clinical trial with PCV7,<sup>38</sup> is unknown and the affected serotypes (4, 6B, 18C) are currently rare in New Zealand. The benefits of achieving broad meningococcal protection as early as possible in immunocompromised infants outweigh the theoretical risk of modest reduction of some pneumococcal antibody levels, so MenACWY-D is recommended at 9 months (see Table 4.4, Table 4.5 and Table 13.5). Note: two doses given at least three months apart are recommended as a primary series; each dose should be given at least four weeks before or after PCV13 to reduce this risk of interference.



## 13.5.2 Recommendations for children and adolescents

In the absence of a universal programme, non-high-risk children and adolescents may be offered meningococcal vaccines, but these are not funded. Table 13.6 suggests the most appropriate ages for this, reflecting the known ages of increased risk. The predominant meningococcal strains in New Zealand in childhood are B, W and C. With the current New Zealand epidemiology, neither MenACWY nor 4CMenB give protection across all prevailing meningococcal groups and both types of vaccine are recommended. For those who are likely to travel, the broadest protection is preferable because of the differing serotype patterns between countries.

**Table 13.6: Recommended schedule for non-funded meningococcal vaccines in children and adolescents**

Note: Vaccine immunity is not long-lasting. The suggested ages of vaccination are not expected to protect individuals through all of childhood but focused on protection during the ages of highest risk. This does not apply to epidemic situations.

Age at time of consultation	Vaccine options (trade name)	Number of doses
6 weeks to <12 months	4CMenB (Bexsero) MenACWY-T (Nimenrix)	2 doses <sup>a,b</sup> plus a booster after 12 months of age 2 doses <sup>a</sup> plus a booster after 12 months of age
12 months to 2 years	4CMenB (Bexsero) MenACWY-D (Menactra) or MenACWY-T (Nimenrix)	2 doses <sup>a,b</sup> 2 MenACWY-D <sup>a,c</sup> doses or 1 MenACWY-T
>2 years to <11 years	4CMenB (Bexsero)	2 doses <sup>a</sup>
Early adolescence (<16 years) <sup>d</sup>	4CMenB (Bexsero) MenACWY-D (Menactra) or MenACWY-T (Nimenrix)	2 doses <sup>a</sup> 1 dose plus a booster at age 16–18
Late adolescence ≥16 years <sup>d</sup>	4CMenB (Bexsero) MenACWY-D (Menactra) or MenACWY-T (Nimenrix)	2 doses <sup>a</sup> 1 dose, no booster required

- Refer to section 13.4.4 and the vaccine data sheets for the intervals between doses.
- Prophylaxis paracetamol (or ibuprofen) is recommended for this age group, see section 13.7.3.
- MenACWY-D should be administered at least 4 weeks after PCV13 (if used).
- In particular, for individuals aged 13–25 years not eligible to funded vaccine, particularly living in crowded private homes, other hostels or student accommodation, or planning overseas travel.

## 13.5.3 Pregnancy and breastfeeding

There are no reports of any adverse effects among pregnant women who have been vaccinated during pregnancy.<sup>37</sup> The vaccine may be given to pregnant women if indicated.<sup>37</sup> Meningococcal vaccine may be given to breastfeeding women.

## 13.5.4 (Re)vaccination

Meningococcal conjugate vaccines, MenC (age under 2 years) and MenACWY-D (from age 9 months) are funded for vaccination or re-vaccination of eligible individuals, as follows. See also section 4.3.

Up to three doses plus booster doses (as appropriate) are funded for individuals:

- pre- or post-splenectomy
- pre- or post-solid organ transplantation
- with functional asplenia
- with complement deficiency (acquired or inherited)
- who are HIV-positive.

Two doses are funded for individuals:

- post-haematopoietic stem cell transplantation
- prior to planned or following immunosuppression for longer than 28 days.

## 13.6 Contraindications and precautions

See also section 2.1.3 for pre-vaccination screening guidelines and section 2.1.4 for general contraindications for all vaccines.

There are no specific contraindications for meningococcal vaccines, except for anaphylaxis to a previous dose or any component of the vaccine.

## 13.7 Potential responses and AEFIs

### 13.7.1 Quadrivalent meningococcal conjugate vaccine

Potential adverse reactions after meningococcal conjugate vaccines include localised pain, irritability, headache and fatigue.<sup>22, 39</sup> Fever is reported by 2–5 percent of adolescents who receive MenACWY-D.

The safety of two doses of MenACWY-D was assessed in a phase III trial of infants: dose one was administered at age 9 months and dose two was administered at age 12 months, with or without routine childhood vaccines.<sup>38</sup> The percentage of participants with solicited systemic reactions after MenACWY-D administration alone at age 12 months (60.6 percent) was lower than after the vaccination at age 9 months (68.2 percent), lower than the control groups at age 12 months (75.2–84.1 percent, depending upon the control vaccine) and lower than when MenACWY-D was administered concurrently with the routine childhood vaccines (68.3–73.2 percent).

The safety profile of MenACWY-T (Nimenrix) is very similar to other meningococcal conjugate vaccines.<sup>22</sup>

## Guillain–Barré syndrome

There is no evidence of an association between meningococcal conjugate vaccines and GBS. An early report in the US of a suspected temporal association between MenACWY-D (Menactra) and GBS was followed by a large retrospective cohort study in the US that found no evidence of an increased risk of GBS following administration of MenACWY-D.<sup>37, 40</sup> If indicated, meningococcal conjugate vaccines may be administered to individuals with a history of GBS.<sup>41</sup>

## 13.7.2 Meningococcal group C conjugate vaccine

A Cochrane Review assessed the safety of MenC against group C disease.<sup>42</sup> MenC vaccines were shown to have an excellent safety profile in infants. The events more frequently reported in infants were fever (1–5 percent), irritability (38–67 percent), crying more than expected (1–13 percent), redness at the site of vaccination (6–97 percent), tenderness at the site of vaccination (11–13 percent) and swelling at the site of vaccination (6–42 percent). Anaphylaxis was reported at a rate of one per 500,000 doses distributed.<sup>4</sup>

## 13.7.3 Meningococcal B recombinant vaccine

There is an increased risk of fever and medically attended fever-related events, such as febrile seizures, associated with 4CMenB in some children age under 2 years.<sup>4, 43, 44, 45, 46</sup> These events peaked at six hours post-vaccination and generally subsided by day 3. Prophylactic paracetamol is recommended 30 minutes prior and six-hourly for up to 48 hours following vaccination for children aged under 2 years. Ibuprofen may be given as an alternative to paracetamol. Some infants will still develop a fever and/or injection-site pain even though they have received paracetamol doses.

In clinical trials, some infants and young children also experienced injection-site tenderness and irritability. Adolescents and adults may experience localised pain, nausea, myalgia, malaise, mild fever and headache.

## 13.8 Public health measures

Invasive meningococcal disease must be notified on suspicion to the local medical officer of health.

The overall rate of secondary cases in untreated adults is around 1 per 300. Adults and children in close contact with primary cases of invasive meningococcal infection are recommended to receive antibiotic prophylaxis, preferably within 24 hours of the initial diagnosis, but prophylaxis is recommended up to 14 days after diagnosis of illness.

Blood or cerebrospinal fluid culture is the main diagnostic method, but blood PCR may be useful if antibiotics are given without prior access to blood culture. It is recommended that in primary care 3–5 mL of blood should be taken in an ethylenediaminetetraacetic acid (EDTA) anticoagulant tube (usually with a purple top) prior to administration of antibiotics unless blood culture is available. This should accompany the patient to hospital.

### 13.8.1 Contacts

A contact is anyone who has had unprotected contact with upper respiratory tract or respiratory droplets from the case during the seven days before onset of illness to 24 hours after onset of effective treatment.<sup>47</sup> Contacts at particular risk include:

- those sleeping at least one night in the same household, dormitory, military barrack or student hostel bunkroom (not residents of nursing or residential homes who sleep in separate rooms) as the case, or who have been in a seat adjacent to the case in a plane, bus or train for more than eight hours
- health care workers who have had intensive unprotected contact (not wearing a mask) with a case during intubation, resuscitation or close examination of the oropharynx
- exchange of upper respiratory tract secretions, including intimate kissing
- other contacts as determined by the medical officer of health on a case-by-case basis, such as children and staff attending an early childhood service.

Prophylaxis is not routinely recommended for health care personnel unless there has been intimate contact with oral secretions (eg, performing mouth-to-mouth resuscitation or suctioning of the case before antibiotic therapy has started).

## 13.8.2 Chemoprophylaxis for contacts

### Recommended antibiotics

The recommended antibiotics are rifampicin, ceftriaxone or ciprofloxacin, preferably given within 24 hours of initial diagnosis, but prophylaxis is recommended up to 14 days after diagnosis of illness.

#### Rifampicin

The recommended dose of rifampicin is 10 mg/kg (maximum dose 600 mg) every 12 hours for two days. For infants aged under 4 weeks, the recommended dose is 5 mg/kg every 12 hours for two days.

Rifampicin should be avoided for pregnant or lactating women.

#### Ceftriaxone

A single dose of intramuscular ceftriaxone (125 mg for children aged under 12 years and 250 mg for older children and adults) has been found to have an efficacy equal to that of rifampicin in eradicating the meningococcal group A carrier state. Ceftriaxone is the drug of choice in a pregnant woman because rifampicin is not recommended later in pregnancy. Ceftriaxone may be reconstituted with lignocaine (according to the manufacturer's instructions) to reduce the pain of injection. A New Zealand study demonstrated that ceftriaxone and rifampicin were equivalent in terms of eliminating nasopharyngeal carriage of *N. meningitidis* group B.<sup>48</sup>

Do not use in infants under aged under 4 weeks.

#### Ciprofloxacin

Ciprofloxacin given as a single oral dose of 500 mg or 750 mg is also effective at eradicating carriage. This is the preferred prophylaxis for women on the oral contraceptive pill and for prophylaxis of large groups.<sup>47</sup>

Ciprofloxacin is not generally recommended for pregnant and lactating women or for children aged under 18 years.<sup>49</sup> Consult the manufacturer's data sheet for appropriate use and dosage of ciprofloxacin in children.

### Use of meningococcal vaccines for close contacts

Close contacts of cases of group A, C, W or Y meningococcal disease may be offered the appropriate meningococcal conjugate vaccine (see section 13.5).

In a multi-occupancy residential meningococcal B outbreak an emergency supply of 4CMenB is available for use. See below for the use of the vaccines for the control of outbreaks, as initiated by the local public health service.

### 13.8.3 Outbreak control

When there is an outbreak of meningococcal disease of a specific vaccine group, an immunisation programme may be recommended and funded for a defined population. The local medical officer of health will determine the necessary action in discussion with the Ministry of Health.

For more details on control measures, refer to the '*Neisseria meningitidis* invasive disease' chapter of the *Communicable Disease Control Manual* (available at [www.health.govt.nz/publication/communicable-disease-control-manual-2012](http://www.health.govt.nz/publication/communicable-disease-control-manual-2012)).

## 13.9 Variations from the vaccine data sheets

The MenACWY-D data sheet states that the vaccine is indicated for use in individuals aged 9 months to 55 years. The Ministry of Health recommends that this vaccine may be used in adults aged over 55 years.<sup>41</sup>

The data sheet states that MenACWY-D should be given as a single dose for individuals aged 2 years and older. The Ministry of Health recommends that two doses are given to individuals at high risk of meningococcal disease (see Table 13.5 and section 4.3), with booster doses every five years. If the first MenACWY-D dose was given before age 7 years, give a booster after three years then five-yearly.<sup>39</sup>

A history of GBS is listed as a precaution in the MenACWY-D data sheet. However, there is no evidence of an association between meningococcal conjugate vaccines and GBS (see section 13.7.2). The Ministry of Health advises that, if indicated, MenACWY-D may be administered to individuals with a history of GBS.<sup>41</sup>

The MenC data sheet states that the first dose of vaccine is not be given earlier than age 8 weeks. However, the Ministry of Health recommends that MenC may be given from age 6 weeks to infants at high risk of meningococcal disease (see Table 13.4 and Table 13.5).

The 4CMenB data sheet states that the vaccine is indicated from age 2 months or older. However, the Ministry of Health recommends that 4CMenB can be given from age 6 weeks to infants at high risk of meningococcal disease (see Table 13.5).

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