4.10 MENINGOCOCCAL DISEASE

4.10.1 Bacteriology

Meningococcal disease is caused by a Gram-negative bacterium, *Neisseria meningitidis*, commonly known as meningococcus. There are 13 known serogroups distinguished by differences in surface polysaccharides of the outer membrane capsule. Globally, serogroups A, B, C, W135 and Y most commonly cause disease. Meningococci can be further classified by differences in their outer membrane proteins.\(^1\)

4.10.2 Clinical features

*N. meningitidis* can cause invasive meningococcal disease (IMD) which includes meningitis and septicaemia. Septicaemia, either on its own or with meningitis, can be particularly severe. *N. meningitidis* can also cause other localised infections, including pneumonia, arthritis and conjunctivitis, but these are less common.

The clinical manifestations of meningococcal septicaemia and meningitis may be non-specific and can include sudden onset of fever, rash (petechial, purpuric or maculopapular), headache, neck stiffness, photophobia, altered consciousness, muscle ache, cold hands, thirst, joint pain, nausea and vomiting.\(^1,3\) Not all symptoms or signs may be present at disease onset. The characteristic rash of meningococcal disease, which does not disappear with gentle pressure on the skin, is not always present. Meningococcal infections can progress rapidly to serious disease or death in previously healthy persons. The overall mortality risk for IMD is high (between 5 and 10%), despite appropriate antibiotic therapy. Approximately 10 to 30% of children and adolescents who survive develop permanent sequelae, including limb deformity, skin scarring, deafness and neurologic deficits.\(^2,4,5\)

Humans are the only reservoir of *N. meningitidis*. Meningococcus is transmitted via droplets or direct contact and has an incubation period of between 2 and 10 days, but commonly 3 to 4 days.\(^7\) A proportion of the population carry *N. meningitidis* without developing disease. The prevalence and duration of asymptomatic nasopharyngeal carriage of meningococci vary over time and in different population and age groups. Prevalence of carriage is known to be higher when groups of people occupy small areas of living space.\(^6,7\)

A number of medical conditions are known to increase the risk of an individual developing IMD. The magnitude of the risk varies with the primary underlying condition. Persons with a complement deficiency have an increased risk of meningococcal disease (estimated to range from 5- to 10 000-fold depending on the specific condition), and are also more likely to have a recurrence of infection.\(^6,9\) Persons with an absent or dysfunctional spleen are at a life-long increased risk of severe bacterial infection,\(^10,11\) including sepsis attributable to meningococcal disease. Other immunocompromising conditions which increase the risk of IMD include HIV infection\(^1,2,13\) and haematopoietic stem cell transplant.

Other individuals at greater risk of meningococcal infection include laboratory workers who handle meningococci, new military recruits,\(^14,15\) and university students living in residential colleges (particularly in their first year).\(^16,19\) Studies have also reported that exposure to smokers (who are more likely to be carriers), intimate kissing with multiple partners, and recent or current viral infection of the upper respiratory tract may also contribute to an individual’s risk of contracting meningococcal disease.\(^1,6,7,20,21\) There is no definitive evidence that there is an increased risk of IMD among men who have sex with men (MSM); however, clusters or community outbreaks of serogroup C IMD among MSM have been reported.\(^22-26\)

4.10.3 Epidemiology

Meningococcal disease may occur sporadically or in epidemics. In Australia, a large proportion of cases are reported during winter and early spring, demonstrating a seasonal trend which is also observed in other countries with temperate climates.\(^27\) The notification rates of IMD among Indigenous persons are several times higher than in non-Indigenous persons for most age groups, except in those aged 15–24 years.\(^28,29\) The dominant meningococcal serogroup(s) varies between geographical regions. Serogroup A disease occurs predominantly in low-income countries, particularly countries in sub-Saharan Africa. Meningococcal serogroup B (‘MenB’) is the major cause of sporadic meningococcal disease in many developed countries. In Australia, serogroup B has predominated, particularly since the meningococcal serogroup C (‘MenC’) conjugate vaccine program began in 2003. Of the 194 cases of meningococcal disease notified in Australia in 2012, for which the serogroup could be determined, 83% were due to serogroup B. The remainder were due to serogroup C (6%), serogroup W135 (4%) and serogroup Y (8%).\(^30\)

Trends in the incidence of meningococcal disease are hard to predict over time due to natural fluctuations in disease. In Australia, notification rates of meningococcal disease have been decreasing, from a peak of 3.5 cases per 100 000 in 2001 to 1.1 per 100 000 in 2011. This is due to a decline in serogroup C disease following the national meningococcal C vaccination program and also a substantial decline in serogroup B disease.\(^27\) In Australia in 2006–2011, the highest incidence of serogroup B disease was in children aged <5 years (5.7 cases per 100 000), particularly infants aged <1 year (14.0 cases per 100 000) and toddlers aged 12–23 months (6.3 cases per 100 000). There was also a lower, secondary peak in late adolescence and early adulthood (2.8 cases per 100 000 aged 15–19 years). The incidence of serogroup C disease has remained low at <0.3 cases per 100 000 since 2009 for all age groups, with no cases reported among those aged <20 years in 2011.\(^27\)
4.10.4 Vaccines

Meningococcal vaccines available in Australia can be broadly categorised according to their formulation type (conjugate, polysaccharide or recombinant) and the serogroups which they are designed to protect against (A, B, C, W_{135} and/or Y). There is no single vaccine that offers protection against all meningococcal serogroups.

Conjugate meningococcal vaccines

**Monovalent meningococcal C vaccines (MenCCV)**

- **Meningitec** – Emerge Health (meningococcal serogroup C–CRM_{197} conjugate). Each 0.5 mL pre-filled syringe contains 10 µg *Neisseria meningitidis* serogroup C oligosaccharide conjugated to approximately 15 µg of non-toxic *Corynebacterium diphtheriae* CRM_{197} protein; aluminium phosphate.

- **Menjugate Syringe** – CSL Limited/Novartis Vaccines and Diagnostics Pty Ltd (meningococcal serogroup C–CRM_{197} conjugate). Lyophilised powder in a monodose vial with a pre-filled diluent syringe. Each 0.5 mL reconstituted dose contains 10 µg *N. meningitidis* serogroup C oligosaccharide conjugated to 12.5–25 µg of non-toxic *C. diphtheriae* CRM_{197} protein; 1.0 mg aluminium hydroxide.

- **NeisVac-C** – Baxter Healthcare Pty Ltd (meningococcal serogroup C–tetanus toxoid conjugate). Each 0.5 mL pre-filled syringe contains 10 µg *N. meningitidis* serogroup C polysaccharide conjugated to 10–20 µg of tetanus toxoid; 0.5 mg aluminium as aluminium hydroxide.

**Combination vaccine that contains meningococcal C (Hib-MenCCV)**

- **Menitorix** – GlaxoSmithKline Australia Pty Ltd (*Haemophilus influenzae* type b [PRP-T]-meningococcal serogroup C–tetanus toxoid conjugate). Lyophilised powder in a monodose vial with a pre-filled diluent syringe. Each 0.5 mL reconstituted dose contains 5 µg Hib capsular polysaccharide (PRP) conjugated to 12.5 µg tetanus toxoid, and 5 µg *N. meningitidis* serogroup C polysaccharide conjugated to 5 µg of tetanus toxoid; traces of tetramethylammonium and sucrose.

**Quadrivalent meningococcal conjugate vaccines (4vMenCV)**

- **Menactra** – Sanofi-Aventis Australia Pty Ltd (meningococcal serogroups A, C, W_{135}, Y–diphtheria toxoid conjugate). Each 0.5 mL monodose vial contains 4 µg each of serogroups A, C, W_{135} and Y polysaccharides conjugated with a total of approximately 48 µg of a diphtheria toxoid protein.

- **Menevo** – CSL Limited/Novartis Vaccines and Diagnostics Pty Ltd (meningococcal serogroups A, C, W_{135}, Y–CRM_{197} conjugate). Lyophilised powder containing serogroup A (MenA) in a monodose vial with a pre-filled vial containing serogroups C, W_{135} and Y (MenCWY) in saline suspension. Each 0.5 mL reconstituted dose contains 10 µg of serogroup A and 5 µg each of serogroups C, W_{135} and Y oligosaccharides individually conjugated with up to 33.3 µg of non-toxic *C. diphtheriae* CRM_{197} protein; sucrose.

- **Nimenrix** – GlaxoSmithKline Australia Pty Ltd (meningococcal serogroups A, C, W_{135}, Y–tetanus toxoid conjugate). Lyophilised powder in a monodose vial with solvent supplied in a pre-filled syringe or ampoule. Each 0.5 mL reconstituted dose contains 5 µg each of serogroups A, C, W_{135} and Y polysaccharides conjugated with a total of 44 µg of tetanus toxoid; tetramethylammonium; sucrose.

Conjugate meningococcal vaccine formulations contain meningococcal serogroup antigens conjugated to a carrier protein. They include vaccines that only offer protection against serogroup C meningococcal disease – monovalent meningococcal C conjugate vaccines (MenCCV) and MenCCV in combination with Hib (Hib-MenCCV) – and vaccines which offer protection against disease caused by four meningococcal serogroups, including meningococcal C (quadrivalent meningococcal conjugate vaccines, 4vMenCV).

**Monovalent meningococcal C vaccines (MenCCV)**

Following extensive assessment in clinical studies, MenCCVs are now routinely delivered to infants and young children in a number of countries, including Australia. The effectiveness of MenCCV following 1 dose has been estimated to range from 83 to 100%. The population-wide use of this vaccine in national vaccination programs has resulted in marked reductions in serogroup C invasive disease in the eligible age groups, including in Australia. There is also evidence that meningococcal C vaccination programs have offered indirect protection to older age groups who were not eligible to receive the vaccine. Although waning of antibody levels has been observed following vaccination with MenCCVs, current serogroup C meningococcal disease epidemiology in Australia suggests ongoing protection in age groups who were previously vaccinated.
Combination vaccine that contains meningococcal C (Hib-MenCCV)

The combination vaccine containing meningococcal serogroup C and *Haemophilus influenzae* type b antigens (Hib-MenCCV) has been used under the National Immunisation Program (NIP) since July 2013. The MenCCV component has similar immunogenicity and safety to monovalent MenCCV.38-43

Quadrivalent meningococcal conjugate vaccines (4vMenCV)

4vMenCVs are designed to provide protection against four serogroups of meningococci: A, C, W135 and Y. As it is not feasible to assess the efficacy of 4vMenCVs in clinical trials, immunogenicity outcomes have been used as a surrogate measure for vaccine efficacy. Each of the registered 4vMenCV formulations have been shown to be immunogenic in infants, children and adults, inducing serum bactericidal antibodies at levels that correlate with clinical protection approximately 1 month after a vaccine dose.44-54 There is some evidence that the immunogenicity of the different 4vMenCV formulations varies among adolescents and adults, but the clinical significance of the differences is uncertain and does not warrant a preference for one formulation over another in these age groups.45,55-58 The vaccine effectiveness of a 4vMenCV adolescent vaccination program in the United States, consisting of a single dose, has been estimated at 80 to 85%.59

Menveo is the only 4vMenCV which has been assessed in young infants (from 2 months of age). A clinical trial has shown that protective levels of antibody to serogroups C, W135 and Y are induced in >70% of infants after 2 vaccine doses, at 2 and 4 months of age, with a lower antibody response to serogroup A.51 However, protective levels of antibodies to all serogroups were achieved in >90% of infants after a 3rd dose at 6 months of age.50

Protective antibody titres from 4vMenCV have been shown to persist for up to 3 years in clinical trials in children.50 In adolescents and adults, a high proportion of vaccine recipients have been shown to maintain seroprotective antibody titres against most of the vaccine serogroups (except serogroup A) until up to 5 years after primary vaccination.61

A few studies have demonstrated a poor immune response to a single dose of meningococcal conjugate vaccine (either MenCCV or 4vMenCV) in children and adults with asplenia62,63 and in HIV-infected persons.64-66 The immune response to some serogroups improves following a 2nd vaccine dose.62,65-67

**Meningococcal B vaccine (MenBV)**

- **Bexsero** – Novartis Vaccines and Diagnostics Pty Ltd (recombinant multicomponent meningococcal serogroup B vaccine). Each 0.5 mL pre-filled syringe contains 50 µg *Neisseria meningitidis* serogroup B Neisseria heparin binding antigen fusion protein, 50 µg *Neisseria meningitidis* serogroup B Neisseria adhesin A protein, 50 µg *Neisseria meningitidis* serogroup B factor H binding protein fusion protein, 25 µg outer membrane vesicles from *Neisseria meningitidis* serogroup B strain NZ98/254 (measured as amount of total protein containing the PorA P1.4), adsorbed onto aluminium hydroxide; sodium chloride; histidine; sucrose. May contain traces of kanamycin. Tip cap may contain traces of natural rubber latex.

MenBV is a recombinant multicomponent vaccine (also known as 4CMenB) designed to provide protection against multiple strains of meningococcal serogroup B. It contains four major protein antigens that are highly conserved across serogroup B strains. This vaccine differs from strain-specific meningococcal B vaccines that have been used in some countries, such as New Zealand, for the control of epidemics dominated by a single serogroup B strain.68

As it is not feasible to assess the efficacy of MenBV in clinical trials, immunogenicity outcomes have been used as a surrogate measure for vaccine efficacy. Clinical studies have shown that MenBV induces bactericidal antibodies specific to the four vaccine antigens in infants, children, adolescents and younger adults at a level that correlates with protection against clinical disease.69-73 There are currently no data on the use of MenBV in persons aged >50 years. MenBV is expected to protect against the majority of circulating meningococcal B strains. Specialised laboratory testing (Meningococcal Antigen Typing System or MATS) has predicted that approximately 76% of all meningococcal B strains that caused disease in Australia from 2007 to 2011 would have been susceptible to effective killing by vaccine-induced antibodies.74

The duration of clinical protection afforded by MenBV is currently unknown due to the limited data on persistence of vaccine-induced immunity.75,78
## Polysaccharide meningococcal vaccines

### Quadrivalent meningococcal polysaccharide vaccines (4vMenPV)

- **Mencevax ACWY** – GlaxoSmithKline Australia Pty Ltd (meningococcal serogroups A, C, W₁₃₅ and Y polysaccharides). Lyophilised pellet in a monodose vial with separate saline diluent. Each 0.5 mL reconstituted dose contains 50 µg of each meningococcal serogroup polysaccharide; 12.6 mg sucrose; 0.1 mg trometamol.

- **Menomune** – Sanofi-Aventis Australia Pty Ltd (meningococcal serogroups A, C, W₁₃₅ and Y polysaccharides). Lyophilised powder in a monodose vial with separate saline diluent. Each 0.5 mL reconstituted dose contains 50 µg of each meningococcal serogroup polysaccharide; 2.5–5 mg lactose.

Quadrivalent polysaccharide vaccine formulations (4vMenPV) contain meningococcal polysaccharide antigens for four serogroups: A, C, W₁₃₅ and Y. Unlike 4vMenCV, the polysaccharide antigens are not conjugated to a carrier protein. This results in a different immunogenicity and efficacy profile to that of the conjugate vaccines. In clinical studies of 4vMenPVs, the vaccines were immunogenic in 90% of recipients >2 years of age, but were poorly immunogenic in children <2 years of age. Compared with 4vMenCV, 4vMenPVs are less immunogenic for all vaccine serogroups in children aged 2–10 years⁷⁹,⁸³–⁸⁵,⁸⁶ and for some vaccine serogroups in adolescents and adults.³⁶,⁷⁵,⁷⁷,⁸¹

Clinical protection following a single dose of 4vMenPV appears to persist for 3 to 5 years in healthy children of school age and adults but with variation between age groups and serogroups. Duration of protection may be shorter for children <10 years of age, particularly for some vaccine serogroups.⁶⁰

Revaccination with polysaccharide meningococcal vaccine formulations has been shown to reduce the antibody response to vaccine serogroups (immunological hyporesponsiveness) compared with the primary immunisation, although a reduction in the clinical effectiveness of 4vMenPV with revaccination has not been demonstrated. This blunting of antibody response is not observed when meningococcal conjugate vaccines are used for the primary immunisation.⁸³

### 4.10.5 Transport, storage and handling

For all meningococcal vaccines, transport according to *National vaccine storage guidelines: Strive for 5*.⁸⁷ Store at +2°C to +8°C. Do not freeze. Protect from light.

#### Conjugate vaccines

Menjugate Syringe must be reconstituted by adding the entire contents of the diluent syringe to the vial and shaking gently until the powder is completely dissolved. Reconstituted vaccine should be used immediately.

Menitorix must be reconstituted by adding the entire contents of the diluent syringe to the vial and shaking well until the powder is completely dissolved. Reconstituted vaccine should be used promptly. If storage is necessary, hold at +2°C to +8°C for not more than 24 hours.

Mencevax ACWY must be reconstituted by adding the entire contents of the liquid MenCWY vial to the lyophilised MenA vial and shaking vigorously until the powder is completely dissolved. Reconstituted vaccine should be used as soon as practicable. If storage is necessary, hold at +2°C to +8°C for not more than 24 hours.

Nimenrix must be reconstituted by adding the entire contents of the pre-filled syringe or ampoule of solvent to the vial and shaking well until the powder is completely dissolved. Reconstituted vaccine should be used promptly. Reconstituted vaccine is stable at temperatures up to 30°C for up to 8 hours.

#### Polysaccharide vaccines

Mencevax ACWY must be reconstituted by adding the entire contents of the diluent container to the vial and shaking until the powder is completely dissolved. Reconstituted vaccine should be used promptly. If storage is necessary, hold at +2°C to +8°C for not more than 8 hours.

Menomune must be reconstituted by adding the entire contents of the diluent container to the vial and swirling until the powder is completely dissolved. Reconstituted vaccine should be used immediately.

### 4.10.6 Dosage and administration

#### Conjugate meningococcal vaccines

The dose of all meningococcal conjugate vaccines (MenCCV, Hib-MenCCV, 4vMenCV) is 0.5 mL, to be given by IM injection.

Meningitec (MenCCV), Menjugate Syringe (MenCCV) and Menitorix (Hib-MenCCV) are registered for use from 6 weeks of age.

NeisVac-C (MenCCV) is registered for use from 8 weeks of age.
The recommended age for use of 4vMenCVs varies between vaccine brands. Menactra can be used from 2 years of age, Nimenrix from 12 months of age and Menveo from 2 months of age (refer to 4.10.13 Variations from product information below).

**Meningococcal B vaccine**

The dose of MenBV is 0.5 mL, to be given by IM injection. Refer to Table 4.10.1 for the recommended doses of MenBV for different age groups.

MenBV is registered for use from 2 months of age. However, the 1st dose can be given as early as 6 weeks of age to align with the schedule for other routine infant vaccines (refer to 4.10.13 Variations from product information below). If the 1st dose is given at 6 weeks of age, the next scheduled doses can be given at 4 and 6 months of age.

**Table 4.10.1: Recommended number of doses of MenBV by age group**

<table>
<thead>
<tr>
<th>Age at commencement of vaccine course</th>
<th>Number of doses required for primary immunisation</th>
<th>Recommended interval between primary doses</th>
<th>Recommended age for single booster dose</th>
</tr>
</thead>
<tbody>
<tr>
<td>6 weeks* – 5 months</td>
<td>3 doses</td>
<td>8 weeks</td>
<td>12 months</td>
</tr>
<tr>
<td>6–11 months</td>
<td>2 doses</td>
<td>8 weeks</td>
<td>12 months, or 8 weeks after previous dose, whichever is later</td>
</tr>
<tr>
<td>≥12 months†</td>
<td>2 doses</td>
<td>8 weeks</td>
<td>No booster required‡</td>
</tr>
</tbody>
</table>

* MenBV is registered for use in persons ≥2 months of age; however, the 1st dose of MenBV can be given as early as 6 weeks of age (refer to 4.10.13 Variations from product information).
† There are currently no data on the use of MenBV in persons aged >50 years; however, it is recommended that MenBV can be used in older persons who are at increased risk of IMD (refer to 4.10.7 Recommendations below).
‡ The need for a booster dose for this age group is as yet uncertain.

**Polysaccharide meningococcal vaccines**

The dose of both 4vMenPVs is 0.5 mL, to be given by SC injection.

4vMenPVs are registered for use in persons ≥2 years of age.

**Co-administration with other vaccines**

Meningococcal vaccines can be administered concurrently with other vaccines (refer to 4.10.13 Variations from product information below).

There is an increased risk of fever following the co-administration of MenBV with other vaccines routinely recommended for children <24 months of age, compared to when these vaccines are given separately (refer to 4.10.11 Adverse events below). Co-administration of MenBV with other routine infant vaccines in this age group is acceptable; however, prophylactic administration of paracetamol to reduce the risk of fever is recommended (refer to 4.10.10 Precautions below). Alternatively, MenBV can be administered separately from other routine infant vaccines, with a minimum interval of 3 days, to minimise the risk of fever. In this circumstance it is important that routinely recommended vaccines are not delayed.

The co-administration of MenBV and 4vMenCV in persons who are at increased risk of meningococcal disease is acceptable based on first principles, although there are no specific data on concomitant administration of these vaccines. In persons for whom multiple vaccines (and thus injections) are recommended at one time, and there is a desire to reduce the number of injections given at one visit. MenBV should be administered earlier than 4vMenCV due to the higher incidence of meningococcal serogroup B compared with other serogroups in Australia (refer to 4.10.3 Epidemiology above).

**Interchangeability of meningococcal vaccines**

The different meningococcal vaccine formulations (conjugate, polysaccharide and recombinant) are not interchangeable.

The different brands of 4vMenCV are not interchangeable. However, in circumstances where the brand of vaccine used for previous dose(s) is not known or is not available, the use of another brand for the subsequent dose(s) is acceptable.88
4.10.7 Recommendations

Meningococcal vaccines are recommended for the following age and risk groups because of their greater risk of IMD.

Infants and children

Meningococcal C vaccines

A single dose of MenCCV-containing vaccine is recommended for all children at the age of 12 months. This can be provided as either MenCCV or the combination vaccine Hib-MenCCV (refer to 4.10.4 Vaccines above). Additional doses of MenCCV-containing vaccine are not recommended based on current disease epidemiology in Australia (refer to 4.10.3 Epidemiology above).

Children who missed receiving a dose of MenCCV-containing vaccine at 12 months of age should be given a single catch-up dose (refer to 2.1.5 Catch-up). Similarly, children (without medical risk factors for IMD) who have received a dose(s) of MenCCV-containing vaccine at age <12 months, such as migrants from overseas countries where different vaccine schedules are used, should be given a single dose at 12 months of age or 8 weeks after their last dose (refer to 2.1.5 Catch-up and 4.10.13 Variations from product information below).

Meningococcal B vaccine

MenBV is recommended for infants and young children, particularly those aged <2 years, due to their higher risk of serogroup B meningococcal disease (refer to 4.10.3 Epidemiology above). The number of doses required depends on the age at which the vaccine course is commenced (refer to Table 4.10.1 in 4.10.6 Dosage and administration above).

Prophylactic administration of paracetamol is recommended with every dose of MenBV in children <2 years of age due to the increased risk of fever following vaccine administration (refer to 4.10.10 Precautions below).

Adolescents and adults

Meningococcal B vaccine

MenBV is recommended in a 2-dose schedule for all adolescents aged 15–19 years due to their higher risk of serogroup B meningococcal disease compared with other ages (refer to Table 4.10.1 in 4.10.6 Dosage and administration above).

MenBV vaccine is particularly recommended for adolescents and young adults living in close quarters, such as new military recruits and students living in residential accommodation. Vaccination should be given prior to entry to such risk settings or as soon as possible after entry (refer to 4.10.2 Clinical features).

Persons with condition(s) associated with an increased risk of meningococcal disease

A number of medical conditions or treatments increase a person’s risk of IMD (refer to List 4.10.1) and additional doses of 4vMenCV and MenBV are recommended for persons with these risk factors.

List 4.10.1: Conditions associated with an increased risk of invasive meningococcal disease (IMD) in children and adults

- defects in or deficiency of complement components, including factor H, factor D or properdin deficiency
- current or future treatment with eculizumab (a monoclonal antibody directed against complement component C5)
- functional or anatomical asplenia
- HIV infection, regardless of stage of disease or CD4+ count
- haematopoietic stem cell transplant

Meningococcal conjugate vaccines

4vMenCV is recommended for persons with conditions in List 4.10.1. The vaccine brand and doses required depend on the age at which the vaccine course is commenced (refer to Table 4.10.2).

Menveo is the only brand of 4vMenCV that should be used in infants <12 months of age. If Menveo is not available, specialist advice should be sought on the most appropriate vaccination schedule.

Persons who require 4vMenCV due to the presence of underlying at-risk conditions, who have previously received 4vMenPV, should receive 2 doses of 4vMenCV as outlined in Table 4.10.2. The first dose of 4vMenCV is recommended approximately 2 years after the most recent dose of 4vMenPV. However, if the first dose of 4vMenCV is required sooner, a minimum interval of 6 months after 4vMenPV is acceptable, based on limited immunogenicity studies.82,84,85
Table 4.10.2: Recommended use of 4vMenCV by age group for persons with medical condition(s) associated with an increased risk of meningococcal disease

<table>
<thead>
<tr>
<th>Age at commencement of vaccine course</th>
<th>Recommended brand</th>
<th>Primary immunisation</th>
<th>Recommended interval between primary doses*</th>
<th>Timing of booster doses</th>
</tr>
</thead>
<tbody>
<tr>
<td>2–6 months</td>
<td>Menevo</td>
<td>3 doses</td>
<td>8 weeks</td>
<td>At age 12–18 months, then 3 years later, then every 5 years thereafter</td>
</tr>
<tr>
<td>7–11 months</td>
<td>Menevo</td>
<td>2 doses</td>
<td>12 weeks</td>
<td>3 years after the primary doses, then every 5 years thereafter</td>
</tr>
<tr>
<td>12–23 months</td>
<td>Menevo or Nimenrix</td>
<td>2 doses</td>
<td>12 weeks</td>
<td>3 years after the primary doses, then every 5 years thereafter</td>
</tr>
<tr>
<td>2–6 years</td>
<td>Menactra, Menevo or Nimenrix</td>
<td>2 doses</td>
<td>8 weeks</td>
<td>3 years after the primary doses, then every 5 years thereafter</td>
</tr>
<tr>
<td>≥7 years</td>
<td>Menactra, Menevo or Nimenrix</td>
<td>2 doses</td>
<td>8 weeks</td>
<td>Every 5 years after the previous dose</td>
</tr>
</tbody>
</table>

* Refer to Table 2.1.7 Minimum acceptable dose intervals for children <10 years of age for advice on minimum intervals.

**Meningococcal B vaccine**

MenBV is recommended for persons with conditions in List 4.10.1. For recommended doses of MenBV by age group refer to Table 4.10.1 in 4.10.6 Dosage and administration above.

**Travellers**

A quadrivalent meningococcal vaccine is recommended for persons who are planning travel involving a greater risk of exposure to meningococcal serogroups A, C, W_135_ and Y.

This includes:

- individuals who intend to travel to or reside in parts of the world where epidemics of group A, C, W_135_ or Y meningococcal disease occur, particularly the ‘meningitis belt’ of sub-Saharan Africa
- individuals who intend to travel to mass gatherings, for example, pilgrims travelling to the Hajj. In some instances documentation of vaccination is required for country entry visas.

The vaccine brand and doses required depends on the age at which the vaccine course is commenced (refer to Table 4.10.3). Use of 4vMenCV is preferred, particularly in children aged <7 years and travellers of any age who anticipate ongoing or periodic travel-related exposure risk. 4vMenPV is suitable, however, when the need for repeat doses is not anticipated, as described in 4.10.4 Vaccines above.

In those with ongoing increased risk due to travel who have previously received 4vMenPV, 1 dose of 4vMenCV is recommended approximately 2 years after the most recent dose of 4vMenPV, with a recommended minimum interval of 6 months, with subsequent 4vMenCV vaccinations as outlined in Table 4.10.3.
Table 4.10.3: Recommended use of 4vMenCV by age group for persons travelling to areas where epidemics of group A, C, W_{135} or Y meningococcal disease occur or to mass gatherings

<table>
<thead>
<tr>
<th>Age at commencement of vaccine course</th>
<th>Recommended brand</th>
<th>Primary immunisation</th>
<th>Recommended interval between primary doses*</th>
<th>Timing of booster doses of 4vMenCV if required</th>
</tr>
</thead>
<tbody>
<tr>
<td>2–6 months</td>
<td>Menveo</td>
<td>3 doses</td>
<td>8 weeks</td>
<td>At age 12–18 months, then 3 years later, then every 5 years thereafter</td>
</tr>
<tr>
<td>7–11 months</td>
<td>Menveo</td>
<td>2 doses</td>
<td>12 weeks</td>
<td>3 years after the primary doses, then every 5 years thereafter</td>
</tr>
<tr>
<td>12–23 months</td>
<td>Either Menveo</td>
<td>2 doses</td>
<td>12 weeks</td>
<td>3 years after the primary dose(s), then every 5 years thereafter</td>
</tr>
<tr>
<td>12–23 months</td>
<td>Or Nimenrix</td>
<td>1 dose</td>
<td>Not applicable</td>
<td></td>
</tr>
<tr>
<td>2–6 years</td>
<td>Menactra, Menveo or Nimenrix†</td>
<td>1 dose</td>
<td>Not applicable</td>
<td>3 years after the primary dose, then every 5 years thereafter</td>
</tr>
<tr>
<td>≥7 years</td>
<td>Menactra, Menveo or Nimenrix†</td>
<td>1 dose</td>
<td>Not applicable</td>
<td>Every 5 years after the previous dose‡</td>
</tr>
</tbody>
</table>

* Refer to Table 2.1.7 Minimum acceptable dose intervals for children <10 years of age for advice on minimum intervals.
† 4vMenCV is preferred. However, 4vMenPV is a suitable alternative for travellers aged ≥7 years when the need for repeat doses is not anticipated (refer to ‘Travellers’ above).

Laboratory personnel who frequently handle Neisseria meningitidis

Laboratory personnel who are at occupational risk of exposure to Neisseria meningitidis are recommended to receive immunisation against all vaccine-preventable meningococcal serogroups as listed below.

Meningococcal conjugate vaccines

4vMenCV is recommended for laboratory personnel to offer protection against serogroups A, C, W_{135} and Y. Those with ongoing occupational exposure risks are recommended to receive a 4vMenCV booster dose every 5 years.

4vMenPV can be used if the risk of exposure is not expected to be ongoing and the need for repeat doses (which can result in immunological hyporesponsiveness, refer to 4.10.4 Vaccines) is not anticipated. However, for most laboratory personnel, there will be ongoing exposure risks and anticipated need for repeat doses of the vaccine and, in these instances, 4vMenCV is preferred.

In those with ongoing occupational exposure risks who have previously received 4vMenPV, a dose of 4vMenCV is recommended approximately 2 years after the most recent dose of 4vMenPV. The minimum interval between the 1st dose of 4vMenCV and the last dose of 4vMenPV is 6 months.\(^{82,84,85}\)

Meningococcal B vaccine

MenBV in a 2-dose schedule is recommended for laboratory personnel to offer protection against meningococcal serogroup B. For recommended doses of MenBV by age group refer to Table 4.10.1 in 4.10.6 Dosage and administration above.

Use of vaccines for close contacts of meningococcal disease cases

Advice on the need for meningococcal vaccination of the close contacts of a meningococcal disease case (i.e. those with household or household-like contact) should be sought from the relevant state or territory public health authority (refer to 4.10.12 Public health management of meningococcal disease below).
4.10.8 Pregnancy and breastfeeding

Meningococcal vaccines are not routinely recommended for pregnant or breastfeeding women, but can be given where clinically indicated (refer to 4.10.7 Recommendations above).

Refer to 3.3 Groups with special vaccination requirements, Table 3.3.1 Recommendations for vaccination in pregnancy for more information.

4.10.9 Contraindications

The only absolute contraindications to meningococcal vaccines are:

- anaphylaxis following a previous dose of any meningococcal vaccine
- anaphylaxis following any vaccine component.

Previous meningococcal disease, regardless of the serogroup, is not a contraindication to administration of any meningococcal vaccine.

Previous vaccination with the strain-specific meningococcal B vaccine used in New Zealand, MeNZB, is not a contraindication for receiving MenBV.

4.10.10 Precautions

Prophylactic administration of paracetamol with MenBV vaccination in children aged <2 years

Prophylactic administration of paracetamol with every dose of MenBV administered to children <2 years of age is recommended due to the increased risk of fever, including high fever, following MenBV (refer to 4.10.11 Adverse events below). This is an exception to the general recommendation to not routinely give paracetamol at the time of vaccinations (refer to 2.3.2 Adverse events following immunisation).

The 1st dose of paracetamol (15 mg/kg/dose) is recommended within the 30-minute period prior to, or as soon as practicable after, vaccination, regardless of the presence of fever. This can be followed by 2 more doses of paracetamol 6 hours apart, regardless of the presence of fever. A clinical trial has shown that the prophylactic use of paracetamol in infancy reduced the likelihood of high-grade fever by approximately half following any vaccine dose, with no overall impact on the immunogenicity of either MenBV or other vaccines given concurrently.

Similarly, the use of prophylactic antipyretics in a population-based MenBV program in a region of Quebec, Canada, reduced the likelihood of fever in the first 48 hours following the 1st dose of MenBV by about 50% among over 1500 children <2 years of age (refer to 4.10.11 Adverse events below).

4.10.11 Adverse events

Conjugate meningococcal vaccines

Meningococcal conjugate vaccines are generally considered safe and well tolerated. Common adverse events are pain, redness and swelling at the injection site, fever, irritability, drowsiness, decreased appetite and headaches. There are some age-related differences in the type of adverse events following vaccination. For example, headache, anorexia, fever and chills are more likely to be reported in adolescents and adults than in children following administration of 4vMenCV. Among recipients of 4vMenCV, rash and nausea are common. However, serious general adverse events are rare.

The range of adverse events occurring after Hib-MenCCV combination vaccine is similar to that after other childhood vaccines. Redness is the most frequently reported local symptom, with irritability the most frequently reported generalised reaction. Concomitant administration of Hib-MenCCV with MMR vaccine is not associated with an increased rate of adverse events for either vaccine.

There is no evidence of an association between meningococcal conjugate vaccines and Guillain-Barré syndrome (GBS). An early report in the United States of a suspected temporal association between Menactra and GBS was followed by a large retrospective cohort study in the United States which found no evidence of an increased risk of GBS with the use of Menactra. Meningococcal conjugate vaccines can be administered to persons with a history of GBS for whom vaccination is indicated (refer to 4.10.13 Variations from product information below).

Meningococcal B vaccine

MenBV has an acceptable safety and tolerability profile based on clinical trial data. In clinical trials, fever was the most notable systemic reaction in infants and young children, particularly those aged 2–12 months. Temperatures were highest 6 hours after vaccination, then decreased on day 2 and generally subsided by day 3. More than a quarter (26 to 41% depending on dose number) of infants who received MenBV alone developed fever ≥38°C and 4 to 8% had fever ≥39°C. In response to a community epidemic, approximately 44 000 individuals between 2 months and 20 years of age in a region of Quebec, Canada, received at least 1 dose of MenBV. About 15% (112/746) of infants who participated in the vaccine safety surveillance reported fever; among those who had their temperature measured in the
first 48 hours \((n=61)\), approximately 32% reported a peak temperature of 39–40.4°C, and <1% reported a peak temperature of ≥40.5°C.\(^\text{92}\)

In a clinical trial, the frequency of fever was about 2 times higher when MenBV was administered with other infant vaccines, specifically DTPa-hepB-IPV-Hib and 7-valent pneumococcal conjugate vaccines, with 51 to 62% of infants reporting fever ≥38°C and 10 to 15% reporting fever ≥39°C within 7 days of any vaccine dose.\(^\text{70}\) Fever in infants given MenBV concurrently with other routine infant vaccines was reduced by prophylactic use of paracetamol.\(^\text{91}\) (Refer also to 4.10.10 Precautions above). In clinical studies, fever and other systemic reactions were less common after the booster dose of MenBV administered at 12 months of age.

Other common adverse events following MenBV included tenderness, swelling, induration and erythema at the injection site, as well as irritability, sleepiness, unusual crying and change in appetite.\(^\text{59}\) These reactions were reported less often with increasing age. Pain at the injection site, malaise and headache were more commonly reported among adolescents and adults.\(^\text{71}\)

### Polysaccharide meningococcal vaccines

Local adverse events after 4vMenPV include erythema, induration, tenderness, pain and local axillary lymphadenopathy. However, these reactions are usually mild and infrequent. Fever and chills occur in approximately 2% of young children, and may persist for 48 hours or longer, but significant general adverse events are rare. Studies have indicated no consistently significant differences in adverse events following 4vMenPV and 4vMenCV.\(^\text{54}\)

### 4.10.12 Public health management of meningococcal disease

Invasive meningococcal disease is notifiable in all states and territories in Australia. Prompt diagnosis and medical treatment of suspected cases of meningococcal disease is important.

The state/territory public health authority should be contacted as soon as possible for guidance on the public health management of suspected cases and their contacts (refer to Appendix 1 Contact details for Australian, state and territory government health authorities and communicable disease control).

Decisions about the need for meningococcal vaccination of the close contacts of a meningococcal disease case (i.e. those with household or household-like contact), or in an outbreak of meningococcal disease in an institutional or community setting, should be made by the local public health unit and/or the state or territory public health authority, according to the national guidelines.\(^\text{34}\)

### 4.10.13 Variations from product information

The product information for meningococcal C conjugate vaccines states that, under the age of 12 months, either 2 (NeisVac-C) or 3 (Meningitec and Menjugate Syringe) doses of vaccine are required. The ATAGI recommends instead that meningococcal C vaccination is routinely not recommended before 12 months of age (unless specifically indicated).

The product information for Meningitec states that an allergic reaction following a previous dose is a contraindication to further doses. The ATAGI recommends instead that the only contraindication is a history of anaphylaxis to a previous dose or to any of the vaccine components.

The product information for NeisVac-C states that this vaccine should not be administered with PRP-OMP \textit{Haemophilus influenzae} type b vaccine unless ‘medically important’. The ATAGI recommends instead that the vaccine may be administered simultaneously with other vaccines in the NIP.

The product information for Bexsero states that this vaccine is indicated for use in persons ≥2 months of age. However, the ATAGI recommends instead that the 1st dose of Bexsero can be given to infants concurrently with other infant vaccines from as early as 6 weeks of age, to align with the routine infant schedule.

The product information for Menveo states that this vaccine is indicated for use in persons ≥11 years of age. The ATAGI recommends instead that Menveo can be given to persons ≥2 months of age (refer to 4.10.4 Vaccines).

The product information for Menacra states that this vaccine is indicated for use in persons between 2 and 55 years of age. The ATAGI recommends instead that this vaccine can be given to persons >55 years of age.

The product information for Nimenrix states that this vaccine is indicated for use in persons between 1 and 55 years of age. The ATAGI recommends instead that this vaccine can be given to persons >55 years of age.

The product information for Menacra states that a previous episode of GBS is a contraindication to vaccination with Menacra. The ATAGI recommends instead that any of the available 4vMenCVs can be administered to a person with a history of GBS.

The product information for all meningococcal vaccines (MenCCV, 4vMenCV, MenBV and 4vMenPV) states that there are no data on the use of these vaccines in lactating women. The ATAGI recommends that breastfeeding women can be vaccinated.
The product information for all 4vMenCVs states that vaccine should be administered as a single dose. The ATAGI recommends that these vaccines can be given in a 2- or 3-dose primary schedule to infants, children and adults who are at increased risk of IMD according to Tables 4.10.2 and 4.10.3.

References

A full reference list is available on the electronic Handbook or website www.immunise.health.gov.au.


44. Gasparini R, Conversano M, Bona G, et al. Randomized trial on the safety, tolerability, and immunogenicity of MenACWY-CRM, an investigational quadrivalent meningococcal glycoconjugate vaccine, administered concomitantly with a combined tetanus, reduced diphtheria, and acellular pertussis vaccine in adolescents and young adults. *Clinical and Vaccine Immunology: CVI* 2010;17:537-44.


70. Gossger N, Snape MD, Yu L.M, et al. Immunogenicity and tolerability of recombinant serogroup B meningococcal vaccine administered with or without routine infant vaccinations according to different immunization schedules: a randomized controlled trial. *JAMA* 2012;307:573-82.


