FactSheet

Following the Department of Health announcement to include meningococcal ACWY vaccine on the NIP, this fact sheet will be updated as more specific information becomes available.

Meningococcal vaccines

NATIONAL CENTRE FOR IMMUNISATION RESEARCH & SURVEILLANCE

FREQUENTLY ASKED QUESTIONS

This fact sheet provides responses to some common questions about meningococcal vaccines, focusing on quadrivalent meningococcal conjugate vaccines (4vMenCVs). More detailed information about meningococcal disease and the available meningococcal vaccines can be found in the NCIRS fact sheet Meningococcal vaccines for Australians and in *The Australian Immunisation Handbook* (Chapter 4.10 Meningococcal disease). Additional information on the use of the meningococcal B vaccine (Bexsero®) is available in the Australian Technical Advisory Group on Immunisation's advice for immunisation providers regarding the use of Bexsero®.

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The Australian Technical Advisory Group on Immunisation (ATAGI) is currently reviewing the use of meningococcal vaccines in Australia and will be updating the meningococcal chapter of *The Australian Immunisation Handbook*. Some of the information contained within this FAQ and the NCIRS fact sheet is not currently in the *Handbook*.

Questions about meningococcal vaccines and vaccine schedules

Q1. Who should be vaccinated with quadrivalent (A, C, W, Y) meningococcal conjugate vaccines (4vMenCV)?

Any person 2 months of age or older can be vaccinated with 4vMenCV to reduce their likelihood of becoming ill with meningococcal disease caused by serogroup A, C, W or Y. Children aged under 2 years have the highest rates of meningococcal W and Y disease, followed by older adolescents (refer also to **Q20**).

Meningococcal bacteria are carried and spread more frequently in older adolescents and young adults, so people living in close conditions, such as military recruits or those in residential accommodation, may particularly benefit from vaccination.

Individuals travelling to parts of the world where serogroup A, C, W or Y disease is more common should also receive 4vMenCV, and 4vMenCV is required for pilgrims attending the annual Hajj in Mecca. Vaccination with both 4vMenCV and the meningococcal B (MenB) vaccine is recommended for people with medical conditions associated with an increased risk of meningococcal disease (refer to **Q6**), and laboratory personnel who frequently handle *Neisseria meningitidis*.

Q2. Which 4vMenCVs are available in Australia, and are there any differences between them?

There are three brands of 4vMenCVs available for use in Australia (Table 1). They differ in the carrier protein that the meningococcal serogroup A, C, W and Y antigens are conjugated to:

- Menactra® (Sanofi Pasteur) – diphtheria toxoid conjugate
- Menveo® (GlaxoSmithKline) – CRM_{197} conjugate
- Nimenrix® (Pfizer) – tetanus toxoid conjugate.

All three vaccines provide protection against meningococcal A, C, W and Y disease. However, the level of immune response that each of them induces in different age groups and to different serogroups varies to some extent. Therefore, there are differences in the dosing schedules for each vaccine. The age ranges for which they are registered for use in Australia also vary. There is currently no preferential recommendation for the use of one brand over another within age groups (Table 1).

Q3. How many doses of 4vMenCV are required?

The number of doses of 4vMenCV required varies by age at which vaccination commences, as shown in Table 1. The intervals given in Table 1 are the minimum intervals between doses; administering subsequent doses at longer intervals does not reduce vaccine effectiveness or necessitate repeating prior doses. Although Menveo® is the only brand that is currently registered in Australia for use in those aged over 55 years, both Menactra® and Nimenrix® can be given to people in this age group, as per *The Australian Immunisation Handbook*.

Given the current supply shortages of all three brands of 4vMenCVs in Australia, there may be times when a particular brand is not available; hence alternative schedules are also provided. The alternative schedules are based on clinical trials demonstrating that they induce adequate antibody responses compared with 4vMenCV schedules registered in Australia, and they are safe. These schedules are also approved by regulatory authorities in Europe or the USA. Refer to the **Appendix** for key references regarding these vaccination schedules.

Table 1: Vaccination schedules for 4vMenCV by age group, for healthy individuals, travellers and laboratory personnel

Age at commencement of vaccine course	4vMenCV vaccine brand	Registered schedule in Australia – number of doses required (and minimum intervals)	Alternative schedule	Source of evidence for alternative schedule
2–6 months	Menveo®	4 doses (8 weeks between doses; 4th dose at 12 months of age or 8 weeks after 3rd dose, whichever is later)	3 doses (8 weeks between 1st and 2nd doses; 3rd dose at 12 months of age)	Clinical trial reports[1-3]
	Nimenrix®	N/R	3 doses (8 weeks between 1st and 2nd doses; 3rd dose at 12 months of age)	Clinical trial report;[4] registered in Europe
	Menactra®	N/R	Not suitable for use*	No published clinical trial data in ages <9 months to date
7–8 months	Menveo®	2 doses (2nd dose at 12 months of age or 8 weeks after 1st dose, whichever is later)	N/A	–
	Nimenrix®	N/R	3 doses (8 weeks between 1st and 2nd doses; 3rd dose at 12 months of age)	Clinical trial report;[4] registered in Europe
	Menactra®	N/R	Not suitable for use*	No published clinical trial data in ages <9 months to date
9–11 months	Menveo®	2 doses (2nd dose at 12 months of age or 8 weeks after 1st dose, whichever is later)	N/A	–
	Nimenrix®	N/R	2 doses (2nd dose at 12 months of age or 8 weeks after 1st dose, whichever is later)	Clinical trial report[5]
	Menactra®	N/R	2 doses (2nd dose at 12 months of age or 12 weeks after 1st dose, whichever is later)	Clinical trial report;[6] registered in 2-dose schedule with 3 months interval in USA
12–23 months	Menveo®	2 doses (8 weeks between doses)	N/A	–
	Nimenrix®	1 dose	N/A	–
	Menactra®	N/R	2 doses (12 weeks between doses)	Clinical trial report;[6] registered in 2-dose schedule with 3 months interval in USA
≥2 years†	Menveo®	1 dose	N/A	–
	Nimenrix®			
	Menactra®			

N/A – not applicable, i.e. there is no alternative schedule available for this vaccine brand and the specified age group

N/R – not currently registered in Australia for use in the specified age group

* There are no published clinical trials data on the use of Menactra® in infants younger than 9 months of age. Given that infants typically have weaker immune responses than toddlers and older children, the clinical effectiveness of Menactra® in young infants is not yet known. Therefore Menactra® is **not recommended** in this age group.

† There is no registered upper age limit for use of Menveo®. Although both Menactra® and Nimenrix® are registered for use up to 55 years of age only, either of these brands can be given to people over 55 years of age, as per *The Australian Immunisation Handbook*.

Q4. Do 4vMenCVs protect against all meningococcal disease?

No. 4vMenCVs (Menactra®, Menveo® and Nimenrix®) provide protection against four meningococcal serogroups (A, C, W and Y), but not against serogroup B. Serogroups W and Y are the two emerging serogroups in Australia (refer to **Q18**). There are also a number of other serogroups that are very rare in Australia and are not currently vaccine preventable.

A meningococcal B vaccine (Bexsero®) is available to protect against serogroup B but may also provide some cross-protective benefit against the currently circulating strains of serogroup W (MenW).[7] This may be particularly relevant for infants (refer to **Q5**), in whom the rate of MenB disease has remained higher than that of MenW disease (refer also to **Q20**). However, vaccination with 4vMenCV is still needed to adequately protect against the A, C, W and Y serogroups.

No vaccine is 100% effective, and an individual may still become infected even after immunisation. However, 4vMenCVs have demonstrated good vaccine effectiveness in populations in which they have been used.[8,9]

Q5. Which vaccine is more important to give, 4vMenCV or Bexsero®?

Epidemiologic data show that the rate of meningococcal disease varies by age and by state and territory. In general, MenB is more common than MenW in young children, especially infants, while MenW tends to affect older age groups. However, given that the epidemiology is constantly changing, ideally both vaccines would be given. They can be administered together on the same day. As the vaccines are currently available through private prescription, financial constraints may also apply. (Refer also to **Q18**, **Q19** and **Q20**.)

Q6. Is there a different vaccine schedule for people at increased risk of meningococcal disease?

Additional doses of 4vMenCV are recommended for individuals with certain medical conditions associated with an increased risk of meningococcal disease, including:

- inherited defects or deficiency of properdin or complement components
- current or future treatment with eculizumab
- functional or anatomical asplenia
- HIV infection
- haematopoetic stem cell transplant.

Refer to Table 4.10.2 in *The Australian Immunisation Handbook* online for details on dosing requirements for these population groups, including requirements for booster doses.

MenB vaccine is also recommended for people with these conditions. For dosing guidelines, refer to Table 4.10.1 in *The Australian Immunisation Handbook* online.

Q7. Are 4vMenCVs safe?

Meningococcal conjugate vaccines (including MenCCV and 4vMenCVs) are generally safe and well tolerated, even in children as young as 6 weeks of age. Limited data suggest no significant differences in frequency or severity of adverse events between brands of 4vMenCV. Additional information on adverse events following meningococcal vaccination can be found in Chapter 4.10 of *The Australian Immunisation Handbook* online. Any reports of adverse events following immunisation can be made to the Therapeutic Goods Administration (TGA) and jurisdictional adverse event surveillance systems. Further information on reporting can be found on the NCIRS website.

Q8. Are there any contraindications to using 4vMenCV?

The only absolute contraindications for 4vMenCV are anaphylaxis following a previous dose of the respective vaccine, or anaphylaxis following any component of the vaccine. Previous meningococcal disease, regardless of the serogroup, is not a contraindication for vaccination.[10]

Q9. Is 4vMenCV or MenB vaccine available for free?

As of July 2017, five states (New South Wales, Queensland, Tasmania, Victoria and Western Australia) have state-funded 4vMenCV vaccination programs for older adolescents via school-based immunisation and/or primary care providers. Refer to state and territory health department websites for further details (refer to **Q21** for relevant links).

In addition, 'B Part of It' is a clinical research study offering the MenB vaccine to students in school years 10 through 12 in participating schools in South Australia. Eligible students will be offered the vaccine in either 2017 or 2018. South Australia does not currently have a 4vMenCV vaccination program.

For other individuals aged 2 months or older, 4vMenCV and MenB vaccines are available through private prescription. Neither the 4vMenCV nor the MenB vaccine is currently free under the National Immunisation Program (NIP).

Q10. Can a different brand of 4vMenCV be used to complete a vaccination course (i.e. are the brands interchangeable), particularly if there are shortages in vaccine supply?

It is preferable to use the same brand of 4vMenCV when giving subsequent doses, especially for completing a primary vaccination course for young children. However, a different brand may be substituted in cases where the initial brand used is unavailable or not known.

Q11. If a 12-month-old child receives 4vMenCV, should they still receive Menitorix® (Hib–MenCCV)?

Administration of Menitorix® at 12 months of age is funded under the NIP and is necessary in accordance with Australian Immunisation Register (AIR) due/overdue rules. To ensure parents remain eligible for Family Tax Benefits A and Child Care Benefits, a dose of MenC vaccine and a Hib booster dose must be given before age 13 months. As 4vMenCV provides protection against MenC as well as other meningococcal serogroups, it may be given in lieu of Menitorix® to satisfy MenC vaccination requirements. However, a booster dose of Hib is also required in the second year of life, ideally before 13 months of age. Presently, monovalent Hib vaccine is in limited supply in Australia and is not available for use under the NIP; therefore, in most instances Menitorix® will be required as the Hib booster dose even if 4vMenCV is given. A minimal interval of 4 weeks between 4vMenCV and Menitorix® is suggested (refer to **Q12**).

Q12. Can a meningococcal vaccine be given concomitantly with other meningococcal vaccines?

4vMenCV with Menitorix® (Hib–MenCCV)

It is preferable that 4vMenCV is not administered concurrently with Menitorix®. There is the potential for interference between the immune responses to the various conjugate carrier proteins and polysaccharide antigens in the vaccines resulting in lower antibody responses. Ideally, the vaccines should be administered at least 4 weeks apart. Either Menitorix® or a 4vMenCV can be administered first.

However, in circumstances where the child may not be able to return to clinic for timely administration of the other vaccine, Menitorix® can be co-administered with a 4vMenCV.

Bexsero® (MenB vaccine) with Menitorix® (Hib–MenCCV) or 4vMenCV

Bexsero® can be co-administered with Menitorix® or 4vMenCV. Prophylactic administration of paracetamol prior to administration is recommended before and after administration of Bexsero® (refer to *The Australian Immunisation Handbook* and ATAGI's advice on the use of Bexsero®).

Q13. Can 4vMenCV be given at the same time as other non-meningococcal vaccines?

Yes, 4vMenCV can be administered concurrently with other routine childhood vaccinations. Clinical trials have reported some variations in antibody responses when 4vMenCVs are co-administered with either 7-valent or 10-valent pneumococcal conjugate vaccines (PCVs) (both of which are not currently used in the NIP);[6,11] however, differences are mostly minor and protective levels of antibodies are attained. Trials on co-administration of 4vMenCVs and 13-valent PCV (Prevenar 13®) are ongoing and results will be reviewed when available.

Q14. For older children and adolescents (aged 10–19 years) who require a catch-up dose of MenC vaccine, is vaccination with a dose of 4vMenCV sufficient?

Yes, vaccination with 4vMenCV provides protection against MenC disease and is accepted by the AIR as a dose of MenC vaccine. It can be given in lieu of monovalent MenC vaccines. Catch-up of the Hib booster dose is not required for children aged over 5 years. Table 2.1.12 in *The Australian Immunisation Handbook* online provides further details on catch-up requirements in people aged 10 years or older, and an Australian Government Department of Health fact sheet provides information on catch-up doses available at no cost under the NIP.

Q15. An adolescent who is currently eligible for a dose of 4vMenCV through the state-based program has received 4vMenCV or a quadrivalent polysaccharide meningococcal vaccine in the past; should they receive this dose through the current program?

Yes. Eligible adolescents can receive a dose of 4vMenCV through a state-based program if they have been vaccinated with 4vMenCV in the past (with at least 4 weeks between doses), even if the previous dose was within the past 5 years. Repeat vaccination can offer a benefit by boosting immunity, and carries minimal risk of adverse events. Adolescents who have previously received a polysaccharide meningococcal vaccine (at any age), which would have provided protection for only a limited period, can be vaccinated with 4vMenCV now, provided that at least 6 months have passed since receiving the last dose of polysaccharide vaccine.

Q16. My patient has received 4vMenCV in the past; do they require a booster dose?

In healthy individuals of any age (i.e. those without risk factors for meningococcal disease, refer to **Q6**), the need for booster doses of 4vMenCV following vaccination with an age-appropriate number of doses has not been established. However, repeat vaccination can benefit the individual as it can boost immunity and clinical trials show no increase in adverse events with multi-dose schedules. There are countries that routinely recommend multiple doses even in older age groups; for example, 2 doses of vaccine with 4–5 years between doses is recommended for adolescents in the USA.

Individuals at increased risk of meningococcal disease due to certain medical conditions (refer to **Q6**), laboratory personnel who handle *Neisseria meningitidis* and repeat travellers to areas with increased risk of meningococcal disease have ongoing risk of infection and should receive regular booster doses, as per the schedules given in Chapter 4.10 of *The Australian Immunisation Handbook* online. Serologic testing to determine immune status is not necessary, nor recommended.

Q17. My patient has been in close contact with someone who has been diagnosed with meningococcal disease. Do they require vaccination?

The relevant state or territory public health authority should be contacted as soon as possible for advice on determining the risk of disease and for guidance on management, including whether to offer clearance antibiotics or vaccination. (Refer also to the NCIRS fact sheet Meningococcal vaccines for Australians, 'Management of meningococcal disease'.)

Questions about meningococcal disease

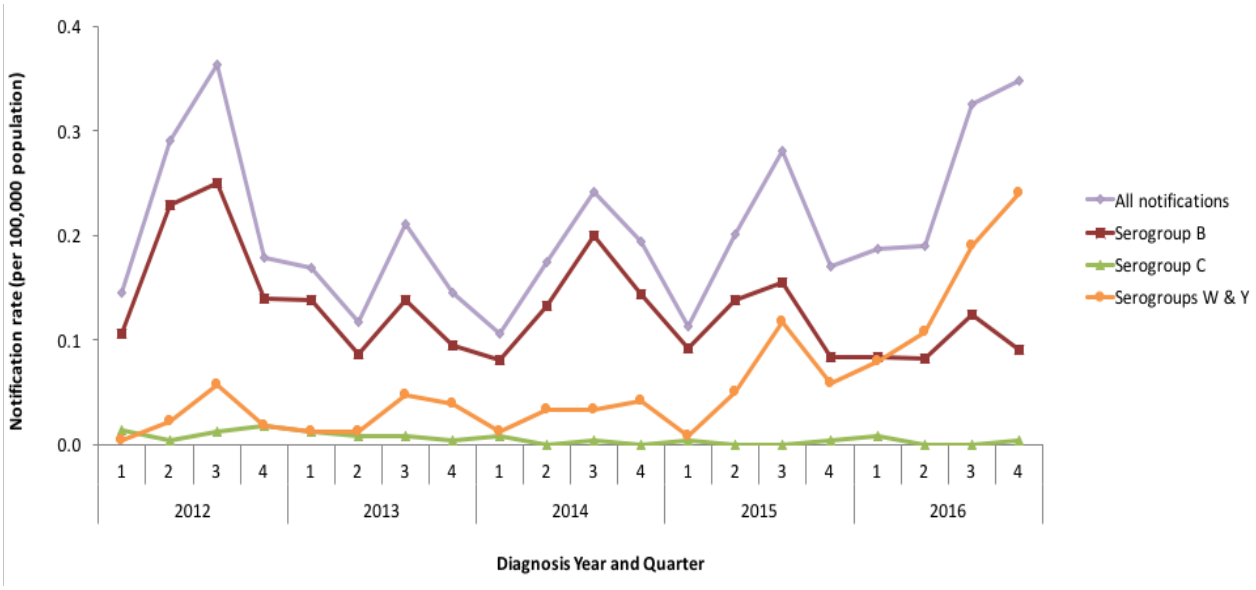
Q18. How has meningococcal disease changed recently?

Nationally, from 2002 to 2015, MenB was the most common serogroup causing invasive meningococcal disease (IMD) in Australia. However, the incidence of IMD caused by MenW has increased since 2013, and more rapidly since mid-2015 (Figure 1). A smaller increase in serogroup Y (MenY) disease incidence has occurred since 2015.

Approximately 20% of MenW cases had an atypical presentation. A higher case fatality rate for MenW compared with MenB disease has also been observed (about 7% for MenW versus about 4% for MenB).

More information on trends in meningococcal disease can be found in the NCIRS fact sheet Meningococcal vaccines for Australians. Information about meningococcal W disease is available on the Australian Government Department of Health website.

Figure 1: Notification rates of invasive meningococcal disease by selected serogroups and year, Australia, 2012–2016



Q19. Does the type of meningococcal disease vary by state or territory?

Yes. While MenW was the dominant strain in some states in 2016 and a growing proportion of all IMD cases compared with previous years, MenB was still the prominent serogroup causing disease in several states. However, the epidemiology of meningococcal disease is constantly changing. Information on the latest trends can be found on the Australian Government Department of Health website. State and territory government health authorities can also provide up-to-date information for your state or territory.

Q20. Which age groups are most at risk of serogroups W and Y meningococcal disease?

Age-specific rates of MenW IMD, while still low overall, have increased in most age groups since 2013. Children aged under 5 years (especially those under 2 years) and adolescents/young adults (aged 15–19 years) have the highest rates of MenW disease. However, since its emergence in Australia, a substantial proportion of all MenW disease has also occurred in adults aged 45 years and over. There has also been an increase in MenY IMD. Table 2 shows age-specific rates of meningococcal disease in Australia in 2016.

Table 2: Age-specific numbers and rates of invasive meningococcal disease (IMD) in Australia, 2016

Age group	Meningococcal W and Y disease		Meningococcal B disease	
	Number of cases	Rate (per 100,000)	Number of cases	Rate (per 100,000)
<12 months	11	3.49	16	5.08
12–23 months	5	1.62	4	1.30
2–4 years	8	0.85	8	0.85
5–14 years	3	0.10	4	0.13
15–19 years	18	1.21	16	1.08
20–24 years	12	0.71	21	1.25
25–44 years	17	0.25	12	0.18
45–64 years	30	0.50	6	0.10
≥65 years	45	1.22	5	0.14

For further information

Q21. Where can I find more information on meningococcal disease and vaccines?

The following links contain the latest updates on meningococcal disease epidemiology, availability of vaccines and general information on meningococcal disease:

- *The Australian Immunisation Handbook*, 10th edition
  www.immunise.health.gov.au/internet/immunise/publishing.nsf/Content/Handbook10-home
- NCIRS fact sheet on meningococcal disease and meningococcal vaccines for Australians
  www.ncirs.edu.au/assets/provider_resources/fact-sheets/meningococcal-vaccines-fact-sheet.pdf
- Immunise Australia website
  www.immunise.health.gov.au
- National Immunisation Program Schedule
  www.immunise.health.gov.au/internet/immunise/publishing.nsf/Content/national-immunisation-program-schedule
- Australian Government Department of Health – Meningococcal W surveillance
  www.health.gov.au/internet/main/publishing.nsf/Content/ohp-meningococcal-W.htm
- Centers for Disease Control and Prevention (USA) – Meningococcal disease
  www.cdc.gov/meningococcal
- Contact details for Australian, state and territory government health authorities and communicable disease control (Appendix of *The Australian Immunisation Handbook*)
  http://immunise.health.gov.au/internet/immunise/publishing.nsf/Content/Handbook10-home~handbook10-tools~handbook10-appendices~handbook10-appendix1
- Jurisdictional meningococcal vaccination programs (as of July 2017):
  - New South Wales
    www.health.nsw.gov.au/Infectious/diseases/Pages/meningococcal-w.aspx
  - Queensland
    www.qld.gov.au/health/conditions/immunisation/adolescents#macwyp
  - Tasmania
    www.dhhs.tas.gov.au/publichealth/communicable_diseases_prevention_unit/immunisation/school_based_immunisation_program/meningococcal_w
  - Victoria
    www2.health.vic.gov.au/public-health/immunisation/vaccination-adolescents/meningococcal-acwy
  - Western Australia
    ww2.health.wa.gov.au/Articles/J_M/Meningococcal-ACWY-Statewide-vaccination-program
- 'B Part of It' South Australian meningococcal B clinical study
  www.bpartofit.com.au/about
- Catch-up schedule to meet No Jab, No Pay – new immunisation requirements for Family Assistance Payments
  www.immunise.health.gov.au/internet/immunise/publishing.nsf/Content/375B788BBCB7EC0FCA257F110017177E/$File/No-Jab-No-Pay-FSheet.pdf
- Communicable Diseases Network Australia (CDNA) National Guidelines for Public Health Units – Invasive meningococcal disease
  www.health.gov.au/internet/main/publishing.nsf/Content/cdna-song-IMD.htm

Appendix

Several alternative dosing schedules for use of 4vMenCVs in infants and children under 2 years of age are summarised below. While these schedules are not currently registered in Australia, use of the schedules may be considered based on published clinical trials and/or registration by regulatory bodies in Europe (EMA) and the USA (FDA).

Infants aged under 12 months

Menactra®: A trial of Menactra® in 9-month old infants found the vaccine was highly immunogenic when given in a 2-dose schedule at 9 and 12 months of age.[6] There are no trials of Menactra® in infants younger than 9 months of age.

Nimenrix®: A 3-dose schedule of Nimenrix® (given at 2, 4 and 12 months of age) in infants as young as 6 weeks of age induced an antibody response as good as that with a 4 dose schedule (2, 3, 4, 12 months).[4] In infants aged 9–12 months, giving 2 doses, at 9 and 12 months of age, was found to be better than giving only 1 dose at 12 months of age.[5]

Menveo®: Clinical trials indicate a 3-dose schedule of Menveo® (2 doses spaced 4–8 weeks apart plus a booster at 12 months of age) induces a comparable antibody response to the 4-dose schedule (3 doses spaced 8 weeks apart plus a booster at 12 months of age) currently registered for infants aged 2–6 months.[1-3,12-14] One study of a 3-dose schedule (given at 2, 4 and 12 months of age) suggests adequate immunity after the first 2 (primary course) doses with a robust booster response at 12 months.[14] Although the immune response after the primary course doses is better with 3 doses than with 2 doses, the differences are less or absent after the 12-month booster vaccination which induces a robust response.[1-3] The level of antibodies 5 years after vaccination does not differ between the two schedules.[15]

Toddlers aged 12–23 months

Menactra®: There are currently no published studies of Menactra® in children aged 12–23 months. However, given that Menactra® has been shown to induce a good immune response using a 2-dose schedule in infants aged 9–12 months, it is likely that this 2-dose schedule would be similarly immunogenic in 12–23 month olds.

Menveo®: In a clinical trial, 1 dose of Menveo® was moderately immunogenic in children aged 12–35 months. There is some variation in response according to meningococcal serogroup. The immune response was significantly improved with an additional dose given 1 month later.[16]

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