Bexsero®: A vaccine to protect against meningococcal group B disease

The Immunisation Advisory Centre

Bexsero is now available for providers to purchase from Healthcare Logistics. This resource has been prepared to assist vaccinators respond to parent questions about meningococcal disease, to increase vaccinator knowledge about the vaccine profile and its administration; and in contrast to other New Zealand (NZ) vaccinations, to outline the recommended use of prophylactic paracetamol to reduce fever with every dose of Bexsero in children aged under 2 years.

What is meningococcal disease?

Meningococcal disease is caused by the bacterium *Neisseria meningitidis*. At least 12 groups have been identified, including groups A, B, C, Y and W (previously called W-135). In NZ over 2009–2016, meningococcal group B caused 53–72% of disease, and meningococcal groups C, Y and W, including the very virulent group W ST-11 type, caused 25–46% of disease. Meningococcal group A rarely causes disease in NZ.

How do you catch it?

Meningococcal bacteria are commonly carried in the nose and throat, and do not usually cause disease. Carriage rates are highest in older teenagers and young adults. The bacteria can be transferred from person to person through contact with saliva, e.g. intimate kissing. In rare cases, the bacteria can invade and rapidly lead to severe disease. The underlying reasons for why invasion occurs in some individuals are not well understood.

How serious is meningococcal disease?

If meningococcal bacteria pass into the blood, the disease usually progresses very quickly. A person with meningococcal disease may develop meningitis (inflammation of the membranes around the brain), septicaemia (blood infection) or pneumonia.

One to two people out of every 10 who survive meningococcal disease have long-term complications, e.g. extensive skin scarring, limb amputation, hearing loss, seizures, or brain injury. Even when the disease is identified and treated early, one to two people out of every 10 will die.

Who is at risk?

In NZ, infants and children aged under 5 years and adolescents aged 15–19 years have an increased risk of meningococcal disease. Māori, particularly infants aged under 1 year, and Pacific peoples have a higher risk of meningococcal disease than other ethnic groups.

What increases the risk?

- Exposure to tobacco smoke, binge drinking, or having another respiratory infection, e.g. influenza.
- Living in close proximity to others, e.g. in a crowded household, at boarding school, in university halls of residence, or in long-term institutional care.
- Being in a household or other close contact of someone carrying the bacteria or with the disease.
- Having a medical condition or receiving treatment that affects the immune system, e.g. functional asplenia, post-splenectomy, or taking disease modifying immunosuppressive medication.

What are the symptoms of meningococcal disease?

The initial symptoms are difficult to distinguish from other infectious illnesses, particularly flu-like illnesses. Symptoms usually progress quickly to a severe illness, often within 24 hours. However, infants may have a more gradual onset than adults.

Infants may have a fever, cry, appear unsettled, feed poorly, vomit, be sleepy or hard to wake, dislike bright light, or have a rash or spots. They may have a bulging fontanelle. Older children and adults may have a fever, malaise, nausea, vomiting, muscle aches and pains, drowsiness, headache, dislike of bright light, neck stiffness, or have a rash or spots. Almost 80% of cases will develop a rash that does not blanch (become pale/go white) when pressed on. This type of rash is often a late sign of infection.

Individuals with disease caused by the very virulent meningococcal group W ST-11 type may present with atypical symptoms, including gastrointestinal symptoms.

Vaccines to protect against meningococcal disease

Meningococcal vaccines are classified by the type of vaccine manufactured and by the meningococcal bacteria groups they protect against. In NZ, conjugate vaccines protect against groups A, C, Y and W (Menactra® or Nimenrix®) or group C only (NeisVac-C®), and the multicomponent recombinant vaccine protects against group B only (Bexsero).

There have been vaccines against the groups A, C, Y and W for more than 20 years but it has taken much longer to develop vaccines that protect against the different types of meningococcal group B. This is because the immune response to group B is different to the immune response to groups A, C, Y and W. For best protection against all meningococcal disease in NZ, separate vaccinations against group B disease and groups A, C, Y and W disease are recommended.

The MeNZB™ vaccine used in NZ between 2004 and 2011 was designed to target a specific type of meningococcal group B bacteria that caused a prolonged epidemic here in NZ. Protection from this vaccine was not long lasting; those who received the MeNZB vaccine are not expected to still have protection against this type of meningococcal B disease. The active component of MeNZB has contributed to the successful development of Bexsero.

Vaccines currently available on the National Immunisation Schedule

NeisVac-C (group C) and Menactra (groups A, C, Y and W) are funded for individuals with a medical condition that increases their risk of meningococcal disease AND is listed on the Pharmaceutical Schedule. NeisVac-C and Menactra for funded individuals can be ordered from ProPharma.

Vaccines available for purchase

Bexsero, NeisVac-C and Menactra for those not covered by the Pharmaceutical Schedule and Nimenrix can be purchased through general practice. Non-funded vaccines can be ordered from Healthcare Logistics. Vaccinators MUST have a prescription or standing order to administer these vaccines.

Who can have Bexsero?

Bexsero is recommended but not funded for individuals at increased risk of infection with or exposure to group B meningococcal bacteria including:

- Individuals pre/post-splenectomy or with functional asplenia.
- HIV positive individuals.
- Individuals with inherited or acquired complement deficiency.
- Pre/post-solid organ transplantation.
- Following stem cell/bone marrow transplantation.
- Prior to immunosuppression for longer than 28 days.
- Other infants and young children aged under 5 years, adolescents and young adults.
  - Particularly adolescents and young adults living in close proximity to each other, e.g. boarding school, university halls of residence or in long-term institutional care.
- Travellers to high-risk countries and Hajj pilgrims.
- Laboratory workers regularly exposed to meningococcal cultures.

How protective is Bexsero?

Meningococcal bacteria can cause disease more quickly than the immune system can generate protection. Therefore, having existing circulating antibodies is required for protection against meningococcal disease.

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How protective is Bexsero? continued

Immunisation generates circulating antibodies. Over time, the antibody levels decrease. The number and quality of antibodies and how long they last depend on what type of vaccine is used, the meningococcal group(s) covered by the vaccine, and the age of the person receiving the vaccine.

As there are generally low numbers of meningococcal disease cases in countries such as Australia, England, Germany, NZ and the United States, it is not possible to determine exactly how many cases of disease are prevented by vaccination or how long protection after vaccination lasts. Instead, the immune system response and antibody levels are used as an alternative measure of how well and how long meningococcal vaccines can protect from disease.

Bexsero is expected to provide protection against disease caused by a broad range of group B meningococcal bacterium types, including the NZ specific type of meningococcal group B. On average in NZ, meningococcal group B causes around two-thirds of meningococcal disease each year.

Table 1 shows the expected protection against group B meningococcal disease after completion of an age appropriate course of Bexsero.

Table 1: Expected protection against group B meningococcal disease after vaccination with Bexsero¥

Age group	Expected protection
Under 2 years	63–100%
2–3 years	72–100%
4–10 years	91–100%
Adolescents	99–100%
Adults	91–100%
Duration of protection	
Under 5 years	1–3 years
Older children, adolescents and adults	Not yet established

¥Based on the proportion of vaccine recipients mounting a protective immune response to the vaccine.

How safe is Bexsero?

Bexsero was first approved for use in Europe in 2013 and is now approved for use in over 40 countries including England and Australia. Bexsero has an excellent safety record. The most common vaccine responses include fever, and discomfort or pain around the injection site. Infants and children may also be irritable, have unusual crying or a decreased appetite. Adolescents and adults may experience headache, muscle or joint aches, malaise or nausea.

Very rarely, a severe allergic reaction (anaphylaxis) to a component in the vaccine occurs. Table 3 on the last page compares possible disease effects with common and rare vaccine responses.

Fever and local vaccine responses

Fever is part of a robust immune system response to Bexsero, usually peaking around 6 hours after vaccination and settling over 24–48 hours. A fever over 38°C is more likely to occur in infants and children aged under 2 years after vaccination with Bexsero compared with other routinely used infant vaccines. When Bexsero is administered at the same visit as other Immunisation Schedule vaccines, a fever over 38°C or 39°C is almost twice as likely as when the Immunisation Schedule vaccines are given alone.

Similarly, redness, swelling and/or mild–moderate pain around the injection site are also common expected immune responses to Bexsero, peaking on the day of vaccination followed by a significant decrease, and settling from around 24 hours after vaccination.

Recommendation for use of prophylactic paracetamol

The advice for the use of prophylactic paracetamol for children aged under 2 years (refer to box 1) only applies to immunisation events when Bexsero is administered, either as the only vaccine or with other vaccines. This is because of the evidence of a robust immune response to Bexsero in young children and that the use of prophylactic paracetamol around vaccination reduces the risk of high fever, especially fever over 39°C, and injection site pain. Some infants will still develop a fever and/or injection site pain even though they have received paracetamol doses.

A review of multiple studies identified that ibuprofen is less effective than paracetamol in preventing a fever of 38°C or higher or injection site pain. Ibuprofen is not recommended to manage the symptoms of a robust vaccination response.

Non-pharmaceutical management of fever or injection site pain

Other strategies that can also be used to help manage fever and injection site discomfort or pain are described in box 2.

Box 1: Use of prophylactic paracetamol in children aged under 2 years to help manage post-Bexsero fever

Note: This advice only applies to immunisation events when Bexsero is administered, either as the only vaccine or with other vaccines.

Prophylactic paracetamol use is recommended with every dose of Bexsero in children aged under 2 years:

- Three doses of paracetamol (15mg/kg) are recommended with 6 hours between each dose, whether the child has a fever or not:
  - The first dose administered 30 minutes prior to Bexsero
    - If the first paracetamol dose has not been given before the child is vaccinated, administer the dose at the time of vaccination
  - The second paracetamol dose is given 6 hours after the first dose, the third dose is given a further 6 hours later.
- If the infant or child is sleeping when the second or third paracetamol dose is due:
  - It is not necessary to wake the child
  - The dose can be given when the child wakes up as long as it is at least 6 hours since the previous dose was given
- Ensure parents:
  - Have the 120mg/5mL paracetamol strength formulation
    - The doctor can provide a prescription for them to fill at the pharmacy
  - Measure the paracetamol dose using a measuring spoon or syringe
- If the child is miserable or distressed because of a fever or injection site pain 6 hours after the third dose of paracetamol and is otherwise well:
  - The parent can continue to administer the paracetamol doses with a minimum of 6 hours between doses until the discomfort resolves or 48 hours after vaccination, whichever occurs first
    - No more than four doses of paracetamol can be given in a 24-hour period
- A child who is miserable or distressed because of a fever or injection site pain 48 hours or more after vaccination is advised to be seen by their doctor

Box 2: Other strategies to help manage fever or injection site discomfort or pain

- If the child has a fever
  - Give lots of breastfeeds or fluids
  - Undress them to a single layer
  - Make sure the room is not too hot or too cold
  - Give lots of cuddles
- If the child has injection site discomfort or pain
  - Do not rub the injection site
  - Hold a cool damp cloth or an ice pack well wrapped in a dry cloth on the injection site
  - Give lots of cuddles

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Vaccine presentation, storage and administration

Bexsero is provided as a 0.5mL suspension in a pre-filled syringe in a single-dose pack. During storage, a fine off-white deposit may form in the syringe. Shake the vaccine well before use to ensure the ingredients are evenly distributed within the vaccine. Store Bexsero between +2°C and +8°C and protect from light.

Bexsero is administered by deep intramuscular injection into the vastus lateralis in infants or deltoid in older children, adolescents and adults.

Bexsero can be administered at the same visit as other vaccines, in separate syringes and at separate injection sites. When giving two intramuscular (IM) injections in the same limb in infants, the vastus lateralis is preferred because of its greater muscle mass. The injection sites should be on the long axis of the thigh and separated by at least 2 cm so that localised reactions will not overlap.

Bexsero is approved for use from 8 weeks of age. The recommended number of Bexsero doses is determined by the age of the individual when they receive their first Bexsero vaccination. The recommended Bexsero vaccination schedules are shown in table 2.

Who should not have Bexsero?

» Anyone with severe allergy (anaphylaxis) to a previous dose of the vaccine or any component of the vaccine should not receive the vaccine.
» Immunisation for any vaccine should be postponed in subjects suffering an acute illness or high fever.
  » The presence of a minor infection is not a reason to delay immunisation.

References

A list of references is available in a separate document on the Written Resources and Bexsero pages of our website.

Table 2: Bexsero vaccination schedules

Age when Bexsero first dose given	Number and timing of doses
Infants 8 weeks–5 months	Option 1 – 2+1 vaccine course[Φ] – 2 doses with a minimum interval of 8 weeks between each dose. – Booster dose aged 12 months or a minimum of 6 months after second dose, whichever is later. Option 2 – 3+1 vaccine course[Φ] – 3 doses with a minimum interval of 4 weeks between each dose. – Booster dose aged 12 months or a minimum of 6 months after third dose, whichever is later.
Infants 6–11 months	– 2 doses separated by 8 weeks – Booster dose aged ≥12 months or a minimum of 2 months after second dose, whichever is later.
Children 12–23 months	– 2 doses separated by 8 weeks – The need for a booster dose has not yet been established
Children 2–10 years‡ Adolescents and adults 11–50 years	– 2 doses separated by 4 weeks – The need for a booster dose has not yet been established

[Φ]How many Bexsero doses for infants aged 8 weeks–5 months?

A small study comparing the 2+1 course in infants receiving their first dose at 3½ months of age with the 3+1 course in infants receiving their first dose at 2½ months of age found similar numbers of infants were expected to be protected from meningococcal group B disease in both groups one month after completing their initial infant dose and also one month after receiving their booster dose.

Parents will need to choose which vaccine course they prefer for their child. Overseas recommendations may assist parents decide:

» The United Kingdom and Australian state of South Australia provide a 2+1 Bexsero vaccine course as part of their routine immunisation schedules (the UK offer Bexsero at 2, 4 and 12–13 months and South Australia at 6 weeks, 4 and 12 months).
» In other parts of Australia, where Bexsero is only available for purchase, the recommended vaccine courses are the 2+1 option for healthy infants or the 3+1 option for infants who have a medical condition that increases their risk of meningococcal disease.

‡Interval between Bexsero doses for children aged 2–10 years

The recommended minimum interval between doses in this age group changed from 8 weeks to 4 weeks. After an 8 week interval between doses 91–100% of children were expected to be protected from meningococcal group B disease compared with 69–100% of children after a 4 week interval. Parents may choose for their child to have an interval of more than 4 weeks between their two Bexsero doses.

Table 3: Comparison of possible effects of disease with vaccine responses

Disease	Possible complications of disease	Possible vaccine responses
Meningococcal disease is caused by the bacterium *Neisseria meningitidis* and can cause meningitis, septicaemia, pneumonia, long-term complications or death	» Inflammation of the membranes around the brain (meningitis) » Blood infection (septicaemia) » Pneumonia » One to two people out of every 10 who survive have long-term complications, e.g. extensive skin scarring, limb amputation, hearing loss, seizures or brain injury » Even when the disease is identified and treated quickly, about one to two people out of every 10 will die	**Common responses** » Fever over 38°C in children aged under 2 years » Redness, swelling and/or mild–moderate pain around injection site » Irritability, unusual crying » Decreased appetite, nausea » Headache, muscle and/or joint aches. » Malaise, drowsiness **Rare responses** » Urticaria (allergic skin reaction) » Anaphylaxis (severe allergic reaction)

Bexsero is a prescription medicine.