The routine infant meningococcal B (MenB) vaccine against meningitis and septicaemia

In the UK and Ireland babies are offered the MenB (meningococcal group B) vaccine, Bexsero, as part of the routine immunisation schedule at 2, 4 and 12 months of age.

A significant number of families in the UK and Ireland are also choosing to pay for MenB vaccination for children who are not covered by national immunisation programmes.

Why do we need MenB vaccines?

For decades, MenB has been the most common cause of bacterial meningitis in the UK and Ireland. Today, meningococcal meningitis and septicaemia remain the leading infectious cause of death for children under five in the UK.

Vaccines are the only way to prevent meningitis and have almost eliminated some other causes of this deadly disease. Since the first meningitis vaccine was introduced against Hib meningitis in 1992, many kinds of meningitis have been reduced or have dwindled to a mere handful of cases, including meningitis caused by Hib and MenC.

Thanks to meningitis vaccines, thousands of children are alive today who would otherwise have died or been left seriously disabled from these deadly diseases. The addition of the MenB vaccine is saving even more, which is why Meningitis Research Foundation and our members have tirelessly campaigned for a MenB vaccine to be made freely available in the UK and Ireland.

Who else is entitled to the MenB vaccine?

MenB vaccination is available free of charge to people in the UK and Ireland with medical conditions that increase the risk of contracting MenB disease, in some circumstances when people have been in close contact with someone who was ill with MenB meningitis and/or septicaemia, and in occupations which put people at increased risk of disease.

Medical conditions

In the UK it is recommended that people with asplenia, splenic dysfunction or complement disorder, including those on Eculizumab therapy are entitled to receive the vaccine because they are at a higher risk of contracting meningococcal disease https://www.gov.uk/government/uploads/system/uploads/attachment_data/file/554011/Green_Book_Chapter_22.pdf.

In Ireland, in addition to the conditions listed above, it is also recommended that those who are HIV positive and haematopoietic stem cell transplant and solid organ transplant candidates and recipients receive the vaccine http://www.hse.ie/eng/health/immunisation/hcpinfo/guidelines/chapter13.pdf.

Close contacts of a case of MenB disease

In Ireland, MenB vaccine is offered to close contacts when there has been a case of MenB disease. In the UK Public Health England (PHE) has written guidance about when the vaccine should be offered to close contacts of people who get meningococcal B disease, see www.gov.uk/government/publications/invasive-meningococcus-capsular-group-b-menb-preventing-secondary-cases

Occupational risk

The vaccine should be offered to laboratory workers who are at risk of exposure to MenB bacteria in their job.

How effective is the MenB vaccine Bexsero?

The effectiveness of a vaccine is determined by many things, including how strong an immune response it produces (its 'immunogenicity'), and how widely it covers disease-causing strains circulating in the country.

The MenB vaccine has been shown to be working well following its introduction to UK infants. Ten months after the programme was introduced, disease surveillance revealed that cases of disease had halved in vaccine eligible age groups. Based on this data, vaccine efficacy against all MenB strain after two doses of vaccine has been calculated to be 83%. However if it is taken into consideration that the vaccine is only predicted to protect against 88% of circulating strains in the UK[1] then the efficacy is 94%, against the strains that it is predicted to cover[2].

Results from the vaccine trials were very encouraging, showing that the vaccine triggers a strong immune response in infants, toddlers and adolescents[3-5]. Studies looking at how well circulating MenB strains match the vaccine have predicted that it will cover approximately 88% of MenB strains circulating in the UK[1], and 78% of MenB in Europe over all[6].

The actual proportion of cases prevented will depend on other things too, including how widely the vaccine is offered and taken up, whether it prevents the bacteria from being carried and passed on and how long protection lasts.

Uptake of the MenB vaccine in the UK is high. Nearly 89% of eligible UK infants had received two doses of the vaccine 10 months after the programme had been introduced. But only babies are routinely offered the vaccine so older age groups remain unprotected.

It may be possible to protect older age groups by immunising teenagers. Teenagers are more likely to carry meningococcal bacteria in the back of the nose and throat and transmit the bacteria to others. However, if the vaccine prevented teenagers from carrying the bacteria, transmission and spread of disease amongst the whole population could be slowed by immunising them. The UK government have commissioned a study to find out whether vaccinating teenagers will stop them from carrying the bacteria. MRF funded some preliminary research which will help inform the methodology for the large UK study (see http://www.meningitis.org/current-projects/study-to-evaluate-prevention-116650)

Is the vaccine safe?

The safety of routine vaccinations is rigorously monitored in the UK and no safety concerns have been raised since the vaccine was routinely introduced in September 2015

As with all drugs, vaccines can cause side effects. Vaccine side effects may include soreness/redness/swelling or hardness of skin at the injection site, fever, lack of appetite, muscle aches, irritability, sleepiness and rashes.

There was already strong safety data from clinical trials involving almost 8,000 people, including more than 5000 infants and toddlers to support the introduction of routine vaccination [3-5, 7-9]. The trials demonstrated that Bexsero® has a good safety profile[10] and a review of the data by the European Commission resulted in vaccine licensure in January 2013 on the basis of the benefits of the vaccine outweighing the risks.

Real-world experience of using Bexsero across the world also continues to grow. Nearly 17,000 students in the US were vaccinated in response to an outbreak of MenB disease at Princeton University in late 2013 and the University of California, Santa Barbara in early 2014. Additionally, in the summer of 2014 over 45,000 people between 2 months to 20 years of age, were vaccinated as part of a public immunisation program in the Saguenay-Lac-St-Jean region of Quebec, Canada[11]. No serious adverse events were reported following the program and rates of fever and local reactions were similar to that of other routine immunisations.

Is it safe for Bexsero® to be given at the same time as other routine vaccines?

Yes. The side effects seen when Bexsero® is given with other vaccines in the routine childhood schedule are the same as those commonly seen with vaccines in general.

Why have I been advised to give my baby paracetamol after vaccination with Bexsero®?

Fever is more common in babies when Bexsero® is given alongside other vaccines. Taking paracetamol as soon as possible after getting vaccinated (or at the same time) reduces the likelihood and severity of fever without affecting the immune response to any of the vaccines[12]. It will also reduce any pain, redness and swelling that vaccination may cause.

How much paracetamol should I be giving and when should I give it?

Liquid paracetamol should be given to babies who are being vaccinated with Bexsero® alongside other routine immunisations at 2 and 4 months of age. You should make sure that you have a supply of liquid paracetamol at home in readiness for your baby's immunisations.

A total of three 2.5ml doses of infant paracetamol suspension 120mg/5ml should be given. The first dose should be administered at the time of vaccination or as soon as possible afterwards. The second and third doses should be administered at 6-8 hourly intervals after the previous dose. Please note that junior paracetamol (six plus) is stronger than infant paracetamol (250/5ml) and should **not** be used in babies.

There is no need to give your baby paracetamol with their vaccinations at 12 months. This is because at that age the risk of fever from administering MenB vaccine with the routine immunisations is the same as when the routine immunisations are given alone. It is fine to give your 12 month old paracetamol after their vaccinations if they develop a fever or appear to be in discomfort however.

More information about giving paracetamol after immunisation with MenB alongside other routine immunisations is available from:
https://www.gov.uk/government/uploads/system/uploads/attachment_data/file/450890/9413-paracetamol-menB-2page-A4-05-web.pdf

What are the ingredients in Bexsero?

The active ingredients that equip our immune system to fight MenB bacteria include four main components of meningococcal bacteria[13]. All of these components have been processed and inactivated and are not part of any living bacteria, but can still stimulate the immune system.

Three of them are proteins found on the surface of the bacteria:

- Factor H Binding Protein (fHbp)
- Neisseria Heparin Binding Antigen (NHBA)
- Neisserial Adhesin A (NadA)

These three components help meningococcal bacteria invade and survive within the human body. In vaccinated people, the immune system can recognise and 'neutralise' these components, so the bacteria cannot make them ill.

The final ingredient is the New Zealand MenB Vaccine (MenZB) derived from the New Zealand outbreak strain of MenB (strain NZ 98/254).

Other ingredients in the vaccine include:

- Aluminium hydroxide (the active ingredients of the vaccine are adsorbed to this to improve immunogenicity)
- Histidine (used to regulate the PH of the vaccine)
- Sodium chloride
- Sucrose

  } *Used to make an isotonic solution (a solution with a similar salt concentration as cells and blood in the body)*

- Water for injections

Are there any safety reasons not to have the vaccine? What about allergies?

People who have previously had an anaphylactic reaction to any of the vaccine components listed above should not get the vaccine.

Anaphylaxis to current vaccines is very rare and is estimated to occur in one in a million doses given, although a recent study[14] found no reports of anaphylaxis following more than 5 million preschool and infant immunisations over an entire year in the UK and Ireland.

People with severe immune system problems cannot have live vaccines, but the new MenB vaccine is not live. Food allergies are not a reason to avoid vaccination. People often worry that eczema, asthma, epilepsy and a family history of reactions to vaccinations are a reason to avoid vaccinations, but this is not true[15].

The tip cap of the syringe may contain natural rubber latex. The risk of developing an allergic reaction is very small, but in case of known severe latex allergy, you should speak to your doctor or nurse before being vaccinated.

Will this vaccine be offered to adolescents free of charge within the health service?

There is no current UK or Irish recommendation for adolescents to be vaccinated.

Typically, meningococcal disease is most common in babies and children under five, with a second peak in adolescence. However, at present the peak age for meningococcal disease is at 5 months of age, and the number of cases in adolescents is even lower than usual.

In theory, vaccinating teenagers could have benefits for the whole population, in addition to directly protecting those vaccinated. Teenagers are the main carriers of meningococcal bacteria, so if vaccinating them could prevent them from carrying the bug and passing it on, it could protect everyone, including people who aren't vaccinated.

However, in the UK the JCVI concluded that there was not enough evidence about the extent to which the MenB vaccine would stop teenagers from carrying and transmitting the bug, nor how long vaccination would directly protect this age group. In order to answer these questions, the UK government has commissioned a study to investigate whether vaccinating adolescents could stop them acquiring the bacteria and carrying them in their throats. If this was the case, then vaccinating teenagers could be the most effective way of protecting everybody because they are the age group largely responsible for transmitting the bacteria amongst the population. A study is currently taking place in Australia which also aims to answer this question.

My child is too old to qualify for the MenB vaccine on the NHS. Should I get them vaccinated privately?

If your child was born before 1 May 2015 they are not eligible to receive any vaccine doses on the NHS.

Babies are at the highest risk of contracting meningococcal disease with peak incidence occurring at around 5 months of age. This is why the vaccine is offered early at 2 and 4 months followed by a booster at 12 months.

Children older than 5 months of age are still at risk of disease, but their risk is substantially lower than that of younger babies which is why routine vaccination on the NHS is focussing on the youngest age groups.

Over the past ten years, the incidence of MenB disease has been steadily declining and at the moment cases of disease are lower than they have been for decades. Current incidence

of disease amongst the under 1s is around 22 per 100,000, reducing to 5 per 100,000 in the 1-4 age groups. The incidence of disease amongst older age groups is substantially less.

MenB is a deadly and disabling disease with such a rapid onset that some parents may wish to have their child protected however small the risk of them contracting disease. MenB vaccination is available privately for parents who wish purchase it.

How can I get the vaccine for my child if s/he is not eligible for it free of charge within the health service?

GPs and travel clinics throughout the UK and Ireland have been informed that the vaccine is available. Start by asking your own GP for the vaccine, as if they can provide it, this is likely to be the least costly option. GPs may not be able to offer the vaccine to their own patients, but they may be able to arrange it via another surgery on private prescription. You can also get the vaccine from a travel vaccination clinic in your area, or a private GP practice. **It is worth asking more than one clinic as prices can vary considerably.** The manufacturer has a customer service line in the UK **for healthcare professionals only**. GPs or other health professionals can ring to get the vaccine: 08457 451500, Mon-Thu 8am-4.45pm and Fri 8am-1pm. **The manufacturer is prohibited by law from speaking to members of the public on this line and any patients who call will be referred back to their healthcare practitioner**.

In Ireland, Bexsero® is available to order through United Drug. Health professionals can ring to get the vaccine on 01 463 2417. They can also email GSKvaccines@united-drug.com

How much will the vaccine cost if I want to get it privately?

As a guideline, the NHS list price of the vaccine is £75 per dose excluding VAT. GPs or clinics can set their own charges for administration – prices in excess of £125/dose are not unusual. More than one dose of the vaccine is needed for sufficient protection – the total number depends on the age of the person being vaccinated.

Table 1 shows the number of doses and the time intervals between doses, as recommended in the Summary of Product Characteristics (part of the licence for Bexsero®)

Table 1: Recommended vaccine dose schedule for Bexsero according to age

Age Group	Primary dose series	Interval	Booster?
2 – 5 months	3	No less than 1 month	Yes, at 12 - 15 months with an interval of at least 6 months after the last primary dose. In case of delay no later than 24 months
3 – 5 months	2	No less than 2 month	
Unvaccinated infants 6 - 11 months	2	No less than 2 month	Yes, at 12 - 23 months with an interval of at least 2 months after the last primary dose
Unvaccinated children, 12 - 23 months	2	No less than 2 month	Yes, between 12-23 months after the last primary dose
Children, 2 - 10 years	2	No less than 1 month	No need yet established
Those over 11 years	2	No less than 1 month	No need yet established

The vaccine is not licensed for children under 8 weeks old because there is not enough information about how well the vaccine works in this age group.

It is likely that Trumenba®, another MenB vaccine now licensed in Europe will also soon be available to purchase privately for adults and children aged 10 and above (see ‘Are there other MenB vaccines?’ section below).

Why has it been so difficult to develop a MenB vaccine?

Meningitis vaccines developed up to now have been made from a fragment of the bacterial sugar coat. When we are vaccinated our immune system learns to recognise and attack this

sugar as a ‘foreign invader’ by producing antibodies which help us destroy bacteria if we come into contact with one with the same sugar coat. However, the sugar coat of MenB bacteria does not trigger an immune response, because it looks like developing human cells. This means that the immune system does not recognise it as a foreign invader, and this protects it from attack. So using the sugar coat just does not work for MenB vaccine development.

The search for a MenB vaccine has focused on other elements of the surface of MenB bacteria but it has been very difficult to find elements which are both ‘visible’ to the immune system and present in every MenB strain. Even elements that are usually present are extremely variable, so the immune response against a vaccine made from one kind of MenB may not be capable of killing all the different MenB strains.

Are there other MenB vaccines?

Yes. Another MenB vaccine, Trumenba®, has been developed by Pfizer and was licensed for 10 to 25 years olds in the United States in November 2014. Trumenba was also licensed in Europe in May 2017 for adults and children aged 10 and above.

The active ingredients in Trumenba® include two variants of Factor H Binding Protein (fHbp) which is found on the surface of meningococcal bacteria. fHbp helps the bacteria survive and go undetected in the human body. Vaccination with Trumenba® helps the immune system to recognise fHbp on the surface of invading bacteria and neutralise them before they can cause serious illness.

Trumenba® is licensed to be given in three doses with a 2 month interval between the first two doses and a 4 month interval between doses two and three. Results from seven clinical trials, which vaccinated a total of 4,282 people aged 11 to 25, have shown that the vaccine has a good safety profile.

Real-world experience of using Trumenba® is also growing. In early 2015 there was an outbreak of MenB disease at the University of Oregon, USA. Six cases were confirmed amongst students in January to February, including one death. In response to this, a campus wide vaccination programme aiming to immunise around 24,000 students began in February 2015.

In addition to the universal vaccines Bexsero® and Trumenba®, vaccines covering just one strain of MenB have been used successfully in New Zealand and Cuba in the past to control

epidemics caused by a single strain. Our research has helped to show that neither the New Zealand or Cuban vaccines would cover the majority of MenB infection in the UK and the rest of Europe.

Why aren't the MenB vaccines Bexsero® and Trumenba® expected to cover all cases?

It is impossible to be certain about the precise extent of coverage. Bexsero® is based on four main protein components found on the bacterial surface across most of the hundreds of different MenB strains. Trumenba® is based on 2 versions of one the same surface proteins included in Bexsero®. However, the structure of each protein can vary a lot and some bacteria have more of a particular protein on their surface than others do. The antibodies we produce after we've been vaccinated may not be able to recognise a protein carried on the surface of invading MenB bacteria if its structure is a bit different to the protein in the vaccine, or if there is not very much protein to latch onto. If our antibodies cannot attach to invading bacteria, our immune system will be unable to destroy them.

In the case of Bexsero® in addition to the main four protein components, other ingredients that are part of the vaccine formulation may also produce immunity. This may add to the coverage predicted for the four main vaccine components.

Now that Bexsero® has been introduced in the UK, it is very important to monitor how well it is working and how much of the disease it covers. Meningitis Research Foundation's Meningococcal Genome Library will help this to happen.

Where can I go for further information?

Free*fone* helpline 080 88 00 33 44
email **helpline@meningitis.org**
Visit our website **www.meningitis.org**
Download our iphone app **www.meningitis.org/iphone**

If using any information from this document in external communications, please credit Meningitis Research Foundation and quote our URL www.meningitis.org.

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