Background

In 2010, the Joint Committee on Vaccination and Immunisation (JCVI) convened a meningococcal subcommittee to conduct a comprehensive and detailed assessment of the evidence on the meningococcal B vaccine development and impact and cost-effectiveness of potential meningococcal B immunisation strategies. In June 2013, the Committee received a request from the Secretary of State for Health for JCVI to provide a recommendation on the possible introduction of a routine meningococcal B immunisation programme.

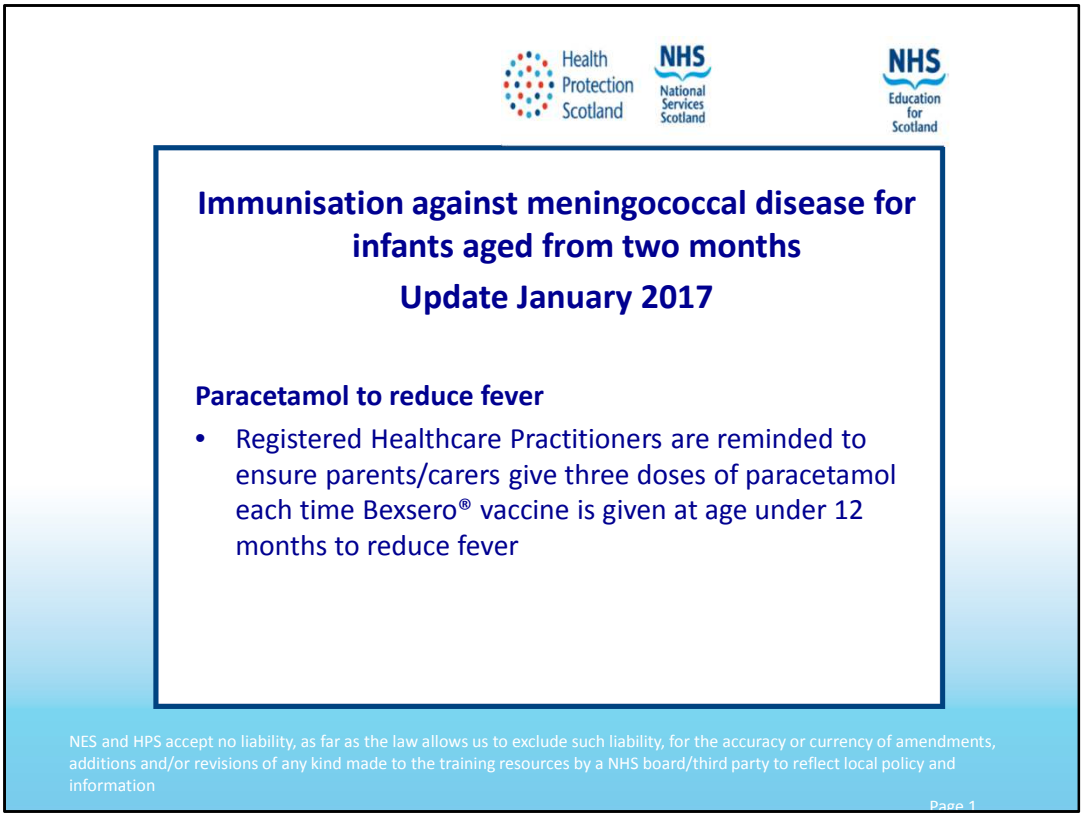
Since 2010, the JCVI has continually reviewed all the available evidence on the disease epidemiology, vaccine efficacy and safety and cost effectiveness of a meningococcal B programme in the UK. As a result, in March 2014[1] the JCVI recommended the introduction of a routine infant meningococcal B immunisation programme following a 2+1 schedule at two, four and twelve months of age. The aim of the routine childhood meningococcal B programme is to reduce the burden and severity of meningococcal meningitis and/or septicaemia caused by Neisseria meningitidis serogroup B in the UK**.**

Rationale of resource

This resource is designed to support registered healthcare practitioners in raising the issue of the importance of immunising infants from two months of age against meningococcal serogroup B disease, providing evidence based information around the implementation and delivery of the meningococcal serogroup B programme in Scotland. Note: Meningococcal serogroup B is commonly known as MenB. For the purpose of this resource MenB is used throughout this document.

This resource does not cover the actual administration techniques involved in vaccination against MenB. Information on immunisation by registered healthcare practitioners is available in chapter 5 of Immunisation against infectious disease, Department of Health, Green Book available at http://immunisation.dh.gov.uk/category/the-green-book/

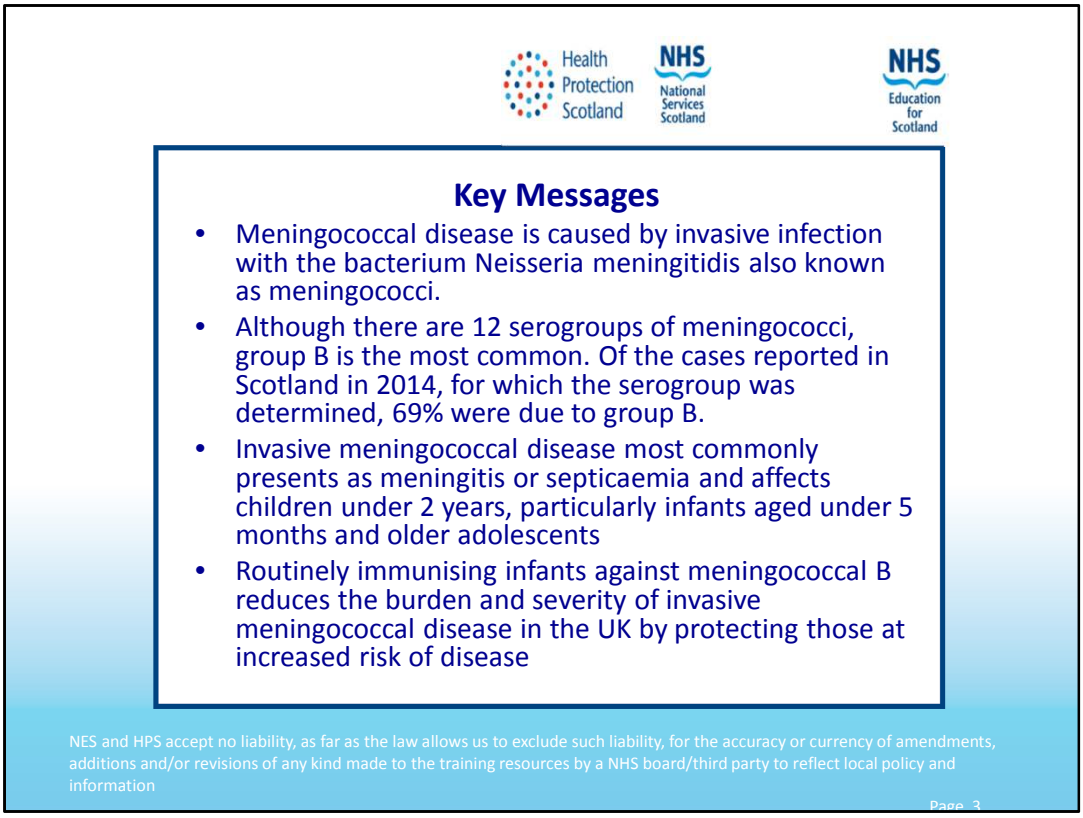
Please note: These educational resources continue to be updated as required to support this programme but do not replace the clinical judgement of practitioners. Practitioners should refer to the Public Health England Green Book Chapter when administering the vaccine.



Please note: These educational resources continue to be updated as required to support this programme but do not replace the clinical judgement of practitioners. Practitioners should refer to the Public Health England Green Book Chapter when administering the vaccine.

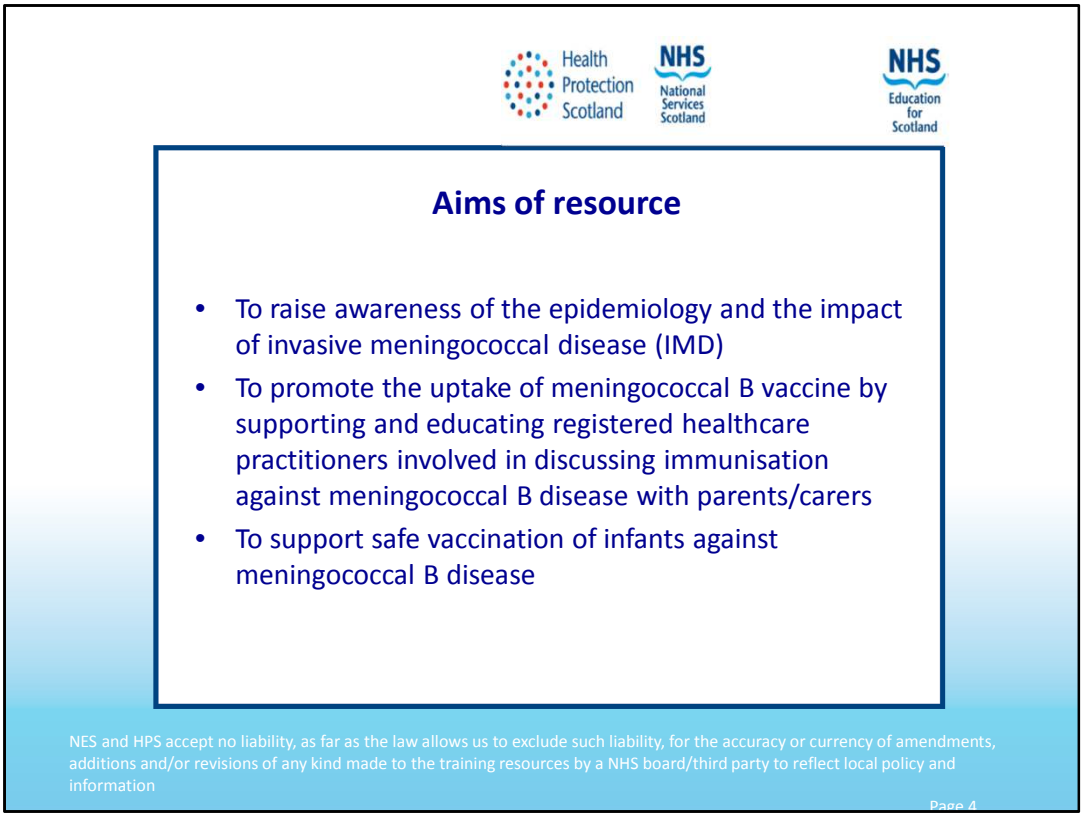
Contents

- What is meningococcal B disease?
- Why routinely immunise infants at eight weeks of age?
- Immunisation against meningococcal B disease and the use of Bexsero®
- The role of registered healthcare practitioners
- Resources



Meningococcal disease can affect all age groups, but the rates of disease are highest in children under two years of age. Meningococcal cases increase from birth and peak at five months before declining gradually until 24 months. Cases remain low until 12 years of age and then gradually increase to a smaller peak at 18 years before declining again.

Individuals with asplenia, splenic dysfunction or complement disorders are also at an increased risk of invasive meningococcal disease and should be immunised in accordance with the schedule for immunisation of individuals with underlying medical conditions; green book chapter 7



Key roles of immunisers in relation to immunisation against meningococcal B disease in infants

Advise parents/carers of infants who are eligible for the routine meningococcal B immunisation programme (those born on or after 1 July 2015) that it is strongly recommended that their infant is immunised against invasive meningococcal B by primary care at the same time as they receive their primary immunisations.

Explain the risks and complications of invasive meningococcal disease in all age groups and in particular explain that infants aged less than 12 months of age are at an increased risk of infection.

Explain to parents/carers that infants receiving meningococcal B vaccine at eight weeks, 16 weeks and 12-13 months of age will be protected against meningococcal B disease and that their child will also be offered protection at 3 months against meningococcal C disease.

Explain what vaccine will be used, the contraindications and possible side effects of immunisation and the evidence for this new immunisation programme.

Advise parents/carers of an increased risk of fever after receiving meningococcal B vaccine and the need for paracetamol suspension around the time of immunisation. Provide parents with clear instructions on how to administer paracetamol and the correct dosage.

Support safe vaccination of infants against meningococcal disease.

Learning outcomes

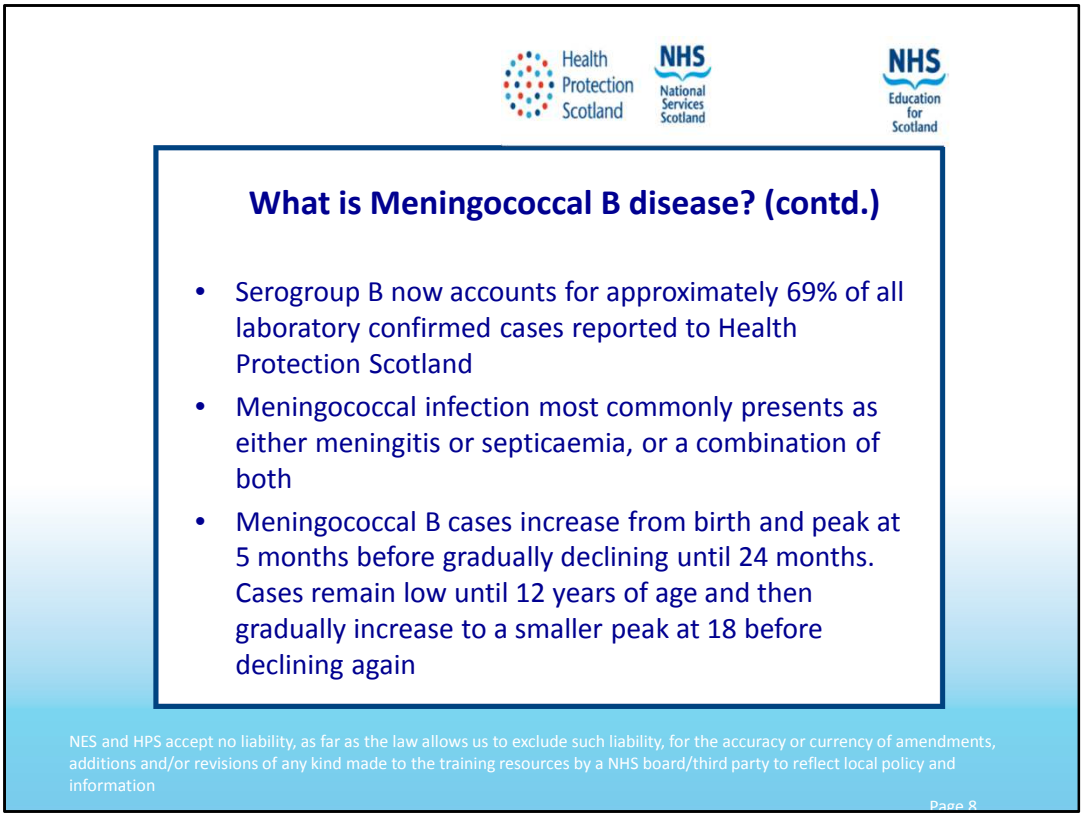
On completion of this resource, registered healthcare practitioners will be able to:

- **Know** the most common types of meningococci in the UK and their relationship in causing invasive meningococcal disease
- **Describe** the aetiology and epidemiology of meningococcal serogroup B disease
- **Advise** and inform parents/carers of the importance of introducing a meningococcal B vaccine in Scotland, providing evidence based information
- **Understand** the registered healthcare practitioners role in supporting the implementation of meningococcal B immunisation programme
- **Safely** administer the meningococcal B vaccine
- **Identify** sources of additional information and resources

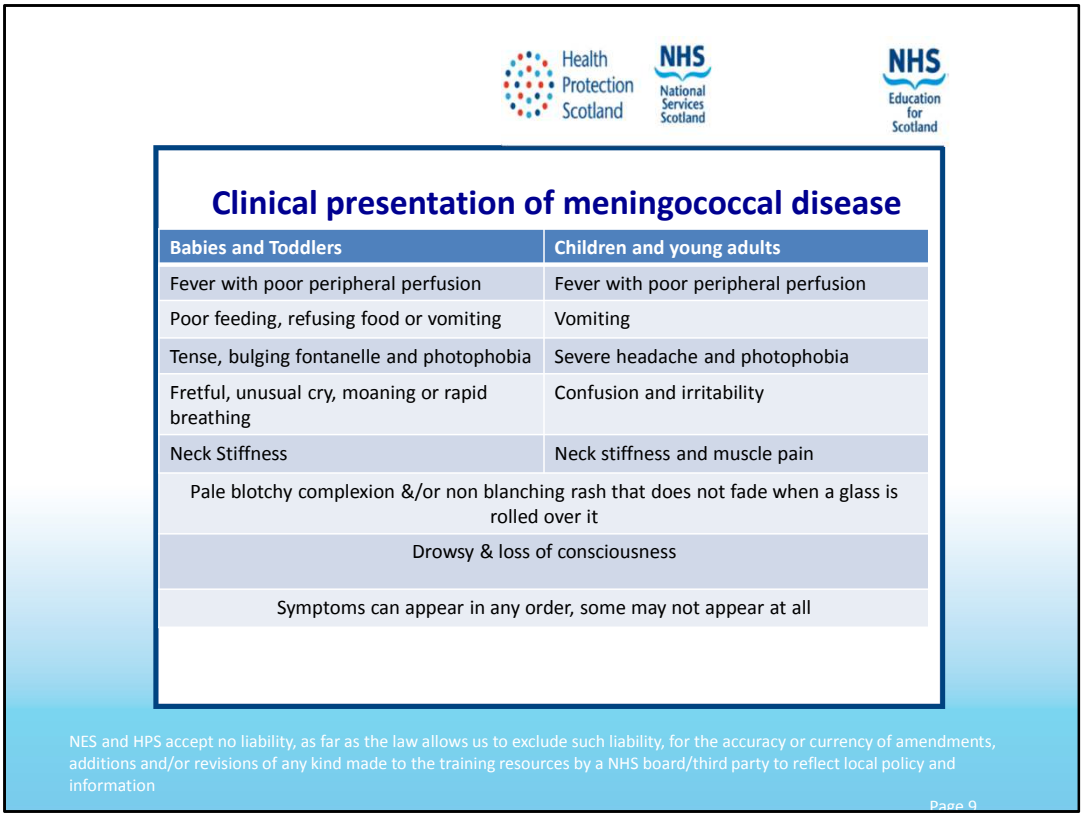
What is Meningococcal B disease?

What is Meningococcal B disease?

- Meningococcal disease occurs as a result of an invasive bacterial infection caused by Neisseria meningitidis also known as meningococci
- There are 12 serogroups of meningococci, of which the most common in the UK historically have been B, C W and Y
- Since the introduction of the routine meningococci C conjugate immunisation programme, cases of invasive meningococcal disease (IMD) in the UK from serogroup C have reduced dramatically



Less commonly, individuals may present with pneumonia, myocarditis, endocarditis, pericarditis, arthritis, conjunctivitis, urethritis, pharyngitis and cervicitis



Please note that some or all symptoms may appear, in any order, and this list is not exhaustive. Table contents based on Meningitis Now https://www.meningitisnow.org/meningitis-explained/signs-and-symptoms/
Onset of disease varies from severe acute and overwhelming features, to insidious with mild prodromal symptoms. Symptoms may be harder to identify in young infants particularly, the onset may be insidious and the signs be nonspecific without classical features of meningitis.

The meningococcal rash

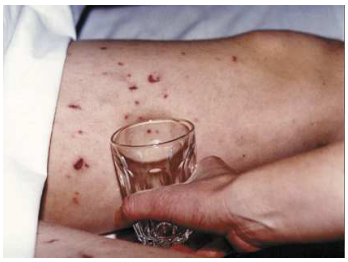


Image courtesy of Meningitis Trust

- A distinctive red rash can appear anywhere on the body
- The rash is formed of tiny “pinpricks” also known as petechiae and appears red in colour. The rash may later develop into purple bruising of the skin
- The meningococcal rash can be distinguished from other rashes by pressing a glass tumbler against it
- A meningococcal rash will not fade when a glass tumbler is rolled over it
- A febrile illness and rash that does not fade is a sign of meningococcal septicaemia

It is important to note that an absence of a rash does not preclude the illness of meningitis.

Transmission, infectivity, incubation and carriage

- Transmission in through person to person spread from respiratory droplets or by direct close contact with respiratory secretions of someone who is carrying the bacteria
- Infectivity of meningococci is relatively low and requires prolonged close contact, for example for those living in the same household or through direct contact with nose and respiratory secretions such as intimate “wet” kissing
- Incubation period ranges from 2 to 7 days with the onset of disease ranging from severe with overwhelming features to insidious mild prodromal symptoms
- Carriage in the nose and throat (without any signs of symptoms) is uncommon in infants and young children but increases to 25% in adolescents

Potential complications of meningococcal disease

- Meningococcal disease is associated with significant case-fatality, ranging from around 5% in infants and young children to 25% in older adults.
- Around a quarter of survivors of meningococcal disease will suffer serious long-term complications after recovering from the infection
- It is estimated that approximately one quarter of those diagnosed with meningococcal disease caused by Neisseria meningitis will suffer complications as a result
- Complications can vary in severity and can either be temporary or permanent. The more severe the disease, the greater the risk of complications

Complications can include:

- Loss of hearing, loss of vision, loss of memory and/or concentration, difficulties in coordination and balance, epilepsy, cerebral palsy, limb amputations and may result in death

Why routinely immunise infants at eight weeks of age?

Immunisation against meningococcal disease for infants aged from eight weeks.

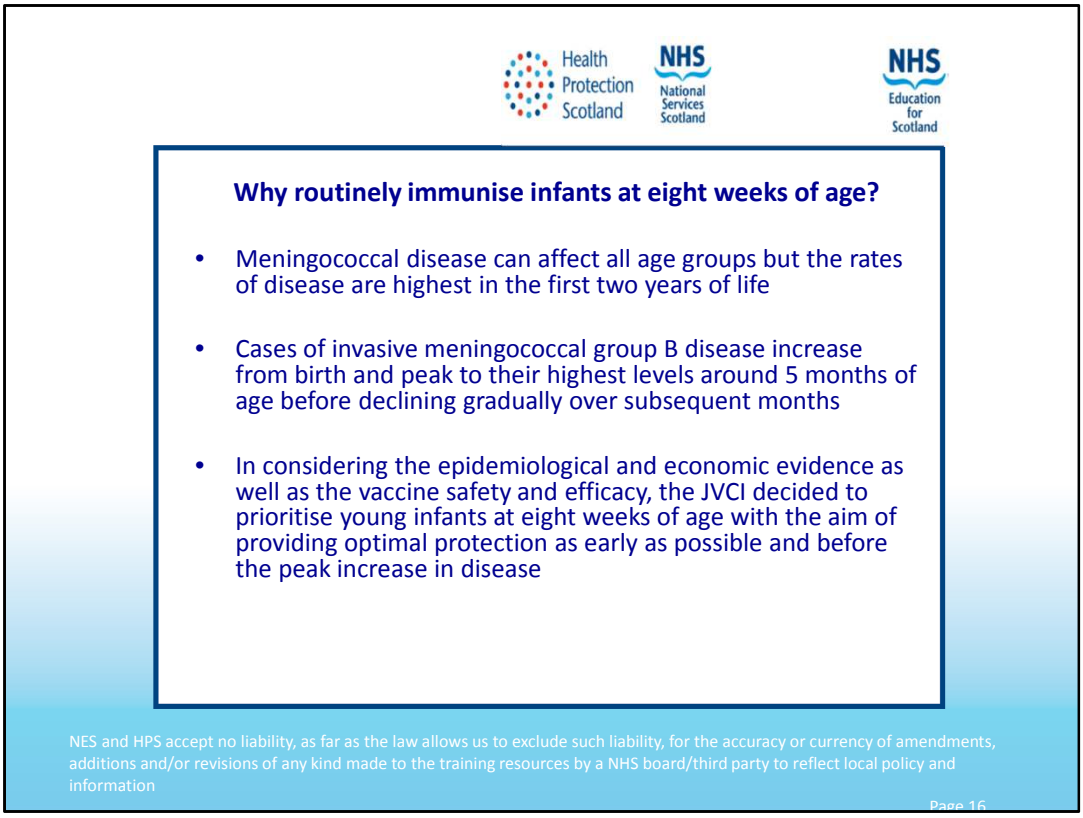
Inclusion criteria

- Born on or after 01 May 2015
- Individuals from age eight weeks requiring primary vaccination as part of the routine immunisation schedule
- Valid consent has been given to receive the vaccine

Immunisation against meningococcal disease for infants aged from eight weeks

Schedule

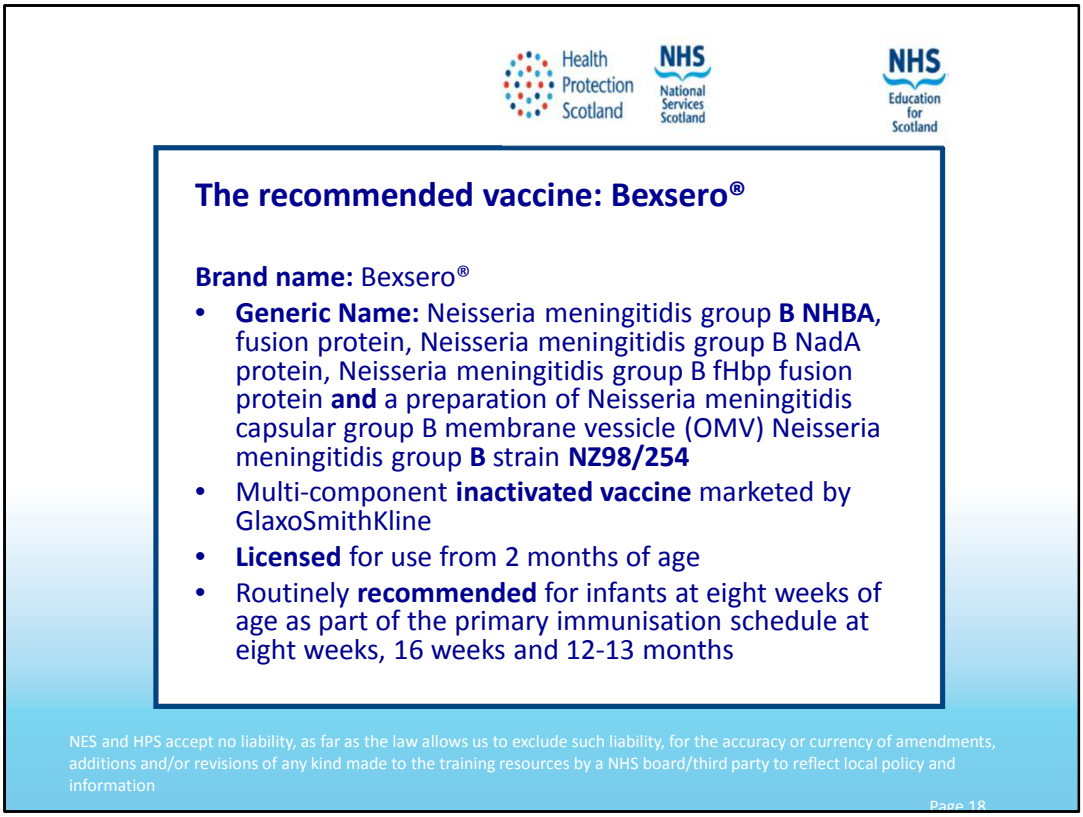
- The primary course consists of two doses with an interval of two months between the doses
- If the primary course is interrupted it should be resumed and not repeated, allowing an interval of two months between the doses.
- The recommended age for immunisation is a dose at eight weeks followed by a dose at 16 weeks.
- All children who have previously received a primary course before 12 months should be offered a reinforcing/booster dose
- The recommended age for the booster is between 12 and 13 months (i.e. within one month of first birthday) but can be given up to the child's second birthday



The JCVI did not recommend a catch-up programme for infants aged 5-12 months (born before the 1 May 2015) after reviewing the cost-effectiveness model. Since the vaccine was only found to be cost-effective at a very low price, a sustainable approach had to be followed for implementation. As meningococcal disease peaks around 5 months of age before declining, the priority of the meningococcal B immunisation programme is to ensure that Bexsero® is offered routinely to infants who are due to receive their routine primary immunisations on or after the 1 September (those born on or after 1 July 2015) with a limited catch up for those infants born from 1 May 2015 to 30 June 2015) which will provide protection to this most vulnerable group prior to the peak in incidence of disease at 5 months of age.

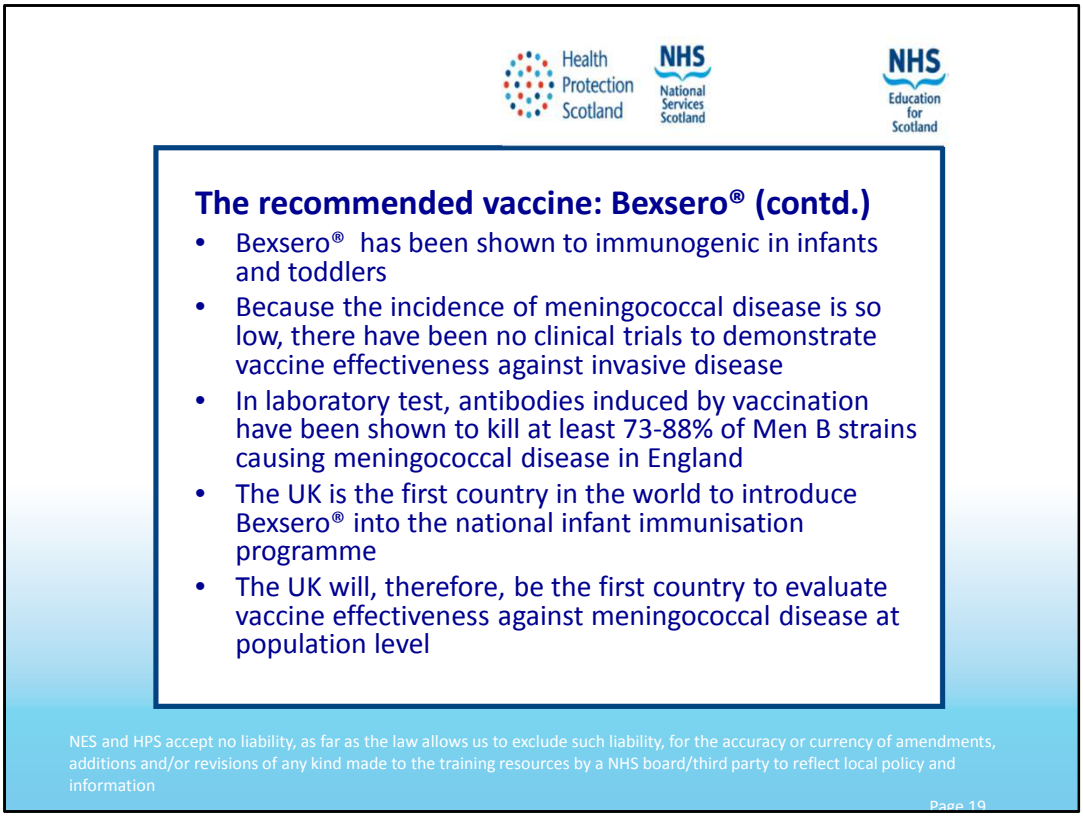
Immunisation against meningococcal B disease

The use of Bexsero® vaccine



The aim of the routine infant meningococcal B immunisation programme is to reduce the burden and severity of invasive meningococcal disease caused by Neisseria meningitidis capsular B in the UK by protecting those at increased risk of disease.

Bexsero® will be available through routine immunisations. Parents attending their GP practice for their child's routine primary immunisations at 8, 12 and 16 weeks of age will be offered meningococcal B vaccine.



Bexsero® has been shown to be immunogenic in infants and toddlers. Vaccine-induced antibodies have been shown to bactericidal (i.e. they kill the bacteria) against most meningococcal strains causing invasive disease in the UK. However, the is as yet no evidence regarding the effectiveness of Bexsero® in preventing meningococcal disease in a populations since the vaccine had not been implemented in any country and the incidence of meningococcal disease is too low for clinical trials to provide a measure of efficacy.

A number of countries such as Cuba, Norway and New Zealand have previously used different MenB vaccines. These were derived from outer membrane vesicles (OMVs) of the specific MenB strains which were causing large outbreaks in these countries. A key limitation of these previous vaccines, however, is that they mainly protect against specific MenB strains and do not provide broad cross-protection against other MenB strains causing invasive disease. In New Zealand, vaccine effectiveness for the OMV component of their vaccine was estimated to be 73%.

The cost-effectiveness model reviewed by the JCVI assumed that 88% of meningococcal B strains causing invasive disease in England would be covered by Bexsero® and the vaccine effectiveness against these strains would be 95%.

The recommended vaccine: Bexsero®

Bexsero® is the recommended vaccine for the routine infant immunisation programme:

- Bexsero® can be ordered from NHS Board vaccine holding centres which supply other childhood vaccines
- It is important immunisers familiarise themselves with the vaccine and its product information to avoid administration errors

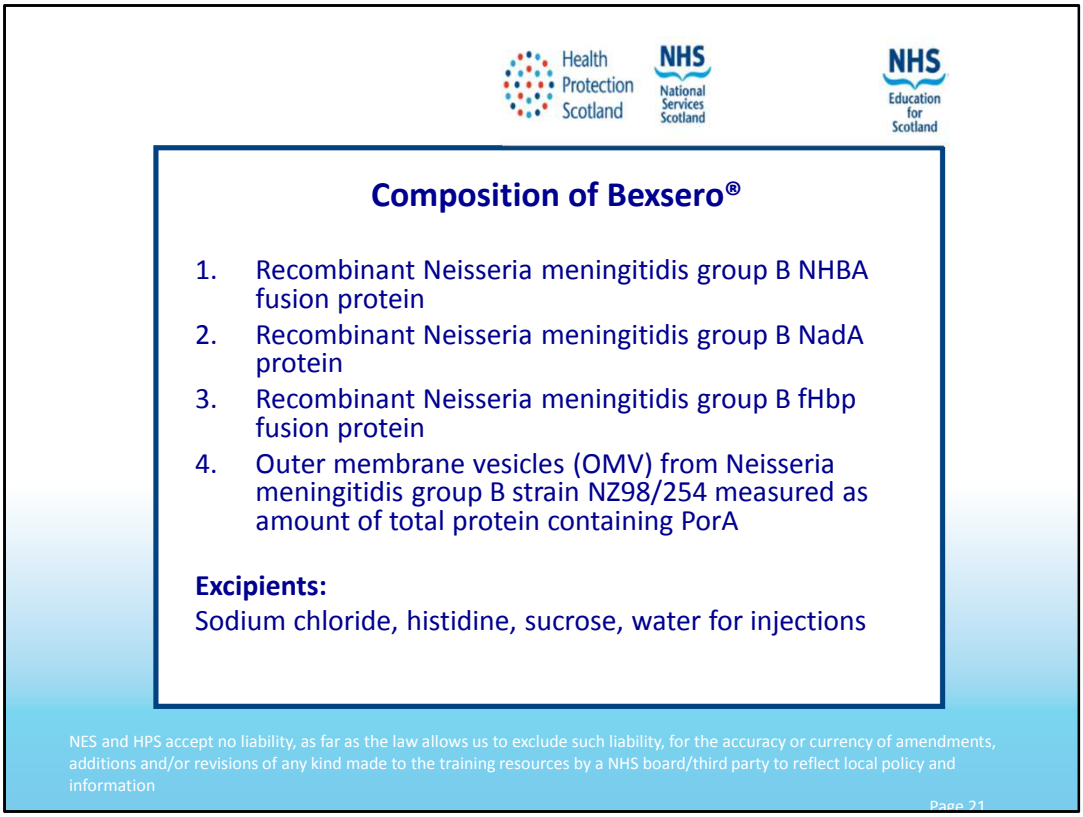
Image courtesy of GlaxoSmithKline

Page

Bexsero® can be ordered from NHS Board vaccine holding centres which supply other childhood vaccines Bexsero® has a shelf life of two years when stored in its original packaging in a refrigerator at the recommended temperatures of +2°C and +8°C. Bexsero® should not be frozen. At the start of the programme the Bexsero® being supplied may have a shorter shelf life and practitioners must check the expiry date of all vaccines being administered.

Registered healthcare practitioners should place small regular orders with their supplying vaccine holding centre.

** GlaxoSmithKline recently acquired Novartis global vaccine business which includes Bexsero® vaccine. Bexsero® is now owned and supplied by GlaxoSmithKline.



Does Bexsero® contain latex?
The tip cap of the syringe may contain natural rubber latex. Although the risk for developing allergic reactions is very small, registered healthcare practitioners should consider the benefit-risk prior to administering this vaccine to subjects with known history of hypersensitivity to latex.
For a full list of excipients, registered healthcare practitioners should read the manufacturers Summary of Products Characteristics (SPCm).

Does Bexsero® contain any preservatives such as thiomersal?
No, Bexsero® does not contain thiomersal. For a full list of excipients, registered healthcare practitioners should read the manufacturers Summary of Products Characteristics (SPCm).

Does Bexsero® contain any porcine gelatin?
No, Bexsero® does not contain porcine gelatin. For a full list of excipients, registered healthcare practitioners should read the manufacturer's Summary of Products Characteristics (SPCm).

Preparation of Bexsero®

- Bexsero® vaccine is supplied in packs containing 10 pre-filled syringes each with a volume of 0.5mls of suspension per syringe
- Registered healthcare practitioners should choose the correct needle size for **intramuscular** administration. Needles for administration of the vaccine need to be ordered by practices as per normal arrangements
- During storage, the contents of the syringe may settle with off-white deposits being noticeable
- Before use, the pre-filled syringe must be **shaken well** so that any observable deposits are thoroughly mixed into the liquid forming an homogenous suspension that should be administered **immediately**
- The vaccine **should not** be administered where there are variations in the physical appearance (i.e. not an homogenous suspension) or signs of foreign particulates are observed after shaking

Administration of Bexsero®

- It is recommended that Bexsero® should be administered via intramuscular injection ideally on its own in the infants left thigh (anterolateral aspect) so that any local reactions can be accurately monitored
- Due to expected local reactivity of Bexsero® it is advised to administer it alone in a separate limb to any other vaccines. This also applies to the 12-13 month appointment
- The vaccine must **not** be injected intravenously, subcutaneously or intradermally and must **not** be mixed with other vaccines in the same syringe

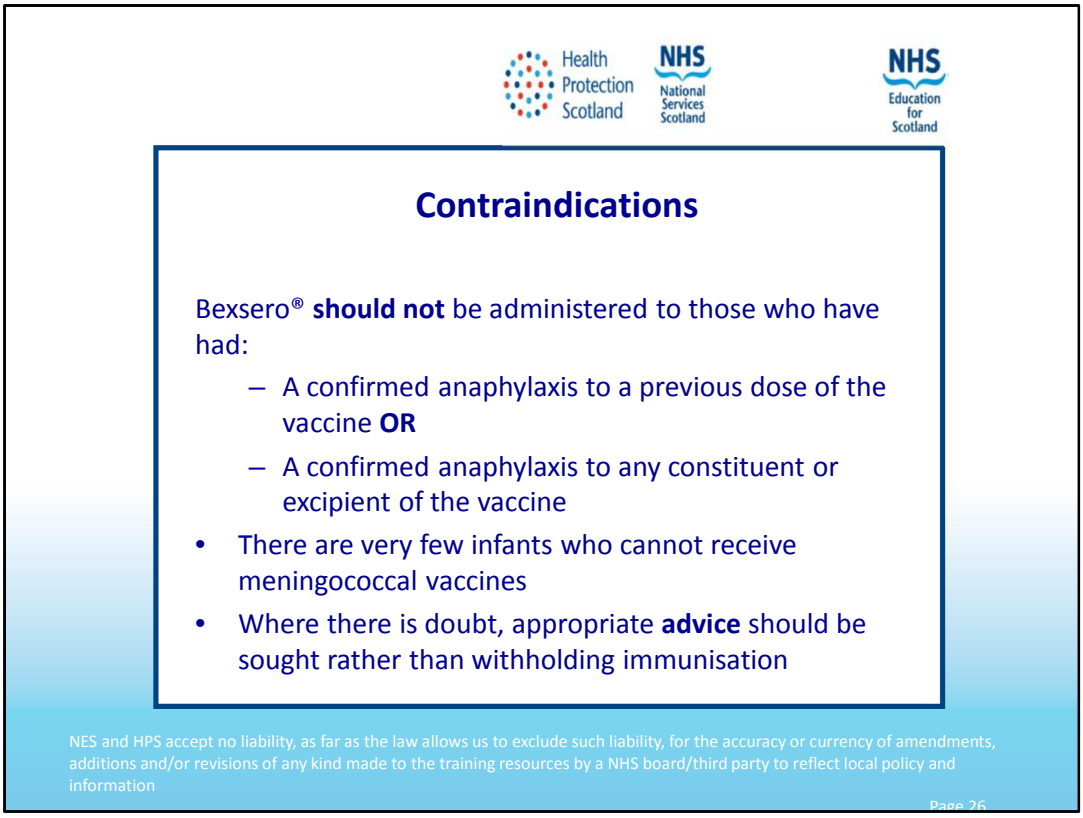
Administration of Bexsero®(contd.)

- Normally, where more than one vaccine is administered at the same time, the vaccines should be given at a separate site, preferably in a different limb
- If more than one vaccine is given in the same limb, they should be given at least 2.5cm apart. The sites at which each vaccine was given should be noted in the individual's health records
- For individuals with a bleeding disorder, the vaccine should be given by **deep** subcutaneous injection to reduce the risk of bleeding

Administration of Bexsero ® (Contd)

Bexsero® should only be administered:

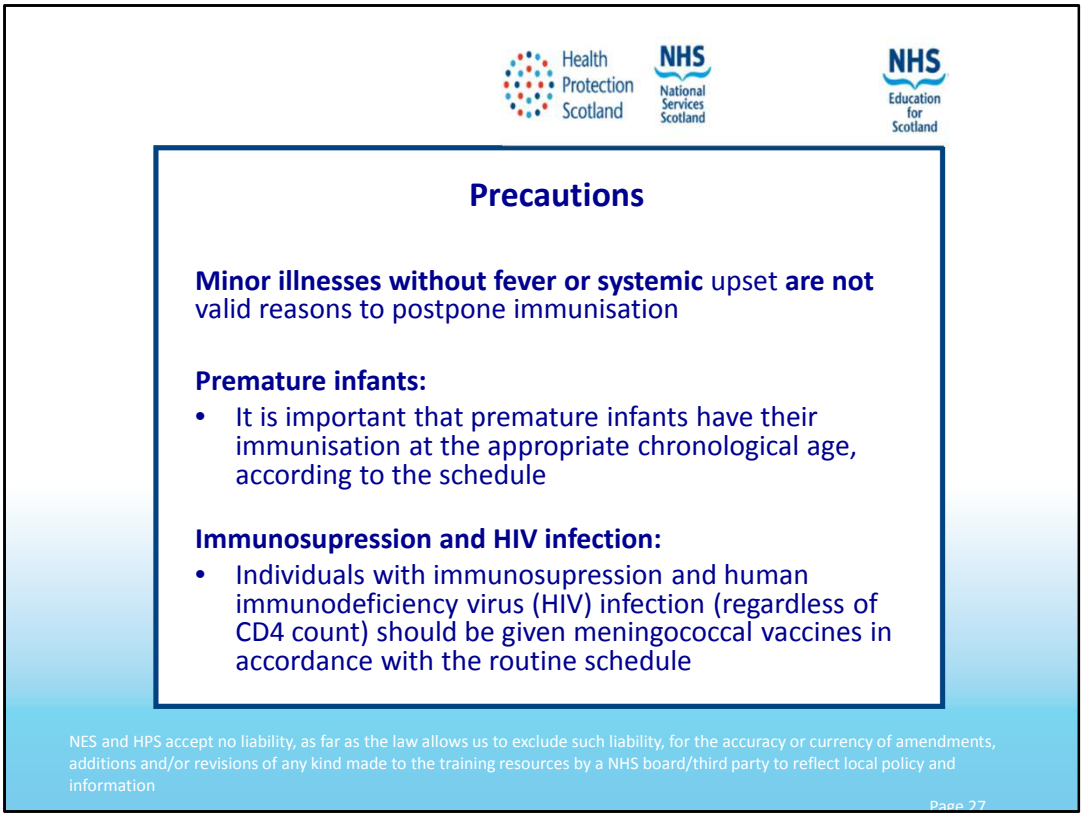
- Against a prescription written manually or electronically by a registered medical practitioner or other authorised prescriber
- Against a Patient Specific Direction
- Against a Patient Group Direction



For the composition and full list of excipients of the vaccine, please refer to the manufacturer's Summary of Product Characteristics https://www.medicines.org.uk/emc/medicine/28407#EXCIPIENTS.

There are very few infants who cannot receive meningococcal vaccines. Where there is doubt, appropriate advice should be sought from your local immunisation coordinator or health protection team rather than withholding immunisation

For further information on contraindications and precautions, please refer to the meningococcal Green Book chapter online at https://www.gov.uk/government/collections/immunisation-against-infectious-disease-thegreen-book

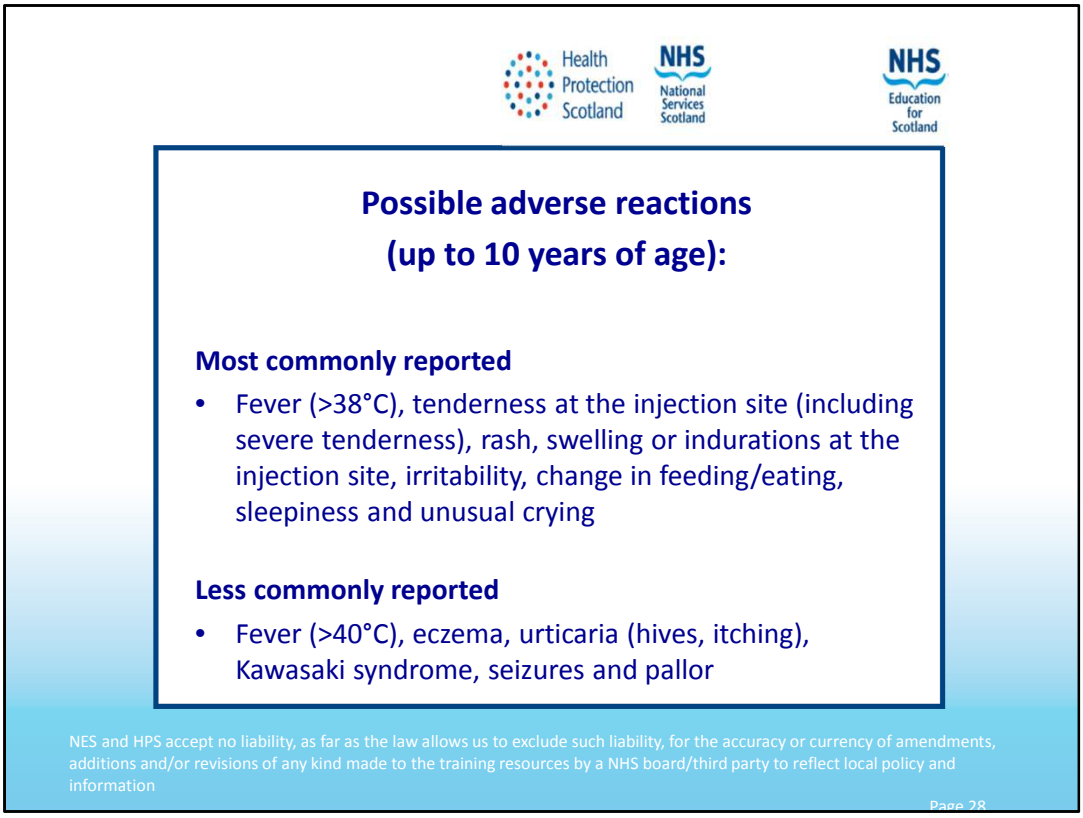


Minor illnesses without fever or systemic upset are not valid reasons to postpone immunisation. If an individual is acutely unwell, immunisation may be postponed until they have recovered fully. This is to avoid confusing the differential diagnosis of any acute illness by wrongly attributing any signs or symptoms to the adverse effects of the vaccine.

Premature infants- It is important that premature infants have their immunisations at the appropriate chronological age, according to the schedule. The occurrence of apnoea following vaccination is especially increased in infants who were born very prematurely. Very premature infants (born @ 28 weeks of gestation) who are in hospital should have respiratory monitoring for 48-72 hrs when given their first immunisation, particularly those with a previous history of respiratory immaturity. If the child has apnoea, bradycardia or desaturations after the first immunisation, the second immunisation should also be given in hospital, with respiratory monitoring for 48-72 hrs (Ohlsson et al., 2004[2]; Pfister et al., 2004[3]; Schulzke et al., 2005[4]; Pourcyrous et al., 2007[5]; Klein et al., 2008[6]). As the benefit of immunisation is high in this group of infants, immunisation should not be withheld or delayed.

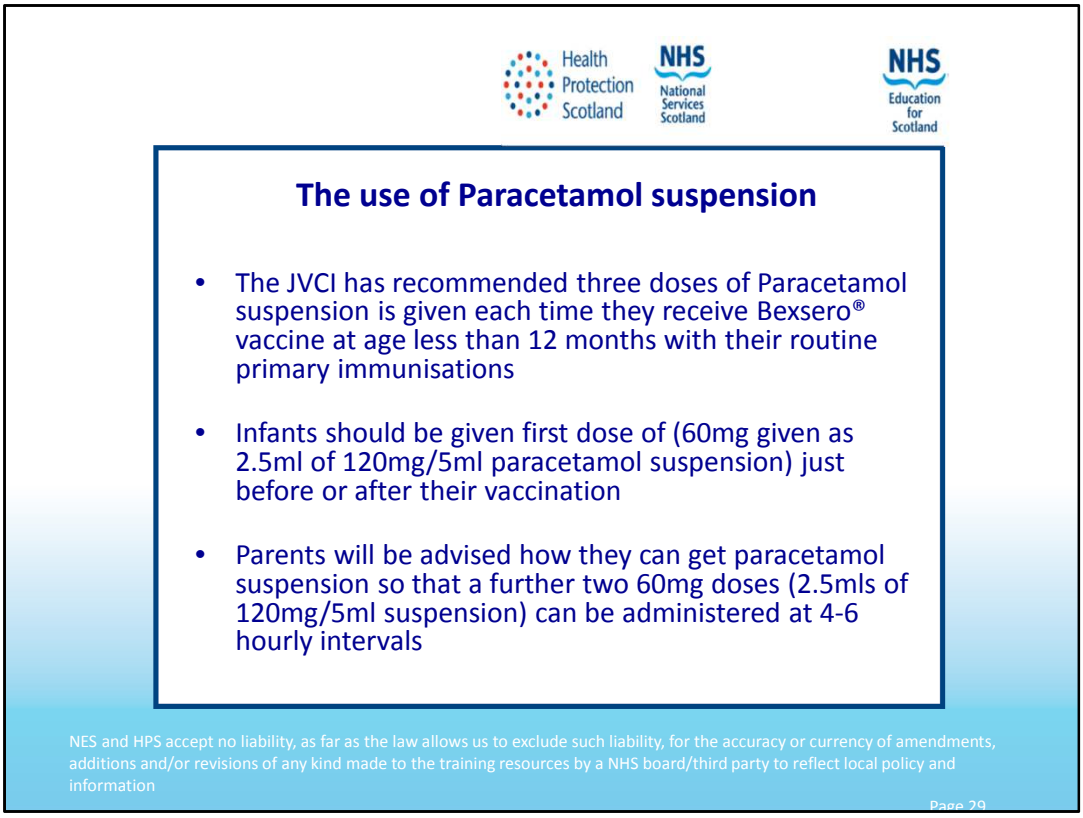
Immunosuppression and HIV infection Individuals with immunosuppression and human immunodeficiency virus (HIV) infection (regardless of CD4 count) should be given meningococcal vaccines in accordance with the routine schedule. These individuals may not make a full antibody response. Re-immunisation should be considered after treatment is finished and recovery has occurred. Specialist advice may be required.
For further information on contraindications and precautions, please refer to the

meningococcal Green Book chapter online at
https://www.gov.uk/government/collections/immunisation-against-infectious-disease-thegreen-book



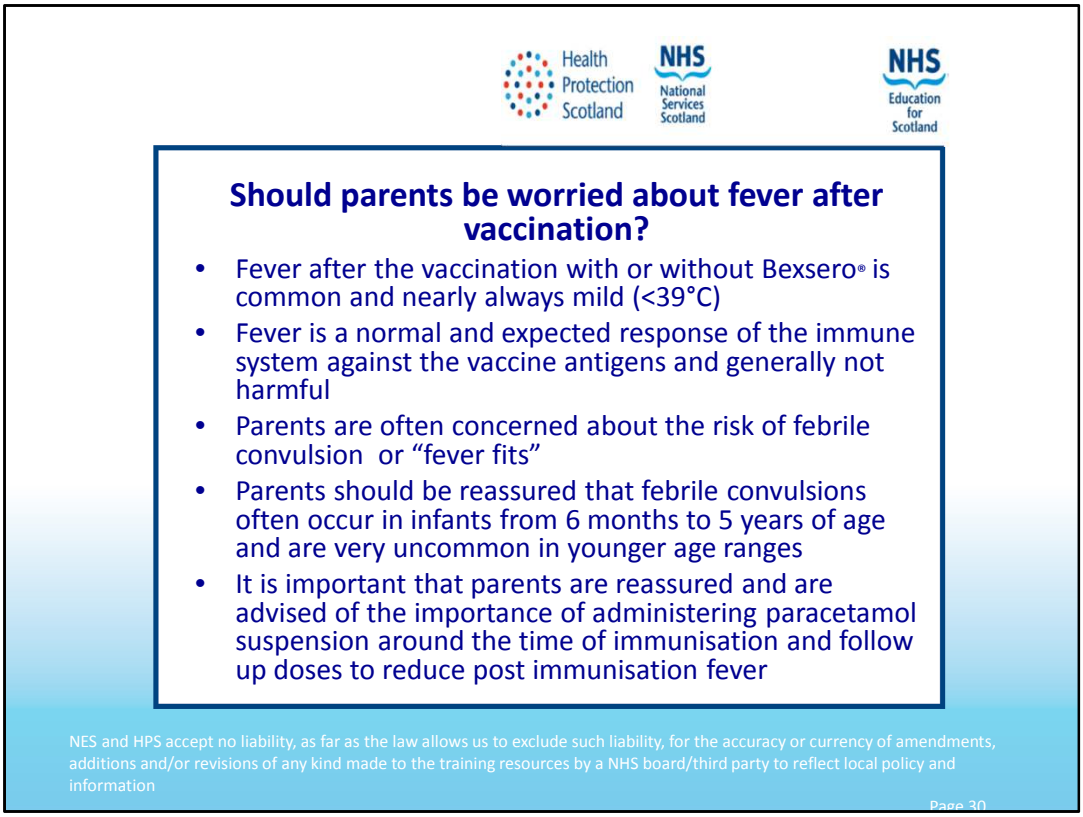
Healthcare registered practitioners should refer to the vaccine manufacturers authorisation holders summary of product characteristics (SPCm). https://www.medicines.org.uk/emc/medicine/28407#EXCIPIENTS [7]

Most commonly
Fever (>38°C**),**tenderness at the injection site (including severe tenderness defined as crying when moving injected limb), rash, swelling or induration at the injection site, irritability, change in feeding/eating, sleepiness and unusual crying.

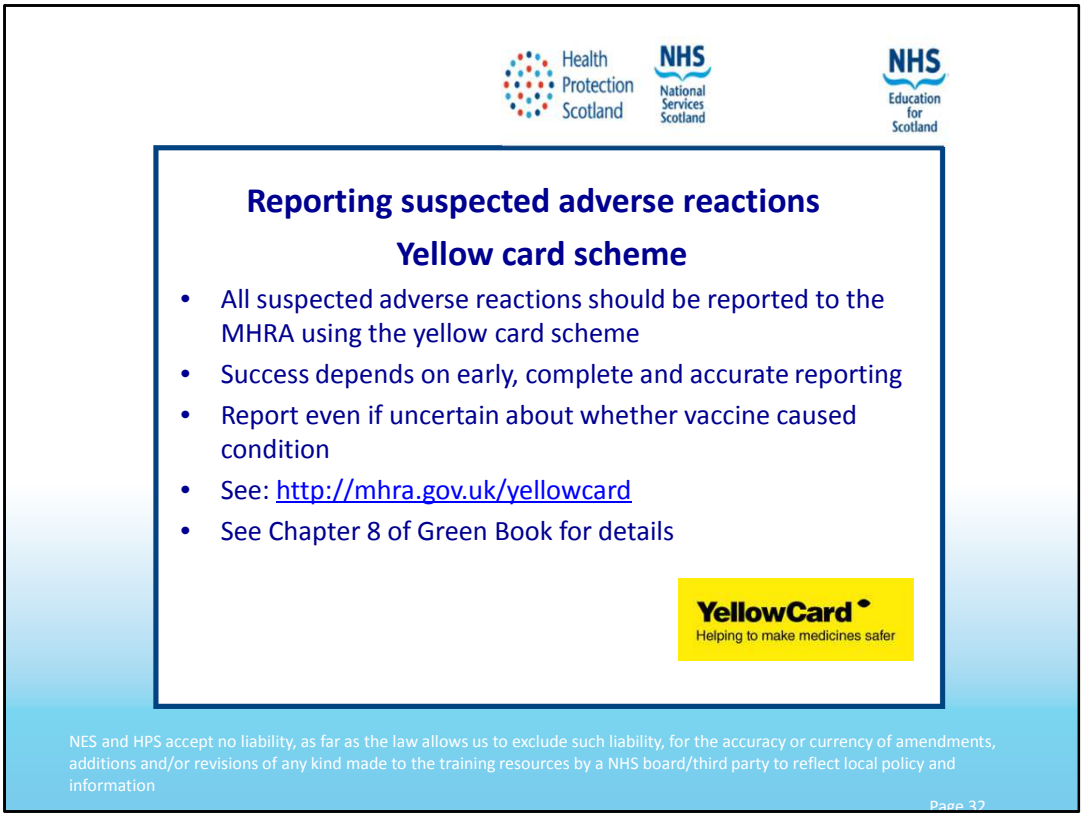


Detailed written instructions will be provided to all parents of infants receiving Bexsero® on how to administer paracetamol suspension, the dose that is required and the timing of the dose.

Practitioners must be aware that some parents may choose to give their paracetemol in advance of vaccination. It is important therefore that practitioners ascertain from parents/carers whether paracetamol has been given to the infant prior to coming for vaccination.



Fever after vaccination with or without Bexsero® is common and nearly always mild (<39°C). Fever is a normal and expected response of the immune system against the vaccine antigens and generally not harmful, but parents are often concerned about the risk of febrile convulsions or "fever fits." Typically, febrile convulsions occur from 6 months to 5 years of age and are very uncommon in younger age groups. In clinical trials involving several thousand infants receiving their routine vaccinations (including Bexsero®), febrile convulsions are very rarely reported. In one of the largest Bexsero® trials, where 1885 infants were recruited and vaccinated at four different visits without paracetamol prophylaxis, only one infant developed a febrile convulsion two days after receiving Bexsero® [8] In the subsequent study of 364 infants receiving Bexsero® with or without paracetamol ([9]) there was not a single case of febrile convulsion after any of the four vaccination visits.



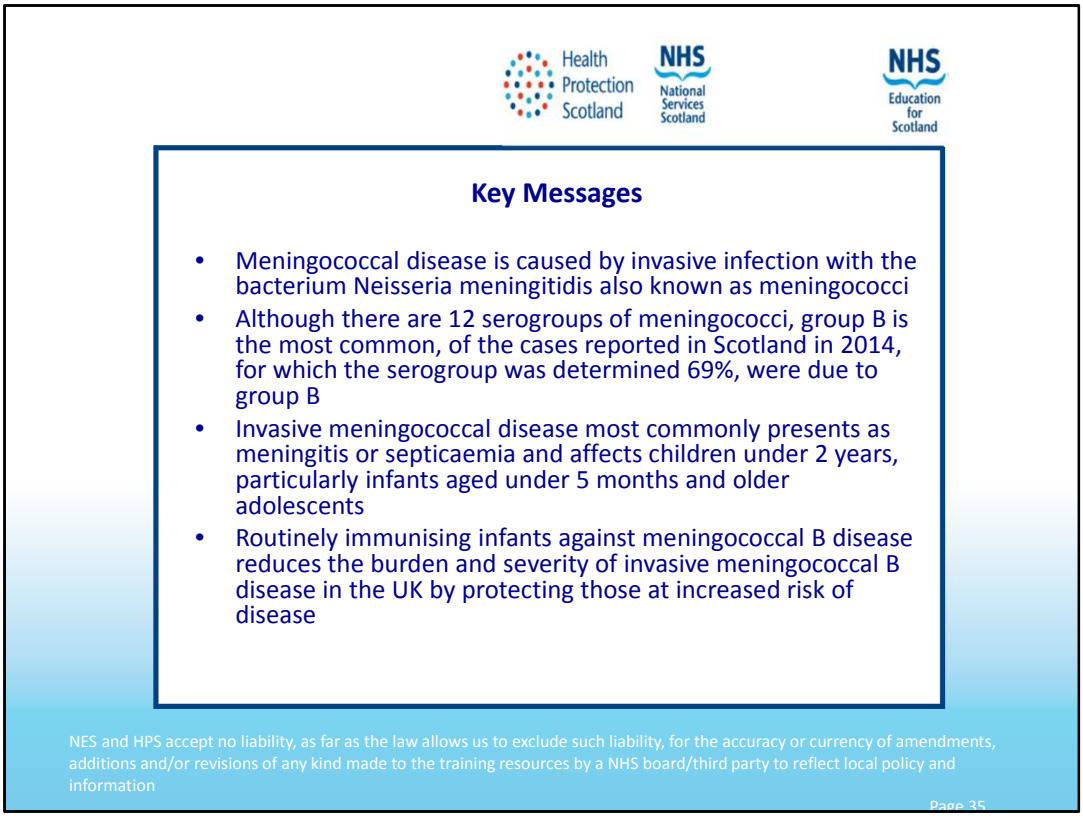
Registered Healthcare practitioners and patients are encouraged to report suspected adverse reactions to the Medicines and Healthcare products Regulatory Agency (MHRA) using the yellow card reporting scheme.

The role of registered healthcare practitioners

- To safely administer the meningococcal vaccine
- To provide clear, concise and accurate information to parents of infants from eight weeks of age receiving Bexsero® as part of their routine primary immunisations
- Every effort should be made by registered healthcare practitioners to maximise uptake of the meningococcal B Vaccine and to ensure that parents are fully informed about the importance of ensuring protection against meningococcal B disease for their child

Resources

- NHS Inform
- http://www.nhsinform.co.uk/health library/articles/m/meningitis/introduction/
- NHS Education for Scotland
- http://www.nes.scot.nhs.uk/education-and-training/by-theme-initiative/public-health/health-protection/immunisation/meningococcal-b-disease-for-infants-aged-from-two-months.aspx
- CMO Letter
- http://www.sehd.scot.nhs.uk/cmo/CMO(2015)17.pdf
- Green Book
- https://www.gov.uk/government/publications/meningococcal-the-green-book-chapter-22
- Meningitis Research Foundation
- http://www.meningitis.org/
- Meningitis Now
- https://www.meningitisnow.org/
- Meningitis Association Scotland
- http://www.menscot.org/



Meningococcal B cases increase from birth and peak at 5 months before declining until 24 months of age. Cases remain low until 12 years of age and then gradually increases again to a smaller peak at 18 years before declining again.

References

1. The Joint Committee on Vaccination and Immunisation (JCVI) position statement on use of Bexsero® meningococcal B vaccine in the UK (2014) accessible at: https://www.gov.uk/government/uploads/system/uploads/attachment_data/file/294245/JCVI_Statement_on_MenB.pdf
2. Ohlsson A and Lacy JB (2004) Intravenous immunoglobulin for preventing infection in preterm and/or low-birth-weight infants. *Cochrane Database Syst Rev* (1): CD000361.
3. Pfister RE, Aeschbach V, Niksic-Stuber V et al. (2004) Safety of DTaP-based combined immunization in very-low-birth-weight premature infants: frequent but mostly benign cardiorespiratory events. *J Pediatr* **145**(1): 58-66.
4. Schulz S, Heininger U, Lucking-Famira M *et al*. (2005) Apnoea and bradycardia in preterm infants following immunisation with pentavalent or hexavalent vaccines. *Eur J Pediatr* **164**(7): 432-5.
5. Pourcyrous M, Korones SB, Arheart KL *et al*. (2007) Primary immunization of premature infants with gestational age <35 weeks: cardiorespiratory complications and C-reactive protein responses associated with administration of single and multiple separate vaccines simultaneously. *J Pediatr* **151**(2): 167-72.
6. Klein NP, Massolo ML, Greene J *et al*. (2008) Risk factors for developing apnea after immunization in the neonatal intensive care unit. *Pediatrics* **121**(3): 463-9.
7. Novartis Vaccines (2015). Bexsero Meningococcal Group B vaccine for injection in pre- filled syringe. [internet] accessed on 11 June 2015. https://www.medicines.org.uk/emc/medicine/28407/SPC/Bexsero+Meningococcal+Group+B+vaccine+for+injection+in+pre- filled+syringe/
8. Gossger N, Snape MD, Yu LM, Finn A, Bona G, Esposito S, Principi N, Diez-Domingo J, Sokal E, Becker B, Kieninger D, Prymula R, Dull P, Ypma E, Toneatto D, Kimura A, Pollard AJ; European MenB Vaccine Study Group (2012). Immunogenicity and tolerability of recombinant serogroup Bmeningococcal vaccine administered with or without routine infant vaccinations according to different immunization schedules: a randomized controlled trial. JAMA. 2012 Feb 8;307(6):573- 82. doi: 10.1001/jama.2012.85.
9. Prymula R1, Esposito S, Zuccotti GV, Xie F, Toneatto D, Kohl I, Dull PM (2014). A phase 2 randomized controlled trial of a multicomponent meningococcal serogroup B vaccine. Hum Vaccin Immunother. 2014;10(7):1993-2004. doi: 10.4161/hv.28666