



Public Health
England

Protecting and improving the nation's health

Immunisation against meningococcal B disease for infants aged from two months

Information for healthcare professionals

About Public Health England

Public Health England's mission is to protect and improve the nation's health and to address inequalities through working with national and local government, the NHS, industry and the voluntary and community sector. PHE is an operationally autonomous executive agency of the Department of Health.

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Background

In 2010, the Joint Committee on Vaccination and Immunisation (JCVI)¹ convened a meningococcal sub-committee 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 this time, the JCVI has regularly reviewed all the available evidence on the disease epidemiology, vaccine efficacy and safety and cost effectiveness of a meningococcal group B immunisation programme in the UK. As a consequence, in March 2014, 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.

What is meningococcal disease ?

Meningococcal disease is caused by invasive infection with the bacterium *Neisseria meningitidis*, also known as the meningococcus. There are 12 identified capsular groups of which groups B, C, W and Y were historically the most common in the UK. Since the introduction of the routine MenC vaccination programme, cases of invasive meningococcal disease (IMD) in the UK due to capsular group C have reduced significantly, with capsular group B (MenB) accounting for approximately 80% of all laboratory-confirmed cases submitted to Public Health England. In 2015, PHE reported a continued increase in meningococcal capsular group W disease across all age groups and all regions in England, demonstrating a year on year increase since 2009 and indicating the strain had become endemic.

¹ The Joint Committee on Vaccination and Immunisation (JCVI) is a statutory expert Standing Advisory Committee. Its purpose is to provide expert impartial advice to the Secretaries of State for Health for England, Scotland, Wales and Northern Ireland on matters relating to communicable diseases, preventable and potentially preventable through immunisation

Immunisation against meningococcal B for infants aged from two months

Invasive meningococcal disease most commonly presents as either meningitis or septicaemia, or a combination of both.

Meningococci commonly colonise the nasopharynx of humans and usually do not cause invasive disease. Between 5 and 11% of adults and up to 25% of adolescents carry the bacteria without any signs or symptoms of the disease. In infants and young children, the carriage rate is low.

The meningococci are transmitted by respiratory aerosols, droplets or by direct contact with the respiratory secretions of someone carrying the bacteria. The incubation period is from two to seven days and the presentation of disease ranges from severe acute and overwhelming features, to insidious with mild prodromal symptoms.

Who does it affect?

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](#)

The Meningococcal B immunisation programme

What is the purpose of the programme?

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.

Who is the vaccine recommended for?

The JCVI recommended the routine immunisation of infants at 2, 4 and 12 month of age, that is, following a 2+1 schedule.

Routine cohort

Starting on the 1 September 2015 all infants born on or after the 1 July 2015 will be eligible for the meningococcal B vaccine which will be administered together with the other primary immunisations at 2 months, 4 months and 12 months.

Catch up cohort

There will also be a catch-up programme for infants born from 1 May 2015 to the 30 June 2015. The JCVI agreed that these infants would be offered the meningococcal B vaccine when they attend for their remaining primary immunisation appointments from 1 September 2015.

Infants aged two, three and four months of age presenting for their routine primary immunisations from 1 September 2015 are eligible to receive the vaccine as outlined below:

Cohort	Dates of birth	Recommended immunisation schedule
Routine	Those born on or after 1 July 2015	2, 4 and 12 month (2+1)
Catch-up	Those born on or after 1 May to the 30 th June 2015	If second routine primary immunisation appointment due on or after 1 September then follow this schedule: 3, 4 and 12 month (2+1)
	Those born before 1 May 2015 are not eligible to receive the meningococcal B vaccine	If third routine primary immunisation appointment due on or after 1 September then follow this schedule: 4 and 12 month (1+1)

*Bexsero will only be offered with routine immunisation appointments

What is the recommended vaccine for the programme?

Bexsero® is the recommended vaccine for the routine infant immunisation programme and is the **only** market authorised meningococcal B vaccine in the UK.

Bexsero® is a multi-component inactivated vaccine made from three *Neisseria meningitidis* proteins produced by recombinant DNA technology (*Neisseria meningitidis* group B NHBA fusion protein, *Neisseria meningitidis* group B NadA protein, *Neisseria meningitidis* group B fHbp fusion protein) **and** a preparation of *Neisseria meningitidis* capsular group B outer membrane vesicle (OMV) *Neisseria meningitidis* group B strain NZ98/254).

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Bexsero® can be ordered via the [ImmForm](#) website. Healthcare professionals should refer to the ImmForm website on a regular basis for up to date information on vaccine availability.

What are the contraindications for receiving Bexsero® ?

There are very few infants who cannot receive meningococcal vaccines. Where there is doubt, instead of withholding immunisation, appropriate advice should be sought from a consultant paediatrician with immunisation expertise, a member of the screening and immunisation team or from your local health protection team .

Bexsero® should **not** be administered to those who have had:


1. A confirmed anaphylaxis to a previous dose of the vaccine OR
2. A confirmed anaphylaxis to any constituent or excipient of the vaccine

For the composition and full list of excipients of the vaccine, please refer to the manufacturer's Summary of Product Characteristics ([SPCm](#)).

What adverse reactions are commonly associated with the administration of Bexsero® ?

In clinical vaccine trials, the most common adverse reaction observed in infants and children under two years of age was a high rate of fever (>38°C) when Bexsero®. was administered with the other routine childhood vaccines (see below).

Other very common (occur in more than 1 in 10 children) adverse reactions observed in infants and children (up to the age of 10 years) are 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.

Bexsero® is a newly licensed vaccine and is subject to additional monitoring under the **black triangle** () labelling scheme by the [Medicines and Healthcare Regulatory Agency \(MHRA\)](#). All suspected adverse reactions should be reported to the MHRA using the [Yellow Card scheme](#).

The manufacturers Summary of Products Characteristics (SPCm) states infants were at an increased risk of fever when Bexsero® was administered at the same time as other routine childhood vaccines. How common is fever and can it be prevented?

In one clinical trial, fever ($\geq 38^{\circ}\text{C}$) was reported in 51- 62% of infants receiving Bexsero® and routine vaccines administered together, although high fever ($\geq 39^{\circ}\text{C}$) was less common (6-12%). Overall, fever ($\geq 38.0^{\circ}\text{C}$) after any vaccination was reported in 76% of infants receiving Bexsero® and routine vaccines together, compared to 51% in infants receiving the routine vaccinations alone. In that study, however, only 6 of the 1,885 recruited infants attended the hospital because of fever within 2 days after vaccination with Bexsero®.

In a subsequent study, 70% of infants receiving Bexsero® had fever $\geq 38.5^{\circ}\text{C}$ at least once in the first 3 days after any primary dose. However, fever was less common (39%) in infants receiving prophylactic paracetamol just before or at the time of vaccination followed by 2 further administrations at 4–6 h intervals after vaccination by parents/guardians. Of note, only ~5% of infants receiving paracetamol had fever $\geq 39^{\circ}\text{C}$ and the frequency of medically-attended fever within 3 days of vaccination was $\leq 2\%$ for any vaccination visit, irrespective of whether the Bexsero® was administered alone or together with the routine vaccinations.

The latter study was also important because it showed that responses to Bexsero® and the routine vaccinations were not affected by administering prophylactic paracetamol at the time of vaccination.

In another vaccine studyⁱ that did not include Bexsero®, infants receiving three doses of paracetamol (at vaccination and at 6-8 hour intervals) were half as likely to develop any post-vaccination fever, and also half as likely to develop high fever ($>39^{\circ}\text{C}$), compared with infants receiving two doses of paracetamol (first dose at 6-8 hours after vaccination and another 6-8 hours later). Thus, the greatest benefit in reducing post-vaccination fever appears to be come from the paracetamol dose give around the time of vaccination.

For the Bexsero® programme, the JCVI has recommended three doses of paracetamol to be given to infants receiving Bexsero® with their routine primary immunisations at 2 and 4 months or as part of the catch up programme at 3 and 4 months. Please refer to “*what adverse reactions are commonly associated with the administration of Bexsero®*” and “*guidance around use of liquid Paracetamol*”.

It is recommend that Bexsero® be administered in the **left thigh**, ideally on it's own, so that any local reactions can be monitored more accurately. If another vaccine needs to be administered in the same limb, then it must be given at least 2.5cm apart. The sites at which each vaccine was given should be noted in the individual's health records.

Guidance on the use of prophylactic infant paracetamol suspension with Bexsero® vaccine

Given that fever has been a very common adverse reaction in trials, and in light of concerns raised that an increase in fever may have a detrimental impact on the uptake of future immunisations, the JCVI recommended the use of prophylactic paracetamol at the time of immunisation with Bexsero®. The JCVI agreed that parents and healthcare professionals needed to be informed and educated about the change in advice regarding the use of prophylactic paracetamol and the reactogenicity of Bexsero® when administered concomitantly with other routine childhood immunisations to reduce anxiety and concerns.

This is a change to previous advice whereby the prophylactic use of antipyretics was not routinely recommended as there was some evidence that antipyretics lowered the immune response to some of the routine infant vaccinations. Additionally, it was also felt that a low grade fever was to be expected following immunisation and such a response was an indication that the vaccine was triggering the appropriate immunological response. The latter remains true. However, the incidence of fever greater than 38°C when Bexsero® is administered at the same time as other childhood vaccines is greatly increased. Additionally, a recent study showed that giving a dose of paracetamol around the time of vaccination followed by a further two doses at 6-8 hourly intervals, significantly reduced the rates of fever associated with vaccination without affecting the immunogenicity of Bexsero® or other routine infant vaccines. Therefore, parents should be advised to give 2.5ml (120mg/5ml) to their babies around the

time of immunisation or as soon as possible after the vaccines are administered. Parents will also be advised to give two further doses at 4-6 hourly intervals. (See Table 1 and 2)

Table 1. Dosage and timing of infant paracetamol suspension (120mg/5ml) for the routine immunisation programme at 2 and 4 months

Age of baby	Dose 1	Dose2	Dose 3
2 months	One 2.5ml as soon as possible after vaccination	One 2.5ml 4-6 hours after 1st dose	One 2.5ml 4-6 hours after 2nd dose
4 months	One 2.5ml as soon as possible after vaccination	One 2.5ml 4-6 hours after 1st dose	One 2.5ml 4-6 hours after 2nd dose

Table 2. Dosage and timing of infant paracetamol suspension (120mg/5ml) for the catch-up programme at 3 and 4 months

Age of baby	Dose 1	Dose2	Dose 3
3 months	One 2.5ml as soon as possible after vaccination	One 2.5ml 4-6 hours after 1st dose	One 2.5ml 4-6 hours after 2nd dose
4 months	One 2.5ml as soon as possible after vaccination	One 2.5ml 4-6 hours after 1st dose	One 2.5ml 4-6 hours after 2nd dose

Healthcare professionals should provide parents with the PHE meningococcal B vaccine leaflet before their 2 month primary vaccination appointment, for example when the parents register their baby at the practice or when they attend the 6-8 week check. This will alert parents to the need to buy liquid paracetamol in preparation for the 2 month immunisation appointment.

Until the programme becomes established, practices will be able to order liquid paracetamol sachets and accompanying syringes via ImmForm to parents who do not have timely access to over-the-counter (OTC) paracetamol and whose infant's are receiving their **first dose** of Bexsero® with their routine immunisations. This sachet is not provided as a "take-home" supply. Parents should be instructed to buy some infant strength liquid paracetamol to complete the two remaining recommended doses of paracetamol at home and in preparation for future meningococcal B vaccines. Most local pharmacies, supermarkets and many local stores stock liquid paracetamol suspension.

What should health professionals advise parents regarding the discrepancy between the Paracetamol packaging and patient information leaflet (PiL) advising a maximum of 2 doses of paracetamol post immunisations for infants aged 2 months.

The Commission on Human Medicines (CHM) has been consulted regarding the licencing restriction on Pharmacy (P) and General Sales List (GSL) paracetamol products which advise consulting a GP or pharmacist if more than 2 doses are required for a 2 month old infant post-immunisation. The reason for this licensing is to ensure early diagnosis of systemic bacterial infection. The CHM supported the PHE recommendations for 3 doses of paracetamol post-immunisation with MenB and supported use of paracetamol for up to 48 hours post immunisations if required to manage post-immunisation fever in 2 month olds. This recommendation is based on the likely-hood that fever is due to immunisation, this recommendation does not extend to fever at any other time and if the infant is otherwise unwell parents should trust their instincts and not delay seeking medical attention for the infant. It is hoped that infant paracetamol suspension manufacturers will update product packaging and literature in due course.

Parents can therefore be reassured that it is appropriate to follow PHE post-immunisation paracetamol dosing recommendations.

Healthcare professionals are reminded that in some circumstances the recommendations regarding vaccines given in the Green Book chapters may differ from those in the Summary of Product Characteristics (SPC) for a particular vaccine. When this occurs, the recommendations in the Green Book are based on current expert advice received from the JCVI and should be followed.

What do nurses need to supply or administer liquid paracetamol to parents of infants receiving Bexsero® ?

Despite liquid infant paracetamol being available to purchase from pharmacists and supermarkets nurses and midwives can only supply or administer medicines using a recognised process as set out in the Nursing and Midwifery Council's Standards for Medicines Managementⁱⁱ

To enable nursing colleagues to practice in accordance with this standard, Public Health England (PHE) will make available a Homely Remedy Protocol for the supply of liquid infant paracetamol.

Nurses should familiarise themselves with the Nursing and Midwifery Councils (NMC) [Standards for Medicines Management](#).

Does liquid paracetamol need to be administered when children receive their 12 months booster dose of Bexsero® ?

In clinical vaccine trials, the most common adverse reaction observed in infants and children under two years of age was a high rate of fever ($>38^{\circ}\text{C}$) when Bexsero®. was administered at the same time as other routine childhood vaccines. As a result, the JCVI recommended the use of prophylactic liquid paracetamol when infants receive Bexsero® at the same time as other routine childhood vaccines such as DTaP/IPV/Hib at 2, 3 and 4 months of age. As these vaccines are not administered as part of the 12 months booster vaccines, there is no additional requirement to offer liquid paracetamol at that time.

Can Ibuprofen be offered as an alternative to paracetamol to reduce post-vaccination fever after Bexsero® is administered with other routine vaccines?

In a head-to-head clinical trial of paracetamol versus ibuprofen to reduce post-vaccination feverⁱ, ibuprofen (two or three doses) did not reduce the rate or intensity of post-vaccination fever compared to the control arm where infants did not receive any anti-pyretic. This finding needs to be validated in further studies but this does suggest that paracetamol should be the only recommended anti-pyretic to reduce post-vaccination fever in infants. Ibuprofen should, therefore, not be recommended as an alternative to paracetamol in this instance.

Should parents be worried about fever after vaccination?

Fever after vaccination with or without Bexsero® is common and nearly always under 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®ⁱⁱⁱ. In the subsequent study of 364 infants receiving Bexsero® with or without paracetamol^{iv}, there wasn't a single case of febrile convulsion after any of the four vaccination visits).

What if my baby still has a fever after having had the three doses of paracetamol?

Some babies may still develop fever after vaccination, even after taking paracetamol. If your baby still has a fever after the first three doses of paracetamol but is otherwise well you can continue giving your baby paracetamol. You should always leave at least four hours between doses and never give more than four doses in a day. You should also keep your child cool by making sure they don't have too many layers of clothes or blankets on, and giving them plenty of fluids. If you are concerned about your baby at any time then trust your instincts and speak to your GP or call 111. Paracetamol is recommended for the prevention and treatment of fever after immunisation as there is evidence that it is safe and effective. If 48 hours after vaccination your baby still has a fever you should speak to your GP or call NHS 111 for advice.

What happens if the infant spits out the paracetamol suspension?

If the infant spits out or regurgitates at least half of the paracetamol suspension, then an additional dose (one dose of 2.5ml spoonful) of liquid paracetamol should be administered.

Does liquid paracetamol affect the immune response to the oral rotavirus vaccine?

Ideally the rotavirus and paracetamol should be given at separate times, but the live vaccine virus should not be affected by close sequential administration of paracetamol syrup. A small volume of paracetamol is unlikely to add significantly to the volume or nature of the fluid present in the gut and therefore should not prevent the vaccine virus replicating to levels that provide a stimulus to the immune system.

Vaccine eligibility for the routine meningococcal B immunisation programme

Why is the national programme being routinely offered to infants aged 2 months?

Meningococcal disease can affect all age groups, but the rates of disease are highest in the first two years of life. Cases increase from birth and peak around 5 months before declining. In considering the epidemiological and economic evidence as well as vaccine safety and efficacy, the JCVI decided to prioritise young infants with the aim of providing optimal protection as early as possible.

How will the programme be delivered?

Bexsero® will be available through General Practitioner (GP) services from the 1 September 2015. Parents attending their GP practice for their child's routine primary immunisations at 2, 3 and 4 months of age will be offered meningococcal B vaccine. The vaccination schedule and interval period administered to infants will be dependent on the child's date of birth and routine primary immunisation appointment due at the start of the programme on the 1 September 2015. Please refer to "*who is the vaccine recommended for?*" for further information on eligibility and scheduling of doses.

How effective is the vaccine

Bexsero® has been shown to be immunogenic in infants and toddlers. Vaccine-induced antibodies have been shown to be bactericidal (i.e. they kill the bacteria) against most meningococcal strains causing invasive disease in the UK. However, there is as yet no evidence regarding the effectiveness of Bexsero® in preventing meningococcal disease in a population since the vaccine has not yet 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 MenB vaccines derived from outer membrane vesicles (OMVs) of specific meningococcal B strains causing large outbreaks in their respective countries. A key limitation of these 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%.

How many doses are required to ensure protection?

Clinical trials for Bexero® in infants initially included three doses followed by a booster in the second year of life. Recent studies, however, indicate that two Bexsero® doses given two months apart at 2 and 4 months will induce bactericidal antibodies against meningococcus group B in nearly all infants. Vaccine responses will also be boosted after the 12-13month dose. Vaccine responses in 3 month-olds receiving 2 priming doses a month apart and 4 month-olds receiving a single priming dose may be lower but will also be boosted after the 12 months dose.

How long does protection last for?

The duration of protection following the recommended routine Bexsero® schedule has not been established, although in reviewing all of the available evidence, the JCVI agreed the most plausible duration of protection is 18 months following a two dose primary course and 36 months following the additional booster dose administered at 12 month. Bexsero® should, therefore, protect infants and toddlers during their period of highest risk of meningococcal B infection.

Should eligible infants born on or after 1 May 2015 who have already completed their primary immunisations be recalled to the practice to receive Bexsero®?

Infants that are born in the eligible cohorts, i.e. born on or after 1 May 2015 are eligible to receive Bexsero® until they reach 2 years of age.

The JCVI recommendation is that all infants in the eligible cohorts should receive the vaccine as part of their routine primary immunisation appointments. Subsequently, an

active call/recall system has not been recommended or agreed with General Practitioners, for those who may have already completed their primary immunisations before the start of the programme.

GPs who wish to immunise this small cohort of infants can use their discretion and recall infants back to the practice, offering additional immunisation appointments where required. GPs who wish to do this can claim the financial payment for administering the vaccine.

Can the vaccine be offered to infants outside of the national programme?

Parents whose children are **not** eligible to receive the vaccine as part of the national programme, but who wish to pay their child to be immunised with Bexsero® privately, should be encouraged to discuss their request with a private provider.

GPs are not able to charge their own patients (i.e. those registered at their practice) a private fee for the vaccine and should **not** use centrally procured stock for the national programme to vaccinate private patients. Parents seeking the vaccine privately should be made aware that they will be liable for the full costs of the vaccine and any additional administration charges that the private provider may apply.

Those of any age in clinical risk groups including an absent or dysfunctional spleen or known complement deficiency should be immunised in accordance with the schedule for [immunisation of individuals with underlying medical conditions; green book chapter 7](#)

Vaccine administration

How is Bexsero® administered?

Bexsero® should be administered via intramuscular injection (IM) into the infant's **left thigh** (antereolataral aspect).

The vaccine comes in a box that contains a prefilled syringe with a volume of 0.5mls. 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 physical appearance (i.e. not an homogenous suspension) or signs of foreign particulate are observed after shaking.

Where is Bexsero administered?

As Bexsero® is a newly licensed vaccine that is subject to additional monitoring under the black triangle labelling scheme by the Medicines and Healthcare Regulatory Agency (MHRA), it is recommended that Bexsero be administered on its own in the **left thigh** so that any local reactions can be monitored more accurately and reported to the MHRA using the [Yellow Card Scheme](#).

Where it is not practically possible to administer Bexsero® on its own, other routine vaccines can be administered in the left thigh at the same time as Bexsero rather than delaying immunisations, i.e at 12 months of age. If more than one vaccine needs to be administered in the same limb, then it must be given at least 2.5cm apart. **The sites at which each vaccine was given should be noted in the individual's health records.**

What is the shelf life of Bexsero®

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. However, initial vaccine supplies will have a shorter-life and expire in **April 2016**. It is recommended that health professionals only order what they need for a 2-4 week period rather than over-ordering.

To ensure vaccines are ordered, stored and monitored as per national recommendations, healthcare professionals should familiarise themselves with Public Health England's [Protocol for ordering, storing and handling of vaccines](#)

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, healthcare professionals should consider the benefit-risk prior to administering this vaccine to subjects with known history of hypersensitivity to latex^v

For a full list of excipients, healthcare professionals 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, healthcare professionals 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, healthcare professionals should read the manufacturer's [Summary of Products Characteristics \(SPCm\)](#).

Should Bexsero® be administered separately to other vaccines?

Bexsero® can be given at the same time as the other vaccines administered as part of the routine childhood immunisation programme, including pneumococcal, measles, mumps and rubella (MMR), diphtheria, tetanus, pertussis, polio and Hib. It is recommended that Bexsero® be given in the **left thigh**, ideally on its own, so that any local reactions can be monitored more accurately. If another vaccine needs to be administered in the same limb, then it must be given at least 2.5cm apart. **The sites at which each vaccine was given should be noted in the individual's health records.**

What should I do if a parent is concerned about the number of vaccines being administered to their child in one session?

It is understandable that some parents may become concerned about the number of vaccines being administered in one session, particularly at 2 and 12 month of age

when four vaccines are scheduled to be administered. Whilst these concerns are understandable, parents should be reassured by confident and knowledgeable healthcare professionals that the aim of immunisation is to provide protection against harmful diseases at the very earliest opportunity. Studies have demonstrated that there are no harmful effects from administering multiple vaccines in one session and there is no evidence to support arguments of “overloading” the immune system. From the moment a child is born, they are continually being exposed to a huge number of bacteria and viruses on a daily basis that the immune system is able to cope with and as a result becomes stronger^{vi}. Additionally, administering multiple vaccines in one session is a routine occurrence in most countries around the world with no evidence of harmful effects.

What should I do if a parent requests Men B vaccine to be administered separately to the other routine primary immunisations?

Parents should be discouraged from delaying immunisation as this inevitably delays protection. The immunisation schedule has been designed to ensure optimal protection against diseases that are most common in the very young such as whooping cough, pneumococcal, Hib and meningococcal disease. These diseases can be life-threatening and it is important for children to receive protection at the earliest possible opportunity.

Those who request for their child’s immunisations to be separated, thus leading to a delay in protection, should be informed of the potential increased risk of disease. Additionally healthcare professionals are encouraged to identify the reasons for such requests as many parents may be concerned about the number of vaccines administered in one session. Whilst it is understandable that parents may be concerned, studies have clearly demonstrated that there are no harmful effects of administering more than one vaccine in one session. Parents can also be reassured that offering multiple vaccines in this way is a routine occurrence around the world with no harmful effects being identified. For further guidance, please see “*What should I do if a parent is concerned about the number of vaccines being administered to their child in one session?*”

What should I do if Bexsero® was not administered at the routine primary immunisation appointment?

In circumstances whereby the GP practice has delayed the administration of Bexsero®, additional immunisation appointments should be offered to ensure that eligible infants are immunised according to their eligibility. As Bexsero® can be administered at any time before or after other routine primary immunisations, GP practices should recall the infant as soon as practically possible.

It is important for infants to be immunised in accordance with the immunisation schedule that they were eligible to receive, observing the recommended minimum interval periods between primary doses. For example, for those eligible to receive the routine schedule, a 2 month interval period should be observed between the first and second primary doses of vaccine.

If Bexsero® is administered separately to other routine primary immunisations, the use of liquid paracetamol does not need to be advised as the risk of fever is reduced.

Can Bexsero® be administered at the same time as MenC or MenACWY vaccines?

Two studies assessing protein-based meningococcal B vaccines given with the MenACWY vaccines reported similar vaccine responses with no significant adverse events. Preliminary results from an on-going, manufacturer-sponsored clinical trial in children receiving the meningococcal B vaccine co-administered with MenC conjugate vaccine in South America, do not indicate any safety concerns. Since Bexsero® is a protein-based vaccine and both MenC and MenACWY are conjugate vaccines with no shared antigens, interference with vaccine responses is unlikely.

Therefore, currently available evidence indicates that Bexsero® can be safely co-administered with MenC and MenACWY conjugate vaccines and other conjugate vaccines (pneumococcal, Hib) without affecting the immune response to either vaccines.

Does Bexsero® provide cross protection against other meningococcal capsular groups, such as Men A, C, W and Y?

Whilst Bexsero has broad coverage against most Men B strains causing invasive meningococcal disease (IMD) in England, it does not offer complete protection. Similarly studies to demonstrate protection against other capsular strains remain on-going. Thus individuals requiring protection against ACWY should receive the ACWY vaccine and should not assume to be protected against these capsular groups even if they have received a complete course of Bexsero®.

The manufacturer's Summary of Product Characteristics (SPCm) states that infants under six months of age should receive three doses of Bexsero® with a minimum of one month interval in addition to the booster dose at 12 month of age. Why is Bexsero® only being recommended as a two dose schedule in infants aged under 6 months?

As yet unpublished findings of a clinical trial have shown that nearly all infants develop bactericidal antibodies against MenB following two doses of Bexsero® given two months apart and this finding formed the basis for the JCVI recommendation for a 2+1 schedule.

Healthcare professionals are reminded that in some circumstances the recommendations regarding vaccines given in the Green Book may differ from those in the Summary of Product Characteristics for a particular vaccine. When this occurs, the recommendations in the Green Book are based on current expert advice received from the JCVI and this advice should be followed.

Why are infants in the 'catch-up' cohort being offered a different schedule (3, 4 and 12 month or 4 and 12 month) to that recommended for the routine cohort (2, 4 and 12 month)?

From the 1 September 2015, children born on or after 1 May 2015 will be offered at least one dose of Bexsero as part of their routine immunisations at 3 and 4 months of age. These children will also receive a booster dose of Bexsero as part of the 12 months booster immunisations.

The aim of this JCVI recommendation is to extend protection to those infants who are most likely to benefit from the vaccine, before reaching an age when they are most at risk of meningococcal B disease, even if immunogenicity data for these modified schedules are limited. Additionally, children receiving a priming dose of Bexsero® in infancy should make a good response to the 12 months booster dose of Bexsero®.

Are infants born before the 1 May 2015 going to be offered Bexsero® as part of a catch up programme?

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.

What should I do if I have inadvertently administered the second dose of Bexsero® at 3 months of age to an infant following the routine schedule (2, 4 and 12 month)?

In the event that the second dose of Bexsero® is administered one month earlier than recommended, infants should be offered an additional dose of vaccine at 4 months to ensure protection against meningococcal B disease.

As Bexsero® has been associated with an increase in fever when administered concomitantly with other routine childhood vaccines, infants inadvertently given Bexsero® at 3 months should be given liquid paracetamol as recommended for the 2-month or 4-month Bexsero®.

Please refer to “what adverse reactions are commonly associated with the administration of Bexsero® ” and “guidance around use of liquid Paracetamol”.

What should I do if an infant following the routine schedule (2, 4 and 12 month) or catch-up schedule (3, 4 and 12 month) misses their second dose of Bexsero® at 4 months?

Bexsero® will only be offered with routine immunisation appointments. Infants who do not attend for their routine appointment at 4 months of age and consequently miss the second dose of Bexsero® should be offered the vaccine at the earliest opportunity or at their next visit to the practice. These infants should be managed according to the “vaccination of individuals with uncertain or incomplete immunisation status” to ensure they are up to date with all immunisations.

What should I do if an infant following the 1+1 catch-up schedule misses their first dose of Bexsero at 4months?

Eligible infants who do not attend for their routine appointment at 4 months of age and consequently miss the first dose of Bexsero® should be offered the vaccine at the earliest opportunity or at their next visit to the practice. Infants born on or after 1 May 2015 are eligible to receive the Men B vaccine until 2 years of age. These infants should be managed according to the “*vaccination of individuals with uncertain or incomplete immunisation status*” to ensure they are up to date with all immunisations.

What should I do if an infant who was born outside of the eligible cohorts inadvertently receives Bexsero®?

Infants born before 1 May 2015 are not recommended to receive Bexsero® and should not be offered additional meningococcal B vaccinations. Healthcare professionals should reassure parents that no further action is required and should report the administration error via their local governance system(s) so that appropriate action can be taken, lessons can be learnt and the risk of future errors minimised.

Parents who wish to complete the Men B vaccination course should be advised to seek the vaccine privately from a private healthcare provider. Please refer to the question “Can the vaccine be offered to infants outside of the national programme?”

What should I do if the vaccine was administered at less than the recommended dose?

In the event that Bexsero® is administered at less than the recommended dose, vaccination will need to be repeated because the dose that the infant received may not be sufficient to evoke a full immune response. Where possible, the dose of Bexsero® should be repeated on the same day or as soon as possible after.

As Bexsero® has been associated with an increase in rates of fever when administered concomitantly with other childhood vaccines, prophylactical paracetamol should be offered with this Bexsero® dose. Please refer to “*what adverse reactions are commonly associated with the administration of Bexsero®*” and “*guidance around use of liquid Paracetamol*”.

In the event that the additional dose of Bexsero cannot be administered at the same visit or day, arrangements should be made to administer the additional dose as soon as possible, thus not to delay future doses.

Where should I administer Bexsero® if four or more vaccines need to be administered at the same time, i.e at 12 month booster?

Infants attending for their routine booster immunisations at 12 months are likely to receive at least four vaccines that are required to be administered at the same time. It is recommended that Bexsero® should be administered in the **left thigh**, ideally on its own, with other booster immunisations being administered into the remaining three limbs. If another vaccine needs to be administered in the same limb, then it must be given at least 2.5cm apart. The sites at which each vaccine was given should be noted in the individual’s health records.

Healthcare professionals are reminded that some infants may receive additional vaccines as part of a selective immunisation programme around 12 months of age, such as Hepatitis B and BCG. Healthcare professionals are reminded that vaccines should not be administered into the same limb as the BCG vaccine for a period of 3

months from administration. Healthcare professionals are encouraged to discuss any recent immunisations at the 12 month booster appointment with parents.

Can Bexsero® be administered earlier than 8 weeks (2 months) to eligible infants travelling abroad?

The immunisation schedule has been designed to provide early protection against infections that are most dangerous for the very young. Recommendations for the age at which vaccines should be administered are informed by the age-specific risk for a disease, the risk of complications and the ability to respond to the vaccine. Therefore, vaccines should be administered as closely to the schedule as possible.

In certain circumstances, some vaccines may be administered slightly earlier, i.e. at 6 weeks for those infants that are due to travel to another country. This is only advisable where the benefit of immunisation outweighs the risk, i.e. in providing early protection against childhood diseases that are common in most other countries. This rationale does not apply to meningococcal B disease as the level of risk is higher in the UK than in other countries. Additionally Bexsero® is only licensed for use from the age of 2 months, thus those wishing to administer the vaccine earlier than recommended will be using an “off-label” licensed vaccine that will require a patient specific direction (PSD).

Administering the vaccine earlier than recommended will also affect the nurse’s ability to supply or administer infant strength liquid paracetamol to infants aged less than 8 weeks as this contraindicates PHE's homely remedy protocol. In these cases, the GP will be required to clinically assess and prescribe liquid paracetamol based on the infant’s weight at the time of vaccination.

For these reasons, we are not recommending that Bexsero® is administered earlier than recommended for travel purposes. Infants should be offered other routine primary immunisations prior to travel and delay the administration of Bexsero® until the child arrives back in the UK.

Useful links

- Public Health England/ NHS England. Introduction of meningococcal B immunisation for infants <https://www.gov.uk/government/publications/menb-vaccination-introduction-from-1-september-2015>
- Public Health England. Immunisation against infectious diseases: meningococcal chapter 22. <https://www.gov.uk/government/publications/meningococcal-the-green-book-chapter-22>
- Public Health England. JCVI recommendation to introduce new MenB vaccine if available at a low price will protect young babies and children. [internet] <https://www.gov.uk/government/news/phe-welcomes-prospect-of-new-meningitis-b-vaccine>
- Meningitis Research Foundation: <http://www.meningitis.org/>
- Meningitis Now. <https://www.meningitisnow.org/>
- NHS Choices. <http://www.nhs.uk/conditions/Meningitis/Pages/Introduction.aspx>
- Joint Committee on Vaccination and Immunisation. <https://www.gov.uk/government/groups/joint-committee-on-vaccination-and-immunisation>

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<https://clinicaltrials.gov/ct2/show/results/NCT01392378?term=paracetamol+vaccine&rank=3§=X01256#all>

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^v 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/>

^{vi} Centre for Disease Control (CDC) 2012. Frequently Asked Questions about Multiple Vaccinations and the Immune System. [internet] accessed 11 June 2015.

<http://www.cdc.gov/vaccinesafety/Vaccines/multiplevaccines.html>