



Public Health
England

Protecting and improving the nation's health

Meningococcal B Vaccination

Information for healthcare professionals

About Public Health England

Public Health England exists to protect and improve the nation's health and wellbeing, and reduce health inequalities. We do this through world-leading science, knowledge and intelligence, advocacy, partnerships and the delivery of specialist public health services. We are an executive agency of the Department of Health and Social Care, and a distinct delivery organisation with operational autonomy. We provide government, local government, the NHS, Parliament, industry and the public with evidence-based professional, scientific and delivery expertise and support.

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Contents

About Public Health England	2
Introduction	4
Meningococcal disease	4
The MenB vaccine (Bexsero)	6
Vaccine response and efficacy	7
The Meningococcal B immunisation programme	9
Adverse reactions commonly associated with the administration of Bexsero	12
Prophylactic paracetamol	13
Vaccine preparation and administration	19
Vaccine administration errors	23
Useful links	25

Introduction

In September 2015, a vaccine against meningococcal B disease (MenB) was added to the childhood immunisation programme as part of the routine schedule in England. This document provides further information for healthcare practitioners about the MenB vaccine Bexsero and the MenB vaccine programme.

Meningococcal disease

Meningococcal disease is caused by invasive infection with the bacterium *Neisseria meningitidis*. 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.

Prior to the introduction of the infant MenB and teenage MenACWY immunisation programme, MenB was responsible for 58% (418/724) of all cases of invasive meningococcal disease in 2014 to 2015¹.

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 2 to 7 days and the presentation of disease ranges from severe acute and overwhelming features, to insidious with mild prodromal symptoms.

¹ Public Health England. Invasive meningococcal disease (laboratory reports in England): 2014/2015 annual data by epidemiological year. Health Protection Report. 9(38): 23 October 2015. Available at: www.gov.uk/government/uploads/system/uploads/attachment_data/file/498057/hpr3815_imd-crrctd.pdf

Risk of meningococcal disease

Meningococcal disease can affect all age groups, but the rates of disease are highest in children under 2 years of age. Meningococcal cases increase from birth and peak at 5 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 MenB vaccine (Bexsero)

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

Bexsero is a multi-component inactivated vaccine made from 3 *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).

Vaccine excipients

Bexsero does not contain thiomersal or porcine gelatine but the tip cap of the syringe may contain natural rubber latex (see section on latex allergy). For a full list of excipients, healthcare professionals should read the [Manufacturer's summary of product characteristics \(SPC\)](#).

Vaccine response and efficacy

Bexsero has been shown to be immunogenic in infants and toddlers. Clinical trials for Bexsero in infants initially included 3 doses followed by a booster in the second year of life. However, clinical trials indicate that 2 Bexsero doses given 2 months apart can induce protective bactericidal antibodies against MenB in nearly all infants². Vaccine responses will also be boosted after the 12-month dose. In the limited catch-up cohort of infants born in May and June 2015, vaccine responses in 12 week olds receiving 2 priming doses a month apart and 16 week olds receiving a single priming dose may have been lower but will have been boosted by the 12-month dose.

Vaccine-induced antibodies have been shown to be bactericidal (they kill the bacteria) against most MenB strains causing invasive disease in the UK. However, Bexsero was licensed on immunogenicity studies because the incidence of MenB disease was 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 responsible for large outbreaks in their respective countries. A key limitation of these vaccines 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 Joint Committee on Vaccination and Immunisation (JCVI) assumed that 88% of meningococcal B strains causing invasive disease in England would be covered by Bexsero and vaccine effectiveness against these strains would be 95%.

Within 10 months of implementing Bexsero in to the UK infant immunisation programme, the vaccine was found to be 83% effective against all MenB disease in vaccine eligible infants, which was equivalent to 94% protection against the predicted 88% vaccine-preventable strains. Moreover, MenB cases in the vaccine-eligible cohort had nearly halved compared to the 4 years prior to Bexsero introduction.³

² Bexsero Summary of Product characteristics (SPC) available at www.medicines.org.uk/emc/product/5168/smpc [Accessed 13 December 2018]

³ Parikh S, Andrews N, Beebeejaun K et al. Effectiveness and impact of a reduced infant schedule of 4CMenB vaccine against group B meningococcal disease in England: a national observational cohort study. *Lancet*. 2016 Dec 3;388(10061):2775-2782. Abstract available at: www.ncbi.nlm.nih.gov/pubmed/28100432

Cross protection against other meningococcal capsular groups

Whilst Bexsero has broad coverage against most MenB strains causing invasive meningococcal disease (IMD) in England, it does not offer complete protection. Studies to demonstrate protection against other capsular strains remain on-going, Although there is some evidence confirming protection against other meningococcal capsular groups, including the current MenW strain responsible for the national outbreak in the UK, individuals requiring protection against meningococcal serogroups A, C, W and Y should receive the MenACWY conjugate vaccine and should not assume to be protected against these capsular groups even if they have received a complete course of Bexsero.

Duration of protection

The duration of protection following the recommended routine Bexsero schedule has not been established, although in reviewing all the available evidence, the JCVI agreed the most plausible duration of protection is 18 months following a 2-dose primary course and 36 months following the additional booster dose administered at 12 months of age. These estimates were based on the waning antibody responses observed in infant clinical trials. Bexsero should, therefore, protect infants and toddlers during their period of highest risk of meningococcal B infection.

Vaccine supply

Bexsero for use in the national programme should be ordered via the ImmForm website. Healthcare professionals should refer to the ImmForm website for up to date information on vaccine availability.

Shelf life of Bexsero

Bexsero has a shelf life of 2 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. It is recommended that health professionals only order what they need for a 2 to 4 week period.

To ensure vaccines are ordered, stored and monitored as per national recommendations, healthcare professionals should familiarise themselves with the recommendations made in [Chapter 3 of the Green book 'Storage, distribution and disposal of vaccines'](#).

The Meningococcal B immunisation programme

Schedule

It is recommended that MenB vaccine be administered together with the other primary immunisations at 8 weeks and sixteen weeks and the third dose on or after their first birthday (2+1 schedule).

These recommendations differ from the [Bexsero Summary of Product Characteristics](#) and healthcare professionals are reminded that where recommendations regarding vaccines given in the Green Book differ from those in the Summary of Product Characteristics for a particular vaccine, the recommendations in the Green Book, which are based on current expert advice received from the JCVI, should be followed.⁴

The basis of the JCVI recommendation for a 2+1 schedule is from studies of clinical trials that have shown that nearly all infants develop bactericidal antibodies against MenB vaccine antigens following 2 doses of Bexsero given 2 months apart².

Eligibility for the meningococcal B immunisation programme

Following review of the epidemiological and economic evidence as well as vaccine safety and efficacy, the JCVI recommended that young infants were prioritised with the aim of providing optimal protection as early as possible because they have the highest disease incidence.

The meningococcal B vaccine, Bexsero, became available through General Practitioner (GP) services from the 1 September 2015. Infants attending their GP practice for their routine primary immunisations at 8 weeks and 16 weeks of age should be offered meningococcal B vaccine along with their routine infant immunisations followed by a booster on their first birthday.

Children remain eligible to receive Bexsero vaccine until they reach 2 years of age.

Infants in the eligible cohort who have not received MenB vaccine at the recommended ages and are still under 2 years of age should commence vaccination only if 2 doses of the vaccine can be administered before their second birthday.

⁴ Public Health England. Immunisation against infectious disease. Immunisation procedures. Chapter 4. [Accessed 13 December 2018]. www.gov.uk/government/publications/immunisation-procedures-the-green-book-chapter-4

If the course is started very late (for example at 23 months of age), the interval between doses can be reduced to 4 weeks to ensure 2 doses can be administered before the infant reaches 2 years of age.

MenB vaccine is not indicated for children after their second birthday unless they are in a risk group.

Catch-up programme

When the MenB vaccination programme commenced on 1 September 2015, a limited opportunistic catch-up (without active recall) was implemented for those infants born between 01 May 2015 and 30 June 2015.

Infants born in May 2015 would have been eligible for Bexsero with their routine 3 and 4-month immunisations, while those born in June 2015 would have been eligible for Bexsero with their routine 4-month immunisations. All infants eligible for the primary Bexsero immunisation schedule should also receive a booster on their first birthday.

Infants born before 1 May 2015

After reviewing the cost-effectiveness model, the JCVI did not recommend a catch-up programme for infants born before 1st May 2015. As 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, the priority of the MenB immunisation programme is to ensure that Bexsero is offered routinely to infants before the peak in incidence of disease.

Children born before 1 May 2015 are not eligible for the MenB vaccine unless they are in a clinical risk group.

Infants aged 6 to 8 weeks of age

Infants may receive their first dose of primary immunisations from 6 weeks of age in exceptional circumstances (such as pre-travel) but it is not routinely recommended to offer infants their primary immunisations before 8 weeks of age.

Bexsero vaccine is licensed from 8 weeks of age. If administered to infants between 6 and 8 weeks of age, a patient specific direction (PSD) will be required as the patient group direction (PGD) does not include infants younger than 8 weeks of age. Parents should also be informed that paracetamol prescribing guidance will usually advise that infants younger than 2 months of age should not receive paracetamol. As paracetamol is

recommended to be administered around the time of Bexsero vaccination, the advice in table 1 should be followed and infants aged 6 to 8 weeks of age should receive the same dose of infant paracetamol suspension (2.5mls) as an 8 week old baby.

Parents should be provided with the PHE leaflet on paracetamol use⁵ and reassured that paracetamol is given to infants younger than 2 months of age when clinically required (for example to infants in SCBU and those admitted to hospital in the first few weeks of life).

Children 2 years of age and older

If Bexsero vaccine is clinically indicated for those aged 2 years and older (for example for those with asplenia, splenic dysfunction or complement disorders), the vaccine can be prescribed but must be sought separately from the national immunisation stock and there will be no reimbursement as part of the national programme.

Some parents may opt to make alternative arrangements to have their child immunised with the MenB vaccine if their child does not meet the eligibility criteria for the routine programme. Parents should be informed that if the vaccine is not clinically indicated and a private arrangement is made for vaccination, the provider may charge for the service as this arrangement is outside of the national programme.

⁵ Using paracetamol to prevent and treat fever after MenB vaccination. NHS 2018 Available at https://assets.publishing.service.gov.uk/government/uploads/system/uploads/attachment_data/file/717281/PHE_paracetamol-menB-A4-2018_01.pdf [Accessed 13 December 2018]

Adverse reactions commonly associated with the administration of Bexsero

In clinical trials, the most common adverse reaction observed in infants and children under 2 years of age was a high rate of fever ($>38^{\circ}\text{C}$) when Bexsero was administered with the other routine childhood vaccines (also see page 13).

Other very common adverse reactions (occurring in more than 1 in 10 children), 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 no longer subject to additional monitoring under the black triangle (▼) labelling scheme by the Medicines and Healthcare Regulatory Agency (MHRA) but all suspected adverse reactions should continue to be reported to the MHRA using the [Yellow Card scheme](#).

Latex allergy

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 latex². For latex allergies other than anaphylactic allergies (for example a history of contact allergy to latex gloves), vaccines supplied in vials or syringes that contain latex can be administered.

For a full list of excipients, healthcare professionals should read the manufacturers' Summary of Products Characteristics (SPC).

Prophylactic paracetamol

Following vaccination, infants may experience symptoms such as fever, irritability and reduced appetite. Infants receiving prophylactic paracetamol when Bexsero is administered with routine immunisations are less likely to experience these symptoms.

Fever and the use of prophylactic paracetamol 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 is 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 were very rarely reported. In one of the largest Bexsero trials, 1,885 infants were recruited and vaccinated at 4 different visits without paracetamol prophylaxis, and only 1 infant developed a febrile convulsion 2 days after receiving Bexsero⁶. In the subsequent study of 364 infants receiving Bexsero with or without paracetamol⁷, there wasn't a single case of febrile convulsion after any of the 4 vaccination visits.

If a parent suspects that their infant has had a convulsion or another serious reaction following administration of any vaccine, including Bexsero, they should be advised to seek medical attention and report it via the Yellow Card Scheme.

Risk of fever when Bexsero is administered at the same time as other routine childhood vaccines

In one clinical trial, fever ($\geq 38.0^{\circ}\text{C}$) was reported in 51% to 62% of infants receiving Bexsero and routine vaccines administered together although high fever ($\geq 39.0^{\circ}\text{C}$) 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.⁶ However, only 6 of the 1,885 recruited infants attended hospital because of fever within 2 days after vaccination with Bexsero in this study.

⁶ Gossger N, Snape MD, Yu LM et al. European MenB Vaccine Study Group. Immunogenicity and tolerability of recombinant serogroup B meningococcal 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.

⁷ Prymula R1, Esposito S, Zuccotti GV et al. 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

In the study conducted by Prymula et al ⁷, 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. Fever was less common (39%) in infants receiving prophylactic paracetamol just before, or at the time of vaccination, followed by 2 further administrations by parents/guardians at 4 to 6-hour intervals after vaccination. Around 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 Bexsero was administered alone or with the routine vaccinations. The Prymula et al 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 study that did not include Bexsero,⁸ infants receiving 3 doses of paracetamol (at vaccination and at 6 to 8 hour intervals) were half as likely to develop post-vaccination fever, and also half as likely to develop high fever ($>39^{\circ}\text{C}$), when compared with infants receiving 2 doses of paracetamol (first dose at 6 to 8 hours after vaccination and another 6 to 8 hours later). This indicates that the greatest benefit in reducing post-vaccination fever appears to come from the paracetamol dose given around the time of vaccination.

For the Bexsero programme, the JCVI has recommended 3 doses of paracetamol to be given to infants receiving Bexsero with their routine primary immunisations at 8 weeks and 16 weeks. Prophylactic paracetamol is not recommended for the 12-month boosters because the infants are older, and rates of fever are similar with and without Bexsero administration at this age. Guidance on the use of liquid prophylactic paracetamol can be found overleaf.

Some babies may still develop fever after vaccination, even after taking paracetamol. Parents can be advised that if their baby still has a fever after the first 3 doses of paracetamol but is otherwise well, they can continue to follow PHE post-immunisation paracetamol dosing recommendations (also see page 17, paracetamol product licencing). There should always be at least 4 hours between doses and they should never give more than 4 doses in a day. The child should also be kept cool by making sure they don't have too many layers of clothes or blankets on, and they should be offered plenty of fluids. If there are any concerns about the baby at any time, advice should be taken from a GP or by calling 111. Information on the use of ibuprofen for post vaccination fever can be found on page 18.

⁸ ClinicalTrials.gov (2014). Study assessing life effect of medications to prevent fever on Prevenar13 (outcomes 18-21). Available at <https://clinicaltrials.gov/ct2/show/results/NCT01392378?term=paracetamol+vaccine&rank=3§=X01256#all> Accessed on 14 December 2018

If Bexsero is administered separately to other routine primary immunisations (for example at a different appointment), liquid paracetamol is not needed as the risk of fever is reduced.

Using prophylactic infant paracetamol suspension with Bexsero vaccine

As 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 as there is evidence that it is safe and effective⁹

The JCVI also advised that parents and healthcare professionals need to be informed and updated 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 any anxiety or concern.

This is a change to previous advice whereby the prophylactic use of antipyretics was not routinely recommended as there was some evidence that they 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, studies^{6,7} have shown that giving a dose of paracetamol around the time of vaccination followed by a further 2 doses at 6 to 8 hourly intervals significantly reduced the rates of fever associated with vaccination without affecting the immunogenicity of Bexsero or other routine infant vaccines.

It is recommended that parents should be advised to give 2.5ml (120mg/5ml) of infant paracetamol to their babies around the time of immunisation or as soon as possible after the vaccines are administered, and to give 2 further doses at 4 to 6 hourly intervals. (See Table 1).

Infants aged 6 to 8 weeks of age who are receiving a first dose of Bexsero early (for example infants travelling to another country before they reach 8 weeks of age), should receive infant paracetamol suspension as described in table 1 for infants aged 8 weeks.

⁹ JCVI position statement on use of Bexsero meningococcal B vaccine in the UK. March 2014. Available at https://assets.publishing.service.gov.uk/government/uploads/system/uploads/attachment_data/file/294245/JCVI_Statement_on_MenB.pdf [Accessed 13 December 2018]

Prophylactic paracetamol is not recommended for the 12-month boosters because the infants are older, and rates of fever are similar with and without Bexsero administration at this age.

Table 1. Dosage and timing of infant paracetamol suspension (120mg/5ml) for the routine immunisation programme at 8 and 16 weeks*

Age of baby	Dose 1	Dose2	Dose 3
8 weeks	One 2.5ml At the time of or as soon as possible after vaccination	One 2.5ml 4 to 6 hours after 1 st dose	One 2.5ml 4 to 6 hours after 2 nd dose
16 weeks	One 2.5ml At the time of or as soon as possible after vaccination	One 2.5ml 4 to 6 hours after 1 st dose	One 2.5ml 4 to 6 hours after 2 nd dose

*For premature babies, the dose should be calculated according to the infant's weight around the time of vaccination

Recommendations for premature babies

Infants born at <32 weeks gestation should receive the vaccine at the appropriate chronological age (age from date of birth) without correction for prematurity. The dose of prophylactic paracetamol should be calculated according to the infant's weight around the time of vaccination.

Alerting parents to the need to buy paracetamol prior to vaccination

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

When the programme was introduced, practices were able to order liquid paracetamol sachets and accompanying syringes via ImmForm. These are no longer available, and parents should be instructed to purchase infant strength liquid paracetamol and ensure that they are able to administer the recommended doses of paracetamol at the time of vaccination and at home for the next 2 days if needed (following both the first and third sets of primary immunisations at 8 and 16 weeks of age). Most local pharmacies, supermarkets and many local stores stock infant liquid paracetamol suspension.

Paracetamol product licencing

The Commission on Human Medicines (CHM) was consulted regarding the previous licencing restriction on Pharmacy (P) and General Sales List (GSL) paracetamol products which advised consulting a GP or pharmacist if more than 2 doses were required for an 8 week old infant post-immunisation. This was to ensure early diagnosis of systemic bacterial infection.

The licence was updated during 2016 and supports PHE recommendations for paracetamol use following Men B vaccination¹⁰ (also see table 1 above).

This recommendation is based on the likelihood 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 their infant. Parents can be reassured that it is appropriate to follow PHE post-immunisation paracetamol dosing recommendations. Advice on bottles and sachets of infant paracetamol has now been changed to reflect the recommendation that paracetamol can be given for relief of fever after vaccinations from 2 months of age. If Bexsero is administered to an infant aged 6 to 8 weeks, the paracetamol recommendations in table 1 should be followed.

Liquid paracetamol supply

There is no longer a central supply of liquid paracetamol for infants having MenB vaccination. 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 Management¹¹

Public Health England (PHE) made available a Homely Remedy Protocol for the supply of liquid infant paracetamol at the time of introduction of the MenB programme. This expired on 31 August 2017. Nurses should advise parents that they need to ensure that they have liquid paracetamol available for their infant at the time of vaccination and at home for the next 2 days if needed.

¹⁰ Public Health England. Using paracetamol to prevent and treat fever after MenB vaccination. Available at: https://assets.publishing.service.gov.uk/government/uploads/system/uploads/attachment_data/file/717281/PHE_paracetamol-menB-A4-2018_01.pdf Accessed 24 December 2018

¹¹ Nursing and Midwifery Council (2008) Standards for Medicines Management. Available at <http://www.nmc.org.uk/standards/additional-standards/standards-for-medicines-management/> Accessed 14 December 2018

Ibuprofen as an alternative to paracetamol to reduce post-vaccination fever after Bexsero

In a head-to-head clinical trial of prophylactic paracetamol versus ibuprofen to reduce post-vaccination fever⁵, ibuprofen (2 or 3 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 suggests that paracetamol should be the only recommended prophylactic anti-pyretic to reduce post-vaccination fever in infants. For this reason, ibuprofen should not be used as an alternative to prophylactic paracetamol at the time of vaccination but can be used for treatment if the infant subsequently develops a post-vaccination reaction, including fever. If an infant still has a fever 48 hours after vaccination or if parents are concerned about their infant's health at any time, then advice should be taken from a GP or NHS 111.

Incomplete dose of liquid paracetamol

If the infant spits out or regurgitates at least half of the paracetamol suspension, then an additional dose (1 dose of 2.5ml spoonful) of liquid paracetamol should be administered. If the second dose is spat out, do not give a third dose.

Administering oral rotavirus vaccine at the same time as liquid paracetamol

If possible, give Rotarix vaccine and prophylactic paracetamol with a short interval between them. Although the live vaccine virus is unlikely to be affected by close sequential administration of a small volume of paracetamol syrup, leaving a short interval between the vaccine and the paracetamol syrup may reduce the chance of the rotavirus vaccine being vomited back up.

Vaccine preparation and administration

Preparing Bexsero vaccine

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 a homogenous suspension that should be administered immediately.

The vaccine should not be administered where there are variations in physical appearance (such as having the appearance of a non-homogenous suspension) or there are signs of foreign particulate observed after shaking.

When newly licensed, Bexsero vaccine was subject to additional monitoring under the black triangle labelling scheme by the Medicines and Healthcare Regulatory Agency (MHRA). Although this vaccine no longer has black triangle status, it is recommended that it continues to be administered on its own into the anterolateral aspect of the left thigh via intramuscular injection. This is to enable accurate monitoring of local reactions which can then be reported to the MHRA using the [Yellow Card Scheme](#).

Administering Bexsero vaccine with other vaccines

Bexsero can be given at the same time as, or at any interval from, all the other vaccines administered as part of the routine childhood immunisation programme.

Bexsero vaccine contraindications

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 the local PHE health protection team.

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

- a confirmed anaphylaxis to a previous dose of the vaccine
- OR
- 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 \(SPC\)](#).

Administering Bexsero to infants less than 12 months of age

It is recommended that Bexsero be administered via intramuscular (IM) injection into the anterolateral aspect of 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 they must be given at least 2.5cm apart. The site at which each vaccine is given should be noted in the individual's health records.

Administering Bexsero at 12 months of age

Infants attending for their routine booster immunisations at 12 months are likely to receive at least 4 vaccines at that same appointment. 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 3 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 encouraged to discuss any recent immunisations at the 12-month booster appointment with parents. This is because some infants may receive additional vaccines, such as Hepatitis B and BCG, as part of a selective immunisation programme at around 12 months of age and additional vaccines should not be administered into the same limb as the BCG vaccine for a period of 3 months from administration.

Administering multiple vaccines in 1 session

Some parents may be concerned about the number of vaccines being administered in 1 session, particularly at 8 weeks and 12 months of age when 4 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 1 session¹² 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 daily that the immune system can cope with⁹. Additionally, administering multiple vaccines in 1 session is a routine occurrence in most countries around the world with no evidence of harmful effects.

Delaying vaccination

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 pneumococcal disease, Hib, meningococcal disease and pertussis (whooping cough). These diseases can be life-threatening, and it is important for children to receive protection at the earliest possible opportunity.

Parents who request for their child’s immunisations to be separated should be informed of the potential risks of delaying protection against a 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 1 session. Such parents can be reassured that studies have clearly demonstrated that there are no harmful effects of administering more than 1 vaccine in 1 session⁹. 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.

¹² Centre for Disease Control (CDC). Frequently Asked Questions about Multiple Vaccinations and the Immune System. www.cdc.gov/vaccinesafety/Vaccines/multiplevaccines.html

Administering Bexsero at the same time as MenC or MenACWY vaccines

A phase II trial in healthy adult laboratory workers explored the safety and immunogenicity of 4CMenB and ACWY-CRM when administered concomitantly. This trial concluded that concomitant use is both safe and immunogenic¹³.

A clinical trial in children receiving the meningococcal B vaccine co-administered with MenC conjugate vaccine in South America, found that immune responses to both the MenB and MenC vaccines were satisfactory and although reactogenicity was higher for concomitant vaccine administration, did not identify any safety concerns¹⁴. Since Bexsero is a protein-based vaccine and both MenC and MenACWY are polysaccharide 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 (for example pneumococcal and Hib vaccines) without affecting the immune response to either vaccine.

¹³ Findlow J, et al. Safety and immunogenicity of a four-component meningococcal group B vaccine (4CMenB) and a quadrivalent meningococcal group ACWY conjugate vaccine administered concomitantly in healthy laboratory workers. *Vaccine* (2015), <http://dx.doi.org/10.1016/j.vaccine.2015.05.027>

¹⁴ Safadi M, Martinon-Torres F, Weck L et al. Immunogenicity and safety of concomitant administration of meningococcal serogroup B (4CMenB) and serogroup C (MenC-CRM) vaccines in infants: A phase 3b, randomized controlled trial. *Vaccine* 11 April 2017, 35(16), 2052-2059

Vaccine administration errors

Bexsero administered earlier than 8 weeks of age

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, the first set of primary immunisations (including MenB) can be administered from 6 weeks of age, for example for infants that are due to travel to another country before they reach 8 weeks of age when the primary immunisations are usually given. However, Bexsero is licensed for use from the age of 8 weeks so if it is administered earlier than this, it should be treated as an “off-label” use of a licensed vaccine and will require a patient specific direction (PSD) for its supply and administration.

If Bexsero is inadvertently given prior to 8 weeks of age but the infant is over 6 weeks of age, this should count as a valid dose and does not need to be repeated. Doses given before 6 weeks of age should be discounted and the scheduled doses should still be given at 8 and 16 weeks of age.

Inadvertent early administration of second dose

If the second dose of Bexsero is inadvertently administered earlier than recommended (for example with the 12-week immunisations), infants should be offered an additional dose of vaccine at 16 weeks 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 12 weeks should be given liquid paracetamol as recommended for the 8 week or 16 week Bexsero dose.

For further information, please refer to the sections titled “adverse reactions commonly associated with the administration of Bexsero” and “using prophylactic infant paracetamol suspension with Bexsero vaccine”.

Missed doses of Bexsero vaccine

Infants who have missed scheduled doses of MenB, or who have not received the recommended number of doses for their age, should be offered the vaccine at the earliest opportunity. These infants should be managed according to the “**vaccination of individuals with uncertain or incomplete immunisation status**” algorithm to ensure they are up to date with all immunisations.

MenB vaccination is offered to children up to their second birthday. Infants younger than 12 months should receive 2 doses of MenB vaccine 2 months apart. They should also then receive a MenB booster vaccine on their first birthday, ensuring at least a 2-month interval between the MenB doses. Children aged 1 year to less than 2 years who received less than 2 doses in their first year of life should receive 2 doses of MenB at least 2 months apart. This interval can be reduced to a minimum of 4 weeks to ensure 2 doses are able to be administered before the age of 2 years.

Vaccine inadvertently administered to child born before 1 May 2015

Children born before 1 May 2015 are not recommended to receive Bexsero and should not be offered additional meningococcal B vaccinations unless they are in one of the identified risk groups recommended to receive the vaccine (asplenia, splenic dysfunction or complement disorders). 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.

Incomplete dose administered

If less than the recommended dose of Bexsero is administered, the 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 as the incomplete dose was administered.

If the additional dose of Bexsero cannot be administered at the same visit or on the same day, arrangements should be made to administer the replacement dose as soon as possible, in order not to delay future doses.

As Bexsero has been associated with an increase in rates of fever when administered concomitantly with other childhood vaccines, prophylactic paracetamol should be offered with replacement Bexsero doses. For further information, please refer to the sections titled “adverse reactions commonly associated with the administration of Bexsero” and “using prophylactic infant paracetamol suspension with Bexsero vaccine”.

Useful links

Public Health England/ NHS England. Introduction of meningococcal B immunisation for infants

www.gov.uk/government/publications/menb-vaccination-introduction-from-1-september-2015

Public Health England. Immunisation against infectious diseases: meningococcal chapter 22.

www.gov.uk/government/publications/meningococcal-the-green-book-chapter-22

Clinical and public health management of meningococcal disease

www.gov.uk/guidance/meningococcal-disease-clinical-and-public-health-management

Meningococcal B (MenB) vaccination programme documents and resources

www.gov.uk/government/collections/meningococcal-b-menb-vaccination-programme

Men B vaccine coverage estimates

www.gov.uk/government/publications/meningococcal-b-immunisation-programme-vaccine-coverage-estimates

Meningitis Research Foundation:

www.meningitis.org/

Meningitis Now.

www.meningitisnow.org/

NHS UK Meningitis overview.

www.nhs.uk/conditions/Meningitis/Pages/Introduction.aspx

Joint Committee on Vaccination and Immunisation.

www.gov.uk/government/groups/joint-committee-on-vaccination-and-immunisation