Immunisation against meningococcal B disease for infants aged from two months

HSC Public Health Agency

Information for healthcare professionals

Disclaimer: This material has been prepared before the updated version of *Immunisation against Infectious Disease - The Green Book* has been published.

Background

In 2010, the Joint Committee on Vaccination and Immunisation (JCVI)† 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 12 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 serogroups, 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 decreased significantly, with capsular group B (MenB) accounting for approximately 80% of all laboratory-confirmed cases in Northern Ireland over the past five years.

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 5–11% 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 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.

† 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.

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 two and four months of age and just after the first birthday, following a 2+1 schedule.

Routine cohort

Starting on 1 September 2015, all infants born on or after 1 July 2015 will be eligible for the meningococcal B vaccine, which will be administered together with the other primary immunisations at two months, four months and just after the first birthday.

Catch-up cohort

There will also be a catch-up programme for infants born from 1 May 2015 to 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 presenting for their routine primary immunisations from 1 September 2015 are eligible to receive the vaccine as outlined here:

Cohort	Dates of birth	Recommended immunisation schedule
Routine	Those born on or after 1 July 2015	Two and four months and just after the first birthday (2+1)
Catch-up	Those born on or after 1 May to 30 June 2015	*If second routine primary immunisation appointment due on or after 1 September then follow this schedule: Three and four months and just after the first birthday (2+1)
		*If third routine primary immunisation appointment due on or after 1 September then follow this schedule: Four months and just after the first birthday (1+1)

*Bexsero® will only be offered with routine immunisation appointments to those in the catch-up cohort.

Infants born before 1 May 2015 are **not** eligible to receive the meningococcal B vaccine.

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).

Bexsero® can be ordered via HSCT pharmacies in the same way as other childhood vaccines.

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 or the Public Health Agency duty room (0300 555 0119).

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).

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 adverse reactions (occur 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 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 manufacturer's Summary of Product Characteristics (SPCm) states infants are at increased risk of fever when Bexsero® is administered at the same time as other routine childhood vaccines.

How common is fever and can it be prevented?

In one clinical trial, fever (≥38°C) was reported in 51–62% of infants receiving Bexsero® and routine vaccines together, although high fever (≥39°C) was less common (6–12%). Overall, fever (≥38.0°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 six of the 1,885 recruited infants attended the hospital because of fever within two days of vaccination with Bexsero®.

In a subsequent study, 70% of infants receiving Bexsero® had fever ≥38.5°C at least once in the first three 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 two further administrations at 4–6 hour intervals after vaccination by parents/guardians. Of note, only ~5% of infants receiving paracetamol had fever

≥39°C and the frequency of medically-attended fever within three days of vaccination was ≤2% for any vaccination visit, irrespective of whether 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 study 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°C) compared with infants receiving two doses of paracetamol (first dose at 6–8 hours after vaccination and another 6–8 hours later).[1] Thus, 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 three doses of paracetamol to be given to infants receiving Bexsero® with their routine primary immunisations at two and four months, or as part of the catch-up programme at three and four months. Please refer to 'What adverse reactions are commonly associated with the administration of Bexsero®' (see page 3) and 'Guidance on the use of prophylactic infant paracetamol suspension with Bexsero® vaccine' (see below).

It is recommended that Bexsero® be administered 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 were administered 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, to reduce anxiety and concerns, 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.

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. 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) of paracetamol to their babies around the time of immunisation or as soon as possible after the vaccines are administered. Parents should also be advised to give two further doses at 4–6 hourly intervals (see Tables 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	Dose 2	Dose 3
2 months	One 2.5ml as soon as possible after vaccination	One 2.5ml 4–6 hours after first dose	One 2.5ml 4–6 hours after second dose
4 months	One 2.5ml as soon as possible after vaccination	One 2.5ml 4–6 hours after first dose	One 2.5ml 4–6 hours after second 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	Dose 2	Dose 3
3 months	One 2.5ml as soon as possible after vaccination	One 2.5ml 4–6 hours after first dose	One 2.5ml 4–6 hours after second dose
4 months	One 2.5ml as soon as possible after vaccination	One 2.5ml 4–6 hours after first dose	One 2.5ml 4–6 hours after second dose

Healthcare professionals should provide parents with the *Immunisations for babies up to a year old* leaflet before their two month primary vaccination appointment, for example when the parents register their baby at the practice or when they attend the 6–8 week check. Healthcare professionals should alert parents to the need to buy liquid paracetamol suspension in preparation for the two month immunisation appointment, and this advice is also contained in the immunisation leaflet. 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 two doses of paracetamol post-immunisations for infants aged two months?

The Commission on Human Medicines (CHM) has been consulted regarding the licensing restriction on Pharmacy (P) and General Sales List (GSL) paracetamol products that advise consulting a GP or pharmacist if more than two doses are required for a two month old infant post-immunisation. The reason for this licensing is to ensure early diagnosis of systemic bacterial infection. The CHM supported JCVI recommendations for three doses of paracetamol post-immunisation with MenB and supported the use of paracetamol for up to 48 hours post-immunisation if required to manage fever in two month olds. 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 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 the JCVI and Green Book post-immunisation paracetamol dosing recommendations.

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 (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.

Does liquid paracetamol need to be administered when children receive the booster dose of Bexsero® just after their first birthday?

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 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 two, three and four months of age. As these vaccines are not administered as part of the booster vaccines just after their first birthday, there is no additional requirement to offer liquid paracetamol at the same 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 fever, 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 six months to five 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, where 1,885 infants were recruited and vaccinated at four different visits without paracetamol prophylaxis, only one infant developed a febrile convulsion two days after receiving Bexsero®.[2] In the subsequent study of 364 infants receiving Bexsero® with or without paracetamol, there wasn't a single case of febrile convulsion after any of the four vaccination visits.[3]

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

Some babies may still develop fever after vaccination, even after taking paracetamol. If a baby still has a fever after the first three doses of paracetamol but is otherwise well, parents

should be advised they can continue giving the baby paracetamol. They should always leave at least four hours between doses and never give more than four doses in a day. They should also keep their child cool by making sure they don't have too many layers of clothes or blankets on and giving them plenty of fluids. If they are concerned about their baby at any time, they should trust their instincts and speak to their GP. Paracetamol is recommended for the prevention and treatment of fever after immunisation as there is evidence that it is safe and effective. If their baby still has a fever 48 hours after vaccination, they should speak to their GP 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. There is no danger of overdosing the baby even if less than half the dose has been spat out.

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

Ideally the rotavirus vaccine and paracetamol should be given at separate times, but the live vaccine virus should not be affected by close sequential administration of paracetamol syrup, ie giving the rotavirus vaccine in clinic and the parent giving the paracetamol shortly afterwards is acceptable and no particular time interval needs to be advised. 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 two 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 at around two 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?

The meningitis B immunisation programme with Bexsero® will start from 1 September 2015. Parents attending their GP practice for their child's routine primary immunisations at two, three and four months of age will be offered meningococcal B vaccine. The vaccination schedule and interval period will be dependent on the child's date of birth and routine primary immunisation appointment due at the start of the programme on 1 September 2015. Please refer to 'Who is the vaccine recommended for?' (see page 2) 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 (ie 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 populations 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 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 two and four months will induce bactericidal antibodies against meningococcus group B in nearly all infants. Vaccine responses will also be boosted after the dose just after their first birthday. Vaccine responses in three month olds receiving two priming doses a month apart and four month olds receiving a single priming dose may be lower but will also be boosted after the dose just after their first birthday.

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 just after their first birthday. Bexsero® should, therefore, protect infants and toddlers during their period of highest risk of meningococcal B infection.

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

The vaccine is licensed for use from the age of two months of age. Parents whose children are not eligible to receive the vaccine as part of the routine national programme (ie born before 1 May 2015) but who wish for their child to be immunised with Bexsero® should speak to their GP to discuss the possibility of obtaining the vaccine directly (privately) from the manufacturer. Parents who request the vaccine privately will be liable for the costs of the vaccine and any additional administration charges. GP's should **not** use centrally procured stock for the national programme.

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) or in the deltoid muscle region of the upper arm in older infants (12–13 months).

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 (ie not a homogenous suspension) or signs of foreign particulate are observed after shaking. **Note:** Needles for administration of the vaccine need to be ordered as per normal arrangements.

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. Other routine vaccines administered at two, three and four months should be administered in the right limb.

Previous guidance that pneumococcal vaccine should be given on its own into a limb no longer applies. 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, ie just after the first birthday. 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.

Healthcare professionals are encouraged to familiarise themselves with local protocols for ordering, storing and handling of vaccines to ensure vaccines are stored and monitored as per recommendations.

At the start of the programme the Bexsero® being supplied may have a shorter shelf life and practitioners must check the expiry date of all vaccines being administered. Practices are reminded to place small regular orders for the vaccine to ensure vaccine is continuously available.

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.[4]

For a full list of excipients, healthcare professionals should read the manufacturer's 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 manufacturer's 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), rotavirus, diphtheria, tetanus, pertussis, polio and Hib. It is recommend 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.**

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 serogroups, such as Men A, C, W and Y?

Whilst Bexsero has broad coverage against most MenB strains causing invasive meningococcal disease (IMD) in England, it does not offer complete protection. Similarly studies to demonstrate protection against other capsular strains remain ongoing. 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 just after their first birthday. Why is Bexsero® only being recommended as a two dose schedule in infants aged under six 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 of 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 (three, four months and just after their first birthday or four months and just after their first birthday) to that recommended for the routine cohort (two, four months and just after their first birthday)?

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 three and four months of age. These children will also receive a booster dose of Bexsero® as part of booster immunisations just after their first birthday.

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 booster dose of Bexsero® just after their first birthday.

Should infants aged four months on the 1 September 2015 who have already received their third primary vaccine be recalled to receive Bexsero®?

Since the Bexsero® programme will begin on the day these infants become four months of age, it is very unlikely that infants will receive their routine four month vaccinations without Bexsero®. If this does occur for any reason (eg Bexsero® was not available in the surgery at the visit or the immunisation nurse omitted the Bexsero® dose at the visit), then the patient should be called back and offered Bexsero® as soon as possible.

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 five 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 five months of age.

What should I do if a child attends for their first primary immunisations before the age of two months?

Bexsero® is not licensed for use in children under two months old and the SPC states that the safety and efficacy of Bexsero® in infants less than eight weeks of age has not yet been established. Practitioners may administer the vaccine to children aged eight weeks or older only. If primary immunisations are being administered early to an infant under two months old for travel reasons, the child should receive Bexsero® on their return.

What should I do if I have inadvertently administered the second dose of Bexsero® at three months of age to an infant following the routine schedule (two, four months and just after their first birthday)?

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 four 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 three months should be given liquid paracetamol as recommended for the two-month or four-month Bexsero®.

Please refer to 'What adverse reactions are commonly associated with the administration of Bexsero®?' (see page 3) and 'Guidance on the use of prophylactic infant paracetamol suspension with Bexsero® vaccine' (see page 4).

What should I do if an infant following the routine schedule (two, four months and just after their first birthday) or catch-up schedule (three, four months and just after their first birthday) misses their second dose of Bexsero® at four months?

Bexsero® will only be offered with routine immunisation appointments. Infants who do not attend for their routine appointment at four 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 four months?

Eligible infants who do not attend for their routine appointment at four 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. 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 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 on the use of prophylactic infant paracetamol suspension with Bexsero® vaccine' (see page 4).

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 vaccines need to be administered at the same time, ie the booster just after their first birthday?

Infants attending for their routine booster immunisations just after their first birthday are likely to receive 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 limbs – left and right arm and right leg.

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

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 two months of age and just after their first birthday 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 it becomes stronger.[5] Additionally, administering multiple vaccines in one session is a routine occurrence in most countries around the world with no evidence of harmful effects.

Useful links

- DHSSPS CMO letter. www.dhsspsni.gov.uk/hss-md-9-2015.pdf
- Public Health Agency leaflet *Immunisation for babies up to a year old.* www.publichealth.hscni.net/publications/immunisation-babies-year-old
- Public Health England. Immunisation against infectious diseases: meningococcal chapter 22. 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. www.gov.uk/government/news/phe-welcomes-prospect-of-new-meningitis-b-vaccine
- Meningitis Research Foundation. www.meningitis.org/
- Meningitis Now. www.meningitisnow.org/
- NHS Choices. 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
- Commission on Human Medicines. www.gov.uk/government/organisations/commission-on-human-medicines

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