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For Action by:
General Practitioners
Immunisation Leads, Health Boards
Chief Executives, Health Boards/Trusts
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Enclosure(s): None

Introduction of MenB immunisation for infants

1. I am writing to advise you that immunisation against meningococcal serogroup B disease (MenB) will be added to the childhood immunisation programme as part of the routine schedule from 1 September 2015**.**

2. This letter provides the information you need to introduce this new vaccine. It includes guidance on those infants eligible for vaccination; clinical advice on use of Bexsero® (the MenB vaccine); details of how to order the vaccine; data collection arrangements to measure vaccine uptake; and funding arrangements.

3. Bexsero® should be offered routinely to all babies at the age of two months and again at four months, when they attend for their first and third routine childhood immunisations from 1 September 2015. A further booster should also be offered at 12-13 months at the same time as current routine immunisations. A limited one-off catch-up programme for infants scheduled to receive their 3 and 4 month routine immunisations after 1 September (born on or after 1 May) will also be offered, as set out in the table below.

		Age of infant		
	Date of birth	**Priming dose**	**Priming dose**	**Booster**
Routine cohort	On or after 01/07/2015	2 months	4 months	12-13 months
Catch-up cohort	01/05/2015 to 30/06/2015	3 months	4 months	12-13 months
		n/a	4 months	12-13 months

4. Further detailed clinical guidance for healthcare professionals is set out in **Annex A**. This notes the importance of clear advice to healthcare professionals and parents/ guardians on the increased risk of fever from the vaccine and the use and supply of infant strength paracetamol following vaccination. Information and resources will be made available at:

   http://nww.immunisation.wales.nhs.uk/meningococcal-b-infant-vaccine-programme

   to support these communications.

5. The meningococcal chapter of the Green Book (*Immunisation against infectious disease*) has been updated and is available to read at:

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

6. The Joint Committee on Vaccination and Immunisation's (JCVI) statement about meningococcal B disease and MenB vaccine is available at:

   JCVI MenB Statement

7. The introduction of MenB immunisation will have a significant impact on reducing cases of meningitis and septicaemia and their complications in infants, and provide reassurance to parents who are concerned about the devastating consequences of this disease. I do not underestimate the additional work the implementation of this routine immunisation will bring, and I would like to take this opportunity to thank all involved in delivering the childhood immunisation programme for their continuing hard work.

Yours sincerely,

DR RUTH HUSSEY OBE
Chief Medical Officer / Medical Director NHS Wales

CLINICAL GUIDANCE ON IMMUNISATION OF INFANTS AGAINST MENINGOCOCCAL B DISEASE

1. This guidance is based on advice from the Joint Committee on Vaccination and Immunisation (JCVI)[1], the UK's independent expert panel on immunisation. Full guidance can be found in the new chapter on meningococcal disease included in *Immunisation against infectious disease* ('the Green Book')[2] at:

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

Background to the introduction of MenB vaccine

2. The incidence of invasive meningococcal disease (IMD) in Wales and England has decreased by more than half since the early 2000s. In 2014, there were 47 confirmed cases of meningococcal disease in Wales, including 36 caused by MenB. Three quarters of all MenB cases in Wales in 2014 occurred in children aged 5 years or younger and more than half were in children aged two years or younger. MenB cases were diagnosed in children in Wales as young as one month and peaked at eight to 12 months of age. The epidemiology of IMD is similar in other countries of the UK. A UK study [3] suggests that around a tenth of survivors of MenB disease have severe physical or neurological disabilities, including amputation, deafness, epilepsy and learning difficulties, and around one third of cases result in less severe physical or neurological disabilities.

3. The declining incidence in IMD in the UK has been attributed to natural secular trends, as often observed with many infectious diseases. Historically, the UK has witnessed many outbreaks of IMD, usually because of a new virulent meningococcal strain into the population, as evidenced by the increase meningococcal group C (MenC) disease in the mid-1990s, which ultimately resulted in the introduction of mass MenC vaccination programme in 1999. Similarly MenW disease is currently increasing rapidly in the UK, requiring an urgent vaccination programme using MenACWY vaccine in teenagers. Therefore, while IMD incidence is currently low, it could increase rapidly at any time.

4. Bexsero® is a novel multi-component, protein-based meningococcal vaccine that took almost 20 years to develop and license. Data from clinical trials show Bexsero® to be immunogenic in infants, children,

[1] JCVI statement: JCVI advice on meningococcal B vaccination.

[2] The meningococcal B chapter can be found at: "The Green Book" reference.

[3] Viner R et al (2012).Outcomes of invasive meningococcal serogroup B disease in children and adolescents (MOSAIC): a case-control study. Lancet Neurol 11:9, 774-783.

adolescents and adults, resulting in high concentrations of bactericidal antibodies that can kill most MenB strains in laboratory tests. These data are used as a proxy for vaccine effectiveness. Direct evidence of clinical effectiveness (i.e. preventing invasive meningococcal disease in humans) is limited because it requires vaccinating thousands of individuals and monitoring disease rates over time. Bexsero® has not been routinely implemented in any country worldwide, but preliminary results from a recent MenB outbreak in Princeton University where more than 17,000 adolescents received Bexsero®, and Québec's Saguenay-Lac-Saint-Jean region where more than 45,000 infants, young children and adolescents were vaccinated with Bexsero®; are encouraging. In the past, countries with large MenB outbreaks have used specific MenB vaccines containing the outer membrane vesicle (OMV) component of the outbreak strain. In New Zealand, the effectiveness of such a vaccine was estimated to be 73%.

5. Bexsero® contains OMV as one of its components along with three other highly-conserved meningococcal surface proteins identified through reverse vaccinology. Given the available data, Bexsero® is estimated to have 95% short-term vaccine effectiveness against most MenB strains causing invasive disease in the UK.

6. Safety data from clinical trials totalling over 6,000 participants and the European Medicines Agency's (EMA) considerations of these data were reviewed by JCVI. These data indicated that infants given Bexsero® along with their routine immunisation rates have higher rates of fever (50-80% above 38^0C) compared to when the infant immunisations are given without Bexsero®. However, administration of prophylactic paracetamol at the time of immunisation reduced fever rates without affecting immunogenicity of the individual vaccine antigens. This is in contrast to a previous study showing that concomitant paracetamol with routine infant immunisations (excluding Bexsero®) lowered the immunogenicity of some of the infant vaccines.

7. The JCVI noted the increased risk of fever when Bexsero® was administered with other childhood immunisations and agreed that there would be a need to educate parents and healthcare professionals on the reactogenicity of Bexsero® given concomitantly with other infant vaccinations under the age of 12 months. Good communications will ensure parents/ guardians have the necessary information they need on the increased risk of fever and the use of paracetamol following vaccination, therefore also reducing parental anxiety. Effective communication on this subject will also reduce the impact on the health service of consultations for fever. Administration of prophylactic paracetamol at the time or as soon as possible after vaccination is recommended, with instructions that a further two doses every four to six hours should be given to reduce the likelihood or intensity of fever.

8. Healthcare professionals should take opportunities to direct parents to information on MenB vaccination and on the use of paracetamol following vaccination ahead of the two month appointment. Written information on the use of paracetamol following MenB vaccination should ideally be

provided to parents before their two month vaccination appointment so that they are aware of the need to purchase an infant liquid paracetamol preparation. This should be reinforced by health professionals during the infant's routine immunisation appointment, and further written information supplied at that time.

Timing

9. The vaccine will be included in the childhood immunisation programme from 1 September 2015. All children scheduled to receive their primary immunisations after that date should be offered the Bexsero® vaccine as set out in the table below:

Routine cohort

		Age of infant		
	DOB (born on or after)	**Priming dose**	**Priming dose**	**Booster**
Routine cohort	01/07/2015	8 weeks (2 months)	16 weeks (4 months)	52-56 weeks (12-13 months)

Catch–up cohort eligibility

All eligible children born from 1st May 2015 will be appointed by the child health system.

Dates of birth	**Recommended immunisation schedule**
*1 May to 30 June 2015.	If third routine primary immunisation appointment at 4 months (16 weeks) is due on or after 1 September then follow this schedule: 4 months and 12-13 months (1+1)
	If second routine primary immunisation appointment at 3 months (12 weeks) is due on or after 1 September then follow this schedule: 3, 4 and 12-13 months (2+1)

*There are a small number of children who may have already received their primary immunisations and these children will be called for their MenB vaccines after 1 September 2015

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

Recommendations for use of the meningococcal group B vaccine (Bexsero®)

Administration

11. Bexsero® is recommended for routine immunisation of infants born on or after 01/05/2015.

12. It is recommend that **all** doses of Bexsero® be given in the left thigh, ideally on their 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.

13. If the infant has a bleeding disorder, the vaccine should be given by deep subcutaneous injection to reduce the risk of bleeding.

14. Please note the information on fever and the administration of paracetamol.

15. Full guidance on the administration technique is included in the relevant chapter of the Green Book.

    https://www.gov.uk/government/publications/immunisation-procedures-the-green-book-chapter-4

Routine Immunisation Schedule

16. The routine immunisation schedule (Infants born on or after 01/07/2015) recommends 0.5mL Bexsero®▼ with their routine vaccinations at:

    - 2 months.
    - 4 months.
    - Booster at 12-13 months.

Catch up cohort

17. Infants born on or after 01/05/2015 who have already had their two month vaccinations on the 1 of September 2015 should receive 0.5mL Bexsero®▼ with their routine vaccinations at their next vaccination visits:

    - 3 months.
    - 4 months.
    - Booster at 12-13 months.

18. Infants born on or after 01/05/2015 who have already had their two month and three month vaccinations on the 1 of September 2015 should receive 0.5mL Bexsero®▼ with their routine vaccinations at their next vaccination visits:

    - 4 months.
    - Booster at 12-13 months.

Vaccination of eligible children (born on or after 01/05/2015) with uncertain or incomplete immunisation status

19. For vaccination of eligible children with uncertain or incomplete immunisation status please refer to the Meningococcal chapter of the Green Book and the *Vaccination of individuals with uncertain or incomplete immunisation status* algorithm:

    https://www.gov.uk/government/publications/vaccination-of-individuals-with-uncertain-or-incomplete-immunisation-status

Contraindications

20. There are very few individuals who cannot receive Bexsero®. Where there is doubt, appropriate advice should be sought from an immunisation coordinator or consultant in health protection rather than withholding vaccination.

21. Bexsero® should not be given to:

    - infants with a confirmed anaphylactic reaction to a previous dose of Bexsero®.
    - infants with a confirmed anaphylactic reaction to any components of the vaccine.

22. Administration of Bexsero® should be postponed in infants suffering from acute febrile illness.

23. Other minor illnesses without fever or systemic upset are not valid reasons to postpone immunisation.

Immunosuppression and HIV infection

24. Bexsero® can be given to infants with HIV infection (regardless of CD4 count) or immunosuppressed in accordance with the routine schedule.

Concomitant administration with other vaccines

25. 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, Hib and MenC. Note it is recommended that Bexsero® be given in the left thigh, ideally on its own

Consent

26. See Chapter Two of *Immunisation against infectious disease* ('the Green Book')

    https://www.gov.uk/government/publications/consent-the-green-book-chapter-2

Pharmacy issues

Vaccine brand name and supplier

27. Bexsero® – supplied by GlaxoSmithKline (NB. Packaging may still say 'Novartis' initially).

Presentation

28. Bexsero® is supplied as a prefilled syringe in a **pack of 10,** without needles with one patient information leaflet (PIL). Additional PILs will be supplied with each pack of 10 Bexsero® ordered.

29. The vaccine is presented as a clear, colourless liquid, free of visible particles, for **intramuscular** administration.

30. The vaccine is ready to use (no reconstitution or dilution is required).

31. The vaccine is to be administered **intramuscularly** without mixing with any other vaccines or solutions.

32. After storage a fine off-white deposit may be observed in the pre-filled syringe containing the suspension. Before use, the pre-filled syringe should be shaken well in order to form a homogeneous suspension. The vaccine should be visually inspected for particulate matter and discoloration prior to administration. In the event of any foreign particulate matter and/or variation of physical aspect being observed, do not administer the vaccine.

33. Any unused medicinal product or waste material should be disposed of in accordance with local requirements.

Vaccine supply

34. Bexsero® should be ordered online via the ImmForm website (www.immform.dh.gov.uk) and is distributed by Movianto UK (Tel: 01234 248631) as part of the national childhood immunisation programme.

35. Centrally purchased vaccines for the national immunisation programme for the NHS can only be ordered via ImmForm and are provided free of charge to NHS organisations. The Bexsero® vaccine is likely to be available to order from August 2015, further details will be published on the ImmForm news item and health boards will be advised as information becomes available. Centrally supplied vaccine may be used for high risk groups as recommended in the Green Book. Vaccines for private prescriptions, occupational health use or travel are NOT provided free of charge and should be ordered from the manufacturer. Further information

about ImmForm is available at ImmForm Helpsheet or from the ImmForm helpdesk at helpdesk@immform.org.uk or Tel: 0844 376 0040.

Paracetamol infant suspension

36. Liquid paracetamol sachets and syringes will also be available to order through ImmForm for a limited period at the start of the programme. These will be bundled with NHS England leaflets; NHS Wales leaflets will be available through the normal channels. Further details on ordering paracetamol will be published on the ImmForm news item and through the Public Health Wales Immunisation e-bulletin available at:

    http://nww.immunisation.wales.nhs.uk/current-e-bulletin.

37. Practitioners should ensure that, at the time of immunisation, parents or guardians have sufficient paracetamol infant suspension (120mg/5ml) in order to administer three 2.5ml doses at intervals of 4-6 hours for babies up to six months. For very premature babies (born before 32 weeks gestation), paracetamol should be prescribed according to the infant's weight at the time of vaccination.

38. Where parents or guardians do not have paracetamol suspension at home it should be provided either by prescription or, where it is immediately necessary to ensure timely administration of paracetamol, by providing liquid paracetamol sachets. Supplies of paracetamol sachets must be made in accordance with the Nursing and Midwifery Council's Standards for Medicines Management.

    http://www.nmc.org.uk/globalassets/siteDocuments/NMC-Publications/NMC-Standards-for-medicines-management.pdf.

39. A template homely remedy protocol will be made available on the Public Health Wales Vaccine Preventable Disease Programme NHS Wales intranet site to support nurses to comply with these standards:

    http://nww.immunisation.wales.nhs.uk/meningococcal-b-infant-vaccine-programme

40. A leaflet will be available about the use of paracetamol and should be provided to the parent or guardian at the time of immunisation. Note the advice to administer a minimum of three doses of paracetamol to infants under three months of age differs from the information contained in the summary of product characteristics, patient information leaflet and labelling of over the counter paracetamol products. The recommendation to use a minimum of three doses was made by JCVI and has been endorsed by the Commission on Human Medicines (CHM).

41. The use of paracetamol for up to 48 hours post immunisation with MenB is supported where it is required to manage post-immunisation fever including in infants between two and three months old where it is likely that the fever is due to immunisation. This recommendation does not

extend to fever at any other time. In all cases if an infant is otherwise unwell parents should be advised to trust their instincts and not delay seeking medical attention. It is hoped that infant paracetamol suspension manufacturers will update product packaging and literature in due course.

42. For further information about vaccines available via ImmForm, please see ImmForm help sheet 13 (ImmForm Helpsheet).

Storage

43. Vaccines should be stored in the original packaging between +2˚C to +8˚C and protected from light. All vaccines may be sensitive to some extent to heat and cold. Do not freeze. Freezing may cause increased reactogenicity and loss of potency for some vaccines. It can also cause hairline cracks in the container, leading to contamination of the contents. **The vaccine should be used immediately after opening.**

Vaccine stock management

44. Please ensure sufficient fridge space is available for the new vaccine. Each site holding vaccine is asked to review current stocks of all vaccines. Two to four weeks of stock is recommended, and higher stock levels should be reduced to this level. Please remember that the vaccine will be supplied in packs of 10. A review of available fridge space will be necessary to ensure adequate storage capacity at the start of the programme.

45. Effective management of vaccines throughout the supply chain is essential to reduce vaccine wastage. Local protocols should be in place to reduce vaccine wastage to a minimum. Even small percentage reductions in vaccine wastage will have a major impact on the financing of vaccine supplies.

46. Any cold chain failures must be documented and reported to the local health board immunisation co-ordinator as appropriate.

Reporting of adverse reactions

47. Bexsero® is a newly licensed vaccine and is subject to additional monitoring under the black triangle labelling scheme. All suspected adverse reactions (ADR) should be reported to the MHRA using the Yellow Card Scheme:

    (www.mhra.gov.uk/yellowcard)

48. Chapter 9 of the Green Book gives detailed guidance which ADRs to report and how to do so:

    https://www.gov.uk/government/publications/surveillance-and-monitoring-for-vaccine-safety-the-green-book-chapter-9

49. Additionally, Chapter 8 of the Green Book provides detailed advice on managing ADRs following immunisation:

https://www.gov.uk/government/publications/vaccine-safety-and-adverse-events-following-immunisation-the-green-book-chapter-8

50. Any reported adverse incidents, errors or events during or post vaccination must follow determined procedures. In addition teams must keep a local log of reports and discuss such events with the local immunisation co-ordinator.

Surveillance

51. The programme will be carefully monitored by Public Health Wales (PHW) and the Medicines and Healthcare products Regulatory Agency (MHRA).

Personal Child Health Record (the "Red Book")

52. Arrangements have been made for the Red Book record of childhood vaccinations to be amended to reflect the changes to the childhood schedule, including MenB vaccination. It is important that information about vaccinations given is recorded in the Red Book, when it is available. Further information on the details to be recorded is given in Chapter Four of the Green Book.

https://www.gov.uk/government/publications/immunisation-procedures-the-green-book-chapter-4

Patient Group Directions

53. The usual method for the supply and administration of vaccines is via a Patient Specific Direction (PSD). The authorisation for this is usually the responsibility of the GP or an independent nurse prescriber. Where a PSD exists, there is no need for a Patient Group Direction (PGD).

54. Where a PSD is not available, a PGD may be used. A PGD is a written instruction that allows for the supply and/or administration of medicines to groups of patients who present for treatment where it offers an advantage to patient care without compromising safety. Template PGDs are available for amendment by health boards to authorise appropriate health professionals to administer the vaccine where a PSD is not available. More information is available from the Public Health Wales Vaccine Preventable Disease Programme NHS Wales intranet site at: http://nww.immunisation.wales.nhs.uk/guidance

Vaccine coverage data collection

55. Practices and health boards are required to provide data to Public Health Wales (PHW) sufficient to carry out surveillance and monitoring of the MenB vaccination programme. Data to monitor vaccine uptake will be collected through the Child Health System in the same way that data for existing childhood immunisation programmes are collected. Immunisation uptake will be reported through the Public Health Wales COVER scheme.

56. For accurate monitoring of immunisation uptake, it is essential that completed lists for scheduled vaccination sessions are returned to Health Board Child Health Offices in a timely manner. It is also essential that any unscheduled MenB vaccinations given opportunistically are reported to Health Board Child Health Offices using an unscheduled form. Timely return of immunisation forms from General Practice is not only important for immunisation uptake monitoring, but also because late return of forms may have consequences for the Child Health System in appointing children for future immunisations.

The Child Health Systems

57. Health boards are responsible for timely updating of their Child Health System Databases. In Wales all health boards use the CCH2000 system for call and recall of infants for routine immunisation and associated Child Health Records, which will be updated by the NHS Wales Informatics Service to allow for call and recall of children for this new vaccination programme. Infants will be called for their immunisation against Men B at their two and four month routine childhood immunisations and at 12-13 months alongside current routine immunisations via the Child Health System.

58. Healthcare professionals administering the vaccine must ensure that information on vaccines administered is documented in the general practice record and parent held record.

59. The healthcare professional must ensure that information on vaccines administered is submitted directly to the Health Board Child Health Office within 7 days.

60. Arrangements continue to be required to inform neighbouring areas when children resident in their area are immunised outside their local area through the child health system.

Funding and service arrangements

61. A practice will receive an item of service (IOS) payment of £7.80 per dose in respect of each child in an eligible cohort who is vaccinated.

62. An additional fee of £2.12 per dose in respect of each child in an eligible cohort who is vaccinated will be paid to GPs from the start of the programme until 31 March 2016 in recognition of the urgency of

implementation and delivery of the programmes and the additional workload this short lead in timeframe will mean for practices.

63. A top-up funding allocation for the MenACWY programme will be made to health boards' block allocations. The top-up allocation will be calculated on the full practice registered population for the health board, adjusted to take into account implementation part way into the financial year. It is expected to see allocated monies translated into resources for appropriate services areas.

Information materials

64. A MenB leaflet, paracetamol leaflet and question and answer sheet will be made available on the NHS Direct (Wales) web site via the link below for the public. Healthcare professionals can order copies of the MenB and paracetamol leaflets by emailing hplibrary@wales.nhs.uk or telephoning 0845 606 4050.

    http://www.nhsdirect.wales.nhs.uk/immunisations#Leaflets

65. Further information for healthcare professionals including a PowerPoint training presentation, will be made available from the Public Health Wales Vaccine Preventable Disease Programme, NHS Wales intranet site at:

    http://nww.immunisation.wales.nhs.uk/meningococcal-b-infant-vaccine-programme