When it comes to MenB* vaccination, targeting 4 antigens **helps to achieve broad coverage**[1,2†]

*Meningococcal disease, serogroup B.

†Indication

BEXSERO is indicated for active immunisation of individuals from 2 months of age and older against invasive meningococcal disease caused by *Neisseria meningitidis* serogroup B.[1]

Please see BEXSERO MOH approved Prescribing Information

BEXSERO
Meningococcal Group B Vaccine
(rDNA, component, adsorbed)

BEXSERO: Why 4 antigens?

BEXSERO uniquely targets 4 distinct antigens—fHbp, NadA, PorA P1.4, and NHBA—which together may help protect against MenB strains which are highly variable in the types and amounts of antigens they express[1,3-6]

BEXSERO contains 4 antigens:

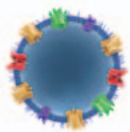
fHbp

Binds factor H, which enables bacterial survival in the blood [7,8]

NadA

Mediates binding to and entry into human epithelial cells[9-11]

PorA P1.4



As part of Outer Membrane Vesicle (OMV), has been shown to induce strain-specific bactericidal response when used in MenZB OMV vaccine[12]

NHBA

Binds heparin, which may promote bacterial survival in the blood[13]

- The Meningococcal Antigen Typing System (MATS) evaluation of **more than 1000 MenB strains from 5 EU countries** from 2007–2008 estimated that 73% to 87% (95% CI: 63–90%) would have been covered by BEXSERO[1]

fHbp=factor H binding protein; MeNZB=meningococcal group B New Zealand; NadA=Neisseria adhesin A; NHBA=Neisserial heparin binding antigen; PorA=porin A.

Expression alone may not be sufficient to provide adequate protection[14,15]

For MenB, only the human complement serum bactericidal assay (hSBA) is reliable as a predictor of protection against disease[16]

Killing in the hSBA of the **MenB** bacterial strain depends on[14]:

- the antigenic similarity of the bacterial and vaccine antigens
- the amount of antigen expressed on the surface

88% of disease-causing strains* have been shown to be killed, in hSBA, by serum from individuals† vaccinated with BEXSERO (95% CI: 72–95%)[17]

By targeting 4 distinct antigens, BEXSERO offers the potential to protect against invasive MenB strains, even when the expression of 1 component is low or antigenically different[2,3,5]

*Using a representative panel of 40 MenB isolates (from England and Wales in 2007–2008).
†Pooled serum derived from 69 infants.

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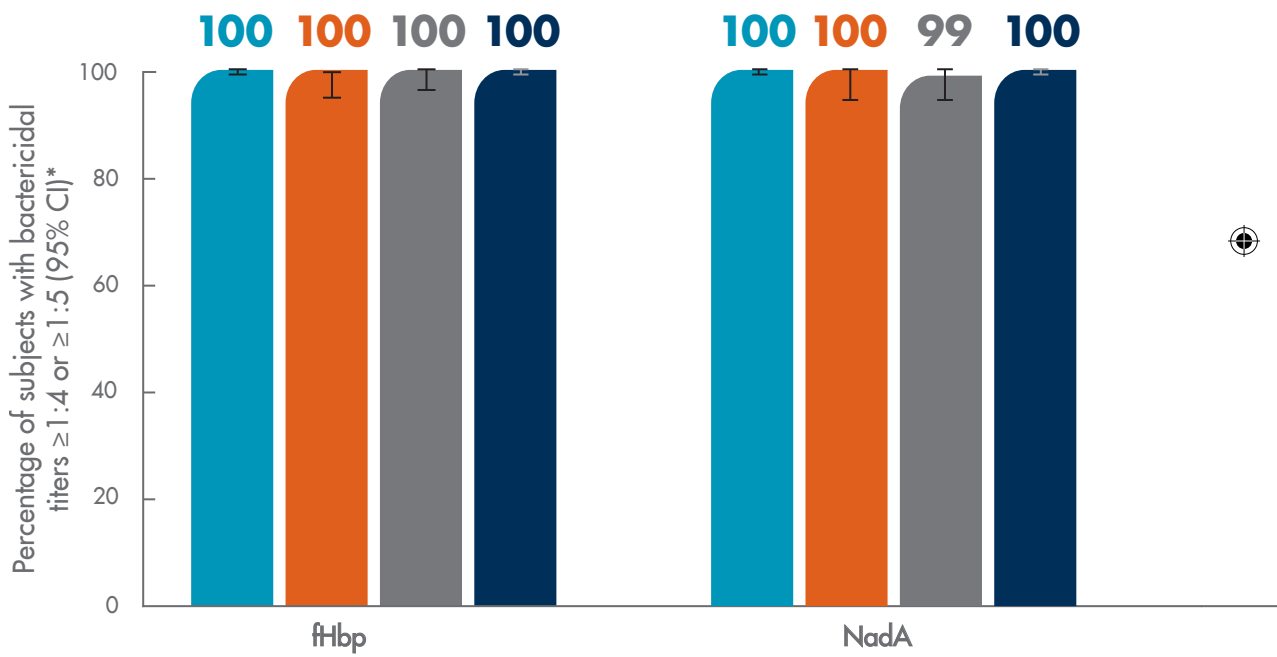
BEXSERO uniquely targets 4 antigens to help optimize MenB protection[1,2]

95%–100% of infants, toddlers, children, and adolescents achieved titers considered protective 1 month after series completion[1,18,19]



*Infants (2–11 months of age), toddlers (12–23 months of age), and children (2–10 years of age): Percentage of subjects who achieved an hSBA ≥1:5.

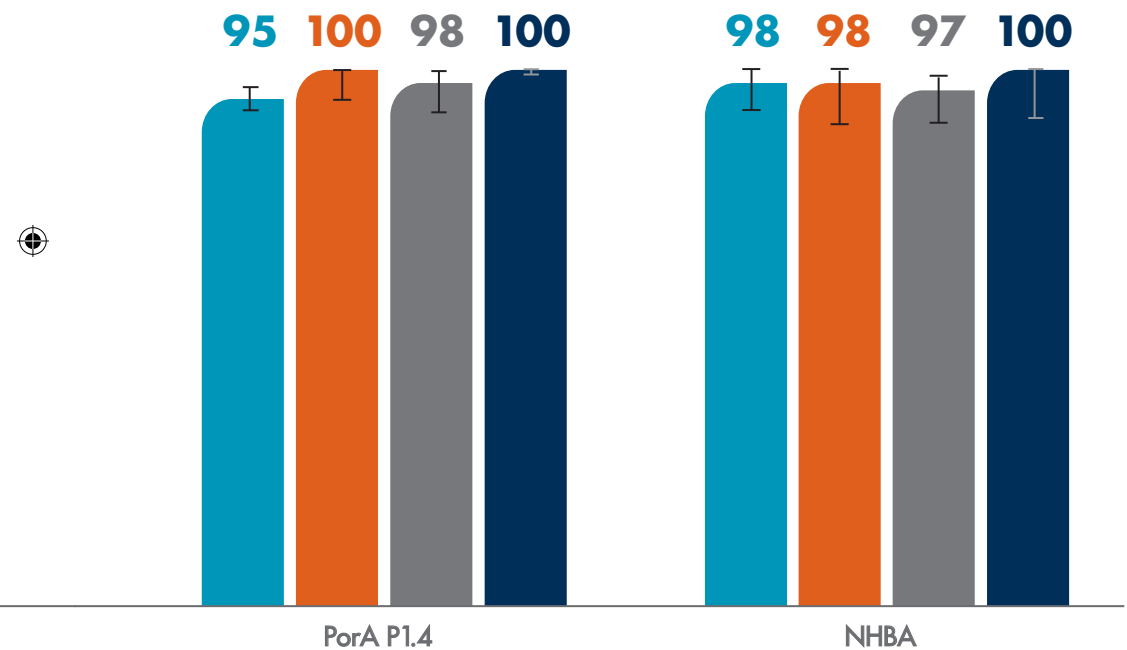
Adolescents (11–17 years of age): Percentage of subjects who achieved an hSBA ≥1:4.

Infants[1]
(2–11 months of age)
3+1-dose schedule†

Toddlers[19]
(12–23 months of age)
2+1-dose schedule‡

Children[1]
(2–10 years of age)
2-dose schedule§

Adolescents[1,18]
(11–17 years of age)
2-dose schedule||



†Vaccinations at 2, 4, and 6 months of age, and booster at 12 months of age; N=421–424; N=100 for NHBA.

‡Vaccinations at 13, 15, and 27 months of age; N=63–67.

§Vaccinations at 24 and 26 months of age; N=100–108.

||Two doses 1 month apart; N=638–639; N=46 for NHBA.

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Important Safety Information

Bexsero™ V 11/2017

For full information see MOH approved prescribing information

Indication: Bexsero is indicated for active immunization of individuals from 2 months of age and older against invasive meningococcal disease caused by Neisseria meningitidis group B
Contraindications: Hypersensitivity to the active substances or to any of the excipients
Special warnings and precautions for use: administration of Bexsero should be postponed in subjects suffering from an acute severe febrile illness. However, the presence of a minor infection, such as cold, should not result in the deferral of vaccination. Appropriate medical treatment and supervision should always be readily available in case of an anaphylactic event following the administration of the vaccine. Do not inject intravascularly. Anxiety-related reactions, including vasovagal reactions (syncope), hyperventilation or stress-related reactions may occur in association with vaccination as a psychogenic response to the needle injection. This vaccine should not be given to individuals with thrombocytopenia or any coagulation disorder that would contraindicate intramuscular injection, unless the potential benefit clearly outweighs the risk of administration. healthcare professionals should be aware that a temperature elevation may occur following vaccination of infants and children (less than 2 years of age). Prophylactic administration of antipyretics at the time and closely after vaccination can reduce the incidence and intensity of post-vaccination febrile reactions. There are no data on the use of Bexsero in subjects above 50 years of age and limited data in patients with chronic medical conditions
Most Common adverse drug reactions (ADRs): in infants and children (less than 2 years of age) the most common local and systemic adverse reactions observed in clinical trials were tenderness and erythema at the injection site, fever and irritability. In adolescents and adults, the most common local and systemic adverse reactions observed were pain at the injection site, malaise and headache. No increase in the incidence or severity of the adverse reactions was seen with subsequent doses of the vaccination series.
For complete data on ADRs, including worldwide voluntary reports, see full approved PI.

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Medical information service: il.medinfo@gsk.com
Adverse events reporting service: il.safety@gsk.com, Tel: 03-9297100

Full PI can be found with a GSK representative

Bexsero Abbreviated PI version 11/2017

For full product information see MOH approved prescribing information

Generic name of the drug and active ingredients: meningococcal group B Vaccine (rDNA, component, adsorbed).

One dose (0.5 ml) contains:

Recombinant Neisseria meningitidis group B NHBA fusion protein [1, 2, 3]- 50 micrograms

Recombinant Neisseria meningitidis group B NadA protein [1, 2, 3] -50 micrograms

Recombinant Neisseria meningitidis group B fHbp fusion protein [1, 2, 3] -50 micrograms

Outer membrane vesicles (OMV) from Neisseria meningitidis group B strain NZ98/254 measured as amount of total protein containing the PorA P1.4 [2] - 25 micrograms

[1] produced in E. coli cells by recombinant DNA technology.

[2] adsorbed on aluminium hydroxide (0.5 mg Al3+).

[3] NHBA (Neisseria Heparin Binding Antigen), NadA (Neisserial adhesin A), fHbp (factor H binding protein).

For the full list of excipients, see full PI.

Therapeutic indications: Bexsero is indicated for active immunization of individuals from 2 months of age and older against invasive meningococcal disease caused by Neisseria meningitidis group B. The impact of invasive disease in different age groups as well as the variability of antigen epidemiology for group B strains in different geographical areas should be considered when vaccinating. See full PI for information on protection against specific group B strains. The use of this vaccine should be in accordance with official recommendations.

Dosage and methods of administration:

Age Group	Primary Immunisation	Intervals between Primary Doses	Booster
Infants, 2 - 5 months	Three doses each of 0.5 ml, with first dose given at 2 months of age	Not less than 1 month	Yes, one dose between 12 and 15 months
Unvaccinated infants, 6 - 11 months	Two doses each of 0.5 ml	Not less than 2 months	Yes, one dose in the second year of life with an interval of at least 2 months between the primary series and booster dose
Unvaccinated children, 12 - 23 months	Two doses each of 0.5 ml	Not less than 2 months	Yes, one dose with an interval of 12 months to 23 months between the primary series and booster dose
Children, 2 - 10 years	Two doses each of 0.5 ml	Not less than 2 months	Need not established
Adolescents (from 11 years of age) and adults	Two doses each of 0.5 ml	Not less than 1 month	Need not established

See full PI for detailed dosing guidelines.

The vaccine is given by deep intramuscular injection, preferably in the anterolateral aspect of the thigh in infants or in the deltoid muscle region of the upper arm in older subjects. Separate injection sites must be used if more than one vaccine is administered at the same time. The vaccine must not be injected intravenously, subcutaneously or intradermally and must not be mixed with other vaccines in the same syringe. For instructions on the handling Bexsero before administration, see full PI.

Contraindications: hypersensitivity to the active substances or to any of the excipients listed in full PI.

Special warnings and precautions for use: as with other vaccines, administration of Bexsero should be postponed in subjects suffering from an acute severe febrile illness. Do not inject intravascularly. As with all injectable vaccines, appropriate medical treatment and supervision should always be readily available in case of an anaphylactic event following the administration of the vaccine. Anxiety-related reactions, including vasovagal reactions (syncope), hyperventilation or stress-related reactions may occur in association with vaccination as a psychogenic response to the needle injection. This vaccine should not be given to individuals with thrombocytopenia or any coagulation disorder that would contraindicate intramuscular injection, unless the potential benefit clearly outweighs the risk of administration. As with any vaccine, vaccination with Bexsero may not protect all vaccine recipients. Bexsero is not expected to provide protection against all circulating meningococcal group B strains. As with many vaccines a temperature elevation may occur following vaccination of infants and children (less than 2 years of age). Prophylactic administration of antipyretics at the time and closely after vaccination can reduce the incidence and intensity of post-vaccination febrile reactions. Immunogenicity data are available in individuals with complement deficiencies, asplenia, or splenic dysfunctions (see full PI). There are no data on the use of Bexsero in subjects above 50 years of age and limited data in patients with chronic medical conditions. The potential risk of apnoea and the need for respiratory monitoring for 48 72 hours should be considered when administering the primary immunisation series to very premature infants (born ≤ 28 weeks of gestation) and particularly for those with a previous history of respiratory immaturity. As the benefit of vaccination is high in this group of infants, vaccination should not be withheld or delayed. The tip cap of the syringe may contain natural rubber latex, healthcare professionals should consider the benefit-risk prior to administering this vaccine to subjects with known history of hypersensitivity to latex. Kanamycin levels in the final vaccine are less than 0.01 micrograms per dose. The safe use of Bexsero in Kanamycin-sensitive individuals has not been established.

Women of childbearing potential/Contraception in females: insufficient clinical data on exposed pregnancies are available. Nevertheless, vaccination should not be withheld when there is a clear risk of exposure to meningococcal infection. There was no evidence of maternal or foetal toxicity, and no effects on pregnancy, maternal behavior, female fertility, or postnatal development in a study in which female rabbits received Bexsero at approximately 10 times the human dose equivalent based on body weights. Breast-feeding: information on the safety of the vaccine to women and their children during breast-feeding is not available. The benefit-risk ratio must be examined before making the decision to immunise during breast-feeding. Fertility: there are no data on fertility in humans. There were no effects on female fertility in animal studies.

The most frequently occurring adverse drug reactions (ADRs): in infants and children (less than 2 years of age) the most common local and systemic adverse reactions observed in clinical trials were tenderness and erythema at the injection site, fever and irritability. In adolescents and adults, the most common local and systemic adverse reactions observed were pain at the injection site, malaise and headache. No increase in the incidence or severity of the adverse reactions was seen with subsequent doses of the vaccination series.

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Refer to the local label and product monograph before prescribing.

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BEXSERO:
4 antigens help achieve broad coverage[1,2]

References: 1. BEXSERO MOH approved Prescribing Information. **2.** Vesikari T, Esposito S, Prymula R, *et al*; the EU Meningococcal B Infant Vaccine Study Group. Immunogenicity and safety of an investigational multicomponent, recombinant, meningococcal serogroup B vaccine (4CMenB) administered concomitantly with routine infant and child vaccinations: results of two randomised trials. *Lancet*. 2013;381:825-835. **3.** Biagini M, Spinsanti M, De Angelis G, *et al*. Expression of factor H binding protein in meningococcal strains can vary at least 15-fold and is genetically determined. *Proc Natl Acad Sci USA*. 2016;113:2714-2719. **4.** Livorsi DJ, Stenehjem E, Stephens DS. Virulence factors of gram-negative bacteria in sepsis with a focus on *Neisseria meningitidis*. *Contrib Microbiol*. 2011;17:31–47. **5.** Hao W, Ma JH, Warren K, *et al*. Extensive genomic variation within clonal complexes of *Neisseria meningitidis*. *Genome Biol Evol*. 2011;3:1406–1418. **6.** Vogel U, Taha M-K, Vasquez JA, *et al*. Predicted strain coverage of a meningococcal multicomponent vaccine (4CMenB) in Europe: a qualitative and quantitative assessment. *Lancet Infect Dis*. 2013;13:416-425. **7.** Madico G, Welsch JA, Lewis LA, *et al*. The meningococcal vaccine candidate GNA1870 binds the complement regulatory protein factor H and enhances serum resistance. *J Immunol*. 2006;177:501-510. **8.** Schneider MC, Prosser BE, Caesar JJE, *et al*. *Neisseria meningitidis* recruits factor H using protein mimicry of host carbohydrates. *Nature*. 2009;458:890-893. **9.** Comanducci M, Bambini S, Brunelli B, *et al*. NadA, a novel vaccine candidate of *Neisseria meningitidis*. *J Exp Med*. 2002;195:1445-1454. **10.** Capecchi B, Abu-Bobie J, Di Marcello F, *et al*. *Neisseria meningitidis* NadA is a new invasin which promotes bacterial adhesion to and penetration into human epithelial cells. *Mol Microbiol*. 2005;55:687-698. **11.** Mazzon C, Baldani-Guerra B, Cecchini P, *et al*. IFN-γ and R-848 dependent activation of human monocyte-derived dendritic cells by *Neisseria meningitidis* adhesin A. *J Immunol*. 2007;179:3904-3916. **12.** Martin DR, Ruijne N, McCallum L, O'Hallahan J, Oster P. The VR2 epitope on the PorA P1.7-2,4 protein is the major target for the immune response elicited by the strain-specific group B meningococcal vaccine MeNZB. *Clin Vaccine Immunol*. 2006;13:486-491. **13.** Serruto D, Spadafina T, Ciucchi L, *et al*. *Neisseria meningitidis* GNA2132, a heparin-binding protein that induces protective immunity in humans. *Proc Natl Acad Sci USA*. 2010;107:3770-3775. **14.** Donnelly J, Medini D, Boccadifuoco G, *et al*. Qualitative and quantitative assessment of meningococcal antigens to evaluate the potential strain coverage of protein-based vaccines. *PNAS*. 2010;107(45):19490-19495. **15.** Medini D, Stella M, Wassil J. MATS: Global coverage estimates for 4CMenB, a novel multicomponent meningococcal B vaccine. *Vaccine*. 2015;33:2629-2636. **16.** Granoff DM, Pelton S, Harrison H. Meningococcal vaccines. In: Plotkin SA, Orenstein WA, Offit PA, eds. *Vaccines*. 6th ed. Philadelphia, PA: Saunders; 2013:388-418. **17.** Frosi G, Biolchi A, Sapio ML, *et al*. Bactericidal antibody against a representative epidemiological meningococcal serogroup B panel confirms that MATS underestimates 4CMenB vaccine strain coverage. *Vaccine*. 2013;31:4968-4974. **18.** Santolaya ME, O'Ryan ML, Valenzuela MT, *et al*. Immunogenicity and tolerability of a multicomponent meningococcal serogroup B (4CMenB) vaccine in healthy adolescents in Chile: a phase 2b/3 randomised, observer-blind, placebo-controlled study. *Lancet*. 2012;379:617-624. **19.** Vesikari T, Prymula P, Merrall E, Kohl I, Toneatto D, Dull PM. Meningococcal serogroup B vaccine (4CMenB): booster dose in previously vaccinated infants and primary vaccination in toddlers and two-year-old children. *Vaccine*. 2015;33:3850-3858.

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