A sneak peek into the future of vaccines

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GSK’s vaccine development pipeline has the potential to help reduce the burden of many communicable diseases\(^1,2\)

### Bacterial
- TB
- Group B Streptococcus
- COPD
- Meningococcal disease
- Shigellosis
- Pneumococcal disease

### Viral
- HIV
- Ebola
- RSV
- Hepatitis C
- Herpes zoster

### Parasitic
- Malaria

### Drivers of vaccine development:
- Poverty
- Paediatric
- Older adults
- Emerging disease
- Maternal
- Therapeutic
- Chronic
- Adolescent

COPD, chronic obstructive pulmonary disease; HIV, human immunodeficiency virus; RSV, respiratory syncytial virus; TB, tuberculosis

GSK is developing innovative vaccines to help prevent diseases

Innovative technologies

- Viral vectors
- Reverse vaccinology
- Generalised modules of membrane antigens
- GSK Adjuvant System
- Self-amplifying mRNA (SAM)
- Bioconjugation

Vaccines for all

- Maternal immunisation
- Infants
- Paediatrics
- Adolescents
- Adults
- Travellers
- Occupational health, e.g. HCW*, military
- Older adults

*HCW = healthcare worker

Bexsero®
Meningococcal Group B Vaccine (rDNA, component, adsorbed)

Bexsero is not registered or available in New Zealand

Bexsero is a registered trademark of the GlaxoSmithKline group of companies.
Neisseria meningitidis are classified into serogroups according to the immunologic reactivity of their capsular polysaccharides.\(^1\)

- The polysaccharide capsule is key in determining virulence.\(^2\)
- Twelve serogroups have been identified based on the structure of their polysaccharide capsule – only six (A, B, C, W, X and Y) cause invasive meningococcal disease.\(^2,3\)

Incidence of Invasive Meningococcal Disease (IMD) by Age

Europe,* 2012

- Incidence highest in infants and young children
- A second, smaller peak in incidence occurs in adolescents and young adults

IMD, invasive meningococcal disease.
Total IMD cases, N=3436 (reported cases for which age information was provided, excluding aggregated data); serogroup B IMD cases, N=2182.
*Countries: Austria, Belgium, Czech Republic, Denmark, Estonia, Finland, France, Germany, Greece, Hungary, Ireland, Italy, Latvia, Lithuania, Luxembourg (total IMD cases only), Malta, Netherlands, Norway, Poland, Portugal, Romania, Slovakia, Slovenia, Spain, Sweden, United Kingdom.

Neisseria meningitidis serogroup distribution varies between regions/countries*

*Serogroup distribution cannot be directly compared across countries due to variability in surveillance data available.

<Further details on surveillance data for each country are shown on next slide for use as back-up, if required>


Figure 1. Neisseria meningitidis serogroup distribution between regions/countries. 57% of USA meningococcal disease was caused by serogroup B in 2014. 36% were ‘other’ serogroups, including serogroup W and non-groupable. Surveillance data only covers some areas of the USA, representing ~43.5 million people2. Serogroup data is across all age groups. Percentages may not total 100 due to rounding.
A conjugate vaccine for Men B?

Vaccines with a single subcapsular antigen component do not offer broad protection against Men B disease.

### Capsular vaccines

- Poorly immunogenic\(^1,2\)
  - Structural homology between the B polysaccharide of the capsule and human tissue\(^1,2\)

### Outer membrane vesicle (OMV) vaccines

- Immunogenic and proven effective for a **single** homologous serogroup B strain\(^4,5\)
- Limited protection against heterologous meningococcal serogroup B strains\(^4,5\)
- Serogroup B strains are highly diverse\(^4,5\)
  - >5000 sequence types identified\(^6\)
  - >600 PorA variants (the dominant antigen in OMV)\(^4\)

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5. Girard MP, *et al.* *Vaccine* 2006;24:4692–4700
**Bexsero contains 4 antigenic components**

Identified using a “reverse vaccinology” approach

**fHbp: factor H-binding protein**
- Binds factor H, which enables bacterial survival in the blood\(^1,2\)

**NHBA: Neisseria heparin-binding antigen**
- Binds heparin, which may promote bacterial survival in the blood\(^6\)
- Present in virtually all strains\(^6,7\)

**NadA: Neisseria adhesin A**
- Promotes adherence to and invasion of human epithelial cells\(^3-5\)
- May be important for colonization\(^4\)

**NZ PorA P1.4: porin A**
- Major OMV protein\(^8\)
- Shown to induce strain-specific bactericidal response when used in MeNZB OMV vaccine\(^^,8\)

\(^*\)Developed by Chiron Vaccines in association with the Norwegian Institute of Public Health.
OMV, outer membrane vesicle.

Multiple antigens may provide synergistic killing, improve strain coverage, and insure against mutations\(^9,10\)

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**Clinical trial experience with Bexsero**

Studies included subjects from 2 months of age

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**Bexsero safety was evaluated in 13 studies including 9 randomised controlled clinical trials**

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**Infants and children 2 months to <2 years of age**
- 5849 received at least 1 dose of *Bexsero*
- 3285 received booster dose in second year of life

**250 children 2 to 10 years of age**

**2677 adolescents (≥11 years of age) and adults**

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**Study in special populations: children and adolescents aged 2 to 17 years**
- 40 with complement deficiency; 107 with asplenia or splenic dysfunction
- 85 age-matched healthy participants

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>9000 subjects received at least 1 dose of the vaccine.

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1. *Bexsero* Product Information
## Bexsero Licensed Immunisation Schedules

### European Union

<table>
<thead>
<tr>
<th>Age group</th>
<th>Primary immunisation</th>
<th>Interval between primary doses</th>
<th>Booster</th>
</tr>
</thead>
<tbody>
<tr>
<td>2–5 months</td>
<td>3 doses</td>
<td>≥1 mo</td>
<td>1 dose age 12–15 mo*</td>
</tr>
<tr>
<td>6–11 months</td>
<td></td>
<td></td>
<td>1 dose in the 2nd year of life</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>≥2 mo post primary series</td>
</tr>
<tr>
<td>12–23 months</td>
<td>2 doses</td>
<td>≥2 mo</td>
<td>1 dose 12–23 mo post primary series</td>
</tr>
<tr>
<td>2–10 years</td>
<td></td>
<td></td>
<td>Need not established</td>
</tr>
<tr>
<td>11+ years</td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

The use of this vaccine should be in accordance with official recommendations.

*In case of delay, the booster should not be given later than 24 months.

*Bexsero® [summary of product characteristics].
**Bexsero Immune Response in Infants Following Vaccination at 2-4-6-12 Months**

2-4-6-12 month schedule with routine vaccines

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Figure adapted and reprinted from *The Lancet*, Vol. 381, Vesikari T et al., Immunogenicity and safety of an investigational multicomponent, recombinant, meningococcal serogroup B vaccine (4CMenB) administered concomitantly with routine infant and child vaccinations: results of two randomized trials, Pages 825-835, Copyright (2013), with permission from Elsevier.


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<table>
<thead>
<tr>
<th></th>
<th>fHbp</th>
<th>NadA</th>
<th>PorA P1.4</th>
<th>NHBA II</th>
</tr>
</thead>
<tbody>
<tr>
<td>Baseline 1,*</td>
<td>100</td>
<td>100</td>
<td>100</td>
<td>100</td>
</tr>
<tr>
<td>Post-primary (7 mo) 1,†</td>
<td>100</td>
<td>99</td>
<td>100</td>
<td>95</td>
</tr>
<tr>
<td>Pre-booster (12 mo) 1,‡</td>
<td>100</td>
<td>100</td>
<td>95</td>
<td>98</td>
</tr>
<tr>
<td>Post-booster (13 mo) 2,§</td>
<td>84</td>
<td>84</td>
<td>33</td>
<td>61</td>
</tr>
</tbody>
</table>

4. N=100.
Routine vaccines given with or without Bexsero at 2, 4, and 6 months of age

**Immunogenicity of Routine Infant Vaccines Administered with Bexsero**

## Tolerability Profile for *Bexsero* in Clinical Trials

<table>
<thead>
<tr>
<th>Infants and children (less than 2 y)</th>
<th>Most common adverse reactions</th>
<th><em>Bexsero</em> given alone</th>
<th><em>Bexsero</em> given with other vaccines* †</th>
</tr>
</thead>
<tbody>
<tr>
<td>Tenderness and erythema at the injection site, fever, and irritability</td>
<td>Frequency of fever was similar to that associated with routine infant vaccines* administered during clinical trials</td>
<td>Higher rate of fever and systemic reactions (irritability, change in eating habits, sleepiness, tenderness at the injection site)</td>
<td></td>
</tr>
</tbody>
</table>

| Adolescents and adults | The most common adverse reactions were pain at the injection site, malaise, and headache; fever rates were similar for *Bexsero*® compared with placebo |

*Pneumococcal 7-valent conjugate vaccine, diphtheria, tetanus, acellular pertussis, hepatitis B, inactivated poliomyelitis, and *Haemophilus influenzae* type b vaccine. †Separate vaccinations can be considered when possible. Separate injection sites must be used if more than one vaccine is administered at the same time.

*Bexsero*® [summary of product characteristics].
**Impact of Prophylactic Paracetamol on Fever**

*When Bexsero is given concomitantly with routine infant vaccines*

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**Post–any dose***

(2-3-4 month schedule)

- **NPP**, no prophylactic paracetamol (N=181–182);

*Subjects received 1 dose of 10–15 mg/kg oral paracetamol before vaccination, followed by 2 additional doses of paracetamol 4–6 hours after vaccination. Routine vaccines: PCV7 and DTaP-HBV-IPV/Hib.*

Summary of Bexsero real-world experience

UK: National MenB vaccination programme

In 2015, Bexsero was introduced to help protect against MenB disease in the UK – ~700,000 infants per year were targeted for vaccination.

Canada: Regional vaccination campaign in Quebec and University outbreak in Nova Scotia

Regional campaign in Saguenay–Lac-Saint-Jean, Quebec

In 2014, 57,038 residents or those in education aged ≥2 months to ≤20 years were targeted for Bexsero vaccination to help protect against the high incidence of MenB disease in the region. Between 5 May and 17 June 2014, 43,740 individuals received the first dose.

Outbreak at Acadia University, Nova Scotia

In 2015, a two-dose MenB vaccination campaign with Bexsero was introduced at Acadia University, Nova Scotia – 4921 individuals received the first dose in February 2015 and 987 participants were assessed in an online safety survey following dose 1.

USA: University outbreaks

Princeton University and University of California at Santa Barbara

In 2013, the FDA authorised vaccination campaigns with Bexsero* in response to two university outbreaks; surveillance data for 15,236 individuals vaccinated with Bexsero have been reported.

Santa Clara

In 2016, a two-dose vaccination campaign with Bexsero was introduced – 4921 individuals received the first dose in February 2016.

*Under IND protocol prior to US approval (January 2015)
*Using a dosing schedule outside of the approved label

References:
Effectiveness and impact of a reduced infant schedule of 4CMenB vaccine against group B meningococcal disease in England: a national observational cohort study

Sydel R Parikh, Nick J Andrews, Kazim Beebeejaun, Helen Campbell, Sonia Ribeiro, Charlotte Ward, Joanne M White, Ray Borrow, Mary E Ramsay, Shamez N Ladhani

National vaccine programme with the entire UK birth cohort

Coverage:
1 dose = 95.5%
2 dose = 88.6%

Sophisticated surveillance

2-dose effectiveness: 82.9% (24.1-95.2)
Summary

- Serogroup B disease affects mainly infants, is easily misdiagnosed, can kill within 24 hours of onset, and may cause serious, lifelong disabilities despite appropriate medical treatment.

- **Bexsero** is a novel meningococcal serogroup B vaccine for active immunisation against invasive MenB disease.

- **Bexsero** offers several schedule options that fit with routine vaccination visits and possible catch-up programs.

- In clinical trials, **Bexsero** has demonstrated a protective immune response in infants, children, adolescents, and adults with or without routine vaccines.

- **Bexsero** has a demonstrated safety profile based on an evaluation of >67,000 subjects in clinical trials and postmarketing studies (from 2 months of age).

- Results from the UK, Canada and USA demonstrate real-world effectiveness of **Bexsero**.

* **Bexsero®** is not expected to provide protection against all circulating meningococcal group B strains.*
Herpes zoster (shingles) and GSK’s adjuvanted subunit vaccine candidate (HZ/su)

HZ/su is not registered or available in New Zealand
HZ is caused by the reactivation of the dormant varicella zoster virus¹

Primary infection: varicella (chickenpox)¹

Reactivation of infection: HZ (shingles)¹

VZV becomes latent in the sensory ganglia nerves¹

Approximately 99.5% of adults ≥40 years of age show serologic evidence of VZV infection, and one in three people develop shingles in their lifetime²


*see footnote
The natural course of HZ is made of an acute phase often followed by chronic complications.

**Prodrome**

- Headache, fever, myalgia

**Acute (2-4 weeks)**

- Localised rash
- Associated acute pain

**Chronic (1–3 months)**

- PHN
- HZO

Others: stroke, bacterial superinfection, hearing loss, palsy, scarring, nerve cell/fiber damage

**Recurrent rate**

- ~5% over years

HZO, herpes zoster ophthalmicus; PHN, postherpetic neuralgia

The risk of HZ increases with the decline in immune system function\(^1\)

**Aging immune system (immunosenescence)\(^1\)**

Older adults (≥50 years of age)

![Image source Shutterstock](image)

**Compromised immune system (immunocompromised)\(^1\)**

Patients on immunosuppressant drugs, with immunodeficient conditions or receiving transplants

![Image source Getty images](image)

HZ/su vaccine composition

HZ/su: for the prevention of HZ and HZ-related complications, such as PHN, in adults ≥50 years of age

**HZ/su vaccine**
Non live

**Antigen**
gE - 50 µg

**Adjuvant system**
AS01B: QS-21* and MPL - 50 µg each

*QS-21 adjuvant licensed from Antigenics Inc, a wholly owned subsidiary of Agenus Inc. a Delaware USA corporation; gE, glycoprotein; MPL, 3-O-desacyl-4’-monophosphoryl lipid A; QS-21, *Quillaja saponaria* Molina, fraction 21

HZ/su pivotal phase III programme: ZOE-50 and ZOE-70\textsuperscript{1,2}

*New England Journal of Medicine, 2015, 2016*

<table>
<thead>
<tr>
<th>Study design and objectives</th>
<th>ZOE-50\textsuperscript{1} (Zoster-006)</th>
<th>ZOE-70\textsuperscript{2} (Zoster-022)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Study design</td>
<td>Randomised, observer-blind, placebo-controlled, multicentre, multinational (North America, Europe, Latin America, Asia-Pacific)</td>
<td></td>
</tr>
<tr>
<td>Schedule</td>
<td>2 doses administered 2 months apart</td>
<td></td>
</tr>
<tr>
<td>Primary objectives</td>
<td>VE\textsubscript{HZ} in subjects ≥50 years of age</td>
<td>VE\textsubscript{HZ} in subjects ≥70 years of age</td>
</tr>
<tr>
<td>Primary objectives (pooled analysis)</td>
<td>VE\textsubscript{PHN} in individuals ≥70 years of age</td>
<td>VE\textsubscript{HZ} efficacy in individuals ≥70 years of age</td>
</tr>
<tr>
<td>Actual enrollment</td>
<td>16160</td>
<td>14816</td>
</tr>
</tbody>
</table>

ZOE-50 and ZOE-70 studies conducted at the same sites
Subjects ≥70 years of age were randomly assigned to ZOE-50 or ZOE-70

PHN, postherpetic neuralgia; VE, vaccine efficacy

Vaccine efficacy against HZ in subjects 50 years and older

<table>
<thead>
<tr>
<th>Age range (years)</th>
<th>ZOE-50 mTVC*</th>
<th>HZ/su N=7,344</th>
<th>Placebo N=7,415</th>
<th>VE (95% CI)†</th>
</tr>
</thead>
<tbody>
<tr>
<td>Overall (≥50)</td>
<td></td>
<td>6</td>
<td>3</td>
<td>9.1</td>
</tr>
<tr>
<td>50−59</td>
<td></td>
<td>3</td>
<td>2</td>
<td>7.8</td>
</tr>
<tr>
<td>60−69</td>
<td></td>
<td>2</td>
<td>8</td>
<td>10.8</td>
</tr>
<tr>
<td>≥70</td>
<td></td>
<td>1</td>
<td>48</td>
<td>9.4</td>
</tr>
</tbody>
</table>

Primary objective  Secondary objective

†p-value for all efficacy comparisons with placebo <0.001
*Excludes subjects not receiving Dose 2 or who developed HZ within 1 month after Dose 2
^Number per 1,000 person-years

Secondary objective

Age independent efficacy

CI, confidence interval; HZ/su, herpes zoster subunit vaccine; mTVC, modified total vaccinated cohort; VE, vaccine efficacy
High efficacy for HZ/su sustained with minimal decline up to 4 years post initial vaccination (ZOE-70)*

<table>
<thead>
<tr>
<th>Vaccine efficacy by year post vaccination</th>
<th>HZ/su</th>
<th>Placebo</th>
<th>( \text{VE}_{HZ} ) (95% CI)‡</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Years†</strong></td>
<td>HZ cases (n)</td>
<td>Rate (cases per 1000 person-years)</td>
<td>HZ cases (n)</td>
</tr>
<tr>
<td>Year 1</td>
<td>2 (8250)</td>
<td>0.2</td>
<td>83 (8346)</td>
</tr>
<tr>
<td>Year 2</td>
<td>7 (8039)</td>
<td>0.9</td>
<td>87 (8024)</td>
</tr>
<tr>
<td>Year 3</td>
<td>9 (7736)</td>
<td>1.2</td>
<td>58 (7661)</td>
</tr>
<tr>
<td>Year 4</td>
<td>7 (7426)</td>
<td>1.0</td>
<td>56 (7267)</td>
</tr>
</tbody>
</table>

*Subjects followed-up for a mean of 3.7 years at the time of this publication
†Year 1: 30–395 days after the second vaccination; Year 2: 396–760 days after the second vaccination; Year 3: 761–1125 days after the second vaccination; Year 4: >1125 after the second vaccination to the last contact date. n=number of subjects within each age group
‡p<0.001 for all comparisons
CI, confidence interval; HZ/su, herpes zoster subunit vaccine; VE, vaccine efficacy

HZ/su greatly reduced HZ complications, such as PHN, among all groups ≥50 years of age*1,2

Pre-specified, pooled analyses from ZOE-50 and ZOE-70

<table>
<thead>
<tr>
<th>Age, years</th>
<th>HZ/su</th>
<th>Placebo</th>
<th>VE$_{HZ}$ (95% CI)†</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>PHN cases (n)</td>
<td>Rate (cases per 1000 person-years)</td>
<td>PHN cases (n)</td>
</tr>
<tr>
<td>≥50</td>
<td>4 (13881)</td>
<td>0.1</td>
<td>36 (8346)</td>
</tr>
<tr>
<td>≥70</td>
<td>4 (8250)</td>
<td>0.1</td>
<td>46 (14035)</td>
</tr>
</tbody>
</table>

• In a post-hoc pooled analysis from ZOE-50 and ZOE-70, HZ/su also reduced non-PHN complications (HZ vasculitis, stroke, disseminated, ophthalmic, neurological and visceral disease)2
  o VE in subjects ≥50 years of age: 93.7% (95% CI 59.5, 99.9)
  o VE in subjects ≥70 years of age: 91.6% (95% CI 43.4, 99.8)

PHN defined as HZ-associated pain rated as ≥3 on a 0–10 scale, occurring or persisting for at least 90 days following the onset of rash using Zoster Brief Pain Inventory questionnaire. Pooled data from ZOE-50 (subjects ≥50 years of age) and ZOE-70 (subjects ≥70 years of age)

*All subjects randomised in the study who received a second dose of the vaccine. Final analysis data cut-off date: July 1, 2014; mean follow-up 3.8 years; †p<0.001 for both comparisons

CI, confidence interval; HZ/su, herpes zoster subunit vaccine; PHN, postherpetic neuralgia; VE, vaccine efficacy

Local adverse reactions to HZ/su were transient; (mean duration 2–3 days)\(^1,2\)

Solicited local symptoms reported during 7 days post vaccination: any grade overall by subject

ZOE-50: Overall median duration of 3 days for pain, redness and swelling\(^3\)
ZOE-70: Overall median duration of 2 days for pain; 3 days for redness and swelling\(^2\)

**Pain**
- ZOE-50: 80%
- Placebo ZOE-50: 55%
- ZOE-70: 40%
- Placebo ZOE-70: 30%

**Redness**
- ZOE-50: 80%
- Placebo ZOE-50: 55%
- ZOE-70: 40%
- Placebo ZOE-70: 30%

**Swelling**
- ZOE-50: 80%
- Placebo ZOE-50: 55%
- ZOE-70: 40%
- Placebo ZOE-70: 30%

n= Number of subjects with at least 1 documented dose
%= Percentage of subjects reporting the symptom at least once when the intensity is maximum

Systemic adverse reactions to HZ/su were transient (mean duration 1–2 days)\textsuperscript{1,2}

Solicited systemic symptoms reported during 7 days post vaccination: any grade overall by subject

- ZOE-50: Median duration of 2 days for fatigue, GI, HA and myalgia; 1 day for fever and shivering\textsuperscript{3}
- ZOE-70: Median duration of 2 days for fatigue, GI, HA myalgia and fever; 1 day for shivering\textsuperscript{2}

*GI symptoms included nausea, vomiting, diarrhoea, and/or abdominal pain

HZ/su provided efficacy across all age groups ≥50 years of age with an acceptable safety and tolerability profile

**Efficacy**

>90% efficacy shown in all age groups – from 50 to over 80 years of age (pooled data from 2 pivotal phase 3 trials)\(^1,2\)

There was no significant decline in efficacy during an ongoing follow-up period (median 4.4 years),\(^2\) and immunogenicity was maintained for at least 9 years\(^3\)

HZ/su eliminated almost all occurrences of PHN and non-PHN complications*\(^2,4,5\)

**Safety**

Adverse reactions were mostly transient and of mild-to-moderate intensity, with a median duration of 3 days\(^2,3,4,6\)

*HZ vaculitis, disseminated disease, ophthalmic disease, neurological disease visceral disease, stroke

Q&A
Prescribing Information— *Bexsero* Meningococcal Group B Vaccine (rDNA, Component, Adsorbed)

**Active ingredients:**

One dose (0.5 ml) contains:

Recombinant *Neisseria meningitidis* group B NHBA fusion protein - 50 µg;

Recombinant *Neisseria meningitidis* group B NadA protein - 50 µg;

Recombinant *Neisseria meningitidis* group B fHbp fusion protein - 50 µg;

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

**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.*

**Method of administration:** The vaccine is given by deep intramuscular injection.

**Dosage information:**

*From 2 to 5 months:* Three doses each of 0.5 ml, with first dose given at 2 months of age, with no less than 2-month interval between primary doses and a booster dose between 12 and 15 months. *Unvaccinated infants, 6 months to 11 months:* Two doses each of 0.5 ml, with no less than 2-month interval and a booster dose in the second year of life, respecting at least a 2-month interval between primary doses and booster dose. *Unvaccinated children, 12 months to 23 months:* Two doses each of 0.5 ml, with no less than 2-month interval between the primary doses and a booster dose, respecting an interval of 12 to 23 months between primary doses and booster dose. *Children, 2 years to 10 years:* Two doses each of 0.5 ml, with no less than 2-month interval between the primary doses. *Adolescents (from 11 years of age) and adults:* Two doses each of 0.5 ml, with no less than 1-month interval between the primary doses. A booster dose was not established in children from 2 to 10 years old, adolescents and adults.

*Bexsero* is not expected to provide protection against all circulating meningococcal group B strains.

*Bexsero* is a registered trademark of the GlaxoSmithKline group of companies.
Prescribing Information—Bexsero Meningococcal Group B Vaccine (rDNA, Component, Adsorbed)

Adverse events: See the local label for details.

Infants and children (up to 10 years): Very common: Eating disorders, sleepiness, unusual crying, diarrhea, vomiting (uncommon after booster), rash (children aged 12 to 23 months, uncommon after booster), fever (≥38°C), erythema, swelling, induration and tenderness at the injection site (including severe injection site tenderness, defined as crying when injected limb is moved), irritability; Common: Rash (children aged between 12 and 23 months); Uncommon: Seizures (including febrile seizures), pallor (rare after booster); Rare: Kawasaki syndrome, urticaria. Adolescents (from 11 years of age) and adults: Very common: headache, nausea, swelling, induration, erythema, and pain at the injection site (including severe injection site pain, defined as unable to perform normal daily activity), malaise, myalgia, arthralgia.

Contraindications:
Hypersensitivity to the active substances or to any of the excipients listed in the formulation.

Interaction with other medicinal products:
The safety profile of the coadministered routine vaccines were unaffected by concomitant administration of Meningococcal group B Vaccine (rDNA, component, adsorbed), except for an increased risk of fever, tenderness at the injection site, change in eating habits, and irritability. The coadministration of whole-cell pertussis with Meningococcal group B vaccine (rDNA, component, adsorbed) has not been studied and therefore is not recommended. When coadministered with other vaccine, the Meningococcal group B Vaccine (rDNA, component, adsorbed) must be applied in a distinct injection site.

Precautions and warnings:
Administration of Meningococcal group B Vaccine (rDNA, component, adsorbed) should be postponed in subjects suffering from acute severe febrile illness. The presence of a minor infection is not a contraindication for immunization. The vaccine should under no circumstances be injected via intravascular. Appropriate medical treatment and supervision should always be available in case of an anaphylactic event following administration of the vaccine. Reactions related to anxiety including vasovagal reactions (syncope), hyperventilation, or stress-related reactions can occur in association with vaccination as a psychogenic response to the needle injection. The vaccine should not be administered in patients with thrombocytopenia or bleeding disorder that may contraindicate intramuscular injection, unless the potential benefit clearly outweighs the risk of administration. As with any vaccine, Meningococcal group B Vaccine (rDNA, component, adsorbed) may not fully protect all of those who are vaccinated. It is not expected that the vaccine provides protection against all meningococcal strains circulating in group B.

Medicinal product subject to medical prescription.

Cost: Please contact the local Key account manager from GSK for pricing information if applicable.

Agency Product Number: EMEA/H/C/002333

Marketing Authorization Holder:

Bexsero is a registered trademark of the GlaxoSmithKline group of companies.
Succinct Safety Statement—*Bexsero* Meningococcal Group B Vaccine (rDNA, Component, Adsorbed)

**Side effects:**

*Infants and children (up to 10 years):* Very common: Eating disorders, sleepiness, unusual crying, diarrhea, vomiting (uncommon after booster), rash (children aged 12 to 23 months, uncommon after booster), fever (≥38°C), erythema, swelling, induration and tenderness at the injection site (including severe injection site tenderness, defined as crying when injected limb is moved), irritability; Common: Rash (children aged between 12 and 23 months); Uncommon: Seizures (including febrile seizures), pallor (rare after booster); Rare: Kawasaki syndrome, urticaria. *Adolescents (from 11 years of age) and adults:* Very common: Headache, nausea, swelling, induration, erythema, and pain at the injection site (including severe injection site pain, defined as unable to perform normal daily activity), malaise, myalgia, arthralgia.

**Interactions:**

The safety profile of the coadministered routine vaccines were unaffected by concomitant administration of Meningococcal group B Vaccine (rDNA, component, adsorbed), except for an increased risk of fever, tenderness at the injection site, change in eating habits, and irritability. The coadministration of whole-cell pertussis with Meningococcal group B vaccine (rDNA, component, adsorbed) has not been studied and therefore is not recommended. When coadministered with other vaccine, the Meningococcal group B Vaccine (rDNA, component, adsorbed) must be applied in a distinct injection site.

**Contraindications:**

Hypersensitivity to the active substances or to any of the excipients listed in the formulation.

**Precautions:**

Administration of Meningococcal group B Vaccine (rDNA, component, adsorbed) should be postponed in subjects suffering from acute severe febrile illness. The presence of a minor infection is not a contraindication for immunization. The vaccine should under no circumstances be injected via intravascular. Appropriate medical treatment and supervision should always be available in case of anaphylactic event following administration of the vaccine. Reactions related to anxiety including vasovagal reactions (syncope), hyperventilation, or stress-related reactions can occur in association with vaccination as a psychogenic response to the needle injection. The vaccine should not be administered in patients with thrombocytopenia or bleeding disorder that may contraindicate intramuscular injection, unless the potential benefit clearly outweighs the risk of administration. As with any vaccine, Meningococcal group B Vaccine (rDNA, component, adsorbed) may not fully protect all of those who are vaccinated. It is not expected that the vaccine provides protection against all meningococcal strains circulating in group B.

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