BEXSERO- neisseria meningitidis serogroup b nhba fusion protein antigen, neisseria meningitidis serogroup b fhbp fusion protein antigen and neisseria meningitidis serogroup b nada protein antigen injection, suspension

GlaxoSmithKline Biologicals SA

HIGHLIGHTS OF PRESCRIBING INFORMATION

These highlights do not include all the information needed to use BEXSERO safely and effectively. See full prescribing information for BEXSERO.

BEXSERO (Meningococcal Group B Vaccine) injectable suspension, for intramuscular use

Initial U.S. Approval: 2015

RECENT MAJOR CHANGES

Indications and Usage (1)	8/2024
Dosage and Administration, Dose and Schedule (2.1)	8/2024

INDICATIONS AND USAGE

BEXSERO is a vaccine indicated for active immunization to prevent invasive disease caused by *Neisseria meningitidis* serogroup B. BEXSERO is approved for use in individuals aged 10 through 25 years. (1)

DOSAGE AND ADMINISTRATION

For intramuscular use. (2)

Two-dose schedule: Administer a dose (0.5 mL) at 0 and 6 months. If the second dose is administered earlier than 6 months after the first dose, a third dose should be administered at least 4 months after the second dose. (2.1)

Three-dose schedule: Administer a dose (0.5 mL) at 0, 1-2, and 6 months. (2.1)

DOSAGE FORMS AND STRENGTHS

Injectable suspension. A single dose is 0.5 mL. (3)

CONTRAINDICATIONS

Severe allergic reaction (e.g., anaphylaxis) to any component of BEXSERO or after a previous dose of BEXSERO. (4)

ADVERSE REACTIONS

The most commonly reported (≥10%) solicited adverse reactions were pain at the injection site (87%-92%), fatigue (45%-49%), headache (37%-41%), nausea (11%-13%), erythema (10%-15%), myalgia (10%-14%), and swelling (10%-14%). (6.1)

To report SUSPECTED ADVERSE REACTIONS, contact GlaxoSmithKline at 1-888-825-5249 or VAERS at 1-800-822-7967 or www.vaers.hhs.gov.

See 17 for PATIENT COUNSELING INFORMATION.

Revised: 8/2024

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FULL PRESCRIBING INFORMATION

1 INDICATIONS AND USAGE

BEXSERO is a vaccine indicated for active immunization to prevent invasive disease caused by *Neisseria meningitidis* serogroup B. BEXSERO is approved for use in individuals aged 10 through 25 years.

2 DOSAGE AND ADMINISTRATION

For intramuscular use.

2.1 Dose and Schedule

Two-dose schedule: Administer a dose (0.5 mL) at 0 and 6 months. If the second dose is administered earlier than 6 months after the first dose, a third dose should be administered at least 4 months after the second dose.

Three-dose schedule: Administer a dose (0.5 mL) at 0, 1-2, and 6 months.

The choice of dosing schedule may depend on the risk of exposure and the individual's susceptibility to meningococcal serogroup B disease.

2.2 Administration

Shake the syringe immediately before use to form a homogeneous suspension. Do not use the vaccine if it cannot be resuspended. Parenteral drug products should be inspected visually for particulate matter and discoloration prior to administration, whenever solution and container permit. Do not use if particulate matter or discoloration is found.

Administer BEXSERO as a 0.5-mL intramuscular injection.

2.3 Use of BEXSERO with Other Meningococcal Group B Vaccines

Sufficient data are not available on the safety and effectiveness of using BEXSERO and other meningococcal group B vaccines interchangeably to complete the vaccination series.

3 DOSAGE FORMS AND STRENGTHS

BEXSERO is an injectable suspension. A single dose is 0.5 mL.

4 CONTRAINDICATIONS

Do not administer BEXSERO to individuals with a history of a severe allergic reaction (e.g., anaphylaxis) to any component of BEXSERO or after a previous dose of BEXSERO *[see Description (11)]*.

5 WARNINGS AND PRECAUTIONS

5.1 Management of Allergic Reactions

Appropriate medical treatment must be immediately available to manage potential anaphylactic reactions following administration of BEXSERO.

5.2 Syncope

Syncope (fainting) can occur in association with administration of BEXSERO. Ensure procedures are in place to avoid injury from falling associated with syncope.

5.3 Limitation of Vaccine Effectiveness

BEXSERO may not protect all vaccine recipients. BEXSERO may not provide protection against all meningococcal serogroup B strains *[see Clinical Pharmacology (12.1)].*

5.4 Altered Immunocompetence

Some individuals with altered immunocompetence may have reduced immune responses to BEXSERO.

Complement Deficiency

Persons with certain complement deficiencies and persons receiving treatment that inhibits terminal complement activation (for example, eculizumab) are at increased risk

for invasive disease caused by *N. meningitidis* serogroup B even if they develop antibodies following vaccination with BEXSERO. *[See Clinical Pharmacology (12.1).]*

6 ADVERSE REACTIONS

The most commonly reported (≥10%) solicited adverse reactions in a Phase 3 clinical trial (Study 1) were pain at the injection site (87%-92%), fatigue (45%-49%), headache (37%-41%), nausea (11%-13%), erythema (10%-15%), myalgia (10%-14%), and swelling (10%-14%).

6.1 Clinical Trials Experience

The safety of BEXSERO was evaluated in 5 clinical studies (Table 1) in which a total of 4,861 participants aged 10 through 25 years received at least 1 dose of BEXSERO. Because clinical trials are conducted under widely varying conditions, adverse reaction rates observed in the clinical trials of a vaccine cannot be directly compared with rates in the clinical trials of another vaccine and may not reflect the rates observed in practice.

Table 1. BEXSERO Clinical Studies

Study (NCT#)	**Participant Age Range**	**Countries**	**BEXSERO Recipients[a]**
Study 1 (NCT04502693)	10-25 years	United States (U.S.), Australia, Canada, Czech Republic, Estonia, Finland, and Turkey	1,803
Study 2 (NCT01423084)	11-17 years	Canada and Australia	342
Study 3 (NCT01214850)	18-24 years	United Kingdom (U.K.)	974
Study 4 (NCT00661713)	11-17 years	Chile	1,622
Study 5 (NCT01272180)	10-25 years	U.S. and Poland	120

[a] Recipients who received at least 1 dose of BEXSERO.

In Study 1, conducted in the United States (U.S.), Australia, Canada, Czech Republic, Estonia, Finland, and Turkey, 1,803 participants aged 10 through 25 years received at least 1 dose of BEXSERO either as a 0-, 2-, 6-month schedule (n = 897) or 0-, 6-month schedule (n = 906). A single dose of MENVEO [Meningococcal (Groups A, C, Y, and W-135) Oligosaccharide Diphtheria CRM_{197} Conjugate Vaccine] was administered 1 month after the third dose in the 0-, 2-, 6-month group and 2 months after the first dose of BEXSERO in the 0-, 6-month group (these participants received saline placebo at month 7). A separate group (n = 178) received a single dose of MENVEO followed 6 months later by 2 doses of BEXSERO administered 1 month apart (these participants received saline placebo at month 2). Approximately 30% of participants were from the U.S. In this trial, the median age was 16 years, males comprised 47%, and 89% of participants were White, 5% were Asian, 4% were Black, and 2% were of other racial groups. Among study participants, 5% were Hispanic.

In Study 2, an uncontrolled study conducted in Canada and Australia, 342 participants aged 11 through 17 years received at least 1 dose of BEXSERO, including 338 participants who received 2 doses of BEXSERO 1 month apart (unapproved dosing schedule). The median age was 13 years, males comprised 55%, and 80% of participants were White, 10% were Asian, 4% were Native American/Alaskan, and 4% were of other racial groups.

In Study 3, conducted in the United Kingdom (U.K.), 974 university students aged 18 through 24 years received at least 1 dose of BEXSERO, including 932 participants who received 2 doses of BEXSERO 1 month apart (unapproved dosing schedule). Comparator groups received 1 dose of MENVEO followed by 1 dose of placebo containing aluminum hydroxide (n = 956) or 2 doses of IXIARO (Japanese Encephalitis Vaccine, Inactivated, Adsorbed) (n = 947). Across groups, median age was 20 years, males comprised 46%, and 88% of participants were White, 5% were Asian, 2% were Black, <1% were Hispanic, and 4% were of other racial groups.

In Study 4, conducted in Chile, 1,622 participants aged 11 through 17 years received at least 1 dose of BEXSERO according to approved and unapproved dosing schedules. A control group of 128 participants received at least 1 dose of placebo containing aluminum hydroxide. In this study, median age was 14 years, males comprised 44%, and 99% were Hispanic.

In Study 5, conducted in the U.S. and Poland, 120 participants aged 10 through 25 years received at least 1 dose of BEXSERO, including 112 participants who received 2 doses of BEXSERO 2 months apart (unapproved dosing schedule); 97 participants received saline placebo followed by MENVEO. Across groups, the median age was 13 years, males comprised 49%, and 60% of participants were White, 34% were Hispanic, 4% were Black, <1% were Asian, and 2% were of other racial groups.

Local and systemic reactogenicity data were solicited from all participants in the trials with the exception of one trial (Study 3) where they were solicited in a subset of participants only. Reports of unsolicited adverse events occurring within the first 7 days after each vaccination were collected in all trials. Reports of unsolicited adverse events occurring within the 30 days after each vaccination were collected in 2 trials (Study 1, Study 5).

Reports of all serious adverse events, medically attended adverse events, and adverse events leading to premature withdrawal were collected throughout the study period of 2 months (Study 2), 8 months (Study 5), or 12 months (Study 1, Study 3, Study 4).

Solicited Adverse Reactions

The rates of local and systemic adverse reactions reported in Study 1 among participants aged 10 through 25 years following each dose of BEXSERO or a single dose of MENVEO are presented in Table 2.

Table 2. Percentage of Participants Aged 10 through 25 Years Reporting Solicited Local and Systemic Adverse Reactions within 7 Days of BEXSERO or MENVEO, by Dose (Solicited Safety Set, Study 1)

	BEXSERO (0, 6 Months) %	**BEXSERO (0, 2, 6 Months) %**	**MENVEO (Single Dose) %**

Solicited Reaction[a]		Dose 1 n = 894	Dose 2 n = 759	Dose 1 n = 885	Dose 2 n = 823	Dose 3 n = 765	Dose 1 n = 178
Local Adverse Reactions							
Pain	Any	92	89	91	87	89	38
	Severe	6	8	6	7	11	0
Erythema	Any	10	12	10	11	15	6
	Severe	1	1	1	1	2	1
Swelling	Any	10	11	10	12	14	6
	Severe	1	2	1	1	1	1
Induration	Any	7	8	7	8	7	4
	Severe	2	1	1	1	1	0
Systemic Adverse Reactions							
Fatigue	Any	46	45	48	45	49	44
	Severe	1	3	2	2	3	2
Nausea	Any	12	11	13	13	12	15
	Severe	1	0.4	1	1	0.3	1
Myalgia	Any	12	14	10	14	14	7
	Severe	1	0.4	0.2	1	1	0
Arthralgia	Any	8	7	6	9	9	10
	Severe	0.3	0	0.2	1	0.4	0
Headache	Any	37	37	41	37	40	39
	Severe	1	1	1	2	2	2
Fever	Any	2	3	2	3	3	2
	Severe	0.1	0	0.1	0	0.1	1

Study 1: NCT04502693.

[a] Erythema, swelling, and induration: Any (≥25 mm); Severe (>100 mm). Pain, fatigue, nausea, myalgia, arthralgia, headache: Any includes Mild (transient with no limitation in normal daily activity), Moderate (some limitation in normal daily activity), and Severe (unable to perform normal, daily activity). Fever: Any (≥38.0°C/100.4°F); Severe (≥40.0°C/104.0°F).

Solicited adverse reactions were also collected in 4 additional clinical trials (Studies 2-5) in participants aged 10 through 25 years who received BEXSERO. Pain was the most common local adverse reaction reported (83% to 96%), with severe pain reported by 8% to 29% of participants, across trials. Among the systemic reactions collected, myalgia (37% to 75%), headache (21% to 47%), and fatigue/malaise (17% to 58%) were the most commonly reported systemic reactions across trials.

Unsolicited Adverse Events

In Study 1, unsolicited adverse events (non-serious and serious) that occurred within 7 days of any dose of study vaccination were reported by 14% of participants in the group receiving BEXSERO as a 0-, 6-month schedule (n = 900), 13% of participants in the group receiving BEXSERO as a 0-, 2-, 6-month schedule (n = 893), and 20% of participants in the MENVEO group (n = 178).

A non-serious event of arthritis with onset 10 days after receipt of BEXSERO in a 24-year-old male was assessed as vaccine-related by the study investigator. The participant, later found to be HLA-B27 positive, may be at increased risk for arthritis

unrelated to vaccination.

In the other controlled trials (Study 3, Study 4, Study 5) (BEXSERO n = 2,221, control n = 2,204), non-serious unsolicited adverse events that occurred within 7 days of any dose were reported by 439 (20%) participants receiving BEXSERO and 197 (9%) control recipients. Unsolicited adverse reactions that were reported among at least 2% of participants and were more frequently reported in participants receiving BEXSERO than in control recipients were injection site pain, headache, injection site induration unresolved within 7 days, and nasopharyngitis.

Serious Adverse Events

In Study 1, serious adverse events that occurred within 30 days of any dose of study vaccination were reported by 1.2% of participants in the group receiving BEXSERO as a 0-, 6-month schedule (n = 900), 1.0% of participants in the group receiving BEXSERO as a 0-, 2-, 6-month schedule (n = 893), and 0% of participants in the MENVEO group (n = 178). None of these events were considered related to BEXSERO.

Overall, in Studies 2-5, among 3,058 participants aged 10 through 25 years who received at least 1 dose of BEXSERO, 66 (2.1%) participants reported serious adverse events at any time during the trial. In the 3 controlled trials (Study 3, Study 4, Study 5) (BEXSERO n = 2,716, control n = 2,078), serious adverse events within 30 days after any dose were reported in 23 (0.8%) participants receiving BEXSERO and 10 (0.5%) control recipients. In Study 4, among participants who received 3 doses of BEXSERO (n = 628), 15 (2.4%) participants reported serious adverse events at any time during the trial.

6.2 Additional Pre-Licensure Safety Experience

In response to outbreaks of serogroup B meningococcal disease at 2 universities in the U.S., BEXSERO was administered as a 2-dose series at least 1 month apart. Information on serious adverse events was collected for a period of 30 days after each dose from 15,351 individuals aged 16 through 65 years who received at least 1 dose. Overall, 50 individuals (0.3%) reported serious adverse events, including one reaction considered related to vaccination, a case of anaphylaxis within 30 minutes following vaccination.

6.3 Postmarketing Experience

The following adverse reactions have been identified during post-approval use of BEXSERO. Because these reactions are reported voluntarily from a population of uncertain size, it is not always possible to reliably estimate their frequency or establish a causal relationship to the vaccine.

Blood and Lymphatic System Disorders

Lymphadenopathy.

General Disorders and Administration Site Conditions

Injection site reactions (including extensive swelling of the vaccinated limb, blisters at or around the injection site, and injection site nodule which may persist for more than 1 month).

Immune System Disorders

Allergic reactions (including anaphylactic reactions), rash, eye swelling.

Nervous System Disorders

Syncope, vasovagal responses to injection.

8 USE IN SPECIFIC POPULATIONS

8.1 Pregnancy

Risk Summary

All pregnancies have a risk of birth defect, loss, or other adverse outcomes. In the U.S. general population, the estimated background risk of major birth defects and miscarriage in clinically recognized pregnancies is 2% to 4% and 15% to 20%, respectively.

There are no adequate and well-controlled studies of BEXSERO in pregnant women in the U.S. Available human data on BEXSERO administered to pregnant women are insufficient to inform vaccine-associated risks in pregnancy.

A developmental toxicity study was performed in female rabbits administered BEXSERO prior to mating and during gestation. The dose was 0.5 mL at each occasion (a single human dose is 0.5 mL). This study revealed no adverse effects on fetal or pre-weaning development due to BEXSERO *(see Data)*.

Data

Animal Data: In a developmental toxicity study, female rabbits were administered BEXSERO by intramuscular injection on Days 29, 15, and 1 prior to mating and on Gestation Days 7 and 20. The total dose was 0.5 mL at each occasion (a single human dose is 0.5 mL). No adverse effects on pre-weaning development up to Postnatal Day 29 were observed. There were no fetal malformations or variations observed.

8.2 Lactation

Risk Summary

It is not known whether the vaccine components of BEXSERO are excreted in human milk. Available data are not sufficient to assess the effects of BEXSERO on the breastfed infant or on milk production/excretion. The developmental and health benefits of breastfeeding should be considered along with the mother’s clinical need for BEXSERO and any potential adverse effects on the breastfed child from BEXSERO or from the underlying maternal condition. For preventive vaccines, the underlying maternal condition is susceptibility to disease prevented by the vaccine.

8.4 Pediatric Use

Safety and effectiveness of BEXSERO have not been established in children younger than 10 years.

8.5 Geriatric Use

Safety and effectiveness of BEXSERO have not been established in adults older than 65 years.

11 DESCRIPTION

BEXSERO (Meningococcal Group B Vaccine) is a sterile, white, opalescent, injectable suspension for intramuscular use. Each 0.5-mL dose of BEXSERO is formulated to contain 50 mcg each of recombinant proteins Neisserial adhesin A (NadA), Neisserial Heparin Binding Antigen (NHBA), and factor H binding protein (fHbp), and 25 mcg of Outer Membrane Vesicles (OMV), 1.5 mg aluminum hydroxide (0.519 mg of Al^{3+}), 3.125 mg sodium chloride, 0.776 mg histidine, and 10 mg sucrose at pH 6.4 to 6.7.

The NadA component is a fragment of the full-length protein derived from *N. meningitidis* strain 2996 (peptide 8 variant 2/3)[1]. The NHBA component is a recombinant fusion protein comprised of NHBA (peptide 2)[1] and accessory protein 953 derived from *N. meningitidis* strains NZ98/254 and 2996, respectively. The fHbp component is a recombinant fusion protein comprised of fHbp (variant 1.1)[1] and the accessory protein 936 derived from *N. meningitidis* strains MC58 and 2996, respectively. These 3 recombinant proteins are individually produced in *Escherichia coli* and purified through a series of column chromatography steps. The OMV antigenic component is produced by fermentation of *N. meningitidis* strain NZ98/254 (expressing outer membrane protein Porin A [PorA] serosubtype P1.4)[2], followed by inactivation of the bacteria by deoxycholate, which also mediates vesicle formation. The antigens are adsorbed onto aluminum hydroxide.

Each dose contains less than 0.01 mcg kanamycin (by calculation).

The tip cap and rubber plunger stopper of the prefilled syringe are not made with natural rubber latex.

12 CLINICAL PHARMACOLOGY

12.1 Mechanism of Action

Protection against invasive meningococcal disease is conferred mainly by complement-mediated antibody-dependent killing of *N. meningitidis*.

NHBA, NadA, and fHbp are proteins found on the surface of meningococci and contribute to the ability of the bacteria to cause disease. OMV derived from the bacterial outer membrane contains PorA and other surface proteins. Vaccination with BEXSERO leads to the production of antibodies directed against NHBA, NadA, fHbp, and OMV. The susceptibility of serogroup B meningococci to complement-mediated antibody-dependent killing following vaccination with BEXSERO is dependent on both the antigenic similarity of the bacterial and vaccine antigens, as well as the amount of antigen expressed on the surface of the invading meningococci.

13 NONCLINICAL TOXICOLOGY

13.1 Carcinogenesis, Mutagenesis, Impairment of Fertility

BEXSERO has not been evaluated for carcinogenic or mutagenic potential or impairment of male fertility in animals.

14 CLINICAL STUDIES

The effectiveness of BEXSERO was assessed by measuring serum bactericidal activity (SBA) in an assay that used endogenous complement preserved in the serum samples collected from study participants (enc-hSBA) and an assay that used an exogenous source of human complement (hSBA).

The enc-hSBA assay was used to assess effectiveness against diverse *N. meningitidis* serogroup B strains. Participants' sera were tested for the presence or absence of bactericidal activity to measure breadth of immune response against a panel of 110 diverse U.S. disease-causing *N. meningitidis* serogroup B strains that were collected between 2000 and 2008. The panel includes most antigen types found among serogroup B isolates circulating in the U.S. between 2000 and 2017, and includes some strains with genetic profiles characterized as hypervirulent. Each participant's serum was tested at a four-fold dilution against a maximum of 35 strains randomly selected from the panel.

The hSBA assay measured bactericidal activity in participants' sera against 4 serogroup B indicator strains, one for each of the 4 antigenic components of BEXSERO.

Breadth of Immune Response Elicited by BEXSERO (enc-hSBA Assay)

Study 1 evaluated enc-hSBA responses in participants aged 10 through 25 years 1 month following dose 2 of a 0-, 6-month schedule and dose 3 of a 0-, 2-, 6-month schedule of BEXSERO using responder-based and test-based analyses.

Responder-based analyses (Table 3) evaluated the percentages of participants whose sera killed ≥70% of the tested strains.

Table 3. Percentage of Participants Whose Sera Killed ≥70% of Meningococcal Serogroup B Strains Tested[a] (Responder-Based) following BEXSERO, Study 1[b]

Group[c]	Dose	N	% Responders[d] (97.5% CI)
0, 6 Months	Dose 2	813	90 (87[e], 92)
0, 2, 6 Months	Dose 3	790	93 (91[e], 95)

Study 1: NCT04502693.
CI = Confidence interval.
[a] Each participant's serum was tested for bactericidal activity (yes/no) against a maximum of 35 strains randomly selected from the 110-strain panel.
[b] Full Analysis Set includes all participants who received at least 1 dose of the study treatment and have post-vaccination immunogenicity data.
[c] enc-hSBA responses were measured one month after the second dose of BEXSERO using the 0-, 6-month schedule and one month after the third dose of BEXSERO using the 0-, 2-, 6-month schedule.
[d] % Responders is defined as percentages of participants whose serum kills ≥70% of strains tested using enc-hSBA.
[e] Predefined criterion (lower limit of the 2-sided 97.5% CI >65%) met. CI calculated using Clopper-Pearson method.

Of the approximately 35 serogroup B strains tested per participant in the enc-hSBA assay at 1 month following vaccination, the median percentage killed by each participant's serum was 88.2% (25^{th} percentile, 80.0%; 75^{th} percentile, 94.3%) after dose 2 of the 0-, 6-month BEXSERO schedule; 88.6% (25^{th} percentile, 80.0%; 75^{th} percentile, 94.3%) after dose 3 of the 0-, 2-, 6-month BEXSERO schedule; and 17.1% (25^{th} percentile, 11.1%; 75^{th} percentile, 26.7%) after MENVEO.

Test-based analyses (Table 4) evaluated the reduction in relative risk of enc-hSBA tests without bactericidal activity against meningococcal serogroup B strains following BEXSERO as compared to MENVEO.

Table 4. Reduction in Relative Risk of a Test[a] without Bactericidal Activity against Meningococcal Serogroup B Strains following BEXSERO (Test-Based), Study 1[b]

Group[c]	Dose	Number of Participants	% of Tests without Bactericidal Activity (n/N)	Reduction in Relative Risk of a Test without Bactericidal Activity[d,e] % (97.5% CI[e])
BEXSERO 0, 6 Months	Dose 2	764	14 (3,777 / 26,142)	82 (80[f], 83)
BEXSERO 0, 2, 6 Months	Dose 3	747	13 (3,412 / 25,596)	83 (82[f], 84)
MENVEO	Dose 1	133	79 (3,456 / 4,374)	-

Study 1: NCT04502693.
CI = Confidence interval, n = number of tests without bactericidal activity, N = total number of tests, RR = Relative Risk.
[a] Each test qualitatively assessed (yes/no) the bactericidal activity of one participant's serum against one of the 110 U.S. meningococcal serogroup B strains. Each participant's serum was tested against a maximum of 35 strains randomly selected from the 110-strain panel.
[b] Per Protocol Set includes all participants in the Full Analysis Set minus participants with protocol deviations that lead to exclusion from the Per Protocol Set.
[c] enc-hSBA responses were measured one month after the second dose of BEXSERO using the 0-, 6-month schedule, one month after the third dose of BEXSERO using the 0-, 2-, 6-month schedule, and one month after the single dose of MENVEO.
[d] Reduction in Relative Risk of enc-hSBA tests without bactericidal activity is defined as 1- RR = (1- percentage of samples without bactericidal serum activity measured by enc-hSBA in the BEXSERO group / percentage of samples without bactericidal serum activity in the MENVEO group) x 100%.
[e] The Relative Risk and corresponding confidence intervals are estimated using a generalized linear model where treatment group and randomization factors were modeled as independent variables.
[f] Predefined criterion (lower limit of the 2-sided 97.5% CI >65%) met.

For each individual strain in the 110-strain panel, the percentage of tests with bactericidal activity following BEXSERO ranged from 4% to 100%; the median was 97%

(25th percentile, 80%; 75th percentile, 99%) for the 0-, 6-month schedule and 98% (25th percentile, 85%; 75th percentile, 99%) for the 0-, 2-, 6-month schedule. For each individual strain, the percentage of tests with bactericidal activity following MENVEO ranged from 0% to 100%; the median was 12% (25th percentile, 3%; 75th percentile, 28%).

Immune Response to BEXSERO (hSBA Assay)

In Study 1, immune responses in participants aged 10 through 25 years were measured following 0-, 6-month or 0-, 2-, 6-month schedules of BEXSERO with hSBA assays using indicator strains representative of each of the 4 antigenic components of BEXSERO (fHbp, NadA, NHBA, and OMV). The proportion of participants who achieved a 4-fold or greater increase in hSBA titer for each of the 4 strains (seroresponse), and the proportion of participants with a titer greater than or equal to the lower limit of quantitation (LLOQ) of the assay for all 4 strains (composite response) at 1 month after dose 2 (0-, 6-month schedule) and doses 2 and 3 (0-, 2-, 6-month schedule) are shown in Table 5.

Table 5. Percentage of Participants with hSBA Seroresponse and Composite Response following BEXSERO, Study 1[a]

	0, 6 Months			**0, 2, 6 Months**					
	Dose 2			**Dose 2**			**Dose 3**		
Seroresponse[b,c,d] Antigen	**N**	**%**	**95% CI[e]**	**N**	**%**	**95% CI[e]**	**N**	**%**	**95% CI[e]**
fHbp	699	78	74, 81	739	67	64, 71	679	81	78, 84
NadA	700	95	93, 97	738	97	95, 98	679	99	98, 99
NHBA	704	69	66, 72	739	58	55, 62	685	67	63, 70
OMV	664	57	53, 61	724	54	50, 57	637	57	53, 60
Composite Response[d,f] Time Point	**N**	**%**	**95% CI[e]**	**N**	**%**	**95% CI[e]**	**N**	**%**	**95% CI[e]**
Baseline (pre-vaccination)	708	0.6	0.2, 1.4	727	1.1	0.5, 2.2	727	1.1	0.5, 2.2
1 Month post-dose 2 or 3	683	80	77, 83	744	74	71, 77	654	82	78, 84

Study 1: NCT04502693.
hSBA = Serum bactericidal activity measured using human complement,
CI = Confidence interval, fHbp = factor H binding protein, NadA = Neisserial adhesin A, NHBA = Neisserial Heparin Binding Antigen, OMV = Outer Membrane Vesicles,
LOD = Limit of detection, LLOQ = Lower limit of quantitation.
[a] Full Analysis Set includes all participants who received at least 1 dose of the study treatment and have post-vaccination immunogenicity data.
[b] Seroresponse is defined as: a post-vaccination hSBA titer at least 4-fold the LOD or ≥LLOQ, whichever is greater, for participants with pre-vaccination hSBA titer <LOD, a post-vaccination hSBA titer at least 4-fold the LLOQ for participants with pre-vaccination hSBA titer ≥LOD and <LLOQ, and a post-vaccination hSBA at least 4-fold the pre-vaccination hSBA titer for participants with pre-vaccination hSBA titer ≥LLOQ.
[c] Antigen (indicator strain) = fHbp (M14459), NadA (96217), NHBA (M13520), OMV (NZ98/254).

[d] LOD = 4 for fHbp (M14459); 6 for NadA (96217); 4 for NHBA (M13520); 4 for OMV (NZ98/254). LLOQ = 5 for fHbp (M14459); 14 for NadA (96217); 6 for NHBA (M13520); 6 for OMV (NZ98/254).
[e] CI calculated using Clopper-Pearson method.
[f] Composite hSBA Response means hSBA ≥LLOQ for all 4 Meningococcal B indicator strains.

In Study 2 and Study 3, hSBA immune responses were measured with hSBA assays using indicator strains for 3 of the 4 antigenic components of BEXSERO: fHbp (strain H44/76), NadA (strain 5/99), and OMV (strain NZ98/254). A 4-fold hSBA response (seroresponse) was defined as a post-vaccination hSBA titer ≥16 for participants with pre-vaccination hSBA titer <4, a post-vaccination titer at least 4-fold the LLOQ for participants with pre-vaccination hSBA titer ≥4 but <LLOQ, and a post-vaccination hSBA titer 4-fold the pre-vaccination titer for participants with pre-vaccination hSBA titer ≥LLOQ. A composite hSBA response was defined as hSBA ≥LLOQ for all 3 indicator strains (≥1:16 for H44/76 and 5/99; 1:8 for NZ98/254).

In Study 2, Canadian and Australian adolescents aged 11 through 17 years received 2 doses of BEXSERO, administered 1 month apart. Among participants in the evaluable immunogenicity population (N = 298-299), the percentage of participants (95% CI) who demonstrated a 4-fold hSBA response were as follows: fHbp 98% (95%, 99%), NadA 99% (98%, 100%), and OMV 39% (33%, 44%). The percentage of participants with a composite response was 0% at baseline and 63% (95% CI: 57%, 68%) at 1 month following dose 2.

In Study 3, University students in the U.K. aged 18 through 24 years received 2 doses of BEXSERO, administered 1 month apart. Among participants in the evaluable immunogenicity population (N = 147-148), the percentage of participants (95% CI) who demonstrated a 4-fold hSBA response were as follows: fHbp 78% (71%, 85%), NadA 94% (89%, 97%), and OMV 67% (58%, 74%). The percentage of participants with a composite response was 24% (95% CI: 18%, 30%; n = 186) at baseline, 88% (95% CI: 82%, 93%; n = 147) at 1 month following dose 2, and 66% (95% CI: 58%, 72%; n = 136) at 11 months following dose 2.

15 REFERENCES

1. Wang X, et al. *Vaccine.* 2011; 29:4739-4744.
2. Hosking J, et al. *Clin Vaccine Immunol.* 2007;14:1393-1399.

16 HOW SUPPLIED/STORAGE AND HANDLING

16.1 How Supplied

BEXSERO is available in 0.5-mL single-dose, disposable, prefilled TIP-LOK syringes (Luer Lock syringes) packaged without needles. TIP-LOK syringes are to be used with Luer Lock compatible needles.

The tip cap and rubber plunger stopper of the prefilled syringe are not made with natural rubber latex.

Table 6. Product Presentation for BEXSERO

Presentation	Carton NDC Number	Components
Prefilled syringe Carton of **10** syringes	58160-976-20	0.5-mL single-dose prefilled syringe NDC 58160-976-02

16.2 Storage and Handling

Do not freeze. Discard if the vaccine has been frozen.

Store refrigerated, at 36°F to 46°F (2°C to 8°C).

Protect from light.

Do not use after the expiration date.

17 PATIENT COUNSELING INFORMATION

Give the patient, parent, or guardian the Vaccine Information Statements, which are required by the National Childhood Vaccine Injury Act of 1986 to be given prior to immunization. These materials are available free of charge at the Centers for Disease Control and Prevention (CDC) website (www.cdc.gov/vaccines).

Inform patients, parents, or guardians about:

- The importance of completing the immunization series.
- Reporting any adverse reactions to their healthcare provider.

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Manufactured by **GSK Vaccines, Srl**

Bellaria-Rosia 53018, Sovicille (SI), Italy

U.S. License No. 1617

Distributed by **GlaxoSmithKline**

Durham, NC 27701

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BXS:8PI

PRINCIPAL DISPLAY PANEL

NDC 58160-976-20

BEXSERO

Meningococcal Group B Vaccine

MenB

GSK

Rx Only

For Use from 10 through 25 Years of Age

10 Disposable Single-Dose Prefilled TIP-LOK Syringes each containing **one 0.5-mL dose**

TIP-LOK syringes to be used with Luer Lock compatible needles

NEEDLES NOT INCLUDED

BEXSERO

Made in Italy

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Rev. 08/23
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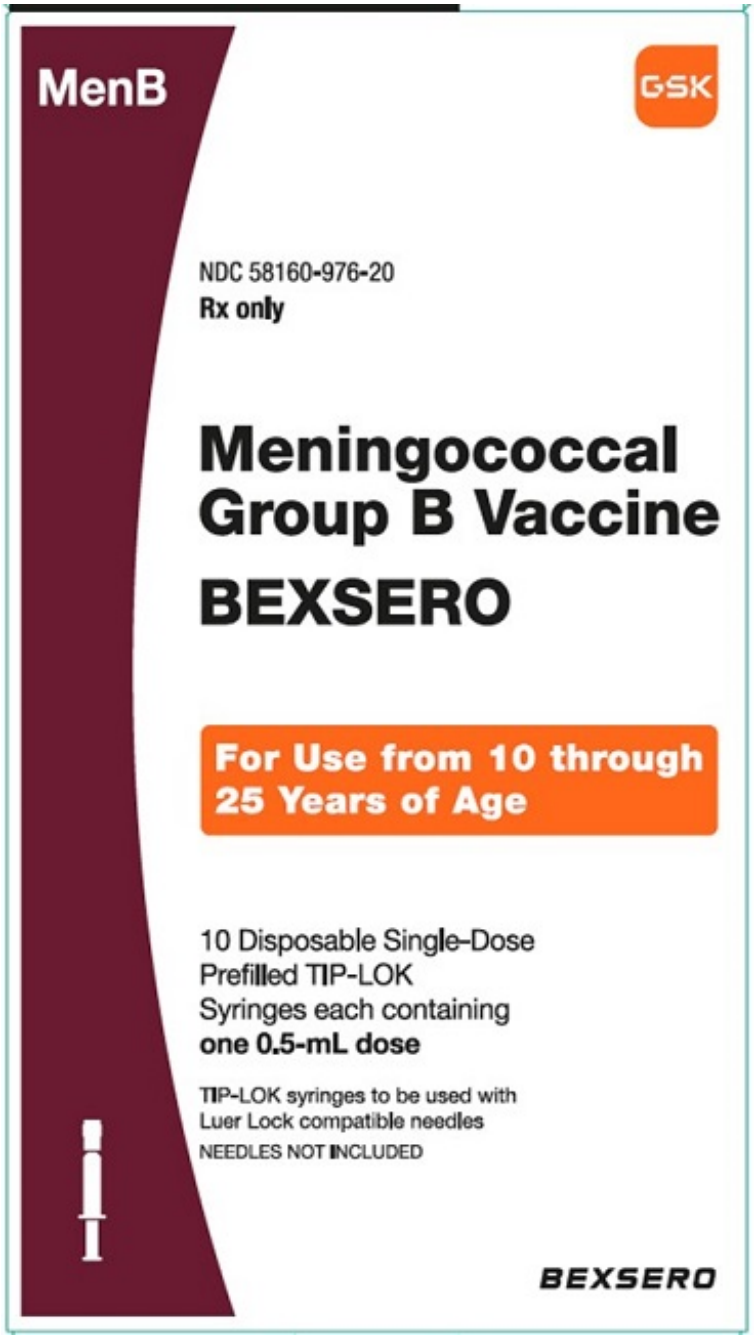
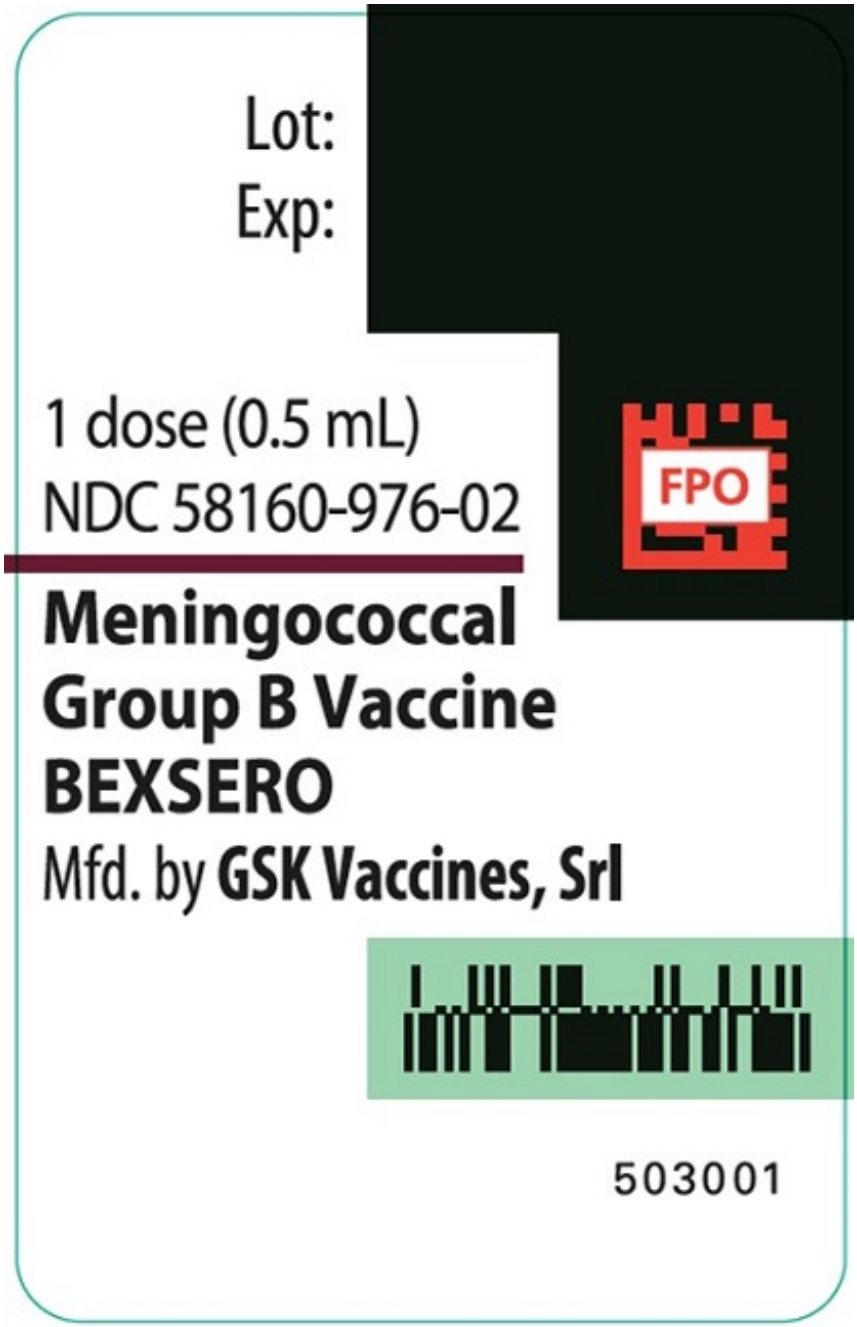


Syringe Label

NDC 58160-976-02

503001



BEXSERO

neisseria meningitidis serogroup b nhba fusion protein antigen, neisseria meningitidis serogroup b fhbp fusion protein antigen and neisseria meningitidis serogroup b nada protein antigen injection, suspension

Product Information			
Product Type	VACCINE	**Item Code (Source)**	NDC:58160-976
Route of Administration	INTRAMUSCULAR		

Active Ingredient/Active Moiety		
Ingredient Name	**Basis of Strength**	**Strength**

NEISSERIA MENINGITIDIS GROUP B NHBA FUSION PROTEIN ANTIGEN (UNII: 28E911Y7AE) (NEISSERIA MENINGITIDIS GROUP B NHBA FUSION PROTEIN ANTIGEN - UNII:28E911Y7AE)	NEISSERIA MENINGITIDIS GROUP B NHBA FUSION PROTEIN ANTIGEN	50 ug in 0.5 mL
NEISSERIA MENINGITIDIS GROUP B FHBP FUSION PROTEIN ANTIGEN (UNII: 25DB599G64) (NEISSERIA MENINGITIDIS GROUP B FHBP FUSION PROTEIN ANTIGEN - UNII:25DB599G64)	NEISSERIA MENINGITIDIS GROUP B FHBP FUSION PROTEIN ANTIGEN	50 ug in 0.5 mL
NEISSERIA MENINGITIDIS GROUP B NADA PROTEIN ANTIGEN (UNII: 1S25R442RS) (NEISSERIA MENINGITIDIS GROUP B NADA PROTEIN ANTIGEN - UNII:1S25R442RS)	NEISSERIA MENINGITIDIS GROUP B NADA PROTEIN ANTIGEN	50 ug in 0.5 mL
NEISSERIA MENINGITIDIS GROUP B STRAIN NZ98/254 OUTER MEMBRANE VESICLE ANTIGEN (UNII: 91523M4S24) (NEISSERIA MENINGITIDIS GROUP B STRAIN NZ98/254 OUTER MEMBRANE VESICLE ANTIGEN - UNII:91523M4S24)	NEISSERIA MENINGITIDIS GROUP B STRAIN NZ98/254 OUTER MEMBRANE VESICLE ANTIGEN	25 ug in 0.5 mL

Inactive Ingredients

Ingredient Name	Strength
ALUMINUM HYDROXIDE (UNII: 5QB0T2IUN0)	
SODIUM CHLORIDE (UNII: 451W47IQ8X)	
HISTIDINE (UNII: 4QD397987E)	
SUCROSE (UNII: C151H8M554)	
WATER (UNII: 059QF0KO0R)	

Packaging

#	Item Code	Package Description	Marketing Start Date	Marketing End Date
1	NDC:58160-976-20	10 in 1 CARTON		
1	NDC:58160-976-02	0.5 mL in 1 SYRINGE; Type 3: Prefilled Biologic Delivery Device/System (syringe, patch, etc.)		

Marketing Information

Marketing Category	Application Number or Monograph Citation	Marketing Start Date	Marketing End Date
BLA	BLA125546	12/01/2016	

Labeler - GlaxoSmithKline Biologicals SA (372748392)

Revised: 8/2024 GlaxoSmithKline Biologicals SA