Bexsero Vaccine, **NAME OF THE MEDICINAL PRODUCT: Bexsero** suspension for injection in pre-filled syringe. Multicomponent meningococcal group B Vaccine (recombinant, adsorbed). **QUALITATIVE & QUANTITATIVE COMPOSITION:** 1 dose (0.5 ml) contains: 1) Recombinant *Neisseria meningitidis* group B NHBA fusion protein[1, 2, 3] 50 micrograms. 2) Recombinant *Neisseria meningitidis* group B NadA protein[1, 2, 3] 50 micrograms. 3) Recombinant *Neisseria meningitidis* group B fHbp fusion protein[1, 2, 3] 50 micrograms Outer membrane vesicles (OMV) from *Neisseria meningitidis* group B. 4) 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 Al^{3+}). [3]NHBA (Neisserial Heparin Binding Antigen), NadA (*Neisseria* adhesin A), fHbp (factor H binding protein). **THERAPEUTIC INDICATIONS: Bexsero** is indicated for active immunization of individuals from 2 months of age & older against invasive meningococcal disease caused by Neisseria meningitidis group B. The use of **Bexsero** should be in accordance with official recommendations. **POSOLOGY :** Infants, 2 - 5 months, primary immunization consists of: either 2 or 3 doses each of 0.5 ml, Intervals between Primary Doses, not less than 2 months for 2 doses schedule or not less than 1 month for 3 doses schedule, with 1 Booster dose in the 2nd year of life with an interval of at least 6 months between the primary series & booster dose [b] . Infants, 6 months to 11 months, primary doses consist of 2 doses each of 0.5 ml, with Not less than 2 months, Booster: one dose in the second year of life with an interval of at least 2 months between the primary series & booster dose [b]. Children, 12 – 23 months, primary doses consist of 2 doses each of 0.5 ml. not less than 2 months apart, with 1 Booster dose & an interval of 12-23 months between the primary series & booster dose [b] . Children, 2 years to 10 years & Adolescents (from 11 years) & adults*, Primary doses, Two doses each of 0.5 ml with a dose interval of Not less than 1 month, A booster dose should be considered in individuals at continued risk of exposure to meningococcal disease, based on official recommendations [b, a] The safety & efficacy of **Bexsero** in infants less than 8 weeks of age has not yet been established. No data are available. [b] See "Pharmacodynamic effects". * The safety & efficacy of **Bexsero** in individuals above 50 years of age have not been established. **METHOD OF ADMINISTRATION:** 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. Contraindications, Hypersensitivity to the active substances or to any of the excipients listed. **SPECIAL WARNINGS & PRECAUTIONS FOR USE**, administration of **Bexsero** should be postponed in subjects suffering from an acute severe febrile illness, presence of a minor infection such as cold, should not result in the deferral of vaccination. Must not be injected intravascularly, subcutaneously or intradermally. Appropriate medical treatment & supervision should always be readily available in case of an anaphylactic event following the administration of the vaccine. Anxiety-related reactions (syncope), hyperventilation or stress-related reactions may occur in association with vaccination as a psychogenic response to the needle injection. Temperature elevation may occur following vaccination of infants & children (less than 2 years of age). Prophylactic administration of antipyretics at the time of & closely after vaccination can reduce the incidence & intensity of post-vaccination febrile reactions. Impaired immune responsiveness individuals, whether due to the use of immuno- suppressive therapy, may have reduced antibody response to active immunisation. Safety & efficacy of **Bexsero** above 50 years old have not been established. Limited data in patients with chronic medical conditions. Potential risk of apnoea & the need for respiratory monitoring for 48-72h should be considered when administering the primary immunisation series to very premature infants (born ≤ 28 weeks of gestation) & particularly for those with a previous history of respiratory immaturity. As the benefit of vaccination is high in this group of infants. Latex-sensitive individuals. Kanamycin level, If present, 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. **INTERACTION WITH OTHER MEDICINAL PRODUCTS & OTHER FORMS OF INTERACTION,** can be given concomitantly with any of the following vaccine antigens, either as monovalent or as combination vaccines: diphtheria, tetanus, acellular pertussis, *Haemophilus influenzae* type b, inactivated poliomyelitis, hepatitis B, heptavalent pneumococcal conjugate, measles, mumps, rubella, varicella, & meningococcal groups A, C, W, Y conjugate. Administration of vaccines containing whole cell pertussis concomitantly with **Bexsero** has not been studied & thus is not recommended. **FERTILITY, PREGNANCY & LACTATION,** There are no data on fertility in humans. Insufficient clinical data on exposed pregnancies are available, vaccination should not be withheld when there is a clear risk of exposure to meningococcal infection. Information on the safety of the vaccine to women & their children during breast- feeding is not available. **ADVERSE REACTION,** In infants & children (less than 2 years of age) the most common local & systemic adverse reactions observed in clinical trials were tenderness & erythema at the injection site, fever & irritability. In adolescents & adults, the most common local & systemic adverse reactions observed were pain at the injection site, malaise & headache. **TO REPORT ANY SIDE EFFECT(S):** *Kingdom of Saudi Arabia,* -National Pharmacovigilance centre (NPC), Fax: +966-11-205-7662, Call NPC at +966-11-2038222, Ext: 2317-2356-2340, Reporting hotline: 19999, E-mail: npc.drug@sfda.gov.sa, Website: www.sfda.gov.sa/npc, GlaxoSmithKline - Head Office, Jeddah, Tel: +966-12-6536666, Mobile: +966-56-904-9882, Email: saudi.safety@gsk.com, Website: https://gskpro.com/en-sa/,P.O. Box 55850, Jeddah 21544, Saudi Arabia. Immunisation with Bexsero is intended to stimulate the production of bactericidal antibodies that recognize the vaccine antigens NHBA, NadA, fHbp, & PorA P1.4 (the immunodominant antigen present in the OMV component) & are expected to be protective against Invasive Meningococcal Disease (IMD). As these antigens are variably expressed by different strains, meningococci that express them at sufficient levels are susceptible to killing by vaccine-elicited antibodies. The Meningococcal Antigen Typing System (MATS) was developed to relate antigen profiles of different strains of meningococcal group B bacteria to killing of the strains in the serum bactericidal assay with human complement (hSBA), & ultimately to predict breadth of strain coverage. The vaccine antigens present in Bexsero are also expressed by strains belonging to meningococcal groups other than group B. Clinical efficacy, Bexsero vaccine efficacy has been inferred by demonstrating the induction of serum bactericidal antibody responses to each of the vaccine antigens. *Immunogenicity in infants 2 months to 5 months of age* at one month after three doses of Bexsero administered at 2, 3, 4 & 2, 4, 6 months of age were high against the fHbp, NadA & PorA P1.4 antigens at both Bexsero vaccination schedules. The bactericidal responses against the NHBA antigen were also high in infants vaccinated at the 2, 4, 6-month schedule. *Two-dose primary series followed by a booster,* The immunogenicity after two doses (at 3 & a half & 5 months of age) or three doses (at 2 & a half, 3 & a half & 5 months of age) of Bexsero followed by a booster has been evaluated in an additional phase 3 clinical study. The percentages of seropositive subjects (i.e. achieving an hSBA of at least 1:4) ranged from 44% to 100% one month after the second dose & from 55% to 100% one month after the third dose. At one month following a booster administered 6 months after the last dose, the percentages of seropositive subjects ranged from 87% to 100% for the two-dose schedule, & from 83% to 100% for the three-dose schedule. Antibody persistence was evaluated in an extension study in children 3-4 years of age. Comparable percentages of subjects were seropositive at 2-3 years after being previously vaccinated with either two doses followed by a booster of Bexsero (ranging from 35% to 91%) or **3** doses followed by a booster (ranging from 36% to 84%). In the same study the response to an additional dose administered 2-3 years after the booster was indicative of immunological memory as shown by a robust antibody. **R**esponse against all Bexsero antigens, ranging from 81%-100% & from 70%-99%, respectively. These observations are consistent with adequate priming in infancy with both a two-dose & a three-dose primary series followed by a booster of Bexsero. *Immunogenicity in infants 6 to 11 months & children 12 to 23 months of age,* Against each of the vaccine antigens, seroresponse rates & hSBA GMTs were high & similar after the two-dose series in infants 6-8 months of age & children 13-15 months of age. *Immunogenicity in children 2 to 10 years of age* The immunogenicity after two doses of Bexsero administered either one or two months apart in children 2 to 10 years of age has been evaluated in an initial phase 3 clinical study & its extension. In the initial study, participants received two doses of Bexsero two months apart In the extension study, in which two doses of Bexsero were administered one month apart in unvaccinated children, high percentages of subjects were seropositive one month after the second dose. An early immune response after the first dose was also evaluated. The percentages of seropositive subjects (i.e. achieving an hSBA of at least 1:4) across strains ranged from 46% to 95% at one month after the first dose & from 69% to 100% at one month after the second dose. This study also evaluated antibody persistence & the response to a booster dose in children who received the two-dose primary series at 2-5 or 6-10 years of age. After 24-36 months, the percentages of seropositive subjects (i.e. achieving an hSBA of at least 1:4) declined, ranging across strains from 21% to 74% in children 4-7 years of age & from 47% to 86% in children 8-12 years of age. The response to a booster dose administered 24-36 months after the primary series was indicative of immunological memory as the percentages of seropositive subjects ranged across strains from 93%-100% in children 4-7 years of age & from 96%-100% in children 8-12 years of age. *Immunogenicity in adolescents (from 11 years of age) & adults,* Adolescents received two doses of

Bexsero with **1,2- or 6-month** intervals between doses; The vaccination schedules of **2** doses administered with an interval of **1** or **2** months showed similar immune responses in both adults & adolescents. Similar responses were also observed for adolescents administered **2** doses of Bexsero with an interval of **6** months. In the study in adolescents, bactericidal responses following two doses of Bexsero were stratified by baseline hSBA less than 1:4 or equal to or greater than 1:4. Seroresponse. Following Bexsero vaccination, a high percentage of subjects were seropositive & achieved 4-fold increases in hSBA titres independent of pre-**vaccination status**. Antibody persistence data for the study in adolescents were obtained in an extension phase 3 study. At approximately 7.5 years after the **2**-dose primary series, the percentages of subjects with hSBA ≥ 1:4 declined, ranging across strains from 29%-84%. The response to a booster dose administered 7.5 years after the primary series was indicative of immunological memory as the percentages of subjects reaching an hSBA ≥ 1:4 across strains ranged from 93%-100%. The same study also evaluated antibody persistence data from an additional **phase 3** initial study in adolescents. At approximately 4 years after the **2-**dose primary series, the percentages of subjects with hSBA ≥ 1:5 generally declined from a range across strains of 68%-100% after the second dose to a range across strains of 9%-84%. The response to a booster dose administered 4 years after the primary series was indicative of immunological memory as the percentages of subjects with hSBA ≥ 1:5 ranged across strains from 92%-100%. SHELF LIFE, 3 years**,** STORE **in Refrigerator (2°C – 8°C). Do not freeze. Protect from light**. Bexsero **is a trademark owned by or licences to GSK group of companies. For any information about this medicinal product, please contact: GlaxoSmithKline - Head Office, Jeddah,** Tel: +966-12-6536666, Mobile: +966-56-904-9882, Email: gcc.medinfo@gsk.com, Website: https://gskpro.com/en-sa/, P.O. Box 55850, Jeddah 21544, Saudi Arabia. **Manufacturer:** GSK Vaccines S.r.l. Bellaria-Rosia, Sovicille, Siena 53018, Italy, Tel: (39) 0577243111, Fax: (39) 0577243401. **Marketing Authorization Holder:** Glaxo Saudi Arabia Ltd.* Jeddah, KSA. Address: P.O. Box 22617 Jeddah 21416 – Kingdom of Saudi Arabia. full prescribing information is available on request