EDA Assessment Report for Biological Medicinal Product

(Scientific Discussion)

Bexsero

Date: August 2024

Assessment report

Bexsero

Unit: Technical Assessment Unit

Administrative information:

Trade name of the medicinal product:	Bexsero
INN (or common name) of the active substance(s):	-Recombinant **Neisseria meningitidis** group B NHBA fusion protein -Recombinant **Neisseria meningitidis** group B NadA protein. -Recombinant **Neisseria meningitidis** group B fHbp fusion protein. -Outer membrane vesicles (OMV) from **Neisseria meningitidis** group B strain NZ98/254 measured as amount of total protein containing the PorA P1.4.
Manufacturer of the finished product	GlaxoSmithKline Vaccines S.r.l., Bellaria-Rosia, 53018 Sovicille, - ITALY
Marketing Authorization holder	GSK Vaccines S.r.l., Via Fiorentina 1, 53100 Siena - ITALY
Applied Indication(s):	Bexsero is indicated for active immunisation 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 section 5.1 for information on protection against specific group B strains. The use of this vaccine should be in accordance with official recommendations.
Pharmaceutical form(s) and strength(s):	-white opalescent liquid Suspension for injection **-Each One dose (0.5 ml) contains:** -Recombinant **Neisseria meningitidis** group B NHBA fusion protein **50 ug;** -Recombinant **Neisseria meningitidis** group B NadA protein **50 ug;** -Recombinant **Neisseria meningitidis** group B fHbp fusion protein **50 ug;** -Outer membrane vesicles (OMV) from **Neisseria meningitidis** group B strain NZ98/254 measured as amount of total protein containing the PorA P1.4 **25 ug;**
Route of administration	Intramuscular use (I.M injection)
Approved pack	Carton box containing Pre-filled syringe (type I glass) with a plunger stopper (butyl rubber) FM457 with a rubber tip cap FM30 not made with natural

	rubber latex with 2 Needles + insert leaflet.

List of abbreviations

EMA	European medicines Agency
CTD	Common Technical Document
GSK	GlaxoSmithKline
AI	Active ingredient
OMV	Outer Membrane Vesicles
IMD	Invasive meningococcal disease
SBA	Serum Bactericidal Assay
OMV NZ	Outer membrane vesicle derived from Neisseria meningitidis serogroup B strain NZ98/254 (New Zealand strain)

Dossier initial submission and evaluation process.

- The product was submitted for registration via reliance level I.
- The dossier evaluation by the registration administration units was started on 18.10.2023 after providing all the required documents (EMA list of questions along with Full CTD for the product).

1. **'General introduction about the product including brief description of the AI, its mode of action and indications:**

- Bexsero is a suspension for injection in pre-filled syringe (PFS) and contains three recombinant proteins (rp), Outer Membrane Vesicles (OMV), and excipients (sodium chloride, histidine, sucrose, aluminium hydroxide and water for injection).
- Bexsero contains 4 different active ingredients, Outer Membrane Vesicles (OMV) which are extracted via detergent from the bacterial membrane of Neisseria meningitidis (N. meningitidis) serogroup B strain NZ98/254 and three N. meningitidis cell surface antigen; Protein 961c, Protein 287-953, Protein 936-741, which are produced in E.coli by recombinant DNA technology.

- The drug substances are adsorbed on aluminium hydroxide (Al (OH)3) as a suspension for injection. The Al (OH)3 concentration in Bexsero is 1.5 mg/ dose which corresponds to 0.5 mg of elemental aluminium per vaccine dose.

- Bexsero is indicated for active immunization against invasive disease caused by Neisseria meningitidis serogroup B strains in individuals from 2 months of age and older. The

efficacy of Bexsero against invasive meningococcal disease (IMD) has been inferred from the ability of the vaccine to induce functional bactericidal antibodies directed against serogroup B meningococci. Immunity to meningococcal disease is mediated primarily by serum antibodies that are specific for bacterial surface components, and are capable of activating complement once bound, resulting in bacteriolysis. Serum bactericidal activity has been accepted as a valid surrogate for predicting the clinical efficacy of serogroup B meningococcal vaccines. Functional bactericidal antibodies induced by vaccination with Bexsero will be measured by the Serum Bactericidal Assay.

- 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.

2. Quality aspects:

- **Manufacturer(s):**
  Drug substance:
  Active substance is manufactured at both GlaxoSmithKline Vaccines S.r.l., Bellaria-Rosia, 53018 Sovicille, - ITALY and Sandoz GmbH, Biochemiestrasse 10, A-6250 Kundl, Austria.
  Drug product:
  Finished product is manufactured at GlaxoSmithKline Vaccines S.r.l., Bellaria-Rosia, 53018 Sovicille, - ITALY

- **Stability**
  Drug substance:
  Approved Storage Conditions of the active substance:
  - OMV: 2-8°C
  - rP 287-953: ≤ -15°C
  - rP 961c: ≤ -15°C
  - rP 936-741: ≤ -15°C
  Approved shelf life for the active substance:
  -OMV: 48 months
  - rP 287-953: 48 months
  - rP 961c: 60 months
  - rP 936-741: 60 months

Drug product:

Approved Storage Conditions:

-Store in a refrigerator (2 °C – 8 °C). Do not freeze.

-Store in the original package in order to protect from light.

Approved shelf life for the finished product: 48 months

3. Non-clinical and clinical aspects:

- The non-clinical program adequately supports the registration of Bexsero. The toxicity profile of Bexsero is sufficiently characterized by the non-clinical data submitted.

- Over all conclusion non-clinical data reveal no special hazard for humans based on repeated dose toxicity and Reproductive and developmental toxicity studies.

- the overall benefit/risk of Bexsero is favourable in the treatment of active immunization of individuals from 2 months of age and older against invasive meningococcal disease caused by Neisseria meningitidis group B.

- **General Conclusion and Recommendations if any:**

Based on the review of CTD modules and other supplementary documents, the product is approved.

For more information, please visit EMA published assessment report link:

https://www.ema.europa.eu/en/documents/assessment-report/bexsero-epar-public-assessment-report_en.pdf