PRODUCT MONOGRAPH
INCLUDING PATIENT MEDICATION INFORMATION

ERVEBO®

Ebola Zaire Vaccine (rVSVΔG-ZEBOV-GP, live)

Solution for intramuscular injection
72 million plaque forming units (pfu) per 1 mL single-dose vial of rVSVΔG-ZEBOV-GP, live

Active immunizing agent

Merck Canada Inc.
16750 route Transcanadienne
Kirkland QC Canada H9H 4M7
www.merck.ca

Date of Initial Authorization:
November 9, 2022

Submission Control Number: 256568

RECENT MAJOR LABEL CHANGES
Not applicable

TABLE OF CONTENTS

Sections or subsections that are not applicable at the time of authorization are not listed.

PART I: HEALTH PROFESSIONAL INFORMATION

1 INDICATIONS

ERVEBO® (Ebola Zaire Vaccine (rVSVΔG-ZEBOV-GP, live)) is indicated for active immunization of individuals 18 years of age or older to protect against Ebola Virus Disease (EVD) caused by Zaire Ebola virus (see 4.2 Recommended Dose and Dosage Adjustment, 7 WARNINGS AND PRECAUTIONS, 14 CLINICAL TRIALS).

1.1 Pediatrics (< 18 years of age)

Based on the data submitted and reviewed by Health Canada, the safety, immunogenicity and efficacy of ERVEBO® in children and adolescents < 18 years of age have not yet been established; therefore, Health Canada has not authorized an indication for pediatric use (see 8 ADVERSE REACTIONS, 14 CLINICAL TRIALS).

1.2 Geriatrics (≥ 65 years of age)

ERVEBO® has been studied in the geriatric population (see 7.1 Special Populations, 14 CLINICAL TRIALS).

2 CONTRAINDICATIONS

ERVEBO® is contraindicated in patients who are hypersensitive to this vaccine or to any ingredient in the formulation, including any non-medicinal ingredient, rice protein, or component of the container. For a complete listing, see 6 DOSAGE FORMS, STRENGTHS, COMPOSITION AND PACKAGING.

4 DOSAGE AND ADMINISTRATION

4.2 Recommended Dose and Dosage Adjustment

Adults (≥ 18 years of age)

Individuals should receive a single dose of 1 mL administered intramuscularly for primary immunization (see 14 CLINICAL TRIALS).
The need for a booster dose has not been established.

Pediatrics (< 18 years of age)

The safety, immunogenicity and efficacy of ERVEBO® in children and adolescents < 18 years of age have not yet been established; Health Canada has not authorized an indication for pediatric use (see 8 ADVERSE REACTIONS, 14 CLINICAL TRIALS).

4.4 Administration

ERVEBO® should be administered by a trained healthcare professional.

For precautions to be taken before administering the vaccine, see 7 WARNINGS AND PRECAUTIONS.

For precautions regarding thawing, handling and disposal of the vaccine, see 11 STORAGE, STABILITY and DISPOSAL, 12 SPECIAL HANDLING INSTRUCTIONS.

ERVEBO® should be administered by the intramuscular (IM) route only. The preferred site is the deltoid area of the non-dominant arm or in the higher anterolateral area of the thigh. Do not inject the vaccine intravascularly (IV). No data are available for administration via the subcutaneous (SC) or intradermal (ID) routes.

Cover the vaccination injection site or any vesicles with an adequate bandage (e.g. any adhesive bandage or gauze and tape) that provides a physical barrier to protect against direct contact (see 7 WARNINGS AND PRECAUTIONS, 16 NON-CLINICAL TOXICOLOGY). The bandage may be removed when there is no visible fluid leakage.

The vaccine should not be mixed in the same syringe with any other vaccines or medicinal products.

5 OVERDOSAGE

No cases of overdose have been reported.

For management of a suspected vaccine overdose, contact your regional poison control centre.

6 DOSAGE FORMS, STRENGTHS, COMPOSITION AND PACKAGING

To help ensure the traceability of vaccines for patient immunization record-keeping as well as safety monitoring, healthcare professionals should record the time and date of administration, quantity of administered dose (if applicable), anatomical site and route of administration, brand name and generic name of the vaccine, the product lot number and expiry date.

ERVEBO® is a solution for injection available in 1 mL single-dose vial (type I glass) with a stopper (chlorobutyl) and a flip-off plastic cap with aluminium seal.

The vaccine is a colorless to slightly brownish-yellow liquid.

Available in pack sizes of 10 vials.

The vaccine vial stopper is not made with natural rubber latex.

Table 1 – Dosage Forms, Strengths, Composition and Packaging

Route of Administration	Dosage Form / Strength/Composition	Non-medicinal Ingredients
Intramuscular injection	Solution for injection Each 1 mL dose contains Ebola Zaire Vaccine (rVSVΔG-ZEBOV-GP[1,2] live, attenuated) ≥72 million pfu[3]. [1]Recombinant Vesicular Stomatitis Virus (rVSV) strain Indiana with a deletion of the VSV envelope glycoprotein (G) replaced with the Zaire Ebola Virus (ZEBOV) Kikwit 1995 strain surface glycoprotein (GP) [2]Produced in Vero cells [3]pfu= plaque-forming units This product contains genetically modified organisms (GMOs). This vaccine contains a trace amount of rice protein. See 2 CONTRAINDICATIONS.	Hydrochloric acid and sodium hydroxide (for pH-adjustments), recombinant human serum albumin, trometamol buffer and water for injection.

7 WARNINGS AND PRECAUTIONS

General

Standard precautions when caring for patients with known or suspected Ebola disease
Vaccination with ERVEBO® does not eliminate the necessity of standard precautions when caring for patients with known or suspected Ebola disease. **All healthcare workers and other ancillary providers who have been vaccinated should not alter their practices with regard to safe injection, hygiene, and personal protective equipment (PPE) after vaccination.**

Healthcare workers caring for patients with suspected or confirmed Ebola virus should apply extra infection control measures to prevent contact with the patient's blood and body fluids and contaminated surfaces or materials such as clothing and bedding. Samples taken from humans and animals for investigation of Ebola infection should be handled by trained staff and processed in suitably equipped laboratories.

Vaccine administrators should counsel vaccinees to continue to protect themselves with adequate measures.

Concurrent illness
Vaccination should be postponed in subjects experiencing moderate or severe febrile illness. The presence of a minor infection should not result in deferral of vaccination.

Protection against filovirus disease
Other than Zaire Ebola virus (ZEBOV), ERVEBO® will not prevent disease caused by other Filoviruses such as Sudan Ebola virus (SUDV) or Marburg virus (MARV).

As with any vaccine, vaccination with ERVEBO® may not protect all recipients. Individuals may not be optimally protected and vaccinees should continue to protect themselves with adequate public health measures.

Driving and Operating Machinery
No studies on the effects of ERVEBO® on the ability to drive and use machines have been performed.

ERVEBO® has no or negligible influence on the ability to drive and use machines. However, some of the effects mentioned under 8 ADVERSE REACTIONS may temporarily affect the ability to drive or use machines.

Hematologic
The vaccine should be given with caution to individuals with thrombocytopenia or any coagulation disorder because bleeding or bruising may occur following an intramuscular administration in these individuals.

Immune
Hypersensitivity
Close monitoring is recommended following vaccination for the early signs of anaphylaxis or anaphylactoid reactions. 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.

Immunocompromised individuals
Safety and efficacy of ERVEBO® have not been assessed in immunocompromised individuals. Immunocompromised individuals may not adequately respond to ERVEBO®. As a precautionary measure, the use of ERVEBO® should be avoided in individuals with known immunocompromised conditions or receiving immunosuppressive therapy, including the following conditions:

- Severe humoral or cellular (primary or acquired) immunodeficiency, e.g. severe combined immunodeficiency, agammaglobulinemia, and AIDS or symptomatic HIV infection. A CD4+ T-lymphocyte count threshold for use in asymptomatic HIV-positive individuals has not been established.
- Current immunosuppressive therapy, including high doses of corticosteroid. This does not include individuals who are receiving topical, inhaled or low-dose parenteral corticosteroids (e.g. for asthma prophylaxis or replacement therapy).
- Diseases of the blood such as leukemia, lymphomas of any type, or other malignant neoplasms affecting the hematopoietic and lymphatic systems.
- Family history of congenital or hereditary immunodeficiency, unless the immune competence of the potential vaccine recipient is demonstrated.

Transmission

Transmission to humans

Vaccine virus might be present in biological fluids such as blood, urine, saliva, semen, vaginal fluids, aqueous humor, breast milk, feces, sweat, amniotic fluid, and placenta. Vaccine virus RNA has been detected by PCR in the plasma of most of the adult subjects. Vaccine virus RNA was mainly detected from Day 1 to Day 7. Shedding of vaccine virus has been detected by PCR in urine or saliva in 19 out of 299 adult subjects and in skin vesicles in 4 out of 10 adult subjects. The vaccine virus RNA was detected in a skin vesicle at 12 days post-vaccination in one of the four subjects.

Transmission of vaccine virus through close personal contact is accepted as a theoretical possibility. Vaccine recipients should avoid close contact with and exposure of high-risk individuals to blood and bodily fluids for at least 6 weeks following vaccination. High-risk individuals include:

- Immunocompromised individuals and individuals receiving immunosuppressive therapy (see section above),
- Pregnant or breast-feeding women (see 7.1.1 Pregnant Women, 7.1.2 Breast-Feeding),
- Children <1 year of age.

Individuals who develop vesicular rash after receiving the vaccine should cover the vesicles until they heal to minimise the risk of possible transmission of vaccine virus through open vesicles. Dispose of contaminated bandages following institutional guidelines or WHO healthcare waste management policy (see 16 NON-CLINICAL TOXICOLOGY).

Inadvertent transmission of vaccine virus to animals and livestock is also theoretically possible, see below.

Individuals administered ERVEBO® should not donate blood for at least 6 weeks post-vaccination.

Transmission to animals and livestock

Transmission of vaccine virus through close contact with livestock is accepted as a theoretical possibility. Vaccine recipients should attempt to avoid exposure of livestock to blood and bodily fluids for at least 6 weeks following vaccination. Individuals who develop vesicular rash after receiving the vaccine should cover the vesicles until they heal. Dispose of contaminated bandages following institutional guidelines or WHO healthcare waste management policy.

Reproductive Health: Female and Male Potential

- **Fertility**

  There are no data on fertility effects in humans.

  Animal studies in female rats do not indicate harmful effects (see 16 NON-CLINICAL TOXICOLOGY).

7.1 Special Populations

7.1.1 Pregnant Women

There is limited amount of data (less than 300 pregnancy outcomes) from the use of ERVEBO® in pregnant women, or women who became pregnant after receiving the vaccine. The safety of ERVEBO® has not been established in pregnant women.

As there are limitations to available data, including the small number of cases, caution should be exercised in drawing conclusions. Lack of reliable data on background rates of pregnancy and neonatal outcomes in the affected regions also makes a contextual assessment of the data challenging. Animal studies do not indicate direct or indirect harmful effects with respect to reproductive toxicity (see 16 NON-CLINICAL TOXICOLOGY).

As a precautionary measure, avoid the use of ERVEBO® during pregnancy. Nevertheless considering the severity of EVD, vaccination should not be withheld when there is a clear and imminent risk of exposure to Ebola infection.

Pregnancy should be avoided for 2 months following vaccination. Women of child-bearing potential should use an effective contraceptive method.

7.1.2 Breast-Feeding

It is unknown whether the vaccine virus is secreted in human milk.

A risk to the newborns/infants from breast-feeding by vaccinated mothers cannot be excluded.

Evaluation of the vaccine virus in animal milk has not been conducted. When ERVEBO® is administered to female rats, antibodies against the vaccine virus were detected in offspring, likely due to acquisition of maternal antibodies via placental transfer during gestation and via lactation (see 16 NON-CLINICAL TOXICOLOGY).

The developmental and health benefits of breastfeeding should be considered along with the mother's clinical need for immunization against Ebola.

7.1.3 Pediatrics (< 18 years of age)

The safety, immunogenicity and efficacy of ERVEBO® in children and adolescents < 18 years of age have not yet been established; therefore, Health Canada has not authorized an indication for pediatric use (see 8 ADVERSE REACTIONS, 14 CLINICAL TRIALS).

7.1.4 Geriatrics (≥ 65 years of age)

Across the clinical development program, the total number of subjects ≥65 years of age who received ERVEBO® was 552.

Clinical studies of ERVEBO® did not include sufficient numbers of subjects 65 years of age and older to determine whether seniors respond differently from younger adult subjects regarding safety and immunogenicity.

8 ADVERSE REACTIONS

8.1 Adverse Reaction Overview

The safety profile of ERVEBO® presented below was evaluated in a Phase III randomized, double-blind, placebo-controlled clinical trial (Protocol 012) conducted in the United States, Canada and Spain. In this study, 1,197 adults 18 years of age and older were randomized to receive ERVEBO® (n=1,061) or saline placebo (n=133). The most commonly reported adverse reactions were pain at the injection site (69.6%), pyrexia (23.2%), headache (22.3%), arthralgia (17.9%), swelling at the injection site (16.6%), erythema at injection-site (12.1%), pain (11.3%), chills (7.3%), fatigue (6.2%), myalgia (6.0%), nausea (5.1%), influenza like illness (5.0%).

8.2 Clinical Trial Adverse Reactions

Clinical trials are conducted under very specific conditions. The adverse reaction rates observed in the clinical trials; therefore, may not reflect the rates observed in practice and should not be compared to the rates in the clinical trials of another drug. Adverse reaction information from clinical trials may be useful in identifying and approximating rates of adverse drug reactions in real-world use.

The clinical development program for ERVEBO® included clinical studies conducted in North America, Europe and Africa, in which 17,415 adults received a dose of ERVEBO®. The number of subjects vaccinated with ERVEBO® in double-blind, placebo-controlled trials was 1,712 and in open-label trials was 15,703.

In one of these studies, Protocol 012, subjects used a memory aid to record solicited local reactions from Days 1 to 5 postvaccination, and daily temperature measurements and solicited joint and skin events from Days 1 to 42 postvaccination. Unsolicited adverse reactions were collected through Day 42 postvaccination. The median age of subjects was 42 years; 46.8% were male; 67.9% were White, 29.2% were Black or African American, 1.4% were Multi-racial, 0.8% were Asian, 0.4% were American Indian or Alaska Native, and 0.3% were Native Hawaiian or Pacific Islander; 14.5% were Hispanic or Latino. Serious adverse events were monitored through 6 months postvaccination and a subset of subjects (n=511) were monitored through 24 months postvaccination. There were no serious adverse events that were considered to be vaccine-related.

Table 2 presents the proportion of subjects reporting adverse reactions that occurred in at least 1% of subjects in Protocol 012.

Table 2 - Incidence of Local and Systemic Adverse Reactions in ≥ 1% of Subjects After Vaccination

	ERVEBO® (N=1,051) n (%)	Placebo (N=133) n (%)
Injection-site Reactions[†]		
Injection-site pain	732 (69.6%)	18 (13.5%)
Injection-site swelling	174 (16.6%)	4 (3.0%)
Injection-site erythema	127 (12.1%)	2 (1.5%)
Injection-site reaction	11 (1.0%)	0 (0.0%)
Injection-site pruritus	10 (1.0%)	0 (0.0%)
Systemic Reactions[‡]		
Pyrexia	244 (23.2%)	1 (0.8%)
Headache	234 (22.3%)	15 (11.3%)
Arthralgia	188 (17.9%)	4 (3.0%)
Pain	119 (11.3%)	2 (1.5%)
Chills	77 (7.3%)	1 (0.8%)
Fatigue	65 (6.2%)	3 (2.3%)
Myalgia	63 (6.0%)	1 (0.8%)
Nausea	54 (5.1%)	1 (0.8%)
Influenza like illness	53 (5.0%)	1 (0.8%)
Back pain	42 (4.0%)	1 (0.8%)
Diarrhea	39 (3.7%)	2 (1.5%)
Joint swelling	35 (3.3%)	0 (0.0%)
Pain in extremity	35 (3.3%)	0 (0.0%)
Oropharyngeal pain	29 (2.8%)	3 (2.3%)
Dizziness	23 (2.2%)	3 (2.3%)
Malaise	23 (2.2%)	0 (0.0%)
Rash	21 (2.0%)	2 (1.5%)
Vomiting	21 (2.0%)	0 (0.0%)
Abdominal pain[§]	20 (1.9%)	3 (2.3%)
Nasopharyngitis	17 (1.6%)	1 (0.8%)
Musculoskeletal pain	15 (1.4%)	1 (0.8%)
Paresthesia	15 (1.4%)	0 (0.0%)
Body temperature increased	14 (1.3%)	0 (0.0%)
Decreased appetite	13 (1.2%)	0 (0.0%)
Muscle spasms	13 (1.2%)	0 (0.0%)
Arthritis	12 (1.1%)	0 (0.0%)
Asthenia	12 (1.1%)	1 (0.8%)
Cough	12 (1.1%)	3 (2.3%)
Musculoskeletal stiffness	12 (1.1%)	0 (0.0%)
Neck pain	12 (1.1%)	2 (1.5%)
Peripheral swelling	12 (1.1%)	0 (0.0%)
Blister	11 (1.0%)	0 (0.0%)
Hypoesthesia	11 (1.0%)	0 (0.0%)
Lethargy	11 (1.0%)	0 (0.0%)

Upper respiratory tract infection	11 (1.0%)	2 (1.5%)
Rhinorrhea	10 (1.0%)	0 (0.0%)
[†] Adverse reactions were solicited Days 1 to 5 postvaccination. [‡] Adverse reactions were solicited Day 1 through Day 42 postvaccination. [§]Abdominal pain includes: abdominal discomfort, abdominal pain, and abdominal pain upper.		

In this study, 29 subjects (2.8%) reported injection-site pain of severe intensity. Severe arthritis (arthritis and joint swelling) was reported by 8 subjects (0.8%) and severe arthralgia was reported by 14 subjects (1.3%). In this study, severe events were defined as incapacitating with inability to work or do usual activity.

Description of Selected Adverse Reactions

Arthralgia and Arthritis

Arthralgia was reported to occur in 7% to 40% of vaccine recipients in blinded, placebo-controlled studies. Arthralgia was generally reported in the first few days following vaccination, was of mild to moderate intensity, and resolved within one week after onset. Severe arthralgia, defined as preventing daily activity, was reported in up to 3% of subjects.

Arthritis (including events of arthritis, joint effusion, joint swelling, osteoarthritis, monoarthritis or polyarthritis) was reported to occur in 0% to 24% of subjects in blinded, placebo-controlled studies in which subjects received ERVEBO® or a lower dose formulation, with all but one study reporting arthritis in <5% of subjects. Most occurrences of arthritis were reported within the first few weeks following vaccination, were of mild to moderate intensity, and resolved within several weeks after onset. In one study conducted in Switzerland, 102 subjects received ERVEBO® or a lower dose formulation. In this study, arthritis was reported to occur in 24% of subjects and severe arthritis, defined as preventing daily activity, in 12% of subjects. Joint effusion samples were obtained from three subjects and all three tested positive for vaccine virus RNA by RT-PCR. Of all 24 subjects with arthritis in this study, six subjects reported recurrent or prolonged joint symptoms lasting up to 2 years following vaccination, the longest follow-up period.

Rash

Rash was reported to occur after administration of ERVEBO® in blinded, placebo-controlled studies, with all but one study reporting rash in <9% of subjects. In one study conducted in Switzerland, rash was reported to occur in 25% (n=4) of ERVEBO® recipients and 7.7% (n=1) of placebo recipients. In this study, cutaneous vasculitis was reported in two subjects who received a lower dose formulation, neither of whom had evidence of systemic vasculitis. Vesicular fluid and skin biopsy samples taken from some subjects reporting rash have tested positive for vaccine virus RNA by RT-PCR.

Table 3 summarizes the incidence of these events in Protocol 012.

Table 3 - Summary of Selected Adverse Events (Composite Term) in Protocol 012

Adverse Events	**ERVEBO® (N=1,051) n (%)**	**Placebo (N=133) n (%)**
Day 1 to Day 42 Postvaccination		
Rash[†]	40 (3.8%)	2 (1.5%)
Vesicular lesions[‡]	16 (1.5%)	0 (0.0%)
Day 5 to Day 42 Postvaccination		
Arthralgia	67 (6.4%)	2 (1.5 %)
Arthritis[§]	37 (3.5%)	0 (0.0%)

[†] Rash is a composite term that includes petechiae, purpura, rash, rash generalized, rash macular, rash papular and rash vesicular.
[‡] Vesicular lesions include events reported as rash vesicular in the rash composite term and reported as blister.
[§] Arthritis is a composite term that includes preferred terms of arthritis, monoarthritis, polyarthritis, osteoarthritis, joint swelling, or joint effusion.

8.3 Less Common Clinical Trial Adverse Reactions

Less frequently reported (<1%) adverse reactions included migraine (0.8%), hyperhidrosis (0.7%), and peripheral arthritis (0.6%). Anaphylactic reaction (0.006%) was reported very rarely and in an open-label study.

8.4 Abnormal Laboratory Findings: Hematologic, Clinical Chemistry and Other Quantitative Data

Transient decrease in white blood cells

Transient decreases in counts of lymphocytes, neutrophils and total white blood cells in the first 3 days following vaccination have been observed very commonly in Phase I/II studies; these events generally resolved after the first week post-vaccination. No adverse events of infections were observed in Phase I/II trials.

8.5 Post-Market Adverse Reactions

There are no post-marketing data available for ERVEBO®.

9 DRUG INTERACTIONS

9.4 Drug-Drug Interactions

No interaction studies have been performed.

As there are no data on co-administration of ERVEBO® with other vaccines, the concomitant use of ERVEBO® with other vaccines is not recommended.

Immune globulin (IG), blood or plasma transfusions should not be given concomitantly with ERVEBO®. Administration of immune globulins, blood or plasma transfusions administered 3 months before or up to 1 month after ERVEBO® administration may interfere with the expected immune response.

It is unknown whether concurrent administration of antiviral medication including interferons could impact vaccine virus replication and efficacy.

9.7 Drug-Laboratory Test Interactions

Following vaccination with ERVEBO®, individuals may test positive for Ebola glycoprotein (GP) nucleic acids, antigens, or antibodies against Ebola GP, which are targets for certain Ebola diagnostic tests. Therefore, diagnostic testing for Ebola should target non-GP sections of the Ebola virus.

10 CLINICAL PHARMACOLOGY

10.1 Mechanism of Action

ERVEBO® consists of a live, attenuated recombinant vesicular stomatitis virus-based vector expressing the envelope glycoprotein gene of Zaire Ebola virus (rVSVΔG-ZEBOV-GP). Immunisation of subjects with the vaccine results in an immune response and protection from Zaire Ebola Virus Disease. The relative contributions of innate, humoral and cell-mediated immunity to protection from Zaire Ebola virus are unknown.

10.2 Pharmacodynamics

Pharmacotherapeutic group: Vaccines, Viral Vaccine, ATC code: J07BX02.

10.3 Pharmacokinetics

Duration of Effect

Vaccination with ERVEBO® may not result in protection in all vaccinees. Vaccine efficacy has been established in the period ≥10 to ≤31 days after vaccination, however the duration of protection is not known (see section 14 CLINICAL TRIALS). **The use of other Ebola control measures should therefore not be interrupted**.

Vaccination of contacts of Ebola cases should occur as soon as possible (see 14 CLINICAL TRIALS).

11 STORAGE, STABILITY AND DISPOSAL

Store and transport frozen at -80°C to -60°C. Do not store or transport outside the recommended temperature range.

After thawing, the vaccine should be used immediately; however, in-use stability data have demonstrated that once thawed, the vaccine can be stored for up to 14 days at 2°C to 8°C prior to use. At the end of 14 days, the vaccine should be used or discarded. Upon removal from the freezer, the product should be marked with both the date that it was taken out of the freezer and also a new discard date (in place of the labelled expiry date). Once thawed, the vaccine cannot be re-frozen.

Keep the vial in the outer carton in order to protect from light.

Special precautions for disposal and other handling

- The vaccine is stored frozen at -80°C to -60°C and should be removed from the freezer and thawed in less than 4 hours until no visible ice is present. Do not thaw the vial in a refrigerator as it is not guaranteed that the vial will thaw in less than 4 hours. The thawed vial should then be gently inverted several times prior to withdrawal with the syringe. The vaccine should appear as a colorless to slightly brownish-yellow liquid with no particulates visible. Discard the vaccine if particulates are present.
- Withdraw the entire content of the vaccine from the vial using a sterile needle and syringe.

12 SPECIAL HANDLING INSTRUCTIONS

Any unused vaccine or waste material should be disposed of in accordance with local requirements.

If breakage/spillage were to occur, disinfectants such as aldehydes, alcohols and detergents are proven to reduce viral infection potential after only a few minutes.

PART II: SCIENTIFIC INFORMATION

13 PHARMACEUTICAL INFORMATION

Drug Substance
ERVEBO® (Ebola Zaire Vaccine (rVSVΔG-ZEBOV-GP, live))

Physicochemical properties: The solution for injection is a colorless to slightly brownish-yellow liquid.

Product Characteristics:
ERVEBO® is a sterile solution for intramuscular injection. ERVEBO® is a live recombinant viral vaccine consisting of a vesicular stomatitis virus (VSV) backbone deleted for the VSV-G envelope glycoprotein and substituted with the envelope glycoprotein (GP) of the Zaire Ebola virus (Kikwit 1995 strain). The vaccine is manufactured in serum-free Vero cell cultures. The virus is harvested from the cell culture medium, purified, and frozen (-80°C to -60°C). The material is then thawed, diluted as needed, mixed, filled into vials, inspected, labeled, packaged, frozen, and stored at -80°C to -60°C.

14 CLINICAL TRIALS

14.1 Clinical Trials by Indication

Table 4 - Summary of patient demographics for clinical trials for Ebola Virus Disease Efficacy, Immunogenicity and Safety

Study #	Study design	Dosage, route of administration and duration	Study subjects (n)	Mean age (Range)	Sex
P009	United States National Institutes of Health: Partnership for Research on Ebola Vaccines in Liberia (PREVAIL); Phase II randomized, double-blind, placebo-controlled study to evaluate safety and immunogenicity of 2 leading Ebola vaccine candidates in adults aged 18 years and older.	1 dose of 1 mL V920 Intramuscular injection V920: 1 dose = 1 mL ($2X10^7$ PFU)	1000	32.2 years (17 to 87 years)	Females: 364 Males: 636
P010	World Health Organization: A randomized trial to evaluate Ebola vaccine efficacy and safety in Guinea, West Africa; cluster randomized ring vaccination; open-label vaccination rings were randomized to immediate vaccination group (vaccinated on Day 0) and delayed vaccination group (vaccinated on Day 21 postrandomization).	1 dose = 1 mL ($2X10^7$ PFU) Intramuscular injection	Immediately vaccinated: 3,796	Median age: 35 years (25-50 years)	Females: 1,223 Males: 2,573
		1 dose = 1 mL ($2X10^7$ PFU) Intramuscular injection	Delayed or never vaccinated: 4,538	Median age: 35 years (25-50 years)	Females: 1,948 Males: 2,589

P011	United States Centers for Disease Control and Prevention: Phase II/III open-label, randomized trial to evaluate vaccine safety and immunogenicity in adults ≥18 years of age working in healthcare facilities or on frontline activities related to the Ebola response in Sierra Leone.	1 dose = 1 mL ($\geq 2X10^7$ PFU) Intramuscular injection	8,651	33.4 years (18.0 to 79.5 years)	Female: 3,407 Male: 5,244
P012	Merck: A Phase III, randomized, double-blind, placebo-controlled, clinical trial to study the safety and immunogenicity of three consistency lots and a high dose lot of rVSVZEBOV-GP (V920 Ebola Vaccine) in healthy adults in the US, Canada, and Spain.	1 dose = 1 mL ($\geq 2X10^7$ PFU) Or 1 mL (2×10^7 PFU), 1 mL (1×10^8 PFU), placebo Intramuscular injection	1,197	41.3 years (18 to 65 years)	Female: 637 Male: 560
P018	World Health Organization: A Phase III randomized, open-label trial to evaluate Ebola vaccine efficacy and Safety in Guinea, West Africa Sub-study Protocol: safety and immunogenicity of VSVΔG/ZEBOVGP among Frontline Workers.	1 mL (2×10^7 PFU) Intramuscular injection	2,115	33,2 years (18 to 75 years)	Female: 541 Male: 1,574

Clinical efficacy and immunogenicity

The clinical development program included five Phase II/III (Protocols 009-012 and 018) clinical trials. All subjects received a single dose of vaccine.

Clinical efficacy of ERVEBO® was assessed in Protocol 010.

Protocol 010 (Ring vaccination study) was a Phase III open-label cluster-randomized trial of ring vaccination (vaccinating contacts and contacts of contacts [CCCs] of index Ebola cases) which evaluated efficacy and safety of ERVEBO® in the Republic of Guinea during the 2014 outbreak. In this trial, 51 clusters were randomized to receive ERVEBO® as an immediate vaccination (immediate vaccination arm) and 47 clusters to receive vaccination 21 days following randomization (delayed vaccination arm). Based on this randomization, 4,160 subjects received ERVEBO® (2,119 subjects were vaccinated in the immediate arm and 2,041 subjects were vaccinated in the delayed arm). The median age of consenting CCCs was 35 years old.

The primary analysis was to assess efficacy against laboratory confirmed EVD by comparing incidence of cases occurring 10 to 31 days post-randomisation for those vaccinated in the immediate vaccination arm versus incidence of cases occurring from Day 0 in the delayed vaccination arm. The primary efficacy analysis included 2,108 subjects (51 clusters) vaccinated in the immediate arm and 1,429 subjects (46 clusters) eligible and consented on Day 0 in the delayed arm. Vaccine efficacy was estimated to be 100% (95% CI: 63.5% to 100%) (0 cases in the immediate arm; 10 cases in 4 rings in the delayed arm). Of the 10 cases, 7 were in contacts, and 3 in contacts-of-contacts. Uncertainties in the findings remain as to the level, duration and type of protection given the methodological limitations and the exceptional circumstances experienced during the trial.

14.4 Immunogenicity

A measure of the immune response that confers protection against EVD is unknown. Four studies assessed antibody responses to ERVEBO® (Protocols 009, 011, 012 and 018), including 477 subjects in Liberia, 506 subjects in Sierra Leone, 915 subjects in the US, Canada, and Spain study, and 1,217 subjects in the Republic of Guinea. *Zaire ebolavirus* (Kikwit) GP-specific immunoglobulin G (IgG) was detected by enzyme linked immunosorbent assay (GP-ELISA). Vaccine virus neutralizing antibody was detected by a plaque reduction neutralization test (PRNT). Antibody responses among subjects in the study conducted in the US, Canada, and Spain were similar to those among subjects in the studies conducted in Liberia, Sierra Leone, and the Republic of Guinea, when the impact of gamma irradiation pretreatment on samples was taken into account. GP-ELISA GMTs reached the peak at 1 month and decreased slightly but remained well above baseline levels up to 12 months in Protocols 009, 011 and 012. PRNT GMTs reached the peak at 1 month and remained consistent up to 12 months in Protocols 009, 011 and 012.

16 NON-CLINICAL TOXICOLOGY

Carcinogenicity: ERVEBO® has not been evaluated for the potential to cause carcinogenicity, as carcinogenicity studies were not considered relevant to this vaccine.

Genotoxicity: ERVEBO® has not been evaluated for the potential to cause genotoxicity, as genotoxicity studies were not considered relevant to this vaccine.

Reproductive and Developmental Toxicology: Non-clinical data reveal no special hazard for humans based on conventional studies of repeated dose toxicity and toxicity to reproduction and development.

In a developmental toxicity study, female rats received a single human dose of ERVEBO® by intramuscular injection on four occasions: 28 days and 7 days prior to mating, gestation day 6 and lactation day 7.

When ERVEBO® was administered to female rats, antibodies against the vaccine virus were detected in foetuses and offspring, likely due to trans-placental transfer during gestation and with the acquisition of maternal antibodies during lactation, respectively (see 7.1.1 Pregnant Women, 7.1.2 Breast-Feeding).

ERVEBO® administered to female rats had no effects on mating performance, fertility, or embryonic/foetal development.

ERVEBO® administered to female rats had no effects on development or behaviour of the offspring.

PATIENT MEDICATION INFORMATION

READ THIS FOR SAFE AND EFFECTIVE USE OF YOUR MEDICINE

ERVEBO®

Ebola Zaire Vaccine (rVSVΔG-ZEBOV-GP, live)

Read this carefully before you are vaccinated with **ERVEBO®**. This leaflet is a summary and will not tell you everything about this vaccine. Talk to your healthcare professional about your medical condition and treatment and ask if there is any new information about **ERVEBO®**.

What is ERVEBO® used for?

- ERVEBO® is a vaccine for adults who are 18 years of age and older.
- ERVEBO® is given to protect you from getting Ebola virus disease caused by the Zaire Ebola virus, which is a type of Ebola virus. This vaccine will not protect you against the other types of Ebola virus or related Filoviruses, such as Sudan Ebola virus or Marburg virus
- Because ERVEBO® does not contain the whole Ebola virus, it cannot give you Ebola virus disease.

Your healthcare professional may recommend that you receive this vaccine in an emergency involving the spread of Ebola virus disease.

How does ERVEBO® work?

The vaccine works by helping your body to make its own antibodies which can protect you against the Ebola Virus Disease caused by Zaire Ebola virus.

What is Ebola?

- Ebola is a serious disease caused by a virus. If you get Ebola, it can kill you. People catch Ebola from people or animals who are infected with Ebola or who died from Ebola.
- You can catch Ebola from blood and body fluids like urine, stools, saliva, vomit, sweat, breast milk, semen and vaginal fluids of people who are infected with Ebola virus.
- You can also catch Ebola from things that have touched the blood or body fluids of a person or animal with Ebola (like clothes or objects in direct contact).
- Ebola is not spread through the air, water or food.

Your healthcare professional will talk to you and then together you can decide if you should receive this vaccine.

What are the ingredients in ERVEBO®?
Medicinal ingredients: Living Vesicular Stomatitis Virus. The surface protein of the virus has been replaced with that of Zaire Ebola Virus (rVSVΔG-ZEBOV-GP).

One dose (1 mL) contains:
Ebola Zaire Vaccine (rVSVΔG-ZEBOV-GP[1,2] live, attenuated) ≥72 million pfu[3]
[1]Recombinant Vesicular Stomatitis Virus (rVSV) strain Indiana with a deletion of the VSV envelope glycoprotein (G) replaced with the Zaire Ebola Virus (ZEBOV) Kikwit 1995 strain surface glycoprotein (GP)
[2]Produced in Vero cells
[3]pfu= plaque-forming units

This product contains genetically modified organisms (GMOs).
This vaccine contains a trace amount of rice protein.

Non-medicinal ingredients: Recombinant human serum albumin, trometamol buffer, water for injections, hydrochloric acid, sodium hydroxide

What ERVEBO® looks like and contents of the pack:
- ERVEBO® is a solution for injection
- ERVEBO® is a colorless to slightly brownish-yellow liquid
- ERVEBO® is available in a pack of 10 vials

Do not use ERVEBO® if:
- are allergic to ERVEBO®, rice, or any of the other ingredients of this vaccine (listed in the section above: **"What are the ingredients in ERVEBO®?"**

You should not receive ERVEBO® if any of the above apply to you. If you are not sure, talk to your healthcare professional.

To help avoid side effects and ensure proper use, talk to your healthcare professional before you get ERVEBO®. Talk about any health conditions or problems you may have, including if you:

Have had allergic reactions to vaccines or medicines
If you have ever had an allergic reaction to a vaccine or medicine, talk to your healthcare professional before you receive this vaccine.

Have a weak immune system
If your immune system is weak (which means your body is less able to fight off diseases), you might not be able to receive ERVEBO®. You might have a weak immune system if:
- you have HIV infection or AIDS,
- you are taking certain medicines that make your immune system weak such as immunosuppressants or corticosteroids,
- you have cancer or a blood problem that makes your immune system weak,
- a member of your family has a weak immune system.

If you think you might have a weak immune system, ask your healthcare professional if you should receive this vaccine. If you do get the vaccine and have a weak immune system, the vaccine may not work as well as in people with a normal immune system.

Are in contact with vulnerable individuals

Tell your healthcare professional if in the 6 weeks after you receive ERVEBO® you might be in close contact with or in the same household as:

- babies who are less than 1 year old,
- someone who may be pregnant or breast-feeding,
- someone who has a weak immune system.

This is because you could pass on the virus in the vaccine to them through your body fluids.

Plan to donate blood

- Do not donate blood for at least 6 weeks after you receive this vaccine.

Are in contact with farm animals

Make sure your blood or body fluids do not come into close contact with farm animals for at least 6 weeks after you receive this vaccine. This is because of a possibility that you could pass on the virus in the vaccine to the animals.

Have a fever (high temperature)

- If you have a fever (high temperature), you should talk to your healthcare professional before receiving ERVEBO®. The vaccination may have to be delayed until your fever is gone.
- A minor infection such as a cold should not be a problem but talk to your healthcare professional before receiving ERVEBO®.

Have a bleeding disorder or bruise easily

- Tell your healthcare professional if you have a problem with bleeding or you bruise easily. ERVEBO® might make you bleed or bruise where the vaccine is injected.

Take a test for Ebola after you receive ERVEBO®

- You may test positive for Ebola virus after you receive ERVEBO®. This does not mean that you have Ebola. Tell your healthcare professional that you have received ERVEBO®. Your healthcare professional might need to do another test.

Are pregnant or breast-feeding

- You are pregnant or breast-feeding, think you may be pregnant or are planning to have a baby, ask your healthcare professional for advice before you receive this vaccine. They will help you decide if you should receive ERVEBO®.
- Do not become pregnant for 2 months after you receive ERVEBO®. Women who are able to become pregnant should use an effective method of birth control. It is not known if ERVEBO® will harm you or your unborn baby. It is also not known if it can pass to your baby through your breast milk.
- If you might be in close contact with, or in the same household as someone who may be pregnant or breast-feeding during the 6 weeks after you receive ERVEBO®, tell your healthcare professional. This is because you could pass the vaccine to them through your body fluids.

Other warnings you should know about:

This vaccine might not protect everyone who receives it and the length of time you are protected from Ebola infection by ERVEBO® is not known.

Continue to follow your healthcare professional's recommendations to protect yourself from Ebola infection after you get this vaccine.

In an area affected by Ebola:
While in an area affected by Ebola, it is important to avoid the following:

- Contact with blood and body fluids (such as urine, feces, saliva, sweat, vomit, breast milk, semen, and vaginal fluids).
- Items that may have come in contact with an infected person's blood or body fluids (such as clothes, bedding, needles, and medical equipment).
- Funeral or burial rituals that require handling the body of someone who died from Ebola.
- Contact with bats, apes and monkeys or with blood, fluids and raw meat prepared from these animals (bushmeat) or meat from an unknown source.
- Contact with semen from a man who had Ebola. You should follow safe sex practices until you know the virus is gone from the semen.

In case of rash:
If you get a rash where the skin is broken after receiving ERVEBO®, cover it until it heals. Put the used plasters and bandages in a sealed container, if possible, and throw them in the waste bin to make sure that people with a weak immune system or animals do not come into contact with the plasters and bandages.

Tell your healthcare professional about all the medicines you take, have recently taken or might take including any drugs, vaccines, vitamins, minerals, natural supplements or alternative medicines.

The following may interact with ERVEBO®:
No studies have looked at how other medicines or vaccines and ERVEBO® might interact with each other. Use of ERVEBO® with other vaccines is not recommended.

If you plan to receive blood or blood products
Do not receive this vaccine at the same time that you get blood or blood products. ERVEBO® might not work as well if you get blood or blood products 3 months before or up to 1 month after vaccination.

How is ERVEBO® given?:

Usual dose:
Adult:
ERVEBO® is given by a healthcare professional. It is given as a single injection (dose of 1 mL) into the muscle (in the top of your arm or the outside of your thigh).

If you have any further questions on the use of this vaccine, ask your healthcare professional.

Children and adolescents
It has not yet been established whether ERVEBO® can be used in children and adolescents younger than 18 years of age.

Overdose:

If you think you, or a person you are caring for, have received too much ERVEBO®, contact a healthcare professional, hospital emergency department, or regional poison control centre immediately, even if there are no symptoms.

Missed Dose:
ERVEBO® is given as a single dose.

What are possible side effects from using ERVEBO®?
Like all vaccines, ERVEBO® can cause side effects, although not everybody gets them.

Serious side effects:
Serious side effects are rare. Get medical care right away if you have symptoms of an allergic reaction, which may include:

- wheezing or trouble breathing,
- swelling of the face, lips, tongue, or other parts of the body,
- generalised itching, redness, flushing or itchy bumps on the skin.

Other side effects:
Very common (may affect more than 1 in 10 people):

- Headache,
- Joint pain,
- Fever,
- Pain,
- Pain, swelling, or redness at the injection site.

Common (may affect up to 1 in 10 people):

- Nausea,
- Chills,
- Influenza like illness
- Muscle aches,
- Feeling tired.

Certain white blood cell counts can decrease below normal after vaccination but this decrease has not resulted in illness and the counts return to normal.

Most side effects go away within a few days. Joint pain and swelling may last for weeks or months in some people. In some people joint pain and swelling may come back after initially going away.

These are not all the possible side effects you may have when taking ERVEBO®. If you experience any side effects not listed here, tell your healthcare professional.

If you have a troublesome symptom or side effect that is not listed here or becomes bad enough to interfere with your daily activities, tell your healthcare worker.

Reporting Suspected Side Effects for Vaccines

For the general public: Should you experience a side effect following immunization, please report it to your healthcare professional.
Should you require information related to the management of the side effect, please contact your healthcare professional. The Public Health Agency of Canada, Health Canada and Merck Canada Inc. cannot provide medical advice.

For healthcare professional**:** If a patient experiences a side effect following immunization, please complete the Adverse Events Following Immunization (AEFI) Form appropriate for your province/territory (http://www.phac-aspc.gc.ca/im/aefi-essi-form-eng.php) and send it to your local Health Unit.

Storage:
ERVEBO® should be stored, supplied and administered by a healthcare professional.

Keep out of reach and sight of children.

If you want more information about ERVEBO®:

- Talk to your healthcare professional
- Find the full product monograph that is prepared for healthcare workers and includes this Patient Medication Information by visiting the Health Canada website: https://www.canada.ca/en/health-canada/services/drugs-health-products/drug-products/drug-product-database.html; the manufacturer's website www.merck.ca, or by calling 1-800-567-2594.

This leaflet was prepared by Merck Canada Inc.

Last Revised November 9, 2022