PUBLIC ASSESSMENT SUMMARY REPORT

Ervebo™, Ebola Zaire Vaccine (rVSVΔG-ZEBOV-GP, live), Merck & Co., Inc. USA

What is Ervebo [Ebola Zaire Vaccine (rVSVΔG-ZEBOV-GP, live)]?

Ervebo (Er-vee-bo), is the Merck & Co., Inc. USA (known as MSD outside the USA and Canada), trade name for its Ebola Zaire vaccine (rVSVΔG-ZEBOV-GP, live). The vaccine is a recombinant vesicular stomatitis virus (rVSV) based vaccine expressing the envelope glycoprotein (G) gene of Zaire Ebola virus (ZEBOV) Kikwit 1995 strain surface glycoprotein (GP) for WHO prequalification listing.

Ervebo is a liquid vaccine, presented in single dose vial (1.0 mL) as a colourless to slightly brownish-yellow solution.

Ervebo is in a single-dose vial presentation and consists of the following composition per 1.0 mL dose:

Components	Quantity (per 1.0 mL)
Active ingredient	
Ebola Zaire Vaccine (rVSVΔG-ZEBOV-GP live), attenuated	≥ 72 million pfu
Excipients	
Recombinant human serum albumin Trometamol buffer Water for injections Hydrochloric acid (for pH-adjustment) Sodium hydroxide (for pH-adjustment)	

The vaccine is supplied in type 1 glass vials closed by a pharmaceutical grade stopper made out of chlorobutyl and flip-off plastic cap with aluminium seal.

The vaccine virus is a Genetically Modified Organism (GMO).

What is Ervebo, [Ebola Zaire Vaccine (rVSVΔG-ZEBOV-GP, live)] used for?

Ervebo 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.

How is Ervebo, [Ebola Zaire Vaccine (rVSVΔG-ZEBOV-GP, live)] used?

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 colourless 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.

Ervebo should be administered by the intramuscular (IM) route. 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. No data are available for administration via the subcutaneous or intradermal 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. 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.

What are Ervebo's [Ebola Zaire Vaccine (rVSVΔG-ZEBOV-GP, live)] storage characteristics?

The vaccine should be stored and transported frozen at -80°C to -60°C, and the assigned shelf-life is 36 months at this temperature, from the date of manufacture. 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.

Vaccine cold chain volume is 16.42 cm3 / dose in the secondary packaging.

Who is the regulatory authority responsible for its oversight vis a vis WHO?

The European Medicines Agency is the authority responsible for the continuing oversight of this WHO prequalified vaccine.

How has Ervebo [Ebola Zaire Vaccine (rVSVΔG-ZEBOV-GP, live)] been studied from the clinical point of view?

The clinical development program included four Phase 2/3 (Protocols 009-012) 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 3 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 Guinea. In this trial, 9,096 subjects ⩾18 years of age who were considered CCCs of an index case with laboratory-confirmed EVD were randomized to immediate (4,539 subjects in 51 clusters) or 21 days delayed (4,557 subjects in 47 clusters) vaccination with Ervebo. Of those 9,096 subjects, 4,160 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 final primary 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.

The final primary analysis was to assess efficacy against laboratory confirmed EVD by comparing incidence of cases occurring 10 to 31 days post-randomization for those vaccinated in the immediate vaccination rings versus incidence of cases for subjects who consented on Day 0 in the delayed vaccination rings. Vaccine efficacy was 100% (unadjusted 95% CI: 63.5% to 100%; 95% CI adjusted for multiplicity: 14.4% to 100%) (0 cases in the immediate arm; 10 cases in 4 rings in the delayed arm). Randomization was stopped after an interim analysis with a p=0.0036 that did not meet the pre-specified alpha level of 0.0027. Of the 10 cases, 7 were in contacts, and 3 in contacts-of-contacts. Uncertainties remain as to the level, duration and type of protection given the methodological limitations and the exceptional circumstances experienced during the trial.

The safety of Ervebo was assessed on the basis of data collected in 15.398 healthy adults in 8 phase 1 studies and 4 phase 2/3 studies. The vaccine was well tolerated by the enrolled subjects. The most common injection-site adverse reactions were injection-site pain, swelling and erythema. The most common systemic adverse reactions reported following vaccination with Ervebo were headache, pyrexia, myalgia, fatigue, arthralgia, nausea, chills, arthritis, rash, hyperhidrosis, and abdominal pain. In general, these reactions were reported within 7 days after vaccination, were mild to moderate in intensity, and had short duration (less than 1 week).

Other information about evaluation of Ervebo [Ebola Zaire Vaccine (rVSVΔG-ZEBOV-GP, live)]

As part of the prequalification process for Ervebo [Ebola Zaire Vaccine (rVSVΔG-ZEBOV-GP, live)], the Common Technical Document and the responses provided by the manufacturer to observations made by WHO have been reviewed for quality, safety and efficacy by a team of WHO experts.

The dossier was prequalified following conditional approval by European Medicine Agency.

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