DATA SHEET

NAME OF THE MEDICINE

VERORAB

Purified inactivated rabies vaccine, prepared on VERO cells.

DESCRIPTION

VERORAB is a sterile freeze-dried powder and diluent for suspension for injection.

Freeze-dried Powder

After reconstitution, each 0.5 mL of reconstituted dose contains:

Rabies virus*, Wistar rabies PM/WI 38 1503-3M strain (inactivated)	≥ 2.5 IU*

* cultured on VERO cells
* IU = International Unit. Potency measured using NIH test in mice

Maltose	26.3 mg
20% Human albumin solution	0.125 mL
BME†	0.025 mL
Water for injection	0.5 mL

† BME: Basal Medium Eagle: mixture of mineral salts, vitamins, dextrose and amino-acids including L-Phenylalanine.

No preservative or adjuvant is added.

Diluent - 0.4% sodium chloride solution

Sodium chloride	2mg
Water for injection	qs 0.5 mL

VERORAB contains bovine serum albumin (not more than 50 nanogram per dose). The vaccine may contain undetectable traces of betapropiolactone, neomycin, streptomycin and polymixin B which are used during vaccine production.

PHARMACOLOGY

Rabies Vaccine

Inactivated vaccine used to prevent rabies in subjects at risk from infection and as a treatment following confirmed or possible infection with rabies virus.

Pre-Exposure

Serum antibody level ≥ 0.5 IU/mL, considered as protective by the WHO, is achieved after the injection of 3 doses at D0, D7 and D28 (or D21). This immunity must be maintained by a first booster dose 1 year later with subsequent boosters every 5 years.

Post-Exposure

Serum antibody level ≥ 0.5 IU/mL, considered as protective by the WHO, is achieved after the third injection by D14.

INDICATIONS

VERORAB is indicated for the prevention of rabies prior to exposure and following proven or suspected exposure.

CONTRAINDICATIONS

Pre-Exposure

Known systemic hypersensitivity reaction to any component of VERORAB or after previous administration of the vaccine or a vaccine containing the same components.

Vaccination must be postponed in case of febrile or acute disease.

In all cases, the risk/benefit ratio should be assessed.

Post Exposure

Since declared rabies infection generally results in death, there are no contraindications to curative vaccination.

PRECAUTIONS

As with any vaccine, VERORAB may not protect 100% of vaccinated individuals.

Do not inject by the intravascular route: ensure that the needle does not penetrate a blood vessel.

Immunoglobulin and rabies vaccine must not be combined in the same syringe or injected at the same site.

In order to reach a sufficient level of protection, recommendations for the use of VERORAB must be strictly followed (see DOSAGE AND ADMINISTRATION) as an insufficient immune response may lead to fatal cases of rabies.

Individuals History

As each dose may contain undetectable traces of neomycin, streptomycin and polymyxin which is used during vaccine production, caution must be exercised when the vaccine is administered to individuals with hypersensitivity to those antibiotics, and other antibiotics of the same class.

In individuals who have a history of serious or severe reaction within 48 hours of a previous injection with a vaccine containing similar components, the course of the vaccination must be carefully considered.

As with all injectable vaccines, appropriate medical treatment and supervision should always be readily available in case of an anaphylactic event following administration of the vaccine.

Serology testing

In order to ensure a continuous protection, a serological test (neutralising antibody assay using the Rapid Fluorescent Focus Inhibition Test (RFFIT) analysis) should be performed every 6 months in individuals with continuous exposure. It may be performed every 2 years after the boosters at 1 and 5 years in individuals with a frequent risk of exposure to rabies.

Using this test, minimum acceptable antibody level is defined as $\geq$ 0.5 IU/mL or as complete virus neutralisation at a 1:5 serum dilution.

If the result is below the acceptable level, a booster should be administered.

Immunocompromised individuals

In individuals with congenital or acquired immunodeficiency, the immune response to the vaccine may be inadequate. Therefore, it is recommended to monitor the serological antibody level in such individuals to ensure that an acceptable response has been induced by the pre-exposure schedule. Additional doses should be given if necessary.

If post-exposure vaccination is needed, rabies immunoglobulin should be given in association with the vaccine for minor (nibbling of uncovered skin, minor scratches or abrasions without bleeding) and severe (single or multiple transdermal bites or scratches, contamination of mucous membrane with saliva from licks, licks on broken skin, exposure to bats) exposures.

Patients with bleeding disorders

Because intramuscular injection can cause injection site haematoma, VERORAB should not be given to individuals with any bleeding disorder, such as haemophilia or thrombocytopenia, or to individuals on anticoagulant therapy unless the potential benefits clearly outweigh the risk of administration. If the decision is made to administer VERORAB in such individuals, it should be given with caution, with steps taken to avoid the risk of haematoma formation following injection.

Use in pregnancy (Category B2)

Pre-exposure
Animal reproductive studies have not been conducted with VERORAB. Data on the use of this vaccine in pregnant women are limited. Therefore, the administration of the vaccine during pregnancy is not recommended. VERORAB should be given to pregnant women only if clearly needed, and following an assessment of the risks and benefit.

Post-exposure
Due to the severity of the disease, pregnancy is not a contraindication.

Use in lactation

It is not known whether this vaccine is excreted in human milk. Caution must be exercised when VERORAB is administered to a nursing mother.

Paediatric use

Safety and effectiveness in children have been established. The indications for infants and children are the same as for adults.

Use in the elderly

Evidence from experience suggests that rabies vaccine is efficacious in the geriatric population.

Effect on laboratory tests

Interference of VERORAB with laboratory tests has not been studied.

INTERACTIONS WITH OTHER MEDICINES

Corticosteroid and immunosuppressive therapy may interfere with the production of antibodies and cause failure of the vaccine; it is therefore advisable to perform a serological test 2 to 4 weeks after the last vaccine injection.

When immunoglobulins against rabies are to be administered with rabies vaccine (see DOSAGE AND ADMINISTRATION), they must not be combined in the same syringe or injected at the same site. If possible, the vaccine should be injected contra-laterally to the immunoglobulin administration sites.

ADVERSE EFFECTS

Data from Clinical Studies

The following adverse events are derived from several clinical studies where VERORAB has been used in both pre-exposure and post-exposure schedule.

Blood and lymphatic system disorders

- Very common: lymphadenopathy

Immune system disorders

- Common: skin allergic reactions rash, pruritus, and oedema
- Uncommon: urticaria, angioedema, dyspnoea

Nervous system disorders

- Common: headache, dizziness, somnolence

Gastrointestinal disorders

- Common: abdominal pain, nausea
- Uncommon: diarrhoea

Musculoskeletal and connective tissue disorders

- Very common: myalgia
- Common: arthralgia, chills

General disorders and administration site conditions

- Very common: injection site pain, fever, malaise
- Common: injection site erythema, injection site pruritus, injection site haematoma, injection site induration, asthenia, influenza-like symptoms
- Uncommon: injection site oedema

Data from Post-Marketing Experience

.Based on spontaneous reporting, the following events have been reported very rarely following commercial use of VERORAB. Because these events are reported voluntarily from a population of uncertain size, it is not always possible to reliably estimate the frequency or establish a causal relationship of exposure to VERORAB.

Immune system disorders

- Anaphylactic reactions
- Serum sickness type reactions

Nervous system disorders

- Encephalitis, convulsions

Ear and labyrinth disorders

- Sudden sensorineural hearing loss

Gastrointestinal disorders

- Vomiting

DOSAGE AND ADMINISTRATION

The vaccine should be administered by the intramuscular route only, in the deltoid muscle in adults and children or in the anterolateral area of the thigh muscle in infants and toddlers.

Do not inject in the gluteal area. Do not administer by the intravascular route.

The vaccination schedule should be adjusted according to the circumstances of the exposure and the individual's rabies immune status.

Pre-Exposure Vaccination

- Primary vaccination: 3 injections at D0, D7, and D21 or D28
- First booster: 1 year later
- Subsequent boosters: every 5 years

Regular serology testing of neutralising antibodies is recommended to assess seroconversion of individuals at increased risk of exposure to rabies virus, with a frequency adapted to that risk.

When antibody titre is below acceptable level, a booster dose is needed.

Post-Exposure Treatment

Local Treatment of Wounds

Prompt local treatment of all bite wounds and scratches is very important and must be performed immediately after exposure. Recommended first-aid procedures include immediate and thorough flushing and washing of the wound for a minimum of 15 minutes with soap and water, povidone iodine or other substances of proven lethal effect on rabies virus. If soap or an antiviral agent is not available, the wound should be thoroughly and extensively washed with water.

Immunisation

Post-exposure vaccination must be carried out under medical supervision and should be started as soon as possible after exposure.

The treatment must be adapted according to the type of contact and the immunisation status of the individual.

a) Vaccination of Non-Immunised Individuals

Administration of immunoglobulin

In the case of severe types of exposure (single or multiple transdermal bites or scratches, contamination of mucous membrane with saliva from licks, licks on broken skin, exposure to bats), rabies immunoglobulin should be given in association with the vaccine.

Complementary passive immunisation at D0 is necessary using:

- Human rabies immunoglobulin (HRIG) 20 IU/kg body weight
- Equine rabies immunoglobulin (ERIG) 40 IU/kg body weight

As much as possible should be infiltrated around the wounds. The remainder should be administered by deep intramuscular injection at a site distant from the vaccine injection site. If possible, the vaccine should be injected contra-laterally to the sites of immunoglobulin administration.

Administration of vaccine

Posology is identical for adults and children: it comprises five 0.5mL injections at D0, D3, D7, D14, and D28.

b) Vaccination of Previously Immunised Individuals (full preventative vaccination confirmed)

According to WHO guidelines, individuals who are not immunocompromised and who have received a complete pre-/post-exposure schedule with cell culture vaccine and have adequate documentation should receive a two-booster series consisting of one intramuscular dose on days 0 and 3. The administration of passive immunisation (immunoglobulin) is not required.

This schedule should not apply to immunocompromised individuals.

In both previously immunised and non-immunised individuals, the treatment should be completed with the administration of antitetanus prophylaxis treatment if necessary and a course of antibiotics to prevent superinfection.

Because VERORAB does not contain any preservative, the reconstituted vaccine should be used immediately.

Preparation

Reconstitution of vaccine:

Introduce the diluent provided into the vial of powder. Shake carefully until complete suspension of the powder is obtained. The suspension should be limpid, homogenous, and free from particles. Withdraw the suspension using a syringe.

Because VERORAB does not contain any preservative, the reconstituted vaccine should be used immediately.

Product is for single use only and must not be used in more than one individual. Discard any remaining unused contents.

OVERDOSAGE

Not applicable

PRESENTATION AND STORAGE CONDITIONS

Presentation

1 dose of freeze-dried vaccine in vial (glass) with 0.5mL of solution in syringe (glass) with plunger stopper. Box of 1 vial and syringe.

Storage

Store at 2º to 8ºC. REFRIGERATE. Do not use after expiry date. Store protected from light.

NAME AND ADDRESS OF THE SPONSOR

sanofi-aventis new zealand limited
Level 8
56 Cawley St
Ellerslie
Auckland

POISON SCHEDULE OF THE MEDICINE

Prescription Medicine

FURTHER INFORMATION

VERORAB has provisional consent under Section 23 of the Medicines Act 1981 due to the limited efficacy data available. VERORAB is only supplied when Merieux Inactivated Rabies Vaccine (MIRV) is unavailable.

DATE OF MOST RECENT AMENDMENT

23 August 2016