VERORAB

PURIFIED INACTIVATED RABIES VACCINE, PREPARED ON VERO CELLS

COMPOSITION

After reconstitution, 1 dose (0.5 mL) contains:

Rabies virus*, WISTAR Rabies PM/WI38 1503-3M strain (inactivated) 3.25 IU**
* Produced in VERO cells
** Quantity measured according to the ELISA test against the international standard (corresponds to ≥ 2.5 IU in the NIH test)

List of excipients
Powder:
- Maltose
- 20% Human albumin solution
- Basal Medium Eagle (mixture of mineral salts including potassium, vitamins, dextrose and amino-acids including L-Phenylalanine)
- Water for injections
- Hydrochloric acid and sodium hydroxide for pH adjustment

Solvent:
- Sodium chloride
- Water for injections

PHARMACEUTICAL FORM

Powder and diluent for suspension for injection.
Before reconstitution, the powder is a white and homogeneous pellet. The solvent is a clear and colorless solution.

THERAPEUTIC INDICATIONS

This medicinal product is a vaccine.

Pre-exposure

This vaccine is recommended for the prevention of rabies in subjects at a high risk of exposure.All subjects at a permanent risk, such as diagnostic, research and production laboratory staff working on rabies virus, should be vaccinated. A serological test is recommended every 6 months. A booster injection should be administered when the antibody titre is below the level considered to guarantee protection: 0.5 I.U./mL. The following categories should be vaccinated given the frequency of exposure to the risk:

- Veterinarians (and assistants), gamekeepers, hunters, forest rangers, slaughter- house personnel, cavers, taxidermists.
- Subjects exposed enzootic areas: children, adults and travelers visiting these areas.

Post-exposure

- After confirmed or suspected exposure, vaccination must be started immediately at the risk of contamination with rabies. It must be performed in a rabies treatment centre. The treatment is adapted to the type of wound and the status of the animal.

POSOLOGY AND METHOD OF ADMINISTRATION

Posology

Once the vaccine is reconstituted with 0.5 mL of solvent, one intramuscular (IM) dose consists of 0.5 mL of reconstituted vaccine and one intradermal (ID) dose consists of 0.1 mL of reconstituted vaccine per injection site.

Pre-exposure prophylaxis

For pre-exposure immunization, individuals can be vaccinated according to the vaccination schedules presented in Table 1 and according to official local recommendations when available.

Table 1: Pre-exposure vaccination schedules

	D0	D7	D21 or D28
Conventional regimen IM route - 0.5 mL	1 dose	1 dose	1 dose

Booster injection 1 years later
Booster injections every 5 year

Post-exposure prophylaxis

Post-exposure prophylaxis includes local non-specific treatment of the wound, vaccination and, where appropriate, passive with rabies immunoglobulins.

Post-exposure prophylaxis should be initiated as soon as possible after suspected exposure to rabies. In all cases, proper wound care (careful washing of all bites and scratches with soap or detergent and copious amounts of water and/or virucidal agents) must be performed immediately or as soon as possible after exposure. It must be performed before administration of vaccine or rabies immunoglobulins, when they are indicated. Post-exposure prophylaxis should be adjusted to the exposure category, the condition of the animal (see Table 3) and the vaccination status of the patient, in accordance with official recommendations (see Table 2, WHO recommendations).

Post-exposure prophylaxis should be performed as soon as possible after exposure under medical supervision and only at rabies treatment center.

If necessary, post-exposure prophylaxis can be supplemented by tetanus prophylaxis and antibiotic therapy to prevent the development of infections other than rabies.

Table 2: WHO Guide for post-exposure prophylaxis depending on severity of exposure (to be adapted according to local official recommendations).

Exposure category	Type of exposure to a domestic or wild animal suspected or confirmed to be rabid or animal not available for testing	Recommended post-exposure prophylaxis
I	Touching or feeding of animals Licks on intact skin (no exposure)	None, if reliable case history is available[a]
II	Nibbling of uncovered skin Minor scratches or abrasions without bleeding (exposure)	Administer vaccine immediately. Discontinue treatment if the animal is in good health after the 10-day observation period[b] or if the rabies test performed using appropriate laboratory method is negative. Treat as category III if bat exposure involved.
III	Single or multiple transdermal bites [c] or scratches, licks on broken skin or contamination of mucous membranes with saliva (licks), exposure to bats (severe exposure).	Administer the vaccine immediately and rabies immunoglobulin, preferably as soon as possible after initiation of post-exposure prophylaxis. Rabies immunoglobulins can be injected up to 7 days after the first dose of vaccine is administered. Discontinue treatment if animal is in good health after the 10-day observation period[b] or if the rabies test performed using appropriate laboratory methods is negative.

(a) If the animal is an apparently healthy dog or cat living in a low-risk area and placed under veterinary observation, treatment may be postponed (see Table 3).

(b) This observation period applies only applies to cats and dogs. With the exception of endangered or threatened species, domestic animals and wild animals suspected to have rabies should be euthanised and their tissues examined using appropriate laboratory methods (see Table 3).

(c) Bites, particularly to the head, neck, face, hands and genitals are classified as Category III exposure due to the extensive innervation of these parts of the body.

Table 3: Course of action after exposure depending on the condition of the animal (WHO recommendations to be adapted according to local recommendations)

Circumstances	Course of action regarding		Comments
	The animal	The patient	

Animal unavailable **Suspect or non-suspect circumstances**		To be taken to a rabies centre for treatment.	Treatment [(b)] is always completed.
Dead animal **Suspect or non-suspect circumstances**	Send the brain to an approved laboratory for analysis.	To be taken to a rabies centre for treatment.	Treatment [(b)] is discontinued if the tests are negative or, otherwise, continued.
Live animal **Non-suspect circumstances**	Place under veterinary supervision [(a)].	Postpone rabies treatment.	Treatment [(b)] is continued according to the results of veterinary supervision of the animal.
Live animal **Suspect circumstances**	Place under veterinary supervision [(a)].	To be taken to a rabies centre for treatment.	Treatment [(b)] is discontinued if veterinary supervision invalidates initial doubts, or, otherwise, continued.

(a) In France, veterinary supervision includes 3 certificates, drawn up at D0, D7, and D14, declaring the absence of signs of rabies. According to WHO recommendations, the minimum observation period under veterinary supervision for dogs and cats is 10 days.
(b) Treatment is recommended depending on the seriousness of the wound: see Table 2.

Post-exposure prophylaxis of previously non-immunised subjects

Individuals not previously immunized can be vaccinated according to one of the vaccination schedules presented in Table 4:

Table 4: Post-exposure vaccination schedules in previously non-immunized subjects

	D0	D3	D7	D14	D21	D28
Essen	1	1	1	1		1
regimen IM route - 0.5 mL	dose	dose	dose	dose		dose
Zagreb regimen IM route - 0.5 mL	2 doses[a]		1 dose		1 dose	

Updated Thai Red Cross regimen ID route - 0.1 mL	2 doses[b]	2 doses[b]	2 doses[b]			2 doses[b]
One week, four-site regimen ID route - 0.1 mL	4 doses[c]	4 doses[c]	4 doses[c]			

a – one injection in each of the two deltoids (for adults and children) or anterolateral thigh sites (infants and toddlers)

b – to be injected in 2 distinct sites, if possible contra-laterally.

c – to be injected in 4 distinct sites

Immunogenicity and safety data in children < 2 years old are limited (see section on clinical studies).

Whatever the regimen used, vaccination must not be discontinued unless the contact animal is declared free from rabies after veterinary supervision (see Table 3).

Rabies immunoglobulins should be administered concomitantly with the vaccine, in case of category III exposure (WHO classification, see Table 2). If possible, the vaccine should be administered contralaterally to the immunoglobulin administration sites.

Refer to the Summary of Characteristics of the rabies immunoglobulins used.

In enzootic areas, the severity of certain exposures due to the severity of the lesions and/or location (proximity of the central nervous system), a late consultation or immune deficiency of the subject may justify, depending on the case, 2 injections on D0.

Post-exposure prophylaxis of previously immunized subjects

In accordance with official recommendations, this applies to subjects who have already received preexposure prophylaxis or post-exposure prophylaxis or who discontinued post-exposure prophylaxis after receiving at least two doses of vaccine prepared in cell culture.

These individuals should receive one dose of vaccine intramuscularly (vaccine dose 0.5 mL) or intradermally (vaccine dose 0.1 mL) on each of days 0 and 3.

Rabies immunoglobulin is not indicated for previously immunized individuals.

Paediatric population

Children should receive the same doses as adults.

Method of administration

Precautions to be taken before handling or administering the medicinal product.

The vaccine is administered via the intramuscular route, in the anterolateral region of the thigh muscle in infants and young children and in the deltoid muscle in older children and adults.

It can also be administered by intradermal (ID) route preferably on upper arm or forearm.

Do not inject in the buttocks region.

Do not inject via the intravascular route.

For instructions on reconstitution of the medicinal product before administration, see Special Precautions for Disposal and other Handling

CONTRAINDICATIONS

This medicinal product MUST NOT BE USED in the following cases:

Pre-exposure

- Severe febrile infection, acute disease, progressive chronic disease (it is preferable to postpone vaccination),
- Known hypersensitivity to any of the ingredients of the vaccine, to polymyxin B, to streptomycin, to neomycin or to any antibiotic of the same group, to a previous administration or to any vaccine containing the same components.

Post-exposure

Due to the fatal progression of declared rabies infection, there are no contraindications to curative vaccination.

Pregnancy: see PREGNANCY– BREASTFEEDING section.

SPECIAL WARNINGS AND PRECAUTIONS FOR USE

Special warnings

As with all vaccines, VERORAB may not protect 100% of people vaccinated.

Use with caution on subjects with a known allergy to neomycin polymyxin B, to streptomycin (present in trace form in the vaccine) or to any antibiotic of the same group.

Do not inject by the intravascular route: make sure that the needle does not enter a blood vessel.

Immunoglobulins and rabies vaccine must not be associated in the same syringe or injected at the same site.

A serological test (neutralizing antibody assay using the RFFIT (Rapid Fluorescent Focus Inhibition Test) test) must be conducted on persons subject to continuous exposure (every 6 months) and maybe conducted every 2 to 3 years after the booster dose after 1 and 5 years in persons subject to discontinuous exposure according to the assessed exposure risk.

For immuno deficient subjects, this test may be conducted 2 to 4 weeks following the vaccination. If the result of the test demonstrates an antibody titre < 0.5 I.U./mL, a booster injection or an additional injection, for immuno deficient subjects, is justified.

This vaccine must never be administered by the intravascular route.

As with all vaccines, VERORAB may not protect 100% of people vaccinated.

Precautions for use

- Inform your doctor in the event of known allergy to neomycin, polymyxin B, streptomycin, or to any antibiotic of the same group due to the use of these substances during production.
- Injection-schedule recommendations should be followed scrupulously.
- As with all injectable vaccines, VERORAB should be administered with caution in subjects with thrombocytopenia or coagulation disorders as intramuscular injection may induce bleeding in these subjects.
- The potential risk of apnoea and the need for respiratory monitoring for 48-72 h should be considered when administering the primary immunization series to very premature infants (born ≤ 28 weeks of gestation) and particularly for those with a previous history of respiratory immaturity. As the benefit of vaccination is high in this group of infants, - vaccination should not be withheld or delayed.
- Anxiety-related reactions, including vasovagal reactions (syncope), hyperventilation or stress-related reactions can occur following, or even before, any vaccination as a psychogenic response to the needle injection. This can be accompanied by several neurological signs such as transient visual disturbance and paraesthesia. It is important that procedures are in place toavoid injury from faints. If there is any doubt, do not hesitate to consult your doctor or your pharmacist. Keep out of the reach of children.

INTERACTION WITH OTHER MEDICINAL PRODUCTS AND OTHER FORMS OF INTERACTION

Corticosteroids and immunosuppressor treatments may interfere with antibody production and cause the vaccination to fail. Therefore, it is preferable to conduct a neutralizing antibody assay 2 to 4 weeks after the last injection of vaccine.

Rabies immunoglobulins and vaccine must never be combined in the same syringe or administered at the same site.

When possible, the vaccine should be administered contra-laterally to the immunoglobulins administration sites.

In order to avoid possible interactions between several medicinal products, any other ongoing treatment should be systematically reported to your doctor or to your pharmacist.

FERTILITY, PREGNANCY AND LACTATION

Pregnancy

The vaccine has not been the subject of animal teratogenicity studies.

In the absence of sufficient human data, it is recommended to postpone pre-exposure vaccination.

For the vaccination of subjects at a high risk of contamination, the benefit/risk ratio must be assessed before administering the injection

In post-exposure vaccination due to the severity of the disease, pregnancy is not a contraindication.

Lactation

As a general rule, during pregnancy and lactation, it is recommended to always ask your doctor or pharmacist for advice before using a medicinal product.

EFFECT ON ABILITY TO DRIVE AND USE MACHINES

Post-vaccination dizziness was frequently reported. It can temporarily affect the ability to drive or use machines.

UNDESIRABLE EFFECTS

Undesirable effects were reported during clinical studies and after commercial use.
Undesirable effects are ranked in terms of frequency:

- very common: ≥ 1/10
- common: ≥ 1/100 and < 1/10
- uncommon: ≥ 1/1 000 and < 1/100
- rare: ≥ 1/10 000 and < 1/1 000
- very rare: < 1/10 000 including isolated cases.

Experience from clinical trials

Blood and lymphatic system disorders

- Very common: adenopathy/lymphadenopathy.

Immune system disorders

- Common: cutaneous allergic reactions such as rash, pruritus, 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, shivering.

General disorders and administration site conditions

- Very common: Injection site pain (IM use), Injection site pain (ID use), Injection site erythema (ID use fever, malaise.
- Common: injection site erythema (IM use), injection site pruritus (IM use), injection site pruritus (ID use) , injection site swelling (IM use), injection site swelling (ID use), injection site haematoma (ID use), injection site induration (IM use), asthenia, influenza-like syndrome.

Experience after commercial use

In addition to the list above, the following undesirable effects were reported. Their exact incidence cannot be calculated as they were spontaneously reported. However, given the number of doses sold, the occurrence of these undesirable effects is very rare (<1/10 000).

Immune system disorders

Anaphylactic reactions, serum sickness-like reactions.

Nervous system disorders

Encephalopathy, convulsions.

Ear and labyrinth disorders
Sudden hearing loss.*
*Which may persist.

Respiratory, thoracic and mediastinal disorders
Apnoea in very premature infants (born ≤ 28 weeks of gestation) (see section "SPECIAL WARNINGS AND PRECAUTIONS)

Gastrointestinal disorders
Vomiting.

OVERDOSE

No cases of overdose were reported.

EXPIRY DATE

3 years

Do not use later than the date of expiry

After reconstitution, the vaccine must be administered immediately.

SPECIAL PRECAUTIONS FOR STORAGE

Keep between + 2°C and +8°C (in a refrigerator). Do not freeze. Store in the original outer package, protected from light.

SPECIAL PRECAUTIONS FOR DISPOSAL AND OTHER HANDLING

Handling instructions:

- Remove the cap of the vial of lyophilised powder.
- Screw the plunger rod into the syringe, if provided separately.
- Inject the solvent into the vial of lyophilised powder.
- Shake the vial gently until homogeneous suspension of the powder is obtained.
- The reconstituted vaccine should be limpid, homogeneous, and free from particles.
- Remove and discard the syringe that was used for vaccine reconstitution.
- Use a new syringe with a new needle to withdraw the reconstituted vaccine.
- Replace the needle used to withdraw the vaccine by a new needle for intramuscular or intradermal injection.
- The length of the needle used for vaccine administration should be adapted to the patient.

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

PACKAGES:

Box, 1 Vial, 1 syringe of diluent @ 0,5 mL NaCl 0,4%,

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Manufactured by: Sanofi Pasteur, Marcy L'Etoile - France

Released by: Sanofi Pasteur, Lyon - France

Registered by: PT Kalventis Sinergi Farma, Jakarta-Indonesia

Pada proses pembuatannya bersinggungan dengan bahan bersumber babi

HARUS DENGAN RESEP DOKTER

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