

VERORAB
POWDER AND SOLVENT FOR SUSPENSION FOR INJECTION
RABIES VACCINE, INACTIVATED

Read all of this leaflet carefully before you start using this medicine because it contains important information for you.

- Keep this leaflet. You may need to read it again.
- If you have any further questions, ask your doctor, pharmacist or nurse.
- This medicinal product was prescribed for you only. Do not pass it on to others.
- If you get any side effects, talk to your doctor, pharmacist or nurse. This includes any possible side effects not listed in this leaflet. See Section 4.

What is in this leaflet:

1. What VERORAB is and what it is used for
2. What you need to know before you use VERORAB
3. How to use VERORAB
4. Possible side effects
5. How to store VERORAB
6. Contents of the pack and other information

1. WHAT VERORAB IS AND WHAT IT IS USED FOR

Pharmacotherapeutic group: rabies vaccines - ATC code: J07BG01.

VERORAB is indicated for the prevention of rabies in children and adults. It can be used before or after exposure to the rabies virus, as a primary vaccination or as a booster dose.

Pre-exposure rabies prevention (pre-exposure vaccination)

Pre-exposure vaccination should be offered to subjects at high risk of contamination by the rabies virus. All those at permanent risk, such as the personnel of a diagnostic, research or production laboratories working with the rabies virus, should be vaccinated. Immunity should be maintained by booster doses (see “**3. HOW TO USE VERORAB**”).

Vaccination is also recommended for the following categories, given the frequency of exposure to risk:

- Veterinarians and veterinarians’ assistants, animal handlers (including those manipulating bats) and forest warden (gamekeepers), taxidermists.
- People in contact with potentially rabid animal species (such as dogs, cats, skunks, raccoons and bats)
- Adults and children living in or travelling to enzootic areas.

Post-exposure rabies prevention (post-exposure vaccination)

Vaccination should be initiated immediately at the slightest risk of rabies contamination.

It must imperatively be performed in a rabies centre under medical supervision.

Post-exposure treatment includes local non-specific treatment of the wound, vaccination and passive immunisation with rabies immunoglobulins. The treatment should be adapted to the nature of the contact or of the wound, the condition of the animal and the patient's rabies vaccination status (see "**3. HOW TO USE VERORAB**"). Local treatment of the wound must be performed in all cases.

2. WHAT YOU NEED TO KNOW BEFORE YOU USE VERORAB**Do not use VERORAB:****Pre-exposure vaccination:**

- If or your child you are allergic to the active substance or any of the other ingredients of this medicine, listed in Section 6. or
- If or your child you developed an allergic reaction during a previous injection of this medicine or of any vaccine with the same composition
- If you or your child are feverish or if you have an acute disease (in this case, it is preferable to postpone vaccination).

Post-exposure vaccination:

- Given the fatal outcome of the declared rabies infection, there are no contraindications to post-exposure vaccination.

Warnings and precautions:

- As with all vaccines, VERORAB may not protect 100% of people vaccinated.
- VERORAB must not be administered via the intravascular route; make sure the needle does not penetrate a blood vessel.
- Use with caution if you are allergic to polymyxin B, to streptomycin or to neomycin (present in trace amounts in the vaccine) or to any antibiotic of the same group.
- As with all injectable vaccines, appropriate medical treatment and supervision must be readily available in case of a rare anaphylactic reaction after vaccine administration.
- Serological tests (assay of neutralising antibodies using the RFFIT – Rapid Fluorescent Focus Inhibition Test – method) should be performed regularly, see Table 1.
- When the vaccine is administered to subjects with a known decreased immunity (immunodeficiency), due to a suppressive disease or to a concomitant immunosuppressive treatment, a serological test should be performed 2 to 4 weeks after vaccination, see "**3. How to use VERORAB**".
- VERORAB should be administered with caution to subjects with a decreased platelet level (thrombocytopenia) or clotting disorders, because of the risk of bleeding that may occur during intramuscular administration.

Talk to your doctor, pharmacist or nurse before using VERORAB.

Using Other Medicines

Corticosteroids and immunosuppressive treatments may interfere with the production of antibodies and lead to vaccination failure, see "Warnings and precautions".

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

VERORAB must not be mixed with other medicinal products or other vaccines.

Tell your doctor or pharmacist if you are taking or have recently taken any other medicines.

VERORAB with food and drink

Not applicable.

Pregnancy and breast-feeding:

Pregnancy

One animal toxicity study on reproduction and development, led with another inactivated rabies vaccine, produced in VERO cells, did not evidence any deleterious effects on female fertility and on pre- and post-natal development.

Clinical use of rabies vaccines (inactivated “WISTAR Rabies PM/WI38 1503-3M strain”) during a limited number of pregnancies did not show any malformative or foetotoxic effects to date. Given the seriousness of the disease, vaccination should be performed during pregnancy, in compliance with the usual vaccination schedule, in case of high risk of contamination.

Breast-feeding

This vaccine can be used during breast-feeding.

If you are pregnant or breast-feeding, think you may be pregnant or are planning to have a baby, ask your doctor or pharmacist for advice before taking this medicine.

Driving and using machines

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

3. HOW TO USE VERORAB

Always use this medicine exactly as your doctor or pharmacist has told you. Check with your doctor or pharmacist if you are not sure.

One dose consists in the administration of 0.5 mL of vaccine via the intramuscular route.

Pre-exposure vaccination

Three doses of 0.5 mL of VERORAB are administered at D0, D7, and D28 for primary vaccination. The dose scheduled at D28 can be administered at D21.

Booster doses and regular serological tests, to assess the subjects’ seroconversion status, are recommended. The frequency of booster doses and serological tests is indicated in Table 1.

Each booster dose consists in the administration of one dose of 0.5 mL.

Table 1: Recommendations for pre-exposure treatment, depending on the nature of the risk

RISK	NATURE OF RISK	TYPICAL POPULATION	PRE-EXPOSURE TREATMENT
CONTINUOUS	Virus present continuously, in high concentrations. Contamination by: aerosols, contact with mucous membrane, bites or scratches. Sources of exposure may be unknown.	Rabies research or production laboratory workers.	Primary vaccination. Serological tests every 6 months. Booster vaccinations when antibody levels are below the protective threshold*.

FREQUENT	Exposure usually episodic. Contamination by: aerosols, contact with mucous membrane, bites or scratches. Sources of exposure may be unknown.	Rabies diagnostic laboratory workers. Veterinarians, cavers, animal handlers and forest warden working in enzootic areas.	Primary vaccination. Booster vaccination after 1 year. Serological tests every 2 years. Subsequent booster vaccinations when antibody levels are below the protective threshold*.
INFREQUENT	Exposure often episodic. Contamination by: contact with mucous membrane, bites or scratches.	Veterinarians, animal handlers and forest warden working in areas of low enzooty. Travellers visiting enzootic areas. Veterinary students.	Primary vaccination. Booster vaccination after 1 year. Subsequent booster vaccinations every 5 years.

* When the level of neutralising antibodies is strictly below the protective threshold (0.5 IU/mL using the RFFIT - Rapid Fluorescent Focus Inhibition Test - method), a booster dose is necessary.

For immunodeficient subjects, a serological test should be performed 2 to 4 weeks after vaccination see "**3. HOW TO USE VERORAB**". If the test result shows antibody titers strictly below 0.5 IU/mL, an additional injection is justified.

Post-exposure vaccination

Post-exposure treatment includes local non-specific treatment of the wound, vaccination and passive immunisation with rabies immunoglobulins. The treatment should be adapted to the nature of the contact or of the wound (see Table 2), the condition of the animal (see Table 3) and the patient's rabies vaccination status.

First Aid: local treatment of the wound

Local treatment of all bites and scratches is very important and must be performed immediately.

First aid recommendations include immediate flushing out of the wound for at least 15 minutes with water and soap, detergent, povidone iodine or any other substance with a proven destructive action on the rabies virus.

If necessary, the treatment can be supplemented by the administration of a prophylactic tetanus treatment and an antibiotherapy in order to prevent the development of infections other than rabies.

Vaccination

Post-exposure vaccination must be performed under medical supervision, only in a rabies centre and as soon as possible following exposure.

Table 2: WHO guidelines on post-exposure treatment depending on the nature of contact and the seriousness of the wound

SERIOUSNESS	TYPE OF CONTACT	TYPE OF EXPOSURE	TREATMENT RECOMMENDED
I		None	

	Touching or feeding of animals Licks on intact skin		None if reliable case history is available
II	Nibbling of uncovered skin Minor scratches or abrasions without bleeding	Minor	Administer vaccine immediately
III	Single or multiple transdermal bites or scratches Licks on broken skin Contamination of mucous membrane with saliva (i.e. licks) Exposure to bats	Severe	Administer rabies immunoglobulin and vaccine immediately

Table 3: Course of action depending on the condition of the animal

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.

Vaccination of non-immunised subjects (subjects who did not receive pre-exposure vaccination)

Five doses of 0.5 mL of VERORAB are administered at D0, D3, D7, D14 and D28.

Vaccination must not be discontinued unless made possible by the animal's health status (see Table 3).

Rabies immunoglobulins should be administered at D0 concomitantly with the vaccine, in case of category III exposure (WHO classification, see Table 2). The rabies immunoglobulins posology is as follows:

- Human rabies immunoglobulins.....20 IU/kg of body weight,
- Equine rabies immunoglobulins 40 IU/kg of body weight

For more information, please see the package leaflet of the rabies immunoglobulins used.

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

For immunodeficient subjects, in the case of Category II exposure (WHO Classification, see Table 2), rabies immunoglobulins should also be administered concomitantly with the vaccine.

Vaccination of subjects already immunized (full pre-exposure vaccination confirmed)

If pre-exposure vaccination was performed less than 5 years before (cell culture rabies vaccine): two booster doses are administered at D0 and D3. Rabies immunoglobulins are not necessary.

This does not apply to immunodeficient subjects.

If pre-exposure vaccination was performed more than 5 years before, if it is incomplete or in case of doubt, the subject's vaccination status is not considered as complete and a full post-exposure treatment should be started (see Vaccination of non-immunised subjects).

If the patient is immunodeficient, a full post-exposure treatment should also be started (see Vaccination of non-immunised subjects).

Use in children

VERORAB can be administered to children and to adults using the same posology.

Method of Administration:

The vaccine is administered by the intramuscular route, generally in the anterolateral region of the thigh muscle until the age of 12 months and in the deltoid muscle after this age.

The intradermal (ID) injection may be used as an alternative, on upper or forearm (1) and approved by national health authorities in some countries such as Thailand. Please refer to the ID Route section at the end of the leaflet.

VERORAB must not be injected in the buttocks region.

The vaccine must not be injected via the intravascular route.

If you have any further questions on the use of this medicine, ask your doctor or pharmacist or nurse.

4. POSSIBLE SIDE EFFECTS OF VERORAB

Like all medicines, this medicine can cause side effects, although not everybody gets them.

- Increase in size of lymph nodes (adenopathy, lymphadenopathy).
- Allergic skin reaction as skin rash with itching (urticarial, pruritus), swelling (oedema). Allergic reaction with respiratory disorders (dyspnea, angioedema). Anaphylactic reaction, serum sickness-like reaction.
- Headache (cephalalgia), dizziness, somnolence.
- Abdominal pain, nausea, diarrhoea, vomiting.
- Muscular pain (myalgia), joint pain (arthralgia).
- At the injection site: pain, erythema (redness) and induration, haematoma, swelling (oedema) and itching (pruritus).
- Fever (hyperthermia), shivering, malaise, influenza-like syndrome.
- Convulsions, encephalopathy.
 - Sudden hearing decrease or loss.
- Fatigue (asthenia).
- In infants born very prematurely (at or before 28 weeks of gestation), respiratory pauses may occur during 2 to 3 days after vaccination.

Reporting of side effects

If you get any side effects, talk to your doctor, pharmacist or nurse. This includes any possible side effects not listed in this leaflet. By reporting side effects you can help provide more information on the safety of this medicine.

5. HOW TO STORE VERORAB

Keep this medicine out of the sight and reach of children.

Do not use this medicine after the expiry date which is stated on the box after EXP. The expiry date refers to the last day of that month.

Store in the refrigerator (+2°C - +8°C). Do not freeze.

Store in the original outer package, protected from light.

After reconstitution, the vaccine must be used immediately.

Do not throw away any medicines via wastewater or household waste. Ask your pharmacist how to throw away medicines you no longer use. These measures will help to protect the environment.

6. Contents of the pack and other information**What VERORAB contains?**

The active substance is:

After reconstitution, 1 dose (0.5 mL) contains:

Rabies virus*, WISTAR Rabies PM/WI38 1503-3M strain (inactivated).....≥ 2.5 IU**

* Produced in VERO cells

** Quantity measured according to the NIH test against the international standard

The other ingredients are:

Powder*: maltose, 20% human albumin solution, Basal Medium Eagle (mixture of mineral salts, vitamins, dextrose and amino-acids including L-Phenylalanine), water for injections.

* Composition of the powder before the freeze-drying step.

Solvent: sodium chloride, water for injections

What VERORAB looks like and contents of the pack ?

VERORAB is a powder and a solvent for suspension for injection (1 dose of powder in vial (≥ 2.5 IU) and 0.5 mL of solvent in prefilled syringe – Box of 1 or 10).

Marketing Authorization Holder :

SANOFI PASTEUR LTD. – Bangkok, Thailand

This leaflet was last revised in 07/2018

The following information is intended for healthcare professionals only:

Injection-schedule recommendations should be followed scrupulously.

To reconstitute the vaccine:

- Take the cap off the vial of powder.
- Inject the content of the prefilled syringe into the vial of powder.

- Shake gently in order to obtain a homogeneous vaccine suspension. The reconstituted vaccine appears as a limpid homogenous liquid.
 - Withdraw 0.5 ml of suspension and inject immediately.
- Any unused medicinal product or waste material should be disposed of in accordance with local requirements.

This medicine product is subject to medical prescription (List I).

INTRADERMAL (ID) ROUTE SECTION: Additional information
Please read this entire section carefully

ID Route can be used as an alternative. (Please refer to your local registration and recommendations). This section provides with additional information specifically related to the use of VERORAB via Intradermal route. All the other information remains valid.

BEFORE YOU USE VERORAB – Intradermal route

Do not use VERORAB – Intradermal route (*Pre-Exposure and Post-exposure vaccination*):

The Intradermal route must not be used in the following instances:

- individuals receiving long term corticosteroid or other immunosuppressive therapy or anti-malarial chemoprophylaxis
- immunocompromised individuals,
- individuals, particularly children, with severe wounds, especially to the head and neck or presenting late for consultation.

Pre-Exposure Vaccination via intradermal route:

Primary-vaccination:

As according to WHO, VERORAB may be given intradermally (0.1 ml dose on day 0, D7 and D21 or D28). However, intramuscular injections are preferable if antimalarial chemoprophylaxis (e.g. chloroquine) is being used concurrently or there is a possibility of an immune-compromised state (antibody response may be impaired if the intradermal method is used) (1).

Post-exposure vaccination via intradermal route:

Intradermal schedule (2)(3) :

This vaccine is of sufficient potency to allow its safe use in the WHO recommended intradermal post-exposure regimen in countries where relevant national authorities have approved the intradermal route for rabies post-exposure treatment (1).

If VERORAB is administered by the intradermal route, the following instructions and warnings must be strictly adhered to.

Dosage and administration for intradermal route:

One intradermal dose comprises 0.1 ml of reconstituted vaccine, i.e. 1/5 of the intramuscular dose. For Verorab, the administration schedule recommended by WHO is:

Non-immunized individuals:

The 2-site Intradermal regimen

- 222011 known as original Thai Red Cross Regimen prescribes 1 injection of 0.1 ml at different sites on D0,D3,D7 and 1 injection at one site on D28 (or D30) and D90
- 22202 known as updated Thai Red Cross regimen prescribes 1 injection of 0.1 mL at 2 sites on D 0, D3, D7, and D28.

Fully immunized individuals:

2 injections on D0, D3. This schedule should not apply to immunocompromised patients.

SPECIAL PRECAUTIONS FOR THE INTRADERMAL ROUTE:

It is essential that intradermal administration of VERORAB be carried out only by medical staff trained in this technique in order to ensure that the vaccine is delivered intradermally and not subcutaneously. For the intradermal route a sterile syringe with fixed needle (insulin type) is preferred. Correct intradermal injection should result in a raised papule with an "orange peel" (peau d'orange) appearance.

If the vaccine is injected too deeply into the skin, and a papule is not seen, the needle should be withdrawn and reinserted nearby. If there is a complete failure to inject intradermally at more than half of the multiple injection sites, an extra intradermal dose should be given in the opposite site. (4)

SPECIAL STORAGE CONDITIONS FOR INTRADERMAL ROUTE

VERORAB does not contain a preservative; therefore, great care must be taken to avoid contamination of reconstituted vaccine. Vaccine may be used up to 8 hours after reconstitution provided it is maintained at +2°C to +8°C. Unused vaccine must be discarded after 8 hours (5). Using aseptic technique, a dose of vaccine may be withdrawn from a vial and the remainder used for another patient provided that the vial is stored in a refrigerator between + 2°C and + 8°C. A new sterile needle and syringe must be used to withdraw and administer each dose of vaccine for each patient to avoid cross infection.

- (1) WHO Current guide for rabies pre and post-exposure treatment in humans- November 2002
- (2) WHO position paper. Rabies vaccines. WER 49-50, 2007, 82, 425-436.
- (3) Report of a W.H.O. consultation on Intradermal Application of Human Rabies Vaccines, Geneva 13-14 March 1995. Published in: Weekly Epidemiological Records (1995), 47, 336-337.
- (4) WHO recommendations on Rabies Post Exposure Treatment and the correct Technique of Intradermal Immunization against Rabies. Page 18
- (5) WHO TRS 931 WHO expert consultation on rabies , 1st report (2005) (Annex 1: Guide for Post Exposure Prophylaxis)

CCDS v.6 (25 July 2016)