VERORAB, powder and solvent for suspension for injection

Clean WHO Package Insert (English)

VERORAB

Powder and solvent for suspension for injection

Rabies vaccine, inactivated

Read all of this leaflet carefully before you or your child are vaccinated 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 has been prescribed for you only or has been prescribed to your child. Do not pass it on to others.
- If you or your child 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

Pharmacotherapeutic group: rabies vaccines, ATC code: J07BG01.

VERORAB is indicated for pre-exposure and post-exposure rabies prophylaxis in all age groups.
VERORAB should be used in accordance with official recommendations.

Pre-exposure prophylaxis should be offered to subjects at high risk of contamination by the rabies virus.

All those at permanent risk, such as the personnel of diagnostic, research or production laboratories working with the rabies virus, should be vaccinated.

Vaccination is also recommended for the following categories:
- chiropterologists and people regularly exposed to the bat rabies virus.
- exposed professionals (veterinary personnel, laboratory personnel handling equipment that is contaminated or likely to be contaminated, slaughterhouse butchers, pound personnel, naturalists, taxidermists, gamekeepers, forest rangers, slaughterhouse personnel).
- adults and children living in or travelling to enzootic areas.

2. What you need to know before you use VERORAB

Do not use VERORAB:

<u>Pre-exposure prophylaxis</u>:

- If you or your child are allergic to the active substance or any of the other ingredients of this medicine, listed in section 6.
- If you or your child 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).

<u>Post-exposure prophylaxis</u>:

- 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 or your child are allergic to polymyxin B, to streptomycin or to neomycin (present in trace amounts in the vaccine) or to any antibiotic of the same class.

- As with all injectable vaccines, appropriate medical treatment and supervision must be readily available in case of a rare anaphylactic reaction after vaccine administration.
- The need for serological tests (to assess seroconversion in the subjects) should be determined in accordance with official recommendations.
- When the vaccine is administered in subjects with a known reduction in immunity (immunodeficiency), due to an immunosuppressive disease or a concomitant immunosuppressive treatment, blood tests must be performed 2 to 4 weeks after vaccination to ensure that a protective immunising response was obtained. In case of post-exposure vaccination, a complete vaccination regimen must be administered. Rabies immunoglobulins should also be administered in association with the vaccine in the event of any category II or III exposure, 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.

Other medicines and VERORAB

Immunosuppressive treatments, including long-term systemic corticosteroid therapy, may interfere with the production of antibodies and lead to vaccination failure. It is therefore recommended to get a serological test 2 to 4 weeks after vaccination; see "**Warnings and precautions**".

VERORAB can be administered in association with a Vi polysaccharide typhoid vaccine during the same vaccination visit using two different injection sites.

Rabies immunoglobulins or any other product and the rabies vaccine must never be combined in the same syringe or injected into the same site.

Given that rabies immunoglobulins interfere with the development of the immune response to the rabies vaccine, the recommendations for administration of rabies immunoglobulins should be strictly followed.

Tell your doctor or pharmacist if you or your child are taking, has recently taken or might take any other medicines.

Pregnancy, breast-feeding and fertility

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 fetotoxic effects to date.

Pre-exposure prophylaxis

Given the seriousness of the disease, in case of high risk of contamination, vaccination should be performed during pregnancy, in compliance with the usual vaccination schedule.

Post-exposure prophylaxis

Given the seriousness of the disease, pregnancy is not a contraindication

Breast-feeding

This vaccine can be used during breast-feeding.

Fertility

VERORAB has not been evaluated in fertility studies.

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 using this medicine.

Driving and using machines

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

VERORAB contains phenylalanine, potassium and sodium

VERORAB contains 4.1 micrograms phenylalanine in each 0.5 mL dose, which is equivalent to 0.068 microgram/kg for a 60 kg person. Phenylalanine may be harmful if you have phenylketonuria

(PKU), a rare genetic disorder in which phenylalanine builds up because the body cannot remove it properly.

VERORAB contains less than 1 mmol of potassium (39 mg) and less than 1 mmol of sodium (23 mg) per dose, that is to say essentially 'potassium-free' and 'sodium-free'.

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.

Intramuscular use (IM): the recommended dose is 0.5 mL of reconstituted vaccine.

Intradermal use (ID): the recommended dose is 0.1 mL of reconstituted vaccine per injection site.

Pre-exposure prophylaxis:

For pre-exposure immunisation, immunocompetent individuals can be vaccinated according to one of the vaccination schedules presented in table 1 and according to official recommendations.

Table 1: Pre-exposure vaccination schedules

	D0	D7	D21 or D28
Intramuscular use (0.5 mL per dose)			
Conventional regimen IM use – 0.5 mL	1 dose	1 dose	1 dose
1-week regimen [(a)] IM use – 0.5 mL	1 dose	1 dose	
Intradermal use (0.1 mL per dose)			
1-week regimen [(a)] ID use - 0.1 mL	2 doses [(b)]	2 doses [(b)]	

[(a)] This regimen should not be used for immunocompromised individuals (see sub-section "Immunocompromised individuals").

[(b)] one injection in each anterolateral thigh (infants and toddlers) or in each arm (children and adults).

Booster doses are determined based on the risk of exposure and on serological tests in accordance with official recommendations.

Post-exposure prophylaxis:

Post-exposure prophylaxis includes local non-specific treatment of the wound, vaccination and, where appropriate, passive immunisation 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 rabies vaccine or rabies immunoglobulin, where 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 3, WHO recommendations).

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

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

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

Exposure category	Type of exposure to a domestic or wild animal, suspected or confirmed to be rabid or not available for testing	Post-exposure prophylaxis recommended
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 methods 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 membrane with saliva (licks), exposure to bats (severe exposure).	Administer rabies 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 the 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 delayed (see Table 3).
[(b)] This observation period 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 in non-immunised subjects

Non-immunised subjects may be vaccinated according to one of the vaccination regimens by intramuscular use (IM) or by intradermal use (ID) presented in table 4.

In all cases, refer to the local official recommendations.

Table 4: Post-exposure prophylaxis of non-immunised subjects

	D0	D3	D7	D14	D21	D28
Intramuscular use (0.5 mL per dose)						
IM Essen protocol IM use - 0.5 mL/dose	1 dose	1 dose	1 dose	1 dose		1 dose
IM Zagreb protocol IM use - 0.5 mL/dose	2 doses[(a)]	-	1 dose	-	1 dose	-
Intradermal use (0.1 mL per dose)						
New Thailand Red Cross (TRC) ID regimen ID use - 0.1 mL/dose	2 doses[(b)]	2 doses[(b)]	2 doses[(b)]	-	-	2 doses[(b)]
Institute Pasteur of Cambodia (IPC) ID regimen ID use - 0.1 mL/dose	2 doses[(b)]	2 doses[(b)]	2 doses[(b)]	-	-	-
4-site 1-week ID regimen ID use - 0.1 mL/dose	4 doses[(c)]	4 doses[(c)]	4 doses[(c)]	-	-	-

[(a)] one IM injection in the anterolateral region of each thigh (in infants and young children) or in each deltoid (in older children and adults).

[(b)] to be injected in 2 separate sites, contralateral if possible.

[(c)] to be injected in 4 separate sites

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 in the event of any category III exposure (WHO classification, see Table 2). If possible, the vaccine should be administered contralaterally to the immunoglobulin administration sites.

Refer to the package leaflet of the rabies immunoglobulins used.

Post-exposure prophylaxis in already immunised subjects

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

Subjects who have already been immunised must receive 1 dose of vaccine (0.5 mL intramuscularly or 0.1 mL intradermally) on D0 and 1 dose on D3.

Alternatively, 4 intradermal injections of 0.1 mL may be administered in 4 separate sites on D0.

Rabies immunoglobulins are not indicated in this case.

Individuals with decreased immunity

Pre-exposure prophylaxis

In individuals with decreased immunity, conventional three-dose regimens should be used (see table 1) and a serological test for neutralising antibodies should be performed 2 to 4 weeks after the last dose of the vaccine to assess the need for a possible additional dose of vaccine.

Post-exposure prophylaxis

In individuals with decreased immunity, a complete vaccination regimen should be administered (see table 4). Rabies immunoglobulins should be administered in association with the vaccine in the event of any category II and III exposure (see Table 1).

Use in children

A child must receive the same dose as an adult (0.5 mL intramuscularly or 0.1 mL intradermally).

Method of administration

- Intramuscular use (IM)
  The vaccine is administered in the anterolateral region of the thigh muscle in infants and young children and in the deltoid muscle in older children and adults.

If the Zagreb regimen is used, one dose should be administered in each deltoid muscle (left and right) in adults at D0, then one dose at D7 and D21.

- Intradermal use (ID)
  The vaccine should ideally be administered in the upper arm or the forearm.

The vaccine 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

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

Serious allergic reactions:

Serious allergic reactions (anaphylactic reactions) can always happen, even if it is very rare. Contact your doctor or health care professional immediately or go to the nearest hospital emergency department immediately if you or your child experience an anaphylactic reaction.

Signs or symptoms of an anaphylactic reaction usually occur very soon after the injection if at all, and may include rash, itching, difficulty breathing, shortness of breath and swelling of the face, lips, throat or tongue.

Other side effects

Most side effects occur within 3 days of vaccination. The effects most often resolve spontaneously within 1 to 3 days of onset. They have been reported with the following frequencies:

Very common: may affect more than 1 in 10 people
- Generally feeling unwell,
- Headache (cephalalgia),
- Muscle pain (myalgia),
- Pain at the injection site,
- Redness (erythema) at the injection site,
- Swelling at the injection site,
- Only in babies: irritability, inconsolable crying and drowsiness.

Common: may affect up to 1 in 10 people
- Fever,
- Increase in size of lymph nodes (lymphadenopathy),
- Allergic reactions, such as rash and itching,
- Flu-like syndrome,
- Itching (pruritus) at the injection site,
- Induration at the injection site,
- Only in babies: difficulty sleeping.

Uncommon: may affect up to 1 in 100 people
- Decreased appetite,
- Nausea,
- Stomach pain (abdominal pain),
- Diarrhoea,
- Vomiting,
- Chills,
- Fatigue, unusual weakness (asthenia),
- Dizziness,
- Joint pain (arthralgia),
- Bruising at the injection site (ecchymosis).

Rare: may affect up to 1 in 1000 people

- Difficulty breathing.

Not known: cannot be estimated from the available data
- Swelling of the face, lips, mouth, tongue or throat, which may cause difficulty swallowing or breathing,
- Sudden hearing loss/decrease.

Reporting of side effects

If you or your child 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 a refrigerator (2°C – 8°C). Do not freeze.

Store in the original outer package, protected from light.

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 protect the environment.

6. Contents of the pack and other information

What VERORAB contains

- The active substance is:

After reconstitution with 0.5 mL solvent, 1 vial contains:

Rabies virus[a], WISTAR Rabies PM/WI38 1503-3M strain (inactivated) .....3.25 IU[b]

[a] Produced in VERO cells

[b] Quantity measured according to the ELISA test against the international standard

- The other ingredients are:

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.

Solvent: sodium chloride, water for injections.

May contain traces of polymyxin B, streptomycin and neomycin, used in the manufacturing process; see “Warnings and precautions”.

What VERORAB looks like and contents of the pack

VERORAB is a powder and a solvent for suspension for injection (powder in vial + 0.5 mL of solvent).

Marketing Authorisation Holder

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The following information is intended for healthcare professionals only:

Injection-schedule recommendations should be followed scrupulously.

Handling instructions:
- Remove the cap of the vial of lyophilised powder.
- Screw the plunger rod into the syringe.

- 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 with a new needle for intramuscular or intradermal injection.
- The length of the needle used for vaccine administration should be adapted to the patient.

If VERORAB is administered intramuscularly, the vaccine must be used immediately after reconstitution.

If VERORAB is administered intradermally, the vaccine may be used up to 6 hours after reconstitution on the condition that is stored at a temperature below 25°C and protected from light. After reconstitution with 0.5 mL of solvent, using aseptic techniques, a 0.1 mL vaccine dose must be taken from the vial. The rest may be used for another patient. Before each withdrawal, shake the vial gently to obtain a homogenous suspension. A new sterile needle and a new sterile syringe must be used to withdraw and administer each vaccine dose to each patient to avoid cross-infection. The unused reconstituted vaccine must be thrown away after 6 hours.

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