VERORAB

VERINC16, VERINC18
VERINC19, 2013.8.5

RABIES VACCINE FOR HUMAN USE, PREPARED ON CELL CULTURES (INACTIVATED)

Please read this entire package leaflet carefully before getting vaccinated.
Keep this package leaflet until you have completed your vaccination schedule. You may need to read it again.
You should follow your doctor's or nurse's recommendations carefully. If you need more information or advice, ask your doctor or nurse.
Ensure that you have completed the entire vaccination schedule. Otherwise, you may not be fully protected.
This vaccine was prescribed for you. Do not pass it on to others.

– The active substance is rabies virus*, Wistar Rabies PM/WI38 1503-3M strain (inactivated) (≥2.5 IU**/0.5 ml)
* produced on VERO cells
** quantity measured according to the international standard and the NIH test
– The other components are:
Powder: maltose and human albumin.
Solvent: sodium chloride and water for injections

Holder/Distributor/Manufacturer:
SANOFI PASTEUR SA - 2, avenue Pont Pasteur - 69007 Lyon, France

1. WHAT VERORAB IS AND WHAT IT IS USED FOR

VERORAB comes in the form of a powder and solvent for suspension for injection (1 dose of powder in a vial and 0.5 ml of solvent in a prefilled syringe. Box of 1).
It is indicated for the prevention of rabies in children and adults. It can be used before or after exposure, as a primary vaccination or as a booster dose.

Pre-Exposure Prevention of Rabies (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 laboratory working with the rabies virus, should be vaccinated. A serological test is recommended every 6 months (see "Take Special Care with VERORAB").
Pre-exposure vaccination should also be considered for subjects at frequent risk of exposure to the rabies virus, such as:
– Veterinarians and their assistants, animal handlers.
– Those who, either by profession or leisure activity, are in contact with species such as dogs, cats, skunks, raccoons, bats or other species likely to have rabies. Examples of such people are gamekeepers, hunters, forestry workers, speleologists and taxidermists.
– Adults and children living or travelling in enzootic areas.
In areas where the enzootic level of rabies is low, veterinarians and assistants (including students), animal handlers and wildlife officers (gamekeepers) are considered to be at occasional risk of exposure and should receive a primary vaccination against rabies.
Serological tests for rabies antibodies should be performed at regular intervals in accordance with the subject's risk exposure.
Systematic booster injections should be administered in accordance with the subject's risk exposure.

Post-Exposure Prevention of Rabies (Post-Exposure Vaccination):
At the slightest risk of contamination, post-exposure vaccination should be performed as soon as possible.
In some countries, vaccination must be performed in a specialized rabies treatment centre.
Post-exposure treatment includes local, non-specific treatment of the injury, passive immunisation with rabies immunoglobulins (RIGs) and vaccination, depending on the type of injury and the status of the animal (see Tables 1 and 2).
Table 1: Course of Action Depending on the Status 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 treatment 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 treatment centre for treatment	Treatment[b] is discontinued if the analyses are negative or, otherwise, continued
Live animal **Non-suspect circumstances**	Place under veterinary supervision[a]	Decision to delay rabies treatment	Treatment[b] is adapted according to the results of veterinary supervision of the animal
Suspect circumstances	Place under veterinary supervision[a]	To be taken to a rabies treatment centre for treatment	Treatment[b] is discontinued if veterinary supervision invalidates the initial doubts, or, otherwise, continued

[a] In France, veterinary supervision includes 3 certificates drawn up on 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 severity of the wound: see Table below.

Table 2: WHO Guidelines on Post-Exposure Treatment Depending on Wound Severity

Category of severity	Type of contact with a wild[a] or domestic animal presumed or confirmed rabid or an animal that cannot be placed under supervision	Recommended treatment
I	Touching or feeding of animals Licks on intact skin	None, if a reliable case history can be obtained
II	Nibbling of uncovered skin Minor scratches or abrasions without bleeding Licks on broken skin	Administer vaccine immediately[b]
III	Single or multiple transdermal bites or scratches Contamination of mucous membrane with saliva (i.e., licks)	Administer rabies immunoglobulins and vaccine immediately[b]

[a] Contact with rodents, rabbits, or hares does not normally necessitate specific rabies treatment.
[b] Discontinue treatment if the animal is in good health after 10 days of observation (for cats and dogs) or if after the animal has been euthanized, the results of the search for rabies by the appropriate laboratory techniques are negative.

2. BEFORE YOU USE VERORAB

Do not use VERORAB:
Pre-Exposure
If you have a fever or an acute illness: vaccination should be postponed.
If you are allergic to the active substance, to one of the excipients, to polymyxine B, to streptomycin or to neomycin.
Post-Exposure
Because rabies is always fatal, there is no contraindication to post-exposure vaccination.

Take Special Care with VERORAB:
As is the case with all injectable vaccines, it is recommended to have appropriate medical treatment readily available in case of anaphylactic reaction immediately after vaccination, particularly a post-exposure vaccination in subjects with a known hypersensitivity to polymyxine B, to streptomycin, or to neomycin.
Do not inject into the gluteal area, because weaker levels of neutralising antibodies have been observed when this area is used.
Regular serological tests are necessary. These serological tests are performed by verifying the complete neutralisation of a reference virus, by the RFFIT method (Rapid Fluorescent Focus Inhibition Test). This test should be done every 6 months in people at permanent risk of exposure, and every 2 to 3 years after each booster injection in subjects at discontinuous risk of exposure. If the antibody level is under that considered to be protective, i.e. 0.5 IU/ml (RFFIT), a booster injection should be administered.

When the vaccine is administered to subjects with a known immunodeficiency due to an immunosuppressive illness or a concomitant immunosuppressive treatment (such as corticosteroids), a serological test of their antibody level should be done 2 to 4 weeks after vaccination. If the antibody level is lower than that considered to be protective, i.e., 0.5 IU/ml (RFFIT), an additional injection should be administered.

Pregnancy and Breast Feeding:

Because of the severity of the disease, the vaccination schedule must not be modified as a result of pregnancy. If you discover that you are pregnant during a vaccination series, quickly consult your doctor: only your doctor can adapt the vaccination program to your situation.

This vaccine may be used during breast feeding.

Ask your doctor or pharmacist for advice before taking any medicine.

Driving and Using Machines:

Post-vaccination dizziness has been frequently reported. This can temporarily affect ability to drive and use machines.

Intake or Use of Other Medicines:

Please tell your doctor or pharmacist if you are taking or have recently taken any other medicines, including medicines obtained without a prescription.

Corticosteroids and other immunosuppressive treatments can interfere with the production of antibodies and lead to the failure of the vaccination (see "Take Special Care with VERORAB").

Immunoglobulins must be administered at a different site from that of the vaccine (the contralateral side).

3. HOW TO USE VERORAB

Before reconstitution, the powder has a uniform white colour.

To reconstitute the vaccine:

– Take the cap off the vaccine vial.

– Inject the solvent from the prefilled syringe into the vial of powder.

– Shake gently to obtain a homogeneous suspension of the vaccine. The reconstituted vaccine appears as a limpid liquid.

– Immediately withdraw 0.5 ml of suspension.

– Inject.

Do not inject by the intravascular route. Ensure that the needle does not penetrate a blood vessel before vaccine injection.

Do not administer by the subcutaneous route.

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

Any unused product or waste should be disposed of in accordance with the regulations in effect.

The vaccination schedule should be adapted in accordance with the circumstances of the vaccination and the subject's rabies immune status.

Pre-Exposure Vaccination:

Three doses of VERORAB (0.5 ml) should be administered on D0, D7, and D28 or D21.

Booster Injection after Pre-Exposure Vaccination:

A booster injection of VERORAB (0.5 ml) will be administered one year after primary vaccination, followed by a booster injection every five years:

Table 3: Recommendations for Primary Vaccination and Booster Injections

Primary vaccination	3 injections	D0, D7 and D28*
1st booster injection	1 year later	
Subsequent booster injections	Every five years	

* The D28 injection can be administered on D21.

VERORAB can be administered as a booster injection after primary vaccination with a rabies vaccine prepared on diploid or Vero cells.

Post-Exposure Vaccination:

First Aid: Local Treatment of the Wound

All bites and scratches should be immediately flushed out and washed with soap or detergent. Doing so can enable efficient elimination of the rabies virus at the infection site.

A 70 % alcohol solution, a tincture (or solution) of iodine, or a 0.1 % quaternary ammonium solution can then be applied (provided that there are no remaining traces of soap, because these products neutralize each other).

Depending on the severity of the injuries, rabies immunoglobulins (RIGs) may need to be administered in association with the vaccine. In this case, refer to the Instructions for Use in the RIG package leaflet.

If necessary, treatment can be supplemented by the administration of a tetanus prophylactic and/or a course of antibiotics.

Fully Immunised Subjects

Two booster doses of VERORAB (0.5 ml) should be administered on D0 and D3.

Administration of rabies immunoglobulins (RIGs) is not necessary and should not be done in this case, since booster injection is always followed by an anamnestic response.

Previously immunised subjects should be able to document the following:

– Full pre- or post-exposure rabies vaccination, by a cell culture vaccine or

– A documented rabies antibody titre ≥0.5 IU/ml

In case of doubt, if the booster injection was administered more than 5 years ago, or in the case of incomplete vaccination, the patient should not be considered to be completely immunised, and complete post-exposure treatment should be initiated.

Table 4: Recommendations for Post-Exposure Rabies Vaccination Depending on Previous Vaccinations

Vaccination within the last 5 years (with a cell culture rabies vaccine)	2 injections: D0 and D3
Vaccination more than 5 years ago or incomplete vaccination	5 injections: on D0, D3, D7, D14 and D28, with RIG administration if necessary

Non-immunised Subjects

Five doses of VERORAB (0.5 ml) should be administered, on D0, D3, D7, D14 and D28.

Rabies immunoglobulins (RIGs) should be administered at the same time as the first injection in the case of a severe injury (category III according to the WHO rabies risk classification). Equine and human immunoglobulins can be used with VERORAB.

Internationally recognized RIG dosage is as follows:

Human rabies immunoglobulins: 20 IU/kg of body weight

Equine rabies immunoglobulins: 40 IU/kg of body weight

Because RIGs may partially inhibit active antibody production, no more than the recommended dose should be administered.

The vaccine should be injected contralaterally to the RIG administration sites.

In enzootic rabies areas, the administration of two injections on D0 may be justified, e.g., in the case of lesions that are extremely severe or located near the nervous system, or when the subject is immunodeficient or did not come in for a medical consultation immediately after exposure.

Method of Administration:

VERORAB is administered by the intramuscular route only, into the deltoid area in adults or the anterolateral aspect of the thigh in infants and toddlers.

If you forget to use VERORAB:

Your doctor will decide when to administer the missing dose.

4. POSSIBLE SIDE EFFECTS OF VERORAB

Like all medicines, VERORAB may have side effects.

Minor local reactions: injection-site pain, injection-site erythema, injection-site oedema, injection-site pruritus and injection-site induration.

General reactions: moderate fever, shivering, malaise, asthenia, headaches, dizziness, arthralgia, myalgia, gastro-intestinal disorders. (Nausea, abdominal pain).

Exceptional cases of anaphylactoid reaction, urticaria, rash.

In babies born very prematurely (at or before 28 weeks of gestation) longer gaps than normal between breaths may occur for 2-3 days after vaccination.

If you notice side effects not mentioned in this package leaflet, inform your doctor or pharmacist.

5. HOW TO STORE VERORAB

Keep out of the reach and sight of children.

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

After reconstitution, the vaccine should be used immediately.

Do not use after the expiry date on the box.

This package leaflet was last approved on 04/2009