PATIENT INFORMATION LEAFLET

SCHEDULING STATUS: S4

VERORAB powder and diluent for suspension for injection

Rabies virus (WISTAR rabies PM/WI 38 1503-3M strain) (inactivated)

Contains sugar: 26,3 mg maltose per dose (following reconstitution).

Read all of this leaflet carefully before you or your child getting vaccinated.

- Keep this patient information leaflet until you or your child 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 or your child's doctor or nurse.
- Ensure that you or your child have completed the entire vaccination schedule. Otherwise, you may not be fully protected.
- This vaccine was prescribed for you or your child. Do not pass it on to others.

What is in this leaflet

1. What VERORAB is and what it is used for

VERORAB contains the active substance rabies virus, WISTAR rabies PM/WI 38 1503-3M strain (inactivated).

VERORAB is indicated for pre-exposure and post-exposure rabies prophylaxis (protection) in children and adults. It can be used before or after exposure, as a primary vaccination or as a booster dose.

Pre-exposure prophylaxis:

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.

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 in or travelling to enzootic (affecting animals in a particular area) 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.

2. What you need to know before you or your child receives VERORAB

Do not use VERORAB

Pre-exposure prophylaxis:

If you have a fever or an acute illness: vaccination should be postponed.

Known allergy to any ingredient (i.e. as defined under section 6 of this leaflet) of VERORAB or after previous administration of the vaccine or a vaccine containing the same components.

Post-exposure prophylaxis:

Because rabies is always fatal, there is no contraindication to post-exposure vaccination.

Warnings and precautions

- 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 polymyxin B, to streptomycin, or to neomycin that may be present in trace amounts in the vaccine.
- As with all vaccines, VERORAB may not protect 100 % of individuals vaccinated.
- VERORAB must not be administered via the intravascular route; the health care provider will make sure the needle does not penetrate a blood vessel.
- Tell your or your child's health care provider if you experienced serious adverse reactions with previous vaccinations.
- Tell your health care provider if you or your child has a known decreased immunity (immunodeficiency), due to a suppressive disease or to concomitant immunosuppressive treatment. It is recommended that serological tests be performed to ensure that an immune response indicative of protection has been induced.

In the case of post-exposure vaccination, all vaccine doses should be administered. Rabies immunoglobulins should also be administered in association with VERORAB in the event of any category II or III exposure (see section 3).

- Your health care provider may prefer to administer VERORAB while you or your child is in a seated position, since anxiety-related reactions may result in fainting and possible injury from falling.
- Your health care provider may consider respiratory monitoring for 48 – 78 hours if your child has been born very prematurely due to the potential risk of breathing that may stop.

Other medicines and VERORAB

Always tell your health care provider if you are taking any other medicine. (This includes

complementary or traditional medicines.)

Corticosteroids and other immunosuppressive treatments can interfere with the production of antibodies and lead to the failure of the vaccination. It is therefore recommended to get a serological test 2 to 4 weeks after vaccination (see Warnings and precautions).

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

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

Pregnancy, breastfeeding and fertility

Pregnancy

If you are pregnant or breastfeeding, think you may be pregnant or are planning to have a baby, please consult your health care provider for advice before receiving VERORAB.

Pre-exposure prophylaxis:

Animal reproductive studies have not been conducted with VERORAB. Data on the use of this vaccine in pregnant women are limited. VERORAB should be given to pregnant women only if clearly indicated, and following an assessment of the risks and benefits.

Post-exposure prophylaxis:

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

Breastfeeding

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

Fertility

VERORAB has not been evaluated in fertility studies.

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 41 micrograms phenylalanine in each 0,5 mL dose, which is equivalent to 0,68 micrograms/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 it is essentially potassium free and sodium free.

3. How to receive VERORAB

The recommended dose is 0,5 mL of reconstituted vaccine administered by the intramuscular route.

Pre-exposure prophylaxis:

Three doses of 0,5 mL of VERORAB are administered at days (D) D0, D7 and D28 by intramuscular route. The dose scheduled at D28 can be administered at D21, if necessary.

Booster doses are determined based on the risk of exposure, serological tests and official local recommendations.

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

Post-exposure prophylaxis:

At the slightest risk of contamination, post-exposure prophylaxis should be performed as soon as possible. Vaccination must be performed under medical supervision.

All bites and scratches should be immediately flushed out and washed with soap or detergent with large quantities of water and/or povidone iodine for at least 15 minutes. Doing so can enable efficient elimination of the rabies virus at the infection site. It must be performed before administration of VERORAB or rabies immunoglobulin, where they are indicated.

Your health care provider will adjust your or your child's post-exposure prophylaxis according to the category of exposure, the condition of the animal (see Table 1 and 2) and the vaccination status of the patient, in accordance with official recommendations.

Table 1: WHO guidelines on post-exposure treatment depending on wound severity

Category of exposure	**Type of exposure with a wild or domestic animal presumed or confirmed rabid or an animal unavailable for testing**	**Recommended post-exposure prophylaxis**
I	Touching or feeding of animals. Licks on intact skin (no exposure).	None, if a reliable case history can be obtained*.
II	Nibbling of uncovered skin. Minor scratches or abrasions without bleeding. Licks on broken skin (exposure).	Administer vaccine immediately. 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 euthanised, the results of the search for rabies by the appropriate laboratory techniques are negative. Treat as category III if bat exposure involved.
III	Single or multiple transdermal*** bites or scratches, contamination of mucous	Administer rabies immunoglobulins and vaccine immediately**.

	membrane with saliva (i.e. licks), exposures due to direct contact with bats (severe exposure).	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 euthanised, the results of the search for rabies by the appropriate laboratory techniques are negative.

* If an apparently healthy dog or cat in or from a low-risk area is placed under observation, treatment may be delayed.

** This observation period applies only to dogs and cats. Except for threatened or endangered species, other domestic and wild animals suspected of being rabid should be euthanised and their tissues examined for the presence of rabies antigen by appropriate laboratory techniques.

*** Bites especially on the head, neck, face, hands and genitals are category III exposures because of the rich innervation of these areas.

Table 2: 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 placed under medical supervision for treatment.	Treatment* is always completed.
Dead animal			
Suspect or non-suspect circumstances	Send the brain to an approved laboratory for analysis.	To be placed under medical supervision for treatment.	Treatment* is discontinued if the analyses are negative or, otherwise, continued.
Live animal			
Non-suspect	Place under	Decision to delay rabies	Treatment* is adapted

circumstances	veterinary supervision.	treatment.	according to the results of veterinary supervision of the animal.
Suspect circumstances	Place under veterinary supervision	To be taken to a rabies treatment centre for treatment. To be placed under medical supervision for treatment.	Treatment* is discontinued if veterinary supervision invalidates the initial doubts, or, otherwise, continued.

***** Treatment is recommended depending on the severity of the wound: see Table 1 above.

Post-exposure prophylaxis of previously immunised subjects:

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.

Two booster doses of VERORAB (0,5 mL) should be administered intramuscularly on D0 and D3 in line with official local recommendation (see section for immunocompromised patients under Special populations).

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 (renewed rapid production of an antibody on the second [or subsequent] encounter with the same antigen).

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.

Post-exposure prophylaxis of previously non-immunised individuals:

Individuals not previously immunised can be vaccinated according to one of the vaccination schedules presented in Table 3 (see Method of administration).

Table 3: Post-exposure vaccination schedules in previously non-immunised individuals

	Day 0	Day 3	Day 7	Day 14	Day 21	Day 28
Essen regimen IM route – 0,5 mL	1 dose	1 dose	1 dose	1 dose	---	1 dose
Zagreb regimen IM route – 0,5 mL	2 doses[a]	---	1 dose	---	1 dose	---

[a] One injection in each of the two deltoids (for adults and children) or anterolateral thigh sites (infants and toddlers).

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). In this case, the vaccine should be administered contralaterally, if possible.

Vaccination must not be discontinued unless the animal is declared not rabid by a reliable laboratory using appropriate diagnostic techniques.

Special populations

Paediatric population:

There are no specificities to dose or vaccination schedule for the paediatric population.

Immunocompromised individuals:

The following recommendation should be followed for immunocompromised individuals (see section 2 and Warnings and precautions).

Pre-exposure prophylaxis:

For immunocompromised individuals, serology testing of neutralising antibodies should be performed 2 to 4 weeks after the vaccination, to assess the possible need for an additional dose of

the vaccine.

If the result of the test shows an antibody titre < 0,5 IU/mL, an additional injection is justified.

Post-exposure prophylaxis:

For immunocompromised individuals, only full vaccination schedule (listed in Post-exposure prophylaxis of previously non-immunised individuals – Table 3) should be administered.

Rabies immunoglobulin should be given in association with the vaccine for both categories II & III exposures.

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. Your health care provider will reconstitute VERORAB before administration.

If you receive more VERORAB than you should

None known.

If you forget to have VERORAB administered

Your doctor will decide when to administer the missing dose.

4. Possible side effects

VERORAB can have side effects.

Not all side effects reported for VERORAB are included in this leaflet. Should your general health worsen or if you experience any untoward effects while receiving VERORAB, please consult your doctor, pharmacist or other health care provider for advice.

Serious allergic reactions

Serious allergic reactions (anaphylactic reactions) can always happen, even if it is very rare.

Contact your doctor or health care provider immediately or go to the nearest hospital emergency

department immediately if you or your child experiences 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.

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 (malaise), headache, muscle pain (myalgia), pain at the injection site, irritability (only in babies/toddlers), inconsolable crying and drowsiness (only in babies/toddlers).

Common *(may affect up to 1 in 10 people):* fever, increase in size of lymph nodes (lymphadenopathy), allergic reactions, such as rash and itching (pruritus), influenza-like symptoms (cold like symptoms) (only in adults), decreased appetite (in children), injection site erythema (redness of the skin), swelling at the injection site, injection site pruritus (itchiness), injection site induration (hardening), difficulty sleeping (insomnia) (only in babies/toddlers).

Uncommon *(may affect up to 1 in 100 people):* urticaria (hives), decreased appetite (in adults), dizziness, somnolence (drowsiness) (only in infants/toddlers), abdominal pain, nausea (only adults), diarrhoea (only in adults), vomiting (only in children), chills (shivering), fatigue, unusual weakness (asthenia) (only in adults), joint pain (arthralgia).

Rare *(may affect up to 1 in 1 000 people):* difficulty breathing (dyspnoea).

In addition, the following side effects have been reported very rarely during monitoring of VERORAB after it was released into the market. 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:

- anaphylactic reactions (life-threatening type reaction), angioedema

- sudden hearing loss.

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

Reporting of side effects

If you get side effects, talk to your doctor or pharmacist. You can also report side effects to:

- The Pharmacovigilance Unit at Sanofi: za.drugsafety@sanofi.com (email) or 011 256 3700 (tel),

  or
- SAHPRA via the "**6.04 Adverse Drug Reaction Reporting Form**", found online under SAHPRA's publications: https://www.sahpra.org.za/Publications/Index/8

By reporting side effects, you can help provide more information on the safety of VERORAB.

5. How to store VERORAB

- Store all medicines out of reach of children.
- Store in the refrigerator (2 – 8 °C). Do not freeze.
- After reconstitution, the vaccine should be used immediately.
- Do not use after the expiry date on the carton.
- Keep vial and prefilled syringe in the carton until required for use to protect from light.

6. Contents of the pack and other information

What VERORAB contains

The active substance is:

After reconstitution, 1 dose (0,5 mL) contains:

3,25 IU** rabies virus* (WISTAR rabies PM/WI 38 1503-3M strain) (inactivated).

* Produced on Vero cells.

** IU = International Unit. *In vitro* potency measured using G protein content by ELISA method.

The other ingredients are:

Freeze-dried powder pellet: maltose, human albumin, BME medium – mixture of mineral salts, vitamins, dextrose and amino acids including L-phenylalanine. The pH of the product is adjusted with hydrochloric acid and/or sodium hydroxide.

May contain traces of polymyxin B, streptomycin and neomycin, used in the manufacturing process (see Warnings and precautions).

Diluent: sodium chloride and water for injections.

What VERORAB looks like and contents of the pack:

The powder is a white homogenous pellet.

The diluent is a colourless and limpid liquid.

After reconstitution, VERORAB is a clear homogenous colourless to pale yellow suspension.

Each carton of VERORAB contains an inserted leaflet with:

- Immunising dose: 1 vial (Type I glass) with grey chlorobutyl stopper and a blue aluminium flip-off cap containing a freeze-dried powder pellet.
- Diluent: 0,5 mL of diluent in a prefilled syringe with a needle (Type I glass with a chlorobutyl or bromobutyl plunger stopper).

Holder of the certificate of registration

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