ינואר, 2026

Verorab

powder and solvent for suspension for injection
Rabies, Inactivated, Whole Virus

ההתוויה המאושרת כיום:
Prevention of rabies in children and adults.
It can be used before and after exposure, as a primary vaccination or as a booster dose.

להלן ההתוויה המעודכנת:
Verorab is indicated for pre-exposure and post-exposure prophylaxis of rabies in all age groups.

חברת סאנופי מבקשת להודיע על עדכון העלון לרופא הכולל את עדכון משטר המינון.

<u>העדכונים העיקריים הינם:</u>
- אפשרות חדשה למתן תוך-עורי (ID, intradermal) בנוסף למתן התוך שרירי (IM) המאושר כיום.
- הוספת משטר מינון מקוצר במתן מניעתי לפני החשיפה (pre -exposure prophylaxis).

<u>בנוסף העלון כולל עדכונים נוספים:</u>
- הנחיות מעודכנות של ה- WHO
- מידע לגבי מדוכאי חיסון
- עדכונים נוספים לאורך העלון

העלון ובו מסומנים העדכונים מצורף למכתב זה, החמרות במידע הבטיחות מסומנות בצהוב.

<u>לתשומת ליבכם : קיים הבדל במשטר המינון בין מתן תוך שרירי ומתן תוך עורי.</u>
<u>מכתב לצוותים הרפואיים הכולל מידע חשוב לגבי מתן תוך עורי (intradermal) מופץ במקביל. יש לעיין במכתב זה לפני השימוש בצורת מתן זו.</u>

העלון המעודכן נשלח לפרסום במאגר התרופות שבאתר משרד הבריאות וניתן לקבלו מודפס על ידי פנייה לבעל הרישום- סאנופי ישראל בע"מ, Greenwork Park, מתחם העסקים בקיבוץ יקום, בניין E (קומה 1), 6097600, יקום או בטלפון: 09-8633081.
להלן הקישור לאתר משרד הבריאות: https://israeldrugs.health.gov.il/#!/byDrug

בברכה,

ד"ר תמר גבע,
רוקחת ממונה

1. NAME OF THE MEDICINAL PRODUCT

Verorab, powder and solvent for suspension for injection

Rabies vaccine, inactivated

2. QUALITATIVE AND QUANTITATIVE COMPOSITION

After reconstitution~~,~~ with 0.5 mL ~~of~~ solvent, 1 vial contains:

Rabies virus*, WISTAR Rabies PM/WI38 1503-3M strain (inactivated) ..... 3.25 IU**

* Produced in ~~VERO~~ Vero cells

** Quantity measured according to the ELISA test against~~by comparison with~~ the international standard

Excipient with known effect~~s~~:
Phenylalanine .....4.1 micrograms

For the full list of excipients, see section 6.1.

Verorab may contain traces of polymyxin B, streptomycin~~,~~ and neomycin, ~~which are~~ used in the manufacturing process (see section 4.3).

3. PHARMACEUTICAL FORM

Powder and solvent for suspension for injection.

Before reconstitution, the powder is ~~a~~ uniform white in colour.

The solvent is a clear, colourless solution.

4. CLINICAL PARTICULARS

4.1. Therapeutic indications

Verorab is indicated for pre-exposure and post-exposure prophylaxis of rabies in all age groups ~~Verorab is indicated for the prevention of rabies in children and adults. It can be used before and after exposure to the rabies virus, as a primary vaccination or as a booster dose.~~

~~**Verorab should be used according to official recommendations.**~~

~~**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 section 4.4).~~

~~Pre-exposure vaccination should also be considered for subjects at frequent risk of exposure to the rabies virus, such as:~~
~~- veterinarians, veterinarians' assistants, and 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.~~
~~A serological test can be performed every 2 to 3 years for those subject to discontinuous exposure.~~
~~In areas where the enzootic level of rabies is low, veterinarians and their 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 of exposure.~~

~~Systematic booster injections should be administered in accordance with the subject's risk of exposure. The frequency of booster injections is described in section 4.2.~~

~~**Post-Exposure Prevention of Rabies (Post-Exposure Vaccination)**~~

Upon the slightest risk of rabies 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)] 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.

4.2 Posology and Method of Administration

Verorab should be used according to official recommendations.

Posology:

The recommended dose is 0.5 mL of reconstituted vaccine intramuscularly (IM) or 0.1 mL of reconstituted vaccine intradermally (ID) in each injection site.

~~VERORAB can be administered to adults and children, using the same posology.~~
~~The vaccination schedule should be adapted in accordance with the circumstances of vaccination and the subject's rabies immune status.~~

4.2.1. Pre-Exposure prophylaxis~~Vaccination~~

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

For primary pre-exposure immunisation, immunocompetent individuals can be vaccinated according to one of the vaccination schedules presented in Table 1 and according to local official recommendations when available:

Table 1: Pre-exposure vaccination schedules

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

a - This regimen should not be used for immunocompromised individuals (see subsection "Immunocompromised individuals")
b - One injection in each arm (for adults and children) or each anterolateral thigh (infants and toddlers)

~~**Booster Injection after Pre-Exposure Vaccination**~~
~~A VERORAB booster injection (0.5 ml) should be administered one year after primary vaccination, followed by a booster injection every 5 years (see Table 3).~~

~~**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.~~

Booster doses are determined based on the risk of exposure and on serological tests to detect the presence of rabies virus-neutralising antibodies (≥ 0.5 IU/ml). A booster dose consists of one dose of 0.5 mL given by intramuscular route or one dose of 0.1 mL given by intradermal route in accordance with WHO recommendations .

VERORAB can be administered as a booster injection after primary vaccination with a cell culture rabies vaccine (a rabies vaccine prepared ~~on~~ in ~~VERO~~ Vero cells or prepared ~~on~~ in human diploid cells (HDCV)).

4.2.2. Post-Exposure prophylaxis~~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 ammonia solution can then be applied (provided that there are no remaining traces of soap, because these two products neutralize each other).~~
~~Depending on the severity of the injuries, rabies immunoglobulins (RIGs) may have 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 prophylaxis treatment and/or antibiotherapy.~~

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.

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 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 the rabies 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 membranes with saliva (licks), exposure to bats (severe exposure).	Administer the rabies vaccine immediately and rabies immunoglobulins, 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 postponed.

[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 for the presence of rabies virus using appropriate laboratory* methods.

[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.

~~***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 performed 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~~

Post-exposure prophylaxis of Non-Immunised *individuals* ~~**Subjects**~~

Non-immunised individuals may be vaccinated according to one of the vaccination regimens by intramuscular use (IM) or by intradermal use (ID) presented in table 3.

Table 3: Post-exposure prophylaxis of non-immunised individuals

	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[d] (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.
[d] See section 5.1

Irrespective of the regimen used, vaccination should not be discontinued unless the animal is declared free from rabies.
~~Five doses of VERORAB (0.5 ml) should be administered on D0, D3, D7, D14 and D28.~~ Rabies immunoglobulins ~~(RIGs)~~ should be administered concomitantly with the vaccine~~, first injection~~ in ~~the~~ case of ~~a severe injury (~~ category III exposure~~,~~ ~~according to the~~ (WHO ~~rabies risk~~ classification~~, see Table 2~~).

~~It can be administered later, but not after the 7th day of vaccination~~. ~~Equine and human immunoglobulins can be used with VERORAB. The internationally recognized RIG posology 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.~~
If possible, each dose of the vaccine should be administered at a body site distant from the immunoglobulin administration sites.
~~In enzootic rabies areas, the administration of two vaccine 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.~~

Post-exposure prophylaxis for already ~~Fully~~ Immunised individuals~~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 performed in this case, since booster injection is always followed by an anamnestic response~~
In accordance with official recommendations, this applies to individuals 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.
Individuals 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.

~~. 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.~~

Immunocompromised individuals

- Pre-exposure prophylaxis

A 3-dose regimen should be used (listed in subsection "Pre-exposure prophylaxis") and serology testing for neutralising antibodies should be performed 2 to 4 weeks following the last dose to assess the possible need for an additional dose of the vaccine.

- Post-exposure prophylaxis

A complete vaccine regimen should be administered post-exposure. Rabies immunoglobulin should be administered concomitantly with the vaccine in case of any category II or III exposure (see table 2).

Paediatric population

Children should receive the same dose as adults.

Method of administration

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

- 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.

- Intradermal use (ID)

The vaccine is administered preferably in the upper arm or the forearm.

~~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.~~

Do not inject in the buttocks region.

Do not inject via the intravascular route.

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

For instructions on reconstitution of the medicinal product before administration, see section 6.6.

4.3. Contraindications

Pre-exposure prophylaxis

Hypersensitivity to the active substance(s) or to any of the excipients listed in section 6.1, to polymyxin B, to streptomycin, to neomycin or to any antibiotic of the same class~~,~~ to a previous administration or to any vaccine containing the same components.

Vaccination should be postponed in ~~the event~~case of ~~acute~~ febrile or ~~febrile~~ acute diseases~~illness~~.

Post-exposure prophylaxis

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

~~Due to the always-fatal course of declared rabies infection, post-exposure vaccination has no contraindications.~~

4.4. Special warnings and precautions for use

Traceability

In order to improve the traceability of biological medicinal products, the name and batch number of the administered product should be clearly recorded. ~~It is recommended to record the batch number as well.~~

Special warnings

~~Like~~ As with all vaccines, Verorab may not protect 100% of ~~those~~ vaccinated individuals.

~~To be u~~Use~~d~~ with caution in ~~individuals~~ people with ~~a~~ known allergie~~sy~~ to polymyxin B, to streptomycin, ~~or~~ to neomycin (present ~~in~~ as trace~~s~~ ~~amounts~~ in the vaccine)~~.~~ or to any antibiotic of the same class.

Precautions for use

Injection-schedule ~~R~~recommendations ~~relating to the injection regimen~~ should be followed scrupulously~~exactly~~.

The need for Serological tests (~~in order~~ to assess ~~the~~ seroconversion in individuals~~of subjects~~) should be determined ~~used~~ in accordance with official recommendations.

When the vaccine is administered in individuals ~~to subjects~~ with known immunodeficiency, due to an immunosuppressive disease or a concomitant immunosuppressive treatment (including corticosteroids), ~~serological~~ blood tests ~~should~~ must be performed 2 to 4 weeks after vaccination ~~in order~~ to ensure that a protective immunising~~immune~~ response was obtained~~has been induced~~. In ~~the~~ case of post-exposure vaccination, a complete ~~course of~~ vaccination regimen must ~~should~~ be administered. Rabies immunoglobulin~~s~~ ~~should~~ must also be administered concomitantly~~in combination~~ with the vaccine in ~~the event~~case of any category II ~~and~~ or III exposure (see Section 4.2).Do not inject ~~by~~ via the intravascular route: make sure the needle does not penetrate a blood vessel.

As with all injectable vaccines, appropriate medical treatment and supervision must be readily available in case ~~any vaccine injection, in the event~~ of a rare anaphylactic reaction ~~occurring~~ after vaccine administration ~~of the vaccine, appropriate medical treatment should be available immediately, and the patient should be monitored~~, particularly in case of post-exposure ~~vaccination~~ in individuals~~subjects~~ with a known hypersensitivity to polymyxin B, to streptomycin, ~~or~~ to neomycin~~,~~ or to any antibiotic of the same class.

As with all injectable vaccines~~any vaccine injection~~, Verorab should be administered with caution in individuals ~~patients~~ with thrombocytopaenia or coagulation disorders~~,~~ as intramuscular injection may induce ~~lead to~~ bleeding in these individuals~~subjects~~.

Anxiety-related reactions, including vasovagal reactions (syncope), hyperventilation or stress-related reactions~~,~~ ~~may~~ can occur ~~after~~following, or even before, any vaccination~~,~~ as a psychogenic response ~~reaction~~ to the needle injection ~~with a needle~~. This ~~may~~ can be accompanied by several neurological signs, such as ~~a~~ transient visual disturbance ~~vision disorder~~ and paraesthesia. It is important that procedures ~~measures~~ are in place to ~~prevent~~ avoid injury from faints.~~in the event of fainting.~~

Verorab contains phenylalanine, potassium and sodium

VERORAB contains 4.1 micrograms ~~of~~ phenylalanine per 0.5 mL dose which is equivalent to 0.068 microgram~~s~~/kg ~~in a~~for a 60 kg person. Phenylalanine may be harmful ~~dangerous~~ for ~~individuals~~ people with phenylketonuria (PKU), a rare genetic disorder in which ~~disease characterised by a defect in the elimination of~~ phenylalanine builds up because ~~and its accumulation in~~ the body cannot remove it properly.

Verorab contains less than 1 mmol ~~(39 mg)~~ of potassium (39 mg), and less than 1 mmol ~~(23 mg)~~ of sodium (23 mg) per dose~~;~~, that is, ~~it is considered~~ to ~~be~~ say essentially "potassium-free" and "sodium-free".

Paediatric population

The potential risk of apnoea ~~and~~ with the need for respiratory monitoring for 48-72 hours ~~should~~ must be carefully taken into account ~~considered~~ when administering the primary vaccination doses in very premature infants (born at ~~≤~~ 28 weeks' ~~of pregnancy~~ gestation or less) and particularly ~~for~~ in those with a history of respiratory immaturity.

4.5. Interaction with other medicinal products and other forms of interaction

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 perform ~~that~~ a serological test ~~is performed~~ 2 to 4 weeks after vaccination ~~the last injection~~ (see section 4.2).

Verorab may be administered concomitantly ~~combined~~ with a Vi polysaccharide typhoid vaccine during the same vaccination ~~session by~~visit, using two different injection sites.

Rabies immunoglobulins or any other product and the rabies vaccine ~~should~~ must never be combined in the same syringe or injected into ~~administered at~~ the same site (see section 6.2).

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

4.6. Fertility, pregnancy and lactation

Pregnancy

~~There is limited~~ D~~d~~ata on the use of VERORAB in pregnant women are limited. Animal developmental and~~. No animal~~

reproductive toxicity studies have not been conducted ~~performed~~ with this vaccine.

Pre-exposure prophylaxis

~~Because of~~Given the seriousness ~~severity~~ of the disease, vaccination ~~the vaccine~~ should be given to pregnant women only ~~be administered during pregnancy~~ if ~~really~~ clearly needed and ~~after~~ following an assessment of the risk~~s~~/ and benefit~~s ratio~~, in compliance ~~accordance~~ with the usual vaccination schedule.

Post-exposure prophylaxis

~~Because~~ Given ~~of~~ the seriousness ~~severity~~ of the disease, the vaccine ~~may~~ can be administered during pregnancy.

Lactation ~~Breast-feeding~~

It is unknown whether VERORAB is excreted in human milk. No risk~~s have~~ has been identified and is anticipated ~~nor are expected~~ for ~~breastfed~~ infants receiving breast milk.

VERORAB ~~may~~ can be administered to ~~a~~ breast-feeding ~~woman~~ women ~~after~~ following an assessment of the risks and ~~/~~benefit~~s ratio~~.

Fertility

Verorab has not been evaluated ~~assessed~~ in fertility studies.

4.7. Effects on ability to drive and use machines

Post-vaccination dizziness was frequently ~~Vertigo has commonly been~~ reported ~~after vaccination~~ (see section 4.8). ~~This may~~It can temporarily affect the ability to drive ~~and~~ or use machines.

4.8. **Undesirable effects**

Summary of the ~~tolerability~~ safety profile

~~More than~~Over 13,000 study participants~~subjects~~, including approximately 1,000 children and adolescents under the age of 18 ~~years of age~~, have received at least one dose of Verorab in clinical studies.

Adverse reactions ~~The undesirable effects~~ were generally moderate in intensity and occurred within 3 days of vaccination. Most ~~of the effects~~reactions resolved spontaneously within 1 to 3 days of their ~~appearance~~onset.

The most common adverse ~~undesirable~~ effects in all age groups (except in infants/young children aged under ~~less than~~ 24 months ~~of age~~) were headache~~s~~, malaise, myalgia and pain at the injection site ~~pain~~. Injection site reactions (pain, erythema and swelling) were more common after an ID injection than an IM injection. Pain was the most common injection site reaction for both administration routes~~at the injection site~~.

Tabulated list of ~~the~~ adverse reactions~~undesirable effects~~

The adverse reactions ~~undesirable effects~~ listed below were reported during ~~are those from~~ clinical studies and worldwide post-marketing surveillance ~~worldwide~~. Within each system organ class, ~~the~~ adverse ~~events~~ reactions are ranked under headings of ~~classified by~~ frequency ~~according~~ using ~~to~~ the following convention:

- very common (≥ 1/10);
- common: (≥ 1/100 ~~to~~ and <1/10);
- uncommon: (≥ 1/1,000 ~~to~~ and <1/100);
- rare: (≥ 1/10,000 ~~to~~ and <1/1,000);
- very rare (<1/10,000);
- Not known (cannot be estimated from the available data).

~~Adverse reactions~~~~Undesirable effects~~	**Adults** ≥ 18 years	**Paediatric population** ~~less than~~under 18 years old
	Frequency	**Frequency**
Blood and lymphatic system disorders		
Lymphadenopathy	Common	Common
Immune system disorders		
Allergic reactions (e.g., rash, urticaria, pruritus)	Uncommon	Uncommon
Anaphylactic reactions and angio-~~e~~edema	Not known	Not known

Adverse reactions~~Undesirable effects~~	**Adults** ≥ 18 years **Frequency**	**Paediatric population** ~~less than~~under 18 years old **Frequency**
Metabolism and nutrition disorders		
Decreased appetite	Uncommon	Uncommon
Nervous system disorders		
Headache	Very common	Very common
Dizziness / Vertigo	Uncommon	-
Irritability (in infants / young children)	-	Very common
Somnolence (in infants / young children)	-	Very common
Insomnia (in infants / young children)	-	Common
Ear and labyrinth disorders		
Sudden ~~loss of~~ hearing loss, which may persist	Not known	Not known
Respiratory, thoracic and mediastinal disorders		
Dyspnoea	Rare	-
Gastrointestinal disorders		
Nausea	Uncommon	-
Abdominal pain	Uncommon	Uncommon
Diarrhoea	Uncommon	-
Vomiting	-	Uncommon
Musculoskeletal and connective tissue disorders		
Myalgia	Very common	Very common
Arthralgia	Uncommon	-
General disorders and administration site conditions		
Injection site pain (IM use)	Very common	Very common
Injection site pain (ID use)	Very common	Very common
Injection site erythema (IM use)	Common	Common
Injection site erythema (ID use)	Very common	Very common
Injection site pruritus (IM use)	Common	-
Injection site pruritus (ID use)	Common	Uncommon
Injection site swelling (IM use)	Common	Common
Injection site swelling (ID use)	Common	Very common
Injection site induration (IM use)	Common	-
Injection site haematoma (ID use)	Uncommon	
Malaise	Very common	Very common
Influenza~~Flu~~-like syndrome	Common	
Fever	Common	Common
Asthenia	Uncommon	-
Chills	Uncommon	Uncommon
Inconsolable crying (in infants / young children)	-	Very common

Reporting of suspected adverse reactions

Reporting of suspected adverse reactions ~~Reporting suspected adverse reactions~~ after authorisation of the medicinal product is important. It allows continued monitoring of the benefit/risk balance of the medicinal product. Any suspected adverse events should be reported to the Ministry of Health according to the National Regulation by using an online form https://sideeffects.health.gov.il/

4.9. Overdose

No cases of overdose ~~have been~~were reported ~~during~~ in clinical ~~studies~~trials.

5. PHARMACOLOGICAL PROPERTIES

5.1. Pharmacodynamic properties

Pharmacotherapeutic group: Rabies vaccines, ATC code: J07BG01.

Mechanism of action

Protection after vaccination is provided ~~ensured~~ by the induction of anti-rabies neutralising antibodies.

Clinical studies have been conducted to assess the immunogenicity of the vaccine ~~as pre- and~~in post-exposure and pre-exposure prophylaxis. ~~A r~~Rabies virus neutralising antibody level~~s~~ of ≥ 0.5 IU/mL ~~is~~ are considered to be protective by the WHO.

Pre-exposure prophylaxis

In clinical trials assessing a 3-dose vaccin~~eation schedule~~ regimen (D0, D7, ~~and~~ D28 [~~(~~or D21])~~)~~ in both adults and children, all study participants achieved an adequate immune response ~~was obtained in all subjects~~ with serum neutralising antibody titres ≥ 0.5 IU/mL ~~on~~ by D14 after the end of the primary vaccine regimen ~~vaccination~~.

A ten-year follow-up in 49 patients who ~~had~~ received a 3-dose regimen (D0, D7 and D28) followed by a booster dose at one year~~,~~ demonstrated a persistent ~~persistence of the~~ immune response, with neutralising antibody titres ~~being~~ maintained for ~~up to~~ 10 years in 96.9% of ~~the~~ vaccinated study participants.~~subjects.~~

The one-week pre-exposure schedule by IM ~~pre-exposure regimen~~route (one 0.5 mL dose ~~on~~ at D0 and one 0.5 mL dose ~~on~~ at D7) was assessed in ~~a~~ one study (VAJ00001) in 75 study participants ~~subjects~~ (including 35 children ~~aged~~ from 2 to 17 years).

~~On~~ At D21, 98.6% study participants reached a ~~of the vaccinated subjects had achieved~~ serum antibody ~~levels~~ titer ≥ 0.5 IU/mL.

One year later, following a simulated PEP with two 0.5-mL doses injected 3 days apart (at D0 and D3) by IM route, a high and rapid anamnestic response was demonstrated in all study participants from D7 (7 days after the 1st PEP dose).

In 5 other supportive studies conducted with Verorab in a total of 392 study participants in the context of a conventional 3-dose regimen assessment (at D0, D7, D21 or D28) by IM route, all study participants reached a serum antibody titer ≥ 0.5 IU/mL, at D21 or D28, after the 2 doses (at D0 and D7), just before injection of the third dose.

The one-week pre-exposure schedule by intradermal route (two 0.1-mL doses at D0 and two 0.1-mL doses at D7) was assessed in one study in 75 study participants (including 36 children from 2 to 17 years).

At D21, 97.2% study participants reached a serum antibody titer ≥ 0.5 IU/mL.

One year later, following a simulated ~~post-exposure prophylaxis (~~PEP~~)~~ with two ~~0.5~~0.1 mL doses injected 3 days apart (~~on~~ at D0 and D3) ~~via~~ by ~~IM~~ ID ~~injection~~route, a high and rapid ~~and robust~~ anamnestic response was demonstrated in all study participants ~~subjects~~ from D7 ~~(7 days after the 1st PPE dose).~~ , except one study participant who remained seronegative at every time points despite completing all study vaccinations.

~~During 5 additional studies conducted with VERORAB in a total of 392 subjects assessing the standard three-dose regimen (on D0, D7, and D21 or D28) by IM injection, all the subjects achieved serum antibody levels ≥ 0.5 IU/mL after two doses (on D0 and D7), just before the third dose on D21 or D28.~~

In another supportive study conducted in 430 study participants who received one 0.1-mL dose of Verorab at D0 and one 0.1-mL dose at D7 by ID route, 99.1% study participants reached a serum antibody titer ≥ 0.5 IU/mL at D21.

Post-exposure prophylaxis

In clinical trials assessing the 5-dose intramuscular Essen regimen (D0, D3, D7, D14 and D28) and the ~~4-dose~~ intramuscular 4-dose Zagreb regimen (2 doses on D0 then one dose on D7 and one dose on D21) in both children and adults, Verorab elicited ~~vaccination with VERORAB resulted in~~ neutralising antibody titres ~~(~~≥0.5 IU/mL~~)~~ in almost all ~~the~~ vaccinated study participants ~~subjects on~~ by D14 and in all ~~the~~ study participants by ~~subjects on~~ D28.

During a phase-3 study including 600 exposed study participants aged from 11 months to 50 years, 2 intradermal post-exposure prophylaxis (PEP) regimens were tested: 1 regimen in 4 sites in 1 week (4 doses on D0, 4 doses on D3 and 4 doses on D7) with or without equine rabies immunoglobulin (ERIG) on D0, and the new Thailand Red Cross regimen (2 doses on D0, 2 doses on D3, 2 doses on D7 and 2 doses on D28) with equine rabies immunoglobulin (ERIG) on D0. The Institute Pasteur of Cambodia (IPC) regimen (2 doses on D0, D3 and D7) was also included in the Thailand Red Cross regimen up to D28. Almost all vaccinated study participants (98.8%) reached rabies neutralising antibody levels ≥ 0.5 IU/mL by D14. A direct comparison of the immunogenicity following ID compared with IM use was not made. Five years later and before the simulated PEP was received, the protective level of rabies neutralising antibodies was maintained in more than 84% of study participants who received a 4-site 1-week regimen with or without ERIG, and in 64.1% (95% CI: 55.1; 72.3) of study participants who received the new Thailand Red Cross regimen with ERIG. Eleven days after the simulated PEP with a 4-dose ID regimen performed in one visit, all the vaccinated study participants reached rabies neutralising antibody levels ≥ 0.5 IU/mL on D14 (geometric mean antibody titre [GMT] between 138 and 193 IU/mL).

The administration of human rabies immunoglobulin (HRIG) or equine rabies immunoglobulin (ERIG) ~~at the same time as~~ concomitantly with the rabies vaccine may cause slightly lower ~~a slight decrease in the~~ mean neutralising antibody titres due to ~~because of~~ immune interference.

The efficacy of Verorab was assessed in 44 adult study participants ~~subjects~~ bitten by ~~rabid~~ animals with rabies in a phase 4 clinical trial. The study participants ~~Subjects~~ received the vaccine according to the 5-dose Essen regimen (D0, D3, D7, D14 and D28 by IM ~~injection~~use) and immunoglobulin~~s~~, if applicable. All study participants ~~the subjects~~ were alive 3 years after the post-exposure prophylaxis.

Paediatric population

There ~~is~~ are no clinically significant differences in the immunogenicity of the vaccine in the paediatric population compared to adults.

In the study (VAJ00001) assessing the one-week pre-exposure schedule by intradermal route (two 0.1-mL doses of Verorab at D0 and two 0.1-mL doses at D7) or by IM route (one 0.5-ml dose of Verorab at D0 and one 0.5-mL dose at D7) in 71 children from 2 to 17 years of age, all children reached a serum antibody titer ≥ 0.5 IU/mL at D21.

One year later, following a simulated PEP with two doses injected 3 days apart (at D0 and D3) by IM or ID route, a high and rapid anamnestic response was demonstrated in all study participants from D7.

5.2. Pharmacokinetic properties

No pharmacokinetic studies ~~have been~~were performed.

5.3. Preclinical safety data

Data in ~~A~~animals ~~data~~, including ~~data from~~ single-dose and repeated- dose studies revealed no~~, did not reveal any~~ unexpected findings ~~or~~ and no target organ toxicity.

~~No a~~Animal developmental and reproductive toxicity studies have not been conducted ~~performed~~ with this vaccine.

6. PHARMACEUTICAL PARTICULARS

6.1. 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).

Hydrochloric acid and sodium hydroxide for pH adjustment.

Water for injections.

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

Solvent:

Sodium chloride.

Water for injections.

6.2. Incompatibilities

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

6.3. Shelf life

The expiry date of the product is indicated on the packaging materials.
After the first opening / reconstitution~~,~~ :

For intramuscular use: the product must be used immediately.

For intradermal use: the physical-chemical stability after reconstitution was shown to last for 6 hours at 25°C protected from light. From a microbiological perspective, the product must be used immediately. In case of non-immediate use, the duration and conditions of storage and use (see section 6.6) are the responsibility of the user.

6.4. Special precautions for storage

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

Store in the original outer package ~~carton in order to~~ protected from light.

For storage conditions after reconstitution of the medicinal product, see section 6.3.

6.5. Nature and contents of container

Powder in ~~a~~ vial (Type I glass) fitted with a stopper (chlorobutyl) and a cap + 0.5 mL of solvent in a pre-filled syringe (Type I glass) fitted with a plunger-stopper with attached needle and needle cap. Box of 1 or 10.
Not all pack size may be marketed.

6.6. Special precautions for disposal and other handling

Handling instructions:

- Remove the cap of the vial of lyophilised powder.
- Screw the plunger rod ~~onto~~ into the syringe, if ~~supplied~~ provided separately.
- Inject 0.5 ml ~~the~~ of solvent into the vial of lyophilised powder.
- Shake the vial ~~G~~gently ~~stir the vial~~ until ~~a~~ homogeneous suspension of the powder is obtained.
- The reconstituted vaccine ~~is a clear, homogeneous, particle-free liquid.~~should be limpid, homogeneous and free from particles
- Remove and discard the syringe that was used for vaccine reconstitution ~~of the vaccine~~.
- 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 ~~to administer the~~ vaccine administration ~~must~~ 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 not exceeding 25°C and protected from light. After reconstitution with 0.5 mL of solvent, using aseptic techniques, each dose of 0.1 mL 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.

8. MARKETING AUTHORISATION HOLDER AND IMPORTER AND ITS ADDRESS:

Sanofi Israel ltd. Greenwork ~~Park~~Complex, P.O Box 47, Yakum ~~.~~

9. MARKETING AUTHORISATION NUMBER: 140-97-31875

Revised in January 2026~~April 2024 according to MoH guidelines~~.