Registration No. 1C 15013/62 (NBC)

Importer/Manufacturer: Bionovel Co., Ltd./SERUM INSTITUTE OF INDIA PVT. LTD.

SUMMARY OF PRODUCT CHARACTERISTICS

1. NAME OF THE MEDICAL PRODUCT

RABIVAX-S

2. QUALITATIVE AND QUANTITATIVE COMPOSITION

Each dose of 1 ml contains:
Purified Rabies Antigen (Rabies virus Pitman-Moore Strain 3218-VERO adapted and grown on vero cells, inactivated by using β-propiolactone) not less than 2.5 IU
Reconstitute with 1 ml of Sterile Water for Injections.

3. PHARMACEUTICAL FORM

RABIVAX-S [Rabies Vaccine Inactivated (Freeze dried)] is a sterile, purified inactivated rabies vaccine prepared on vero cells. RABIVAX-S is freeze dried and is provided with diluent (1 dose of powder in vial and 1 ml of diluent in ampoule). The vaccine has the appearance of a white dry cake.

4. CLINICAL PARTICULARS

4.1 Therapeutic indications

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

a) Pre-Exposure prophylaxis

Pre-exposure vaccination should be offered to subjects at high risk of contamination by the rabies virus. This vaccination is particularly recommended for veterinarians, veterinary medicine students, animal keepers, hunters, forestry workers, animal handlers, butchers, personnel in rabies research laboratories etc., children at high risk of exposure or prior to visit to areas in which rabies is endemic.

b) Post-Exposure prophylaxis

RABIVAX-S is indicated in post-exposure prophylaxis of rabies infection, when given to individuals with suspected rabies exposure. RABIVAX-S must always be used as per recommendations of the World Health Organization (WHO), depending on the type of contact with a suspected rabid animal.

Category	Type of contact	Recommended treatment
I	Touching or feeding animals, licks on the intact skin.	No treatment is required.
II	Nibbling of uncovered skin, minor scratches or abrasions without bleeding.	Immediate vaccination.
III	Single or multiple transdermal bites or	Immediate vaccination and

	scratches, contamination of mucous membrane with saliva from licks, licks on broken skin, exposure to bats.	administration of immunoglobulin.

For all categories, immediate washing and flushing of all wounds and scratches is recommended. If indicated tetanus prophylaxis should also be given with tetanus toxoid.

Treatment should be started as early as possible after exposure, but in no case should it be denied to exposed persons whatever time interval has elapsed.

4.2 Posology and method of administration

RABIVAX-S should be reconstituted only with the entire contents of the diluent supplied (Sterile Water for Injections) using a sterile syringe and needle, with gentle shaking until the dried cake is easily dissolved. After reconstitution the vaccine should be used immediately

The vaccine vial monitor (see figure at the end of this package insert), for this type of vaccine is attached to the vial cap and should be discarded when the vaccine is being reconstituted.

The diluent and reconstituted vaccine should be inspected visually for any foreign particulate matter and/or variation of physical aspects prior to administration. In the event of either being observed, discard the diluent or reconstituted vaccine.

For adults and children aged ≥ 2 years, the vaccine should always be administered in the deltoid area of the arm; for children aged < 2 years, the anterolateral area of the thigh is recommended. Rabies vaccine should not be administered in the gluteal area, as the induction of an adequate immune response may be less reliable.

Intradermal regimen may be used for people with category II and III exposures in countries where the intradermal route has been endorsed by national health authorities.

a) Pre-Exposure prophylaxis

The following schedule should be followed for pre-exposure prophylaxis in high risk populations.

Route	Dose	Number of doses	Schedule
Intramuscular	1 ml	2	Day 0 and 7
Intradermal	0.1 ml	2	Day 0 and 7

In case of immunocompromised individuals, veterinarians and high risk populations, 1 dose of 1 ml given by intramuscular route or 1 dose of 0.1 ml given by intradermal route on Day 0, 7, 21 or 28 (totally 3 doses) are recommended (Thai Red Cross Regimen).

Periodic booster injections are recommended as an extra precaution only for people whose occupation puts them at continual or frequent risk of exposure. For people who are potentially at risk of laboratory exposure to high concentrations of live rabies virus, antibody testing should be done every 6 months. Those professionals, who are not at continual risk of exposure through their activities, should have serological monitoring every 2 years. Because vaccine-induced immunity persists in most cases for years, a booster should be administered if rabies virus neutralizing antibody titres fall to <0.5 IU/ml.

b) Post-Exposure prophylaxis

In order to remove as much of the rabies virus as possible, immediately cleanse the wound with soap and wash thoroughly with water. Then treat with alcohol (70%) or an iodine tincture.

The following schedule should be followed for post-exposure prophylaxis in persons who have not received complete schedule of rabies vaccination in the past (pre-exposure or post-exposure prophylaxis).

Route	Dose	Number of doses	Schedule
Intramuscular	1 ml	5	Day 0, 3, 7, 14 and 28
Intradermal	0.1 ml, 0.1 ml (2 different sites)	4	Day 0, 3, 7 and 28

For intradermal route, four doses should be administered (2 injections of 0.1 ml at 2 different sites) as per the Updated Thai Red Cross regimen (2-2-2-0-2) as given above.

In those previously immunized by complete vaccination schedule (pre-exposure or post-exposure prophylaxis), 2 doses of 1 ml given by intramuscular route or 2 doses of 0.1 ml by intradermal route on Day 0 and Day 3 are recommended. Rabies immunoglobulin is not required for such individuals.

In cases of Category III exposures and of category II exposures in immunodeficient patients, human rabies immunoglobulin (20 IU per kg) or equine rabies immunoglobulin (40 IU per kg) should be given in conjunction with RABIVAX-S on Day 0. If anatomically feasible, the full dose of rabies immunoglobulin should be thoroughly infiltrated in the area around and into the wounds only. Rabies immunoglobulin may be diluted to a volume sufficient for all wounds to be effectively and safety infiltrated if there are multiple wounds.

If rabies immunoglobulin is not available at the time of the first vaccination, it must be administered no later than 7 days after the first vaccination since later administration would result in interference with immune response of the vaccine.

4.3 Contraindication

a) Pre-Exposure prophylaxis

In case of fever or an acute illness, vaccination should be postponed. In case of previous severe reaction to any components of the vaccine, RABIVAX-S is contraindicated

b) Post-Exposure prophylaxis

Because of the life-threatening risk of rabies, there are no contraindications to the administration of post-exposure prophylaxis using RABIVAX-S. The intradermal route must not be used in the individuals receiving long term corticosteroid or other immunosuppressive therapy or chloroquine for malaria treatment or prophylaxis and in immunocompromised individuals. Such individuals may have a reduced response to intradermal rabies vaccination and should instead receive the vaccine intramuscularly.

4.4 Special warnings and precautions for use

1. Special care should be taken to ensure that the product is not injected into a blood vessel. RABIVAX-S must not be administered intravenously.
2. Under no circumstances should RABIVAX-S be administered in the same syringe or at the same site as rabies immunoglobulin.

3. The possibility of allergic reactions in individuals sensitive to components of the product should be evaluated. Adrenaline hydrochloride Solution (1:1000) and other appropriate agents should be readily available for immediate use in case an anaphylactic or acute hypersensitivity reaction occurs as per the current recommendations.
4. A separate sterile needle and syringe must be used for each individual patient to prevent the transmission of infectious agents.
5. As with all preparations given intramuscularly, bleeding complications may be encountered in patients with bleeding disorders.

SPECIAL PRECAUTIONS FOR THE INTRADERMAL ROUTE

It is essential that intradermal administration of RABIVAX-S be carried out only by medical staff trained in this technique in order to ensure that the vaccine is delivered intradermally and not subcutaneously. For the intradermal route, a sterile syringe with fixed needle (insulin type) is preferred. Correct intradermal injection should result in a raised papule with an "orange peel" (peau d' orange) appearance. If the vaccine is injected too deeply into the skin, and a papule is not seen, the needle should be withdrawn and reinserted nearby. If papule is not seen after 2 successive attempts, the patient should be given the dose intramuscularly.

RABIVAX-S does not contain preservative; therefore, great care must be taken to avoid contamination of reconstituted vaccine. Vaccine may be used up to 6 hours after reconstitution provided it is maintained at 2°C to 8°C. Unused vaccine must be discarded after 6 hours. A new sterile needle and syringe must be used to withdraw and administer each dose of vaccine for each patient to avoid cross infection.

4.5 Interaction with other medical products and forms of interaction

Corticosteroids, chloroquine and other immunosuppressive treatments can interfere with the immune response of the vaccine and lead to the failure of the vaccination. Immunoglobulins must be administered at a different site from that of the vaccine (the contralateral side). The recommended dose of rabies immunoglobulin should not exceed nor should repeated doses of the same be administered once the vaccination course has been started since a higher dose could interfere with the immune response to rabies vaccine.

4.6 Pregnancy and lactation

RABIVAX-S is safe, non-teratogenic and did not cause developmental toxicity in a prenatal developmental toxicity study in pregnant rats.

It is not known whether RABIVAX-S can cause fetal harm when administered to a pregnant woman or can affect reproductive capacity. It is also not known whether RABIVAX-S is secreted in breast milk.

It is advisable to carefully weigh expected benefits against potential risks prior to pre-exposure prophylaxis with RABIVAX-S during pregnancy and breast feeding.

Because of the life-threatening risk due to rabies, pregnancy and lactation are not contraindications for post-exposure prophylaxis with RABIVAX-S.

4.7 Effects on the ability to drive and use machines
Effect of Rabivax-S on ability to drive and use machines is not known

4.8 Undesirable effects
RABIVAX-S may cause injection site reactions such as pain, erythema, oedema, pruritus and induration and systemic reactions such as fever, shivering, faintness, asthenia, headache, dizziness, myalgia, nausea, abdominal pain and arthralgia. Usually these reactions are mild in severity, transient and resolve uneventfully. Rarely erythema multiforme has been reported with other tissue culture rabies vaccines.

4.9 Overdose
No cases of overdose are reported

5 PHARMACOLOGICAL PROPERTIES
5.1 Pharmacodynamic properties
Not applicable

5.2 Pharmacokinetic properties
Not applicable

5.3 Preclinical safety data
Not applicable

6 PHARMACEUTICAL PARTICULARS
6.1 List of excipients
Diluent: Sterile Water for Injections I.P.
Excipients: Sucrose, glycine, human serum albumin (HSA).

6.2 Incompatibilities
Not applicable

6.3 Shelf life
36 months

6.4 Special precautions for storage
The vaccine should be stored between 2°C and 8°C. The diluent should not be frozen, but should be kept cool.
After reconstitution, immediate use is recommended.

6.5 Nature and contents of container
RABIVAX-S is supplied as:
1 dose – 1 ml vial plus diluent (1 ml)

6.6 Special precautions for disposal and other handling

Not applicable

7 MARKETING AUTHORISATION HOLDER

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8 MARKETING AUTHORISATION NUMBER(S)

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9 DATE OF FIRST AUTHORISATION/RENEWAL OF THE AUTHORISATION

February 1, 2019

10 DATE OF REVISION OF THE TEXT

April, 2021