Summary of Product Characteristics

1. Name of the medicinal product

Rabix-vc Vaccine

Rabies Vaccine(Human) BP

Available in 1 ml strength.

2. Qualitative and quantitative composition

Freeze-dried vaccine. Each vial contains lyophilized preparation of Rabies Vaccine (Human) BP containing purified, inactivated rabies virus (Pasteur PV-2061strain) produced on vero cell, after reconstitution 1ml gives potency ≥ 2.5 IU.

3. Pharmaceutical form

Freeze-dried vaccine

4. Clinical particulars

4.1 Therapeutic indications

Pre-exposure immunization

This vaccination is particularly recommended for:

- Professional groups exposed to frequent contamination
- Veterinary surgeons (including students at veterinary colleges)
- Technical personnel working with veterinary surgeons
- Laboratory personnel handling material contaminated with rabies virus
- Personnel in abattoirs and knackers yards
- Taxidermists
- Gamekeepers, forestry workers and naturalists in enzootic areas
- Infants particularly exposed to the risk of rabies

Post-exposure immunization

- Treatment of subjects bitten by rabid animals or those suspected of being so
- Treatment of contact subjects

4.2 Posology and method of administration

To reconstitute the vaccine, transfer content of supplied diluents into the vial containing freeze- dried preparation. Do not shake. After reconstitution the solution should be homogenous, clear and free from any particles. Vaccine must be injected immediately after reconstitution and the syringe should be destroyed after use.

- ✓ Method of administration for intramuscular use
  The 1ml dose of Rabix-vc should be given intramuscularly in the deltoid in adults and in the anterolateral aspect of the thigh muscle in children under 1 year. It should not be injected into the gluteal region.
  Do not inject intravenously.
- ✓ Method of administration for intradermal use
  The 0.1 ml dose of Rabix-vc (per site) should be administered intradermally in the upper arm, over the deltoid.

a) Pre-exposure immunization

1ml for children and adults

Primary-vaccination:

According to the WHO recommendations 1 injection by the intramuscular route on days D0, D7, D21 or D28, followed by a booster dose one year later.

Boosters:

Thereafter, one injection every 5 years or when the titre is found to be less than 0.5 IU/ml.

b) Post-exposure immunization

Local treatment of the wound:

1. Prompt and gentle thorough washing with soap or detergent and flushing the wound with running tap water for at least 15 minutes.
2. After washing, disinfectants like either ethanol (700ml/l) or tincture or aqueous solution of iodine or povidone iodine must be applied.
3. Don't bandage or suture the wound.

Vaccination of non-immunized subjects

Intramuscular schedules: One Intramuscular (IM) dose comprised of 1ml**.**

Standard intramuscular (1-1-1-1-1) regimen:

Day 0: 1 injection of 1ml

Day 3: 1 injection of 1ml

Day 7: 2 1 injection of 1ml

Day 14: 1 injection of 1ml

Day 28 : 1 injection of 1ml

Or

Abbreviated multisite (2-1-1) regimen:

Day 0: 2 injections each of 1ml at separate sites

Day 7: 1 injection of 1ml

Day 21: 1 injection of 1ml

Intradermal schedules: One Intradermal (ID) dose is comprised of 0.1ml

Thai Red Cross (2-2-2-0-1-1) schedule:

Day 0: 2 injections each of 0.1 ml at separate sites

Day 3: 2 injections each of 0.1 ml at separate sites

Day 7: 2 injections each of 0.1 ml at separate sites

Day 28: 1 injection of 0.1 ml

Day 90: 1 injection of 0.1 ml (Optional).

Or

WHO Modified Thai Red Cross (2-2-2-0-2)

Day 0: 2 injections each of 0.1 ml at separate sites

Day 3: 2 injections each of 0.1 ml at separate sites

Day 7: 2 injections each of 0.1 ml at separate sites

Day 28: 2 injections each of 0.1 ml at separate sites

In case of severe (WHO category III) wounds, rabies immunoglobulin should be administered as soon as possible with the first dose of rabies vaccine. The anti-rabies immunoglobulin should be used as local wound soakage injections as much as possible, with the rest part for muscle injection. The rabies vaccine should be administered in different injection site.

Vaccination of immunized subjects: If vaccine administered in less than 5 years of exposure (cell culture rabies vaccine): 2 injections, one on each of D0, D3.

If vaccine administered in more than 5 years of exposure or incomplete vaccination: 5 injections on D0, D3, D7, D14 and D28 with administration of immunoglobulin if required.

Post- exposure vaccination must be administered on the basis of severity under medical supervision.

WHO guideline on post- exposure treatment depending on wound severity

Category	Type of contact with a suspect or confirmed rabid domestic or animal available for observation	Recommended treatment
1	Touching or feeding of animal, licks on intact skin	None, if reliable case history is available
2.	Nibbling of uncovered skin, minor scratches, superficial bites (except on head, neck, shoulder, girdle, arms or hands) or abrasion without bleeding, licks on broken skin.	Administer vaccine immediately on Day 0, D3, D7, D14 and D28.Stop treatment if animal remains healthy throughout the observation period of 10 days of if animal is killed humanely and found to be negative by appropriate laboratory techniques.
3.	Single or multiple transdermal bites or scratches especially on head, neck, shoulder girdle, arms or hands. Contamination of mucus membrane with saliva (i.e. licks on broken skin).	**Administer rabies immunoglobulin immediately with the first dose of rabies vaccine.** Administer rabies vaccine immediately on Day 0, D3, D7, D14 and D28.Stop treatment if animal remains healthy throughout the observation period of 10 days of if animal is killed humanely and found to be negative by appropriate laboratory techniques.

4.3 Contraindication

a) Pre-exposure and booster immunization

- Severe fever, febrile infection, acute disease, progressive chronic disease
- Known hypersensitivity reactions to rabies vaccine or any of its components

b) Post-exposure immunization

- No contraindication to post- exposure treatment, because rabies is lethal disease, any contraindication to exposure, treatment should be considered carefully before disqualifying an individual for anti rabies treatment.

4.4 Special warnings and precautions for use

- To be used with care in cases of true allergy to streptomycin and/or neomycin (traces present in the vaccine).
- In cases of severe bites, it is recommended by the WHO that a treatment of 40 IU. per kg of purified rabies serum of equine origin, be given on the first day of vaccination (D0). This immunoglobulin provides protective antibodies immediately and as much as possible should be administered locally at the wound site(s).

  Wound cleaning: In accordance with WHO recommendations, prompt and gentle thorough washing with soap or detergent and flushing the wound with running tap water for at least 15 minutes. After washing, disinfectants like either ethanol (700ml/l) or tincture or aqueous solution of iodine or povidone iodine must be applied. Don't bandage or suture the wound.

Special precautions for the intradermal route:

1. It is essential that intradermal administration of vaccine be administered only by medical staff trained in the ID technique in order to ensure that the vaccine is delivered intradermally and not subcutaneously.
2. For the intradermal route a sterile syringe with fixed needle (insulin type) is preferred.
3. A sterile needle and syringe must be used to withdraw and administer each dose of vaccine for each patient to avoid cross infection. Correct intradermal injection should result in a raised papule with a "peau d orange" (orange peel) appearance. If the vaccine has been injected too deeply and a papule is not seen, the needle should be withdrawn and re-inserted nearby.
4. This vaccine doesn't contain a preservative; therefore, great care must be taken to avoid contamination of reconstituted vaccine.
5. Any reconstituted vaccine should be used as soon as possible. It must be stored in a refrigerator at $+2^0$C to $+8^0$C and used within 8 hours after reconstitution or discarded.
6. ID route must not be used in the following conditions:
    - Patient receiving immunosuppressive therapies, including irradiation, antimetabolites, alkylating agents, cytotoxic drugs and corticosteroids.
    - Immunocompromised individuals.

4.5 Interaction with other medical products and forms of interaction

Corticosteroid and immunosuppressive treatment may interfere with antibody production and cause vaccination failure. In these cases, a titration of neutralizing antibodies should be performed.

4.6 Fertility,Pregnancy and lactation

Pregnancy

No cases of harm attributable to use of Rabix-vc during pregnancy have been observed.

Rabix-vc may be administered to pregnant women when post-exposure prophylaxis is required.

The vaccine may also be used for pre-exposure prophylaxis during pregnancy if it is considered that the potential benefit outweighs any possible risk to the foetus.

Breastfeeding

While it is not known whether Rabix-vc enters breast milk, no risk to the breast-feeding infant has been identified. Rabipur may be administered to breastfeeding women when post-exposure prophylaxis is required.

The vaccine may also be used for pre-exposure prophylaxis in breastfeeding women if it is considered that the potential benefit outweighs any possible risk to the infant.

Fertility

Non clinical reproductive and developmental toxicity studies have not been performed.

4.7 Effects on ability to drive and use

Some of the adverse effects described in section 4.8, may affect the ability to drive and use machines.

4.8 Undesirable effects

Minor local reactions like pain, erythema, edema, pruritus and indurations at the injection site and lasting to 24-48 hours. Moderate fever, shivering, fainting, asthenia, dizziness, respiratory manifestations (dyspnoea, wheezing), fever, abdominal pain, vomiting and allergic skin reactions (urticaria, rash, itching).

4.9 Overdose

Not applicable

5.Pharmacological properties

5.1 Pharmacodynamic properties

5.1.1. Pharmacotherapeutic group

Rabies vaccine

5.1.2.Mechanism of action

Rabix-vc induces stimulation of lymphocytes and antibody-secreting plasmocytes resulting in production of RVNAs.

5.2 Pharmacokinetic properties

Not applicable

5.3 Preclinical safety data

Preclinical data including single-dose, repeated dose and local tolerance studies revealed no unexpected findings and no target organ toxicity. No genotoxicity, carcinogenicity and reproductive toxicity studies have been performed.

6. Pharmaceutical particulars

6.1 List of excipients

Human Serum Albumin

Dextran 40

Sodium Dihydrogen Phosphate

Disodium Hydrogen Phosphate Dodecahydrate

Sodium Chloride

Water for Injection

6.2 Incompatibilities

In the absence of compatibility studies, Rabix-vc must not be mixed in the same syringe with other medicinal products.

6.3 Shelf life

3 years from the date of manufacturer when stored at 2 – 8 °C.

6.5 Special precautions for storage

- Keep out of the reach and sight of children
- Store at + 2°C and + 8°C. Transportation should also be at 2°C and + 8°C
- Protect from light
- Do not freeze

6.5 Nature and contents of container

Each box contains 1 vial lyophilized preparation of Rabies Vaccine (Human) BP, 1ampoule containing 1ml WFI and a sterile disposable syringe.

6.6 Special precautions for disposal and other handling

- Intravenous injection is prohibited.
- The vaccine and anti-rabies immunoglobulin must not be administered with same syringe and in the same injection site.
- Before use, please carefully check package, label, appearance and the validity period.
- After reconstitution, the freeze- dried rabies vaccine should be administered as soon as possible.
- Don't shake during and after reconstitution.

7. Marketing authorization holder

Incepta Vaccine Ltd. Dhaka, Bangladesh

8. Drug authorization number(s)

363-09-069

9. Date of first authorization/Renewal of the authorization

11 February, 2011

10. Date of revision of the text

May, 2021