Registration No.: 1C 18/53(B)

Importer/Manufacturer: BioNet-Asia Co., Ltd / Bharat Biotech International Limited

SUMMARY OF PRODUCT CHARACTERISTICS

1. NAME OF THE MEDICAL PRODUCT
   INDIRAB™

2. QUALITATIVE AND QUANTITATIVE COMPOSITION
   One vial of Lyophilized Vaccine contains:
   Purified β Propiolactone Inactivated Rabies Virus 2.5 I.U*.
   (Prepared on Vero cells; Pitman-Moore strain of Rabies virus) of one immunizing dose.
   Thiomersal as preservative ........................................ 0.01%
   Maltose ................................................................. up to 1 immunizing dose
   Human Serum Albumin ............................................. up to 1 immunizing dose
   Such that the protective power is greater than or equal to 2.5 I.U before and after heating at +37°C for
   4 weeks.
   Diluent: 0.3% w/v Sodium Chloride for Solution ........... 0.5 ml.
   The 0.5 ml presentation is suitable for all WHO recommended Intramuscular / Intradermal pre-exposure & post-
   exposure vaccination schedule.

3. PHARMACEUTICAL FORM
   Lyophilized powder for injection along with diluent ampoule.

4. CLINICAL PARTICULARS
   4.1 Therapeutic indications
   Pre-Exposure prophylaxis:
   This vaccination is specially recommended for high risk professionals e.g. veterinarians, animal care
   personnel, hunters, doctors, rabies laboratory personnel, production personnel, army personnel,
   postmen and children who are exposed to the risk of rabies.
   Post-Exposure prophylaxis:
   Treatment of subjects bitten by suspicious/ rabid animals.

   4.2 Posology and Method of Administration:
   4.2.1 Posology:
   Dose for Children and Adult is 0.5 ml for Intramuscular route.
   Dose for Children and Adult is 0.1 ml per site for Intradermal route.
   The vaccination schedule should be adapted according to the category of exposure and the subject’s
   rabies immune status.
   Pre-exposure Vaccination by Intramuscular/Intradermal route:
   This vaccine is recommended for the prevention of rabies in subjects at a high risk of exposure.
   All subjects at a permanent risk, such as diagnostic, research and production laboratory staff
   working on rabies virus, should be vaccinated (Table - 1).
Table-1: Schedule (Intramuscular/Intradermal Administration)

<table>
<thead>
<tr>
<th></th>
<th>Intramuscular</th>
<th>Intradermal</th>
</tr>
</thead>
<tbody>
<tr>
<td>1st dose</td>
<td>Zero day</td>
<td></td>
</tr>
<tr>
<td>2nd dose</td>
<td>Day 7</td>
<td></td>
</tr>
<tr>
<td>3rd dose</td>
<td>Day 28</td>
<td></td>
</tr>
<tr>
<td>1st Booster Dose</td>
<td>1 year later</td>
<td></td>
</tr>
<tr>
<td>Booster dose</td>
<td>Every 5 years</td>
<td></td>
</tr>
</tbody>
</table>

**Post Exposure Vaccination by Intramuscular/Intradermal injection:**
After confirmed or suspected exposure, vaccination must be started immediately.
The treatment is instituted according to the type of wound/exposure and the status of the animal.

**First aid treatment:**
The treatment of wounds is very important and must be performed promptly after the bite. It is recommended first to wash the wound with large quantities of water and soap or detergent and then apply 70% alcohol/ tincture of iodine.

Post exposure vaccination must be administered under medical supervision (Table-2).

Table-2: Schedule (Intramuscular/Intradermal Administration)

<table>
<thead>
<tr>
<th>Route of Administration</th>
<th>Intramuscular</th>
<th>Intradermal</th>
</tr>
</thead>
<tbody>
<tr>
<td>1st dose</td>
<td>Zero day</td>
<td>Zero day</td>
</tr>
<tr>
<td>2nd dose</td>
<td>Day 3</td>
<td>Day 3</td>
</tr>
<tr>
<td>3rd dose</td>
<td>Day 7</td>
<td>Day 7</td>
</tr>
<tr>
<td>4th dose</td>
<td>Day 14</td>
<td>Day 28</td>
</tr>
<tr>
<td>5th dose</td>
<td>Day 28</td>
<td>-</td>
</tr>
</tbody>
</table>

Table 3: Guide for Post Exposure Treatment (WHO) Vaccination of non-immunized subjects against rabies:

The schedule includes 0.5 ml injections on D0, D3, D7, D14 and D28 with Intramuscular or 0.1 ml injections on D0, D3, D7 and D28 with Intradermal administration Table category II & III.

In the case of category III exposure (see Table-3), rabies immunoglobulin / Rabies immuneserum must be administered in association with the vaccine.

<table>
<thead>
<tr>
<th>Category</th>
<th>Type of contact with a suspect rabid domestic or wild animal or animal unavailable for observation</th>
<th>Recommended Treatment</th>
</tr>
</thead>
<tbody>
<tr>
<td>I</td>
<td>Touching or feeding of animal, licks on intact skin, contact with animal but definitely not with its saliva</td>
<td>None; if reliable case history is available. In case of doubts vaccinate on D0, D7 and D28 by Intramuscular or Intradermal route.</td>
</tr>
</tbody>
</table>
Additional passive immunization on day 0 is required with:

Human rabies immunoglobulin (HRI) 20 I.U./Kg of body weight or equine rabies immunoglobulin 40 I.U./kg of body weight. The vaccine should be injected on one side and the immunoglobulin administration on the other side. In enzootic areas, the severity of certain exposures due to the severity of the lesions and/or location (proximity of the central nervous system), a late consultation or immunodeficiency of the subject may justify, depending on the case 2 injections on Day Zero.

Vaccination of subjects already immunized against Rabies:

If vaccine administered in less than 6 months of exposure (cell culture rabies vaccine): Then 1 injection on D0 is recommended.

If vaccine administered in more than 6 months of exposure (cell culture rabies vaccine): Then 2 injections on D0, D3 are recommended.

Post Exposure vaccination by Intradermal route: Two schedules are recommended by WHO

a) Modified TRC-ID regimen (“2-2-0-2-2” regimen):

The schedule for the updated Thai Red Cross intradermal regimen is as follows: One dose of vaccine, in a volume of 0.1 mL is given intradermally at two different lymphatic drainage sites, usually the left and right upper arm on days 0, 3, 7, and 28.

b) TRC-ID regimen (“2-2-0-1-1”):

The schedule for the Original Thai Red Cross regimen is as follows: One dose of vaccine, in a volume of 0.1 mL is given intradermally at two different lymphatic drainage sites, usually the right and left upper arm on days 0, 3, 7 and one site in upper arm day, 28 and 90. Using aseptic technique, reconstitute the vial of freeze-dried vaccine with the diluents supplied by the manufacturer. With 1 ml syringe with hypodermic needle (insulin syringe) draw 0.2 ml (upto 20
units if a 100 units syringe is used or 8 units if a 40 units syringe is used) of vaccine needed for one patient (i.e 0.1mL per ID site x 2 sites) for intradermal administration using the above mentioned regimens.

The potency as well as immunogenicity and safety based on clinical trial allow safe use of this vaccine by intradermal route.

* WHO guide for post exposure prophylaxis (TRS 931, 2005).

** WHO/EMC/ZOO/96.6 WHO recommendations on rabies post-exposure treatment and correct technique of intradermal immunization against rabies.

4.2.2 Mode and Route of Administration:

Reconstitute the vaccine with 0.5 ml of diluents supplied in ampoule, into the lyophilized vial and shake gently thoroughly until the powder is completely dissolved. The solution should be homogenous, clear and free from particles. Withdraw required quantity of the solution in a syringe.

The vaccine must be injected immediately after reconstitution and the syringe must be destroyed after use. The reconstituted vaccine can be administered intradermal as per schedule below.

<table>
<thead>
<tr>
<th>Modified TRC-ID regimen *</th>
<th>TRC-ID regimen **</th>
</tr>
</thead>
<tbody>
<tr>
<td>Day 0 3 7 28</td>
<td>Day 0 3 7 28 90</td>
</tr>
<tr>
<td>ID Sites X2 X2 X2 X2</td>
<td>ID Sites X2 X2 X2 X1 X1</td>
</tr>
</tbody>
</table>

Rabies immunoglobulin

**Intramuscular route:** The 0.5 ml dose of vaccine is administered by intramuscularly in the deltoid in adults and in the antero-lateral region of the thigh in young children. Do not inject in the gluteal region.

**Intradermal route:** The 0.1 ml dose of vaccine is administered intradermally in each upper arm (over the left & right deltoids). Vaccine administered intradermally must raise a visible and palpable “bleb” in the skin. In the event that a dose of vaccine is inadvertently given subcutaneously or intramuscularly, a new dose should be administered intradermally immediately in the near by site.

4.3 Contraindications:

This vaccine must not be used in the following cases:

**Pre-exposure:**
- It is preferable to postpone vaccination in severe febrile infection, acute disease, progressive chronic disease.
- Known hypersensitivity to any of the ingredients of the vaccine.

**Post-exposure:**
- Due to the fatal progression of declared rabies infection, there are absolutely no contraindications to curative anti-rabies vaccination.
4.4 Special warnings and Precautions for use:
- Intradermal injections must be administered by staff trained in this technique. Vaccine vials should be stored between 2°C to 8°C after reconstitution and the total content should be used as soon as possible, but at least within 8 hours.
- Do not inject by the intravascular route, make sure that the needle does not enter a blood vessel. Immunoglobulin and rabies vaccine must not be associated in the same syringe or injected at the same site. Keep out of the reach of children.

4.5 Interaction with other medicinal products and other forms of interaction:
Corticosteroids and immunosuppressive treatment may interfere with antibody production and cause vaccine failure. In order to avoid possible interactions between several medicinal products any other ongoing treatment should be systematically reported to your doctor. If any contraindications exist the risk of prophylactic vaccination should be weighed against those of a possible infection and if necessary, the vaccination should be carried out taking appropriate precautions.

4.6 Pregnancy and lactation:
Adequate human data on use during pregnancy or lactation and adequate animal reproductive studies are not available. It is recommended to postpone pre-exposure prophylaxis. In post-exposure vaccination as rabies is a dreaded disease, pregnancy is not a contraindication. For the vaccination of subjects at a high risk of contamination, the benefit/risk ratio must be assessed before administering the injection. During pregnancy and lactation, it is recommended to ask your doctor for advice using the vaccine.

Additional information:
Wound should not be sutured for 7 days but any case, RIG should always be administered before suturing. Antibiotics can be prescribed and the tetanus vaccination status should be checked and if needed institute antitetanus procedures. In case of severe bites (Category III) half of the calculated dose of rabies immunoglobulin should be infiltrated deep into the wound and around the wound. Sensitivity to heterologous (equine) immunoglobulin must be determined before it is administered. Rabies immunoglobulin should not be administered more than once or at higher doses than the recommended dose since there is a risk that this may interfere with antibody induction after vaccination.

4.7 Effect on ability to drive and use machines:
Not Applicable.

4.8 Undesirable Effects:
- Minor local reactions: pain, erythema, oedema, pruritus and induration at the injection point.
- Systemic reactions: moderate fever, shivering, fainting, asthenia, headaches, dizziness, arthralgia, myalgia, gastro-intestinal disorders (nausea, abdominal pains).
- Exceptional cases of anaphylactic reactions are observed.
Report to your doctor any unwanted and disturbing effects which might not be mentioned in this leaflet.

4.9 Over dose:
Not Applicable.
5. PHARMACOLOGICAL PROPERTIES

5.1 Pharmacodynamic Properties
   Not applicable

5.2 Pharmacokinetic Properties
   Not applicable

5.3 Preclinical Safety Data
   Not applicable

6. PHARMACEUTICAL PRATICULARS

6.1 List of excipients
   Thiomersal, Maltose, Human Serum Albumin and buffer solution containing Disodium Hydrogen Orthophosphate, Sodium Dihydrogen Orthophosphate, Sodium Chloride and water for injection.

6.2 Incompatabilities:
   This medicinal product should not be mixed with other medicinal products.

6.3 Shelf life:
   2 years from the date of manufacture.

6.4 Special precautions for storage:
   Do not use the vaccine after expiry date. Vaccine vials should be stored between 2°C to 8°C after reconstitution and the total content should be used within 8 hours. Do not Freeze. Keep out of the reach of children.

6.5 Nature and contents of container:
   Mono pack contains one vial of lyophilized vaccine, diluent and disposable syringe with needle. Multi pack contains ten vials of lyophilized vaccine and ten ampoules of diluent. Separate syringes and needles to be used for IM/ID use.

6.6 Special precautions for disposal and other handling:
   N/A

7. MARKETING AUTHORIZATION HOLDER
   BioNet - Asia Co.,Ltd. Bangkok, THAILAND

8. MARKETING AUTHORIZATION NUMBER(S)
   1C 18/53(B)

9. DATE OF FIRST AUTHORIZATION/RENEWAL OF THE AUTHORISATION
   August 31, 2010

10. DATE OF REVISION OF THE TEXT
    May 9, 2018