PRODUCT INFORMATION

NAME OF THE MEDICINE

MERIEUX INACTIVATED RABIES VACCINE (MIRV)

Inactivated Rabies Vaccine

DESCRIPTION

MIRV is lyophilised, stabilised suspension of inactivated Wistar rabies virus strain PM/W1381503-3M. It is cultured on human diploid cells and inactivated by ß-propiolactone. These human diploid cells are a cell line derived from human embryonic lung tissue in the 1960s.

The powder is pinkish beige to orangey yellow. After reconstitution with the diluent supplied it turns a pinkish colour due to the presence of phenol red.

The potency of the reconstituted vaccine is not less than 2.5 IU, the WHO International Standard per dose (1 mL). Each vial contains, in addition, between 100 and 150 microgram of neomycin and up to 70 mg of human serum albumin.

The manufacture of this product includes exposure to bovine materials. No evidence exists that any case of vCJD (considered to be the human form of bovine spongiform encephalopathy) has resulted from the administration of any vaccine product.

PHARMACOLOGY

Following a single deep subcutaneous injection, an antibody response can be detected after a variable period of up to 7 days, in all subjects. Peak antibody levels are reached at about 30 days and then start to decline.

INDICATIONS

Pre-exposure immunisation in persons at special risk of contracting rabies. Post exposure immunisation against rabies.

CONTRAINDICATIONS

Pre-Exposure

Known systemic hypersensitivity reaction to any component of MIRV or after previous administration of the vaccine or a vaccine containing the same components.

Vaccination must be postponed in case of febrile or acute disease.

Post-Exposure

Since rabies infection generally results in death, there are no contraindications to post-exposure vaccination.

PRECAUTIONS

Do not administer intravenously or intradermally.

As with all injectable vaccines, appropriate medical treatment and supervision should always be readily available in case of an anaphylactic event following administration of the vaccine.

As with any vaccine, vaccination with MIRV may not protect 100% of vaccinated individuals.

The full course of immunisation should be completed in order to obtain sustained antibody response.

As each dose may contain undetectable traces of neomycin which is used during vaccine production, caution must be exercised when the vaccine is administered to individuals with hypersensitivity to this antibiotic and other antibiotics of the same class.

Immunocompromised individuals

In individuals with congenital or acquired immunodeficiency, the immune response to the vaccine may be inadequate.

Therefore, it is recommended to monitor serological antibody level in such individuals to ensure that an acceptable response has been induced. Additional doses should be given as necessary.

Moreover, if post-exposure vaccination is needed, rabies immunoglobulin should be given in association with the vaccine for both categories II& III exposures.

Bleeding Disorders

Because intramuscular injection can cause injection site haematoma, MIRV should not be given to individuals with any bleeding disorder, such as haemophilia or thrombocytopaenia, or to individuals on anticoagulant therapy unless the potential benefits clearly outweighs the risk of administration. If the decision is made to administer MIRV in such individuals, it should be given with caution, with steps taken to avoid the risk of haematoma formation following injection.

Use in pregnancy - Category B2

Pre-exposure

The vaccine has not been studied in animal teratogenicity studies. Data on the use of this vaccine in pregnant women are limited. Therefore, the administration of the vaccine during pregnancy is not recommended.

For the vaccination of individuals at a high risk of exposure, the risk/benefit ratio must be assessed before administering the vaccine.

Post-exposure

Due to the severity of the disease, pregnancy is not a contraindication.

Use in Lactation

It is not known whether MIRV is excreted in human milk. Therefore, caution must be exercised when the vaccine is administered to a nursing woman.

Paediatric use

MIRV is indicated for use in paediatric population.

Use in the elderly

MIRV is indicated for use in elderly.

Genotoxicity

MIRV has not been evaluated for genotoxic potential.

Carcinogenicity

MIRV has not been evaluated for carcinogenic potential.

Effect on laboratory tests

Interference of MIRV with laboratory and/or diagnostic tests has not been studied.

INTERACTIONS WITH OTHER MEDICINES

Corticosteroids and immunosuppressive treatments may interfere with antibody production and cause the failure of the vaccination. It is therefore advisable to perform a neutralizing antibody assay 2 to 4 weeks after the last injection.

When immunoglobulins against rabies are to be administered with rabies vaccine (see Dosage and Administration), they must not be combined in the same syringe or injected at the same site. If possible, the vaccine should be injected contra-laterally to the immunoglobulin administration sites.

ADVERSE EFFECTS

Adverse event information is derived from clinical trials and worldwide post-marketing experience.

Data from Clinical Studies

Two studies where MIRV has been studied in randomised controlled trials in both children (N=199) using pre-exposure schedule (3 doses, IM) and adults (n=124) using the post exposure schedule (5 doses, IM) have been selected to represent safety clinical data.

Blood and lymphatic system disorders

- Very common: adenopathy

Immune system disorders

- Common: allergic reactions with skin disorders such as urticaria and rash, or respiratory manifestations such as dyspnoea and wheezing
- Uncommon: angioedema

Nervous system disorders

- Very common: headache
- Common: dizziness

Gastrointestinal disorders

- Very common: nausea
- Common: abdominal pain, vomiting, diarrhoea

Musculoskeletal and connective tissue disorders

- Very common: myalgia

- Common: arthralgia

General disorders and administration site conditions

- Very common: injection site pain, erythema, and induration (swelling/hardness) hematoma, malaise

- Common: injection site pruritus (itching) fever, chills (shivering)

Data from Post-Marketing Experience

In addition, the following adverse events have been reported very rarely (<1/100000) during the post marketing surveillance of MIRV. Based on spontaneous reporting, their frequencies have been estimated using number of reports and estimated number of patients. However, exact incidence cannot be precisely calculated.

Immune system disorders

- Anaphylactic reactions

- Serum sickness type reactions

These reactions have been associated with the presence of betapropiolactone-altered human albumin in the Human Diploid Cell Vaccine (HDCV).

Nervous system disorders

- Paraesthesia

- Neuropathy

- Convulsion, encephalitis

General disorders and administration site conditions

- Asthenia

DOSAGE AND ADMINISTRATION

One dose consists of 1 mL of vaccine administered by the intramuscular route, in the deltoid area for adults and children or the anterolateral area of the thigh muscle in infants and toddlers.

The vaccination schedule should be adapted in accordance with the circumstances of the exposure and the individual's rabies immune status. For further information, refer to the current Immunisation Handbook.

Product is for single use in one patient on one occasion only. Discard any residue.

Pre-Exposure Vaccination

- Primary vaccination: 3 injections at day 0, day 7, and day 21 or day 28 (as per WHO recommendations)

Regular serology testing of neutralising antibodies is recommended to assess seroconversion of individuals at increased risk of exposure to rabies virus, with a frequency adapted to that risk. When antibody titre is below acceptable level, a booster dose is needed. For further information on booster dose recommendations, refer to the current Immunisation Handbook.

According to the Immunisation Handbook, WHO current recommendations state that booster doses are not required for persons who are travelling to, or living in, an area of high rabies risk and who have completed a primary course, either pre- or post-exposure, using currently available cell culture derived vaccine.

Post-Exposure Treatment

Post-exposure treatment consists of local treatment of the wound, initiated as soon as possible after an exposure, followed by the administration of the vaccine and of passive immunisation, if indicated.

Immunisation

The vaccination must be administered under medical supervision and should be started as soon as possible after exposure.

The treatment must be adapted according to the type of contact and the immunisation status of the subject. For further information, refer to the current Immunisation Handbook.

Vaccination of Non-Immunised Individuals

Administration of immunoglobulin

In the case of severe types of exposure, rabies immunoglobulin should be given in association with the vaccine for non-immunised individuals:

On day 0, a complementary passive immunisation is required using:

- Human rabies immunoglobulin (HRIG) 20 IU/kg body weight

As much as possible should be infiltrated around the wounds. The remainder should be administered by deep intramuscular injection at a site distant from the vaccine injection site. If possible, the vaccine should be injected contra-laterally to the immunoglobulin administration sites.

Administration of vaccine

Vaccine should be administered on day 0, day 3, day 7 and day 14 (4 injections of 1 mL). The posology is the same for adults and children.

Vaccination of Previously Immunised Individuals (full preventative vaccination confirmed)

In this case, administration of immunoglobulin is not required. Two injections of vaccine should be administered at day 0 and day 3.

This schedule should not apply to immunocompromised individuals.

In both previously-immunised and non-immunised individuals, consideration should also be given to the possibility of tetanus and other wound infections, and appropriate measures taken as per the Current Immunisation Handbook.

Preparation

Reconstitution of vaccine:

Reconstitute the freeze-dried vaccine by introducing the diluent in the pre-filled syringe into the vial of powder. Shake carefully until complete suspension of the powder is obtained. Withdraw the suspension from the vial into a separate syringe, and administer via intramuscular injection with an appropriate needle for each individual.

Once reconstituted, the vaccine must be used immediately.

After use, any remaining vaccine and container must be disposed of safely, preferably by heat inactivation or incineration, according to locally agreed procedures.

OVERDOSAGE

Not documented.

PRESENTATION AND STORAGE CONDITIONS

Vial (powder for reconstitution), 1 mL solvent (distilled water): 1's.

Store refrigerated (2° to 8°C). Do not freeze. Use immediately after reconstituting the vaccine.

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POISON SCHEDULE OF THE MEDICINE

S4 – Prescription Only Medicine

DATE OF FIRST INCLUSION IN THE AUSTRALIAN REGISTER OF THERAPEUTIC GOODS (ARTG)

21 October 1991

DATE OF MOST RECENT AMENDMENT

24 August 2017