MÉRIEUX INACTIVATED RABIES VACCINE

PREPARED ON HUMAN DIPLOID CELLS
WISTAR RABIES PM/WI 38-1503-3M STRAIN

For pre or post-exposure immunization

COMPOSITION

For one immunizing dose:

• Powder: – Freeze-dried rabies vaccine (WISTAR RABIES PM/WI 38-1503-3M strain rabies virus, obtained from culture on human diploid cells, inactivated with beta-propiolactone) ..... 1 immunizing dose*
• Diluent: – Water for injections ..... 1 ml

* Such that the activity is equal to or greater than 2.5 I.U. before and after heating for one month at 37°C.

PHARMACEUTICAL DOSAGE FORM

Powder and diluent for suspension for injection.

MARKETING AUTHORIZATION HOLDER

Aventis Pasteur SA
2, avenue Pont Pasteur, F-69007 Lyon

INDICATIONS

This medicinal product is a vaccine.

Pre-exposure

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. A serological test is recommended every 6 months. A booster injection should be administered when the antibody titre is below the level considered to guarantee protection: 0.5 I.U./ml.
The following categories should be vaccinated given the frequency of exposure to the risk:
– veterinarians (and assistants), gamekeepers, hunters, forest rangers, slaughterhouse personnel, cavers, taxidermists,
– subjects exposed enzootic areas: children, adults and travellers visiting these areas.

Post-exposure

After confirmed or suspected exposure, vaccination must be started immediately at the slightest risk of contamination with rabies. It must be performed in a rabies treatment centre.
The treatment is adapted to the type of wound and the status of the animal.

Table 1

Circumstances	Course of action		Remarks
	For the animal	For the patient	
Animal unavailable			
Suspect or non-suspect circumstances		Treatment by the rabies treatment centre.	The treatment** must always be completed.
Dead animal			
Suspect or non-suspect circumstances	Send the brain to an approved laboratory for analysis.	Treatment by the rabies treatment centre.	Stop the treatment** if the analyses are negative, otherwise, continue.
Live animal			
Non-suspect circumstances	Place under veterinary supervision*.	Decision to postpone rabies treatment.	Continue the treatment** according to the veterinary supervision of the animal.
Suspect circumstances	Place under veterinary supervision*.	Treatment by the rabies treatment centre.	Stop the treatment** if the supervision invalidates the initial doubts, otherwise, continue.

* In France, veterinary supervision includes 3 certificates issued on D0, D7 and D14 certifying the absence of signs of rabies. According to W.H.O. recommendations, the minimum veterinary supervision observation period is 10 days for dogs and cats.
** The treatment is recommended according to the severity of the wound: see table 2.

Table 2

Severity	Type of contact	Recommended treatment
I	Touching or feeding of animals. Licks on intact skin.	None, if reliable case history is available.
II	Nibbling of uncovered skin. Minor scratches or abrasions without bleeding. Licks on broken skin.	Administer vaccine immediately.
III	Single or multiple transdermal bites or scratches. Contamination of mucous membrane with saliva (i.e. licks).	Administer immunoglobulins and rabies vaccine immediately.

CONTRAINDICATIONS

This medicinal product MUST NOT BE USED in the following cases:

Pre-exposure

– severe febrile infection, acute disease, progressive chronic disease (it is preferable to postpone vaccination),
– known hypersensitivity to any of the ingredients of the vaccine.

Post-exposure

Due to the fatal progression of declared rabies infection, there are no contraindications to curative vaccination.

Pregnancy: see PREGNANCY - BREAST FEEDING section.

If there is any doubt, it is essential to consult your doctor or your pharmacist.

SPECIAL WARNINGS

Use with caution on subjects with a known allergy to neomycin (present in trace form in the vaccine).
Do not inject by the intravascular route: make sure that the needle does not enter a blood vessel.
Immunoglobulins and rabies vaccine must not be associated in the same syringe or injected at the same site.
A serological test (neutralizing antibody assay using the RFFIT [Rapid Fluorescent Focus Inhibition Test] test) must be conducted on persons subject to continuous exposure (every 6 months) and may be conducted every 2 to 3 years after the booster dose after 1 and 5 years in persons subject to discontinuous exposure according to the assessed exposure risk.
For immunodeficient subjects, this test may be conducted 2 to 4 weeks following the vaccination.
If the result of the test demonstrates an antibody titre < 0.5 I.U./ml, a booster injection or an additional injection, for immunodeficient subjects, is justified.
This vaccine must never be administered by the intravascular route.

PRECAUTIONS FOR USE

Inform your doctor in the event of known allergy to neomycin, due to the use of these substances during production.

If there is any doubt, do not hesitate to consult your doctor or your pharmacist.

Keep out of the reach of children.

DRUG INTERACTIONS AND OTHER INTERACTIONS

Corticosteroids and immunosuppressor treatments may interfere with antibody production and cause the vaccination to fail. Therefore, it is preferable to conduct a neutralizing antibody assay 2 to 4 weeks after the last injection of vaccine.

In order to avoid possible interactions between several medicinal products, any other ongoing treatment should be systematically reported to your doctor or to your pharmacist.

PREGNANCY - BREAST FEEDING

The vaccine has not been the subject of animal teratogenicity studies.
In the absence of sufficient human data, it is recommended to postpone pre-exposure vaccination.
For the vaccination of subjects at a high risk of contamination, the benefit/risk ratio must be assessed before administering the injection.
In post-exposure vaccination, due to the severity of the disease, pregnancy is not a contraindication.
As a general rule, during pregnancy and breast feeding, it is always recommended to ask your doctor's or pharmacist's advice before using a medicinal product.

DOSAGE

The vaccination schedule should be adapted according to the circumstances of the vaccination and the subject's rabies immune status.

Preventive or pre-exposure vaccination

– primary vaccination: 3 injections on D0, D7, D28,
– booster injection 1 year later,
– booster injections every 5 years.
The injection scheduled on D28 may be administered on D21.

"Curative" vaccination (prevention of rabies after confirmed or suspected exposure)

First aid treatment
The treatment of wounds is very important and must be performed promptly after the bite. It is recommended firstly to wash the wound with large quantities of water and soap or detergent and then apply 70° alcohol, tincture of iodine or a 0.1 per cent quaternary ammonium solution (provided that no soap remains as these two products neutralize each other).
Curative vaccination must be administered under medical supervision and only in a rabies treatment centre.

Vaccination of non-immunized subjects

The dosage is the same for adults and for children: it includes 5 x 1 ml injections on D0, D3, D7, D14 and D28.
In the case of category III exposure (see INDICATIONS - Table 2), rabies immunoglobulins must be administered in association with the vaccine. Additional passive immunization on day 0 is required with:
– human rabies immunoglobulin (HRI) ..... 20 I.U./kg of body weight
– equine rabies immunoglobulin ..... 40 I.U./kg of body weight
If possible, the vaccine should be injected on the side opposite the immunoglobulin administration sites.
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 D0.

Vaccination of subjects already immunized

Vaccination administered less than 5 years previously (cell culture rabies vaccine): 2 injections: D0, D3.
Vaccination administered over 5 years previously or incomplete: 5 injections: D0, D3, D7, D14 and D28 with administration of immunoglobulins if required.
In practice, if the last booster dose was administered over 5 years previously or if the vaccination is incomplete, the subject is considered to have an uncertain vaccination status.

MODE AND ROUTE OF ADMINISTRATION

To reconstitute the vaccine, introduce the diluent into the vial of powder and shake thoroughly until the powder is completely suspended. The solution should be homogenous, clear and free of any particles. Withdraw the solution in a syringe.
The vaccine must be injected immediately after reconstitution and the syringe must be destroyed after use.
The vaccine is administered by the intramuscular route only in the deltoid in adults and in the antero-lateral region of the thigh muscle in children. Do not inject in the gluteal region.

SIDE EFFECTS

Like any active product, this medicinal product may in certain persons cause effects which are disturbing to a greater or lesser extent:
– Minor local reactions: pain, erythema, oedema, pruritus and induration at the injection point.
– Systemic reactions: moderate fever, shivering, faintness, asthenia, headaches, dizziness, paraesthesia, arthralgia, myalgia, gastro-intestinal disorders (nausea, abdominal pains), allergic skin reactions (urticaria, rash, pruritus, oedema).
– In particular, after readministration, possibility of immediate (24 hours) or delayed (1-2 weeks) hypersensitivity reaction, which may be similar to serum sickness and include rash, urticaria, dyspnea, Quincke's oedema and arthralgia. This signs are generally benign and diminish in 2- 4 days.
– Exceptional cases of neuropathy have been reported. A causal relationship with the vaccine has not been established.

Report to your doctor or to your pharmacist any unwanted and disturbing effects which might not be mentioned in this leaflet.

STORAGE

Do not exceed the expiry date stated on the external packaging.

SPECIAL PRECAUTIONS OF STORAGE

Keep between + 2°C and + 8°C (in a refrigerator).

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