

**ROUVAX**  
LIVE HYPERATTENUATED VIRUS VACCINE  
AGAINST MEASLES (SCHWARZ STRAIN)

**COMPOSITION**

Each vaccine dose contains:

Lyophilizate:

- Hyperattenuated live measles virus  
SCHWARZ strain . . . . . at least 1000 CCID<sub>50</sub>\*
- Human albumin . . . . . q.s. for lyophilization

Solvent:

- Water for injections . . . . . q.s. 0.5 ml

\*CCID<sub>50</sub> = Cell culture infectious dose 50 percent.

This vaccine contains traces of neomycin.

This vaccine also contains lactose.

This vaccine is in conformity with WHO specifications.

**PHARMACEUTICAL DOSAGE FORM**

Suspension for injection, obtained by reconstitution of the lyophilizate with the solvent.

Lyophilizate: 1 dose or 10 dose vial

Solvent: 1 dose ampoule or syringe (0.5 ml)  
10 dose vial (5 ml)

**MARKETING AUTHORIZATION HOLDER**

PASTEUR M'RIEUX S'rums et Vaccins  
58 avenue Leclerc, 69007 LYON - FRANCE

**INDICATIONS**

The attenuated live measles vaccine is recommended for the vaccination of any child susceptible to measles infection.

**Indicated Age**

Administration of the measles vaccine is recommended from 12 months of age.

**Vaccination Program**

It is usually recommended as a combined vaccine (Measles, Mumps, Rubella - MMR).

Vaccination against measles is particularly important for children living in a community, and for children at risk (malnutrition, chronic, cardiac and pulmonary diseases).

Note:

1. Even children, who have a past history of measles, but without laboratory confirmation, will be immunized with the vaccine.
2. Children, who were vaccinated against measles before reaching one year of age (for instance, during an outbreak), will be reimmunized with the measles vaccine after reaching 12 months of age.

At 6 years of age (first grade), the MMR booster will be given together with the OPV booster.

**Supplementary Measles Vaccine**

In the supplementary measles vaccine program, for children who did not receive the vaccine, children who have a past history of the measles infection without serological confirmation will be included.

Considered "Immunized Against Measles"

- A child in the 6-17 year age group who received two doses of the vaccine against measles (or MMR), from 12 months of age and up, with a space of at least one-month between doses.

Note: Children between the ages of 1-5 years are considered immune if they received one dose of the vaccine within the routine vaccine program.

- Whoever has in his possession laboratory confirmation of an antibody titer which immunizes against measles (titer of HI antibodies against measles whose level is 1:4 or more).

**CONTRAINDICATIONS**

- Those of all vaccinations in general: the attending physician remains the only judge of the appropriateness of vaccination.
- Sudden illness with high fever – defer the vaccine until recovery. Nevertheless, a mild illness without fever or with a low fever (under 38°C), such as mild upper respiratory infection, otitis media or mild diarrhea, are not reasons to defer the vaccine.
- Severe reaction to a previous dose, such as anaphylactic reaction.
- Knowledge of immediate sensitivity - of the anaphylactic type – to ingredients of the vaccine, such as to egg protein or to gelatin or to the antibiotic included in the preparation, according to the information in the patient's leaflet (such as neomycin). These cases are extremely rare.

Note: Cases of delayed sensitivity of the non-anaphylactic type to eggs, or contact dermatitis to neomycin, are not contraindications to the preparation.

- Severe immune deficiency

Primary (such as agammaglobulinemia, hypogammaglobulinemias, combined immunodeficiency, etc).

Malignant diseases such as leukemia, lymphoma, carcinomatosis.

During the remission period of these diseases, the administration of the measles vaccine (or MMR) can be considered not earlier than 3 months after cessation of treatment with immunosuppressants.

Immunosuppressant therapy, such as radiation, cytotoxic drugs, antimetabolites, steroids.

The measles vaccine (or MMR) may be administered 3 months after cessation or end of treatment, with the condition that there is a remission in the fundamental disease.

Individuals with a family history of congenital or hereditary immunodeficiency, until the immune competence of the potential vaccine recipient is demonstrated.

- HIV infection

1. HIV-positive without clinical symptoms:

The measles vaccine (or MMR) may be administered in cases of HIV-positive carriers without clinical symptoms. However, the vaccinees should be monitored closely for vaccine-preventable diseases because immunization may be less effective than for uninfected persons.

2. HIV-positive patients with clinical symptoms – AIDS:

If there are no signs of severe immune deficiency, it is usually recommended to give the measles vaccine (or MMR) to those vulnerable to measles (according to serologic tests); this is because in these cases the measles infection can be severe.

It is not recommended to give the measles vaccine (or MMR) to symptomatic HIV-positive carriers with severe immune deficiency for fear of serious complications.

Severe immune deficiency is defined as:

CD4+ T-lymphocyte count less than 750 for patients under the age of 12 months, less than 500 for ages 1-5 years and less than 200 for the age of 6 years and above.

- Special case of children born to seropositive HIV mothers:

The obligatory passage of maternal antibodies of the IgG type through the placenta makes it impossible to interpret the serology of the child up to about 9-10 months (persistence of maternal antibodies has been detected up to 14 months). It is therefore necessary to wait until the child becomes seronegative as determined by immunotransfer (Western blot) with the support, if necessary, of techniques for detecting the viral genome, before it is possible to confirm that the child is not infected.

1. If the child is not infected: the vaccination timetable can be applied normally.

2. If the child is infected: it is imperative to seek the opinion of a paediatric team.

- Active untreated tuberculosis.

- Recent injection of immunoglobulins.

- Do not give to pregnant females; the possible effects of the vaccine on fetal development are unknown at this time. If vaccination of postpubertal females is undertaken, pregnancy should be avoided for three months following vaccination. However, vaccination against measles carried out during pregnancy does not justify recommending termination of pregnancy (see below).

### PRECAUTIONS FOR USE

The vaccine contains lactose and may cause harm in lactose-sensitive patients.

The vaccine has been produced from a culture of chicken embryo cells. There is a possibility of a hypersensitivity reaction in patients exhibiting hypersensitivity to egg proteins (anaphylactic reaction after ingestion of eggs).

Due caution should be employed in administration of measles vaccine to persons with a history of cerebral injury, individual or family histories of convulsions, or of any other condition in which stress due to fever should be avoided. The physician should be alert to the temperature elevation that may occur following vaccination.

Vaccination should be deferred for at least 3 months following blood or plasma transfusions, or administration of human immune serum globulin.

There are no reports of transmission of live attenuated measles virus from vaccinees to susceptible contacts.

It has been reported that attenuated measles virus vaccine, live, may result in a temporary depression of tuberculin skin sensitivity.

Therefore, if a tuberculin test is to be done, it should be administered either before or simultaneously with ROUVAX (see below).

Children under treatment for tuberculosis have not experienced exacerbation of the disease when immunized with live measles virus vaccine; no studies have been reported to date of the effect of measles virus vaccines on untreated tuberculous children.

As for any vaccine, vaccination with ROUVAX may not result in seroconversion in 100% of susceptible persons given the vaccine.

### Pregnancy

Animal reproduction studies have not been conducted with ROUVAX.

It is also not known whether ROUVAX can cause fetal harm when administered to a pregnant woman or can affect reproduction capacity. Therefore, the vaccine should not be administered to pregnant females; furthermore, pregnancy should be avoided for three months following vaccination (see CONTRAINDICATIONS).

Reports have indicated that contracting of natural measles during pregnancy enhances fetal risk. Increased rates of spontaneous abortion, stillbirth, congenital defects and prematurity have been observed subsequent to natural measles during pregnancy. There are no adequate studies of the attenuated (vaccine) strain of measles virus in pregnancy. However, it would be prudent to assume that the vaccine strain of virus is also capable of inducing adverse fetal effects for up to three months following vaccination.

Vaccine administration to postpubertal females entails a potential for inadvertent immunization during pregnancy. Theoretical risks involved should be weighed against the risks that measles poses to the unimmunized adolescent or adult. Advisory committees reviewing this matter have recommended vaccination of postpubertal females who are presumed to be susceptible to measles and not known to be pregnant. If a measles exposure occurs during pregnancy, one should consider the possibility of providing temporary passive immunity through the administration of immune globulin (human).

### Nursing Mothers

It is not known whether measles vaccine virus is secreted in human milk. Therefore, because many drugs are excreted in human milk, caution should be exercised when ROUVAX is administered to a nursing woman.

### Administering an anti-measles preparation under special circumstances

After fresh exposure to a measles patient, the administration of the measles vaccine (or MMR) should not be postponed.

If the preparation is given soon after exposure (within the first 72 hours), the development of the measles infection can be arrested.

Simultaneously, long-term immunization is achieved.

Note: In cases of susceptible exposure to measles, when more than 3 days have passed (and up to 6 days) after exposure or if there is a contraindication to the measles vaccine, standard immunoglobulin IG can be administered, especially to children under one year of age.

Susceptible exposure – without laboratory confirmation – of measles, or if not immunized against measles with at least one dose from 12 months of age and upwards.

It is not recommended to administer IG to exposed people who were immunized with one dose, except for those who are immunosuppressed.

The dose of IG is 0.25 ml/kg, intramuscularly (the maximum dose should not exceed 15 ml):

- In the first three days following exposure, IG usually prevents the development of the clinical disease.

- Between 4-6 days following exposure, IG usually causes the disease to occur in a milder form.  
Administer the measles vaccine (or MMR) 3 months after giving IG (if there is no contraindication and not before 12 months of age). In the case of immunosuppression (following a disease or immunosuppressant treatment), IG will be given as soon as possible following exposure at a dose of 0.5 ml/kg intramuscularly (up to 15 ml), except in cases of patients with immunodeficiency who are receiving regular immunoglobulin.

The presence of pregnant women or immunosuppressed persons in the immediate vicinity of a person waiting for a measles vaccine does not constitute a contraindication.

Reactions of hypersensitivity following administration of the antimeasles preparation are rare and usually mild.

If the child is used to eating eggs (or foods which contain eggs), it is permissible to vaccinate with this preparation which is prepared with chicken embryo cells.

Vaccination can take place in cases where there is a history of nonanaphylactic, delayed hypersensitivity to eggs, chicken flesh or to feathers since they are not at a higher risk for developing allergic reactions. An antihistamine drug is recommended before vaccination. It should be given under the direction of a doctor and proper precautionary measures should be taken.

Nevertheless, when there is a known immediate allergic reaction of the anaphylactic type only to egg protein, avoid vaccinating.

These cases are extremely rare.

Note:

- Immediate anaphylactic reaction to egg protein, means immediately after ingesting eggs there is a reaction such as swelling of lips and tongue or difficulty breathing, or urticaria or another type of widespread rash, or general edema or loss of consciousness.

- Delayed non-anaphylactic reaction, means a reaction that may occur several hours after vaccination and may be expressed by redness, itching, limited urticaria or other localized rash.

History of convulsions or nervous system damage that is currently at a static, stable stage:

Vaccination may take place, since the advantage of vaccination in preventing complications of natural infections is greater than the danger of developing side effects following the vaccination.

In these cases, take precautionary measures as follows:

1. Instruct parents to carefully monitor their child following vaccination, especially for the early detection of fever, and about giving appropriate antipyretic treatment in order to reduce the risk of fever-induced convulsions.

2. Children who are taking anticonvulsants must continue to take them also after receiving the preparation. It is questionable whether to start prophylactic treatment for seizures especially before administering the vaccine, since most of the anticonvulsant medicines are effective only after a specific time.

There is no need to carry out a tuberculin test routinely before the measles vaccine since it has not been proven that the anti-measles preparation can cause an outbreak of tuberculosis as occurs with the natural measles infection. It is permissible to give the measles vaccine even if the tuberculin test is positive.

If there is a need to give the tuberculin test, it can be given before or concomitantly with the measles vaccine. Assessment of the test will be done at the normal time.

If there is a need to carry out the tuberculin test after administering the measles vaccine, its administration should be postponed for 4 weeks. That is because the vaccine can cause a temporary delay in the reaction to the tuberculin test.

Steroid treatment in normal children with diseases that are not related to immune deficiency, such as asthma, etc.

1. It is possible to give the vaccine concomitantly with steroid treatment in doses that do not reach immunosuppressive levels:

- Short-term treatment (less than 2 weeks) at a high daily dose (e.g. in children, prednisone 2 mg/kg and upward per day or a daily dose above 20 mg for children who weigh more than 10 kg).

- Long-term treatment or intermittent treatment at low-medium doses of short-acting steroids (e.g. in children, prednisone less than 2 mg/kg a day or less than a total of 20 mg per day for children above 10 kg).

- Treatment at maintenance physiologic doses.

- Local treatment (e.g. in the nose, inhalation, skin, eyes, joints).

2. Avoid administering the vaccine during treatment with steroids at high doses, which may cause a state of immunosuppression (e.g. in children who receive prednisone for two weeks or more, at a dose of 2 mg/kg and upwards per day or a daily dose above 20 mg for children who weigh more than 10 kg). The vaccine may be given at least one month after cessation or end of treatment.

Children with a history of thrombocytopenia or thrombocytopenic purpura may develop, on rare occasions, thrombocytopenia after receiving a measles vaccine. The advantage of the vaccine outweighs the potential risk, especially since the risk of thrombocytopenia is ten times greater after contacting measles. Therefore, in these cases, the measles vaccine may be administered.

Nevertheless, if thrombocytopenia occurs within 6 weeks after receiving the measles vaccine, it is recommended to refrain from receiving an additional dose. In these cases, it is recommended that the specific level of immunity to measles be checked.

## **DRUG INTERACTIONS**

### **Administering measles vaccine and other preparations**

The measles vaccine can be given concomitantly with other vaccines, live-attenuated (e.g. BCG, YF, OPV) or inactivated (e.g. HAV, HBV, Hib, DTP, IPV) at different sites on the body.

If the vaccines are not given simultaneously:

There is no need for a time delay between the measles vaccine and other inactivated vaccines.

Maintain an interval of 4 weeks between administering the measles vaccine and other live-attenuated vaccines except for OPV.

Measles and OPV can be given with any time interval between the two.

Administration of immunoglobulin (standard or specific), blood transfusion or blood products:

After administering immunoglobulin (standard or specific) or blood transfusion or blood products, delay the measles vaccine for three months.

If the measles vaccine is nonetheless given within this time frame, repeat the vaccine three months after receiving IG (unless the serology tests indicate immunization).

After administering the measles vaccine, delay, as much as possible, the administration of IG for at least two weeks.

If there is a need for administering IG within this time period, repeat the vaccine three months after receiving IG (except of course in cases when the level of specific antibodies is checked and found to be satisfactory).

## **DOSAGE**

The measles vaccination involves only a single injection, which is recommended between 12 and 15 months. However, for children vaccinated before the age of 1, in particular those living in communities, a second vaccination is recommended six months later. In countries where the incidence of measles and the death rate for measles are high during the first year of life, it is recommended to carry out the vaccination as early as possible after the age of 9 months.

## **MODE AND ROUTE OF ADMINISTRATION**

Dissolve the lyophilizate by adding:

- 0.5 ml of solvent to a 1 dose vial

- 5 ml of solvent to a 10 dose vial

Rehydration is immediate. Shake well before use. After reconstitution, the vaccine can be used within a maximum period of one day, provided it is stored between 0°C and 8°C, and protected from light.

Inject 0.5 ml of the reconstituted vaccine subcutaneously using a sterile syringe.

Do not inject intravenously.

## **INJECTION SITE**

Disinfect the area before injection and wait until the skin dries.

The reconstituted preparation will be injected subcutaneously in the upper quadrant of the arm, in the deltoid area. Do not inject intravenously.

## **SIDE EFFECTS**

Side effects to the measles vaccine are not influenced by the age at which the vaccine is given and are generally observed among those without immunity. The risk for effects is not greater if the preparation is given to immunized persons, e.g. after receiving a prior vaccine or after the natural illness.

Local reactions such as redness and local pain, swelling at the injection site, are rare.

Allergic reactions such as rash and urticaria are rare and pass quickly.

Anaphylactic shock – extremely rare.

A rise in temperature to around 38-39°C may occur in 5-15% of those vaccinated, 5-12 days after receiving the vaccine and lasts for a few days.

A temporary rash may occur 5-12 days after vaccination, in about 5% of the vaccinees.

Erythema multiforme has also been reported rarely.

Congestion, coughing, inflammation of the throat, and eye infection: may occur 5-12 days after immunization.

Less Common

High fever (over 103°F/39.4°C).

Diarrhea has been reported after vaccination with measles-containing vaccines.

Transient convulsions occur infrequently due to a rise in temperature.

The measles vaccine does not cause chronic convulsive disorders or permanent neurologic damage.

Syncope, particularly at the time of mass vaccination, has been reported.

Thrombocytopenia up to 2 months after vaccination – a rare effect, passes without damage.

Purpura has occurred rarely.

Vasculitis has been reported rarely.

Forms of optic neuritis, including retrobulbar neuritis, papillitis, and retinitis may infrequently follow viral infections, and have been reported to occur 1 to 3 weeks following inoculation with some live virus vaccines.

There have been rare reports of ocular palsies, Guillain-Barre syndrome, or ataxia occurring after immunization with vaccines containing live attenuated measles virus. The ocular palsies have occurred approximately 3-24 days following vaccination. No definite causal relationship has been established between either of these events and vaccination.

Subacute Sclerosing Panencephalitis (SSPE) is a rare effect, that is reported every one per million injections (compared to 8 per million cases in measles patients) and it is possible that among the cases reported after the vaccination were children who were previously ill with non-detected measles. It is clear that the measles vaccination caused a significant reduction in the cases of SSPE by reducing the number of measles outbreaks.

Rarely, local severe reactions that require hospitalization, including prolonged high fevers, panniculitis, and extensive local reactions, have been reported.

## **STORAGE AND TRANSFER OF PREPARATION**

### **Storage of preparation**

Store the preparation in a regular refrigerator, at a temperature between 2°C and 8°C. Avoid exposing the preparation to light. There is no need to store the solvent that comes with the preparation in the refrigerator, but it should be stored in a cool place.

### **Transporting the preparation**

Place in an ice box with ice packs (preferably) or in thermos bottles that contain ice.

Ensure that both during transport and when preparing the vaccine the preparation is kept at a temperature that does not exceed 8°C and that it is not exposed to light.

Manufacturer: Aventis Pasteur S.A., Lyon-France

Importer: Promedico Ltd., 4 Baltimore Street, Petach-Tikva