

	Serum Institute of India Pvt. Ltd.	MODULE 1: ADMINSTRATIVE/ LEGAL INFORMATION Measles and Rubella Vaccine, Live Attenuated (Freeze Dried)	MER/MA/IN/18-V-00
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1.2.5.10 Summary of product characteristics as per Annex C:



Serum Institute of
India Pvt. Ltd.

SUMMARY OF PRODUCT CHARACTERISTICS

Measles and Rubella Vaccine (Live) I.P.

1. NAME OF THE MEDICINAL PRODUCT

Measles and Rubella Vaccine (Live) I.P.

Brand name: MR-VAC

2. QUALITATIVE AND QUANTITATIVE COMPOSITION

MR (Measles Rubella Virus Vaccine Live) is a live, lyophilized vaccine for vaccination against measles (rubella) and rubella. The vaccine is prepared from the live, attenuated strains of Edmonston - Zagreb measles virus and Wistar RA 27/3 rubella virus. The measles and rubella viruses are propagated on human diploid cells (HDC). The vaccine meets the requirement of WHO when tested by the methods outlined in WHO, TRS 840 (1994).

Each single human dose when reconstituted in a volume of 0.5 ml contains not less than 1000 CCID₅₀ of Measles virus and 1000 CCID₅₀ of Rubella virus.

3. PHARMACEUTICAL FORM

Injectable, Freeze-dried powder for injection

4. CLINICAL PARTICULARS

4.1 Therapeutic indications

Measles and Rubella vaccine is indicated for active immunization against measles and rubella in infants, children, adolescents and young adults at risk. Immunization of susceptible non-pregnant adolescent and adult females is indicated if certain precautions are observed (see CONTRAINDICATIONS).

4.2 Posology and method of administration

Posology

0.5 ml of the reconstituted vaccine constitutes one dose.

Method of administration

FOR SUBCUTANEOUS USE ONLY.

The vaccine should be reconstituted only with the entire diluent supplied (Sterile Water for Injections I.P.) using a sterile syringe and needle. With gentle shaking the dried cake is easily dissolved. After reconstitution the vaccine should be used immediately.

A single dose of 0.5 ml should be administered by deep subcutaneous injection into the anterolateral aspect of upper thigh in infants and toddlers and upper arm in older children and adults.

If the vaccine is not used immediately then it should be stored in the dark between +2°C and +8° C for no longer than 6 hours. Any opened container remaining at the end of a session (within six hours of reconstitution) should be discarded.

The diluent supplied is specially designed for use with the vaccine. Only this diluent must be used to reconstitute the vaccine. Do not use diluents from other types of

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vaccine or for MR vaccine from other manufacturers. Water for Injections must not be used for this purpose. Using an incorrect diluent may result in damage to the vaccine and/or serious reactions to those receiving the vaccine. Diluent must not be frozen but should be kept cool.

The diluent and reconstituted vaccine should be inspected visually for any foreign particulate matter and / or variation of physical aspects prior to administration. In the event of either being observed, discard the diluent or reconstituted vaccine.

4.3 Contraindications

- Persons with a history of hypersensitivity to the active substance(s) or to any of the excipients should not be vaccinated. The vaccine may contain traces of neomycin. Anaphylactic or anaphylactoid reactions to neomycin, history of anaphylactic or anaphylactoid reactions are absolute contraindications. There are extremely rare reports of hypersensitivity reactions with MMR vaccines in individuals who are allergic to cow's milk. Such individuals should not receive the vaccine.
- Pregnancy: MR vaccine should not be administered in pregnant women because of the theoretical but never demonstrated teratogenic risk. Inadvertent receipt of MR vaccine during pregnancy is not an indication for an abortion. Since MR vaccine is recommended in adults, if pregnancy is planned, then an interval of one month should be observed after MR vaccination. No cases of CRS have been reported in several pregnant women who inadvertently received rubella-containing vaccine in early pregnancy.
- The vaccine should not be given in acute severe infectious diseases, febrile states, leukaemia, severe anemia and other severe diseases of the blood system, severe impairment of renal function, decompensated heart diseases, following administration of gammaglobulin or blood transfusions. Low grade fever, mild respiratory infections or diarrhoea, and other minor illness should not be considered as contraindications. It is particularly important to immunize children with malnutrition.
- The vaccine is contraindicated in persons who are severely immunocompromised as a result of congenital disease, HIV infection, advanced leukaemia or lymphoma, serious malignant disease, or treatment with high-dose steroids, alkylating agents or anti-metabolites, or in persons who are receiving immunosuppressive therapeutic radiation.

4.4 Special warnings and special precautions for use

- Individuals receiving corticosteroids, other immuno-suppressive drugs or undergoing radio-therapy may not develop an optimal immune response.
- Measles and Rubella vaccine may be used in children with known or suspected HIV infection.
- As with all injectable vaccines, appropriate medical treatment should always be readily available in case of rare anaphylactic reactions following the administration of the vaccine.

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4.5 Interaction with other medicinal products and other forms of interaction

Due to the risk of inactivation, the Measles and Rubella vaccine should not be given within the 6 weeks, and if it is possible within 3 months, after an injection of immunoglobulins or blood product containing immunoglobulins (blood, plasma). For the same reason, immunoglobulins should not be administered within the two weeks after the vaccination.

Tuberculin positive individuals may transitionally become tuberculin negative after vaccination.

Measles and Rubella vaccine can be safely and effectively given simultaneously with DTP, DT, TT, Td, BCG, Polio vaccine (OPV and IPV), Haemophilus influenzae type b, Hepatitis B, Yellow fever vaccine and vitamin A supplementation.

Concomitant vaccines should be given by separate injections.

4.6 Pregnancy and lactation

Measles and Rubella vaccine is contraindicated (see 4.3) in pregnancy. No studies on the effects on lactation have been performed.

4.7 Effects on ability to drive and use machines

No studies on the effects on the ability to drive and use machines have been performed.

4.8 Undesirable effects

The type and rate of severe adverse reactions do not differ significantly from the measles and rubella vaccine reactions described separately.

Measles vaccine may cause within 24 hours of vaccination mild pain and tenderness at the injection site. In most cases, they spontaneously resolve within two to three days without further medical attention. A mild fever can occur in 5-15% of vaccinees 7 to 12 days after vaccination and last for 1-2 days. Rash occurs in approximately 2% of recipients, usually starting 7-10 days after vaccination and lasting 2 days. The mild side effects occur less frequently after the second dose of a measles-containing vaccine and tend to occur only in person not protected by the first dose. Encephalitis has been reported following measles vaccination at a frequency of approximately one case per million doses administered although a causal link is not proven.

The rubella component may commonly result in joint symptoms manifested as arthralgias (25%) and arthritis (10%) among adolescent and adult females that usually last from a few days to 2 weeks. However, such adverse reactions are very rare in children and in men receiving Measles and Rubella vaccine (0%-3%). Symptoms typically begin 1-3 weeks after vaccination and last 1 day to 2 weeks. These transient reactions seem to occur in non-immunes only, for whom the vaccine is important. Low-grade fever and rash, lymphadenopathy, myalgia and paraesthesiae are commonly reported. Thrombocytopenia is rare and has been reported in less than 1 case per 30,000 doses administered.

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Anaphylactic reactions are also rare. In susceptible individuals the vaccine may very rarely cause allergic reactions like urticaria, pruritis and allergic rash within 24 hours of vaccination.

Clinical experience has exceptionally recorded isolated reactions involving the CNS. These more serious reactions have however, not been directly linked to vaccination.

Following adverse events have been reported in clinical trials of Measles and Rubella vaccine irrespective of causal relationship to the vaccine and frequencies are reported as:

Very common ($\geq 1/10$), Common ($\geq 1/100$ to $< 1/10$), Uncommon ($\geq 1/1,000$ to $< 1/100$), Rare ($\geq 1/10,000$ to $< 1/1,000$) and Very rare ($\geq 1/100,000$ to $< 1/10,000$).

General disorders and administration site conditions:

Common: Pyrexia, injection site pain, injection site erythema.

Uncommon: Injection site induration, injection site nodule.

Musculoskeletal and connective tissue disorder:

Uncommon: Arthralgia, arthritis.

Skin and subcutaneous tissue disorders:

Uncommon: Rash

Infections and infestations:

Common: Nasopharyngitis, rhinitis

Blood and lymphatic system disorders:

Uncommon: Lymphadenitis

Eye disorders:

Common: Ocular hyperaemia

Reproductive system and breast disorders:

Rare: Menstrual disorder.

4.9 Overdose

No case of overdose has been reported.

5. PHARMACOLOGICAL PROPERTIES

5.1 Pharmacodynamic properties

Pharmacotherapeutic group: Viral vaccine, ATC code: J07BD53

Effectiveness of the vaccine is proved in mass immunisation campaigns conducted across countries; Albania and South Korea. The campaigns had a dramatic impact on the epidemiology of these two diseases in these countries. The measles and rubella cases reduced significantly with complete elimination of measles from South Korea.

Immunogenicity of measles and rubella vaccine was established in 2 controlled clinical trials. Immunogenicity was measured by measuring circulating antibodies by ELISA (enzyme linked immunosorbent assay) test. The seropositivity after the vaccination ranges from 96 % to 100 % for measles and 92 % to 100 % for rubella vaccine.

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An epidemiological study in Iran evaluated immunity against rubella after MR vaccination. 98% of the susceptible group acquired immunity against rubella 1 month after vaccination.

5.2 Pharmacokinetic properties

Pharmacokinetic studies are not applicable for vaccines.

5.3 Preclinical safety data

No formal animal testing has been carried out for non-clinical assessment. However as part of the quality control every batch of the vaccine is tested in mice and guinea pigs for general safety and innocuity.

6. PHARMACEUTICAL PARTICULARS

6.1 List of excipients

Gelatin (Partially hydrolyzed), D-Sorbitol, L-Histidine, L- Alanine, Tricine, L-Arginine hydrochloride, Lactalbumin hydrolysate, Minimum Essential Medium (MEM)

6.2 Incompatibilities

In the absence of compatibility studies, this medicinal product must not be mixed with other medicinal products

6.3 Shelf life

30 Months

6.4 Special precautions for storage

Store and transport refrigerated at 2°C – 8°C.

Protect both the lyophilised and reconstituted vaccine from light

The long term storage (unlabelled containers), it is recommended to store the lyophilised vaccine in the freezer at -20°C

The diluent should not be frozen.

6.5 Nature and contents of container

Packaging/ Container closure system of vaccine

Lyophilised Measles and Rubella vaccine is a yellowish-white friable mass and is filled in 5ml amber coloured vials (Type I glass)

Sr. no.	Container Closure	Description
1	Glass Vials	5mL, USP Type-I, amber, tubular European blowback glass vials Height 50 mm, Body diameter 16.50 mm
2	Rubber Closures	13mm, Datwyler FM460, grey coloured rubber stopper and 13mm, Aptar Stelmi GS6740, grey coloured rubber stopper Flange Diameter 12.45 mm, Flange thickness 1.98
3	Flip-off Aluminium Seals	Flip-off seal 13mm AF, Pantone 220C (Violet colour)

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Packaging/ Container closure system of Diluent (sWFI)

Based on the dose of the vaccine the Packaging/ Container closure of the diluent is classified as below. The OPC mechanism ampoules are tested as per SOP 130 0224.

Dose	Ampoule Type	Volume	Dimensions
1 Dose	Type 1, clear, tubular glass ampoule with One Point Cut (OPC) mechanism	1 ml	Height 65 mm Body Diameter 10.25 mm Base to Constriction height 28 mm
2 Dose	Type 1, clear, tubular glass ampoule with One Point Cut (OPC) mechanism	1 ml	Height 65 mm Body Diameter 10.25 mm Base to Constriction height 31 mm
5 Dose	Type 1, clear, tubular glass ampoule with One Point Cut (OPC) mechanism	3 ml	Height 75 mm Body Diameter 14.75 mm Constriction height 30 mm
10 Dose	Type 1, clear, tubular glass ampoule with One Point Cut (OPC) mechanism	5 ml	Height 87 mm Body Diameter 14.75 mm Constriction height 52 mm

6.6 Special precautions for disposal

The vaccine should be reconstituted only with the diluent (sterile water for injection) using a sterile syringe and needle. With gentle shaking the dried cake is easily dissolved.

If the vaccine is not used immediately then it should be stored in the dark at 2°C – 8°C for no longer than 6 hours.

Any unused product or waste material should be disposed of in accordance with local requirements.

7. MARKETING AUTHORIZATION HOLDER

SERUM INSTITUTE OF INDIA PVT. LTD.,

212/2, Hadapsar, Pune 411028, India

Fax No: 020-26993945

E-mail: ssj@seruminstitute.com

8. MARKETING AUTHORISATION NUMBER(S)

Manufacturing License number: 10 (in form 28-D)

9. DATE OF FIRST AUTHORISATION/RENEWAL OF THE AUTHORISATION

Date of First Authorization: 13th April, 1989

Date of Renewal of the Authorization: 01st January, 2017



MEASLES AND RUBELLA VACCINE (LIVE) I.P. (Freeze-Dried) MR-VAC®

DESCRIPTION

MR-VAC® (Measles and Rubella Vaccine (Live) I.P.) (freeze-dried) is prepared from the live, attenuated strains of Edmonston-Zagreb measles virus and Wistar RA 27/3 rubella virus.

POTENCY

Each dose of 0.5ml contains NOT LESS THAN 1000 CCID50 of Measles virus 1000 CCID50 of Rubella virus Dose : 0.5 ml by subcutaneous injection.

INDICATIONS

MR vaccine is indicated for active immunization against measles and rubella in infants, children, adolescents and young adults at risk.

The World Health Organization recommends that all the children receive two doses of a measles containing vaccine. The first dose of vaccine can be administered as early as 9 months of age.

The vaccine can be safely and effectively given simultaneously with DTP, DT, TT, Td, BCG, Polio vaccine (OPV and IPV), Haemophilus influenzae type b, Hepatitis B, Yellow fever vaccine and vitamin A supplementation.

APPLICATION AND DOSAGE

The vaccine should be reconstituted only with the entire diluent supplied (Sterile Water for Injections I.P.) using a sterile syringe and needle. With gentle shaking the dried cake is easily dissolved.

Any opened container remaining at the end of a session (within six hours of reconstitution) should be discarded.

The diluent supplied is specially designed for use with the vaccine. Only this diluent must be used to reconstitute the vaccine. Do not use diluents from other types of vaccine or for MR vaccine from other manufacturers.

CLOSE ATTENTION SHOULD BE PAID TO THE CONTRAINDICATIONS LISTED.

The diluent and reconstituted vaccine should be inspected visually for any foreign particulate matter and / or variation of physical aspects prior to administration.

ADVERSE REACTIONS

The type and rate of severe adverse reactions do not differ significantly from the measles and rubella vaccine reactions described separately.

Measles vaccine may cause within 24 hours of vaccination mild pain and tenderness at the injection site. In most cases, they spontaneously resolve within two to three days without further medical attention.

The rubella component may commonly result in joint symptoms manifested as arthralgias (25%) and arthritis (10%) among adolescent and adult females that usually last from a few days to 2 weeks.

DRUG INTERACTIONS

Due to the risk of inactivation, the measles and rubella vaccine should not be given within the 6 weeks, and if it is possible within 3 months, after an injection of immunoglobulins or blood product containing immunoglobulins (blood, plasma).

For the same reason, immunoglobulins should not be administered within the two weeks after the vaccination. Tuberculin positive individuals may transitionally become tuberculin negative after vaccination.

CONTRAINDICATIONS AND WARNINGS

Individuals receiving corticosteroids, other immuno-suppressive drugs or undergoing radio-therapy may not develop an optimal immune response. The vaccine should not be given in febrile states, pregnancy, acute infectious diseases, leukaemia, severe anaemia and other severe diseases of the blood system, severe impairment of the renal function, decompensated heart diseases, following administration of gammaglobulin or blood transfusions or to subjects with potential allergies to vaccine components.

The vaccine may contain traces of neomycin. Anaphylactic or anaphylactoid reactions to neomycin, history of anaphylactic or anaphylactoid reactions are absolute contraindications.

MR vaccine should not be administered in pregnant women because of the theoretical but never demonstrated teratogenic risk. Inadvertent receipt of MR vaccine during pregnancy is not an indication for an abortion.

IMMUNE DEFICIENCY

Measles and Rubella vaccine may be used in children with known or suspected HIV infection. The vaccine is contraindicated in persons who are severely immunocompromised as a result of congenital disease, HIV infection, advanced leukaemia or lymphoma, serious malignant disease, or treatment with high-dose steroids, alkylating agents or anti-metabolites, or in persons who are receiving immunosuppressive therapeutic radiation.

RECOMMENDED STORAGE

IT IS IMPORTANT TO PROTECT BOTH THE FREEZE-DRIED AND RECONSTITUTED VACCINE FROM THE LIGHT. The vaccine should be stored in the dark at a temperature between +2°C and +8°C.

SHELF LIFE

The expiry date of the vaccine is indicated on the label and packaging.

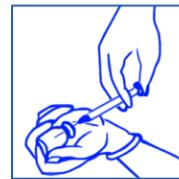
PRESENTATION

- 1 Dose vial plus diluent (0.5 ml) 2 Dose vial plus diluent (1 ml) 5 Dose vial plus diluent (2.5 ml) 10 Dose vial plus diluent (5 ml)

MOST IMPORTANT WARNING

- 1. Please ensure that the vaccine is administered by subcutaneous route only. In rare cases anaphylactic shock may occur in susceptible individual and for such emergency please keep handy 1:1000 adrenaline injection ready to be injected intramuscularly or subcutaneously. For treatment of severe anaphylaxis the initial dose of adrenaline is 0.1-0.5 mg (0.1-0.5 ml of 1:1000 injection) given s/c or i/m. Single dose should not exceed 1 mg (1 ml). For infants and children the recommended dose of adrenaline is 0.01 mg/kg (0.01 ml/kg of 1:1000 injection). Single paediatric dose should not exceed 0.5 mg (0.5 ml). This will help in tackling the anaphylactic shock/reaction effectively. 2. The mainstay in the treatment of severe anaphylaxis is the prompt use of adrenaline, which can be lifesaving. It should be used at the first suspicion of anaphylaxis. As with the use of all vaccines the vaccinee should remain under observation for not less than 30 minutes for possibility of occurrence of rapid allergic reactions. Hydrocortisone and antihistaminics should also be available in addition to supportive measures such as oxygen inhalation.

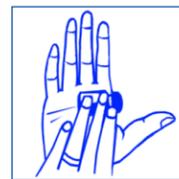
FREEZE-DRIED PREPARATIONS Instructions for use



1) Draw the diluent from the ampoule into a syringe, pierce the bung of the vial with the needle and gently inject the diluent into the vial.



2) Detach the syringe, leaving the needle in vial bung. After 15 seconds remove the needle.



3) Rotate the vial gently between your palms till the material dissolves. Avoid shaking the vial as this would cause frothing.



4) Withdraw the reconstituted solution into the syringe, now ready for administration.



Manufactured by: SERUM INSTITUTE OF INDIA PVT. LTD.

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Protection from birth onwards

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Table with 5 columns: Reason for issue, Customer, Product, Item Code number, Specification No., Artwork made to, Supercedes Item Code, Dimensions, and five departmental columns: PACKAGING DEVELOPMENT, QUALITY CONTROL, REGULATORY AFFAIRS, MEDICAL DEPARTMENT, QUALITY ASSURANCE.