SUMMARY OF PRODUCT CHARACTERISTICS

1 NAME OF THE MEDICINAL PRODUCT

Measles, Mumps & Rubella Vaccine Live Attenuated, (Freeze-Dried)

2 QUALITATIVE AND QUANTITATIVE COMPOSITION

Each single human dose when reconstituted in a volume of 0.5 ml contains not less than 1000 CCID 50 of measles virus, 5000 CCID 50 of mumps virus and 1000 CCID 50 of Rubella virus

3 PHARMACEUTICAL FORM

Injectable, Powder for Injection.
The vaccine is prepared from the live, attenuated strains of Edmonston-Zagreb measles virus, Leningrad-Zagreb (L-Z) mumps virus and Wistar RA 27/3 rubella virus. The measles and rubella viruses are propagated on human diploid cells (HDC) and the mumps virus is grown on chick fibroblasts from SPF eggs (Specific pathogen free eggs). The vaccine is freeze-dried and is provided with diluent. The product has the appearance of a Yellowish white friable mass may or may not contain bubbles and / or indentations.

4 CLINICAL PARTICULARS

4.1 Therapeutic indications

For active immunization against measles, mumps and rubella in children from 12 months to 10 years of age. Second dose of MMR is usually advocated any time before the age of 6 years (elementary school entry 4-6 years). In children above 10 years, adolescents and adults, Measles and Rubella (MR) vaccine is recommended. Revaccination may seroconvert primary failures or boost antibody titres of previously vaccinated individuals whose titers have declined. The Advisory Committee on Immunization Practices (ACIP) recommends administration of the first dose of MMR at 12-15 months of age and administration of the second dose of MMR at 4-6 years 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, or Yellow fever vaccine or vitamin A supplementation.

4.2 Posology and method of administration

The vaccine should be reconstituted only with the entire diluent supplied (Sterile water for injections) 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 toddlers and upper arm in older children. If the vaccine is not used immediately

then it should be stored in the dark at 2-8ºC 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 vaccine vial monitor (see figure), for this type of vaccine is attached to the vial cap and should be discarded when the vaccine is being reconstituted. 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 MMR 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.
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. In the event of either being observed, discard the diluent or reconstituted vaccine.

4.3 Contraindications

Individuals receiving corticosteroids, other immuno-suppressive drugs or undergoing radiotherapy 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 gamma-globulin 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 to eggs (Hypersensitivity to eggs), are absolute contraindications. There are extremely rare reports of hypersensitivity reactions with MMR vaccine in individuals who are allergic to cow's milk.
Such individuals should not receive the vaccine. 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.
MMR vaccine should not be administered in pregnant women because of the theoretical but never demonstrated teratogenic risk. Inadvertent receipt of MMR 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 any pregnant women who inadvertently received rubella-containing vaccine in early pregnancy.

IMMUNE DEFICIENCY

Measles, Mumps 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.

4.4 Special warnings and precautions for use

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 (0.01ml/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.

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 vaccine 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.

4.5 Interaction with other medicinal products and other forms of interaction

Due to the risk of inactivation, the MMR vaccine should not be given within the 6 weeks, and if it is possible the 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.

4.6 Fertility, pregnancy and lactation

MMR vaccine should not be administered in pregnant women because of the theoretical but never demonstrated teratogenic risk. Inadvertent receipt of MMR 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 any pregnant women who inadvertently received rubella-containing vaccine in early pregnancy.

4.7 Effects on ability to drive and use machines

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

4.8 Undesirable effects

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

The 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 mumps component may result in parotitis and low grade fever. Febrile seizures and orchitis may also occur. However, moderate fever occurs rarely and aseptic meningitis has been reported very rarely. Vaccine-associated meningitis resolves spontaneously in less than 1 week without any sequelae. The onset of aseptic meningitis is delayed, which may limit the ability to detect these cases by passive surveillance. Vaccine associated aseptic meningitis is observed between 15-35 days post immunization.

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 MMR 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 30000 doses administered. 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.

4.9 Overdose
No case of overdose has been reported.

5. PHARMACOLOGICAL PROPERTIES

5.1 Pharmacodynamic properties
Pharmacotherapeutic group: Viral vaccines,
Measles, Mumps & Rubella live attenuated, ATC code: JO7BD52
MMR vaccine is a mixture of live attenuated measles, mumps and rubella viruses to provide active immunization against these diseases.

5.2 Pharmacokinetic properties
Not applicable

5.3 Preclinical safety data
Single dose toxicity studies were conducted in mice and Beagle dogs with MMR vaccine live attenuated (Freeze-dried) by subcutaneous route. No toxicological effects were observed in mice and Beagle dogs after a single subcutaneous administration of MMR vaccine. The approximate lethal dose of MMR vaccine live attenuated (Freeze dried) was more than 80 times and 6.3 times the expected clinical dose, respectively.

In a repeated dose toxicity study in mice with MMR vaccine live attenuated (Freeze dried) by subcutaneous route no treatment related toxic effects were observed. There were no significant macroscopic and histopathological findings. The approximate lethal dose of MMR vaccine live attenuated (Freeze-dried) was more than 80 times the expected clinical dose in mice.

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

IT IS IMPORTANT TO PROTECT BOTH THE LYOPHILIZED AND RECONSTITUTED VACCINE FROM THE LIGHT.

The vaccine should be stored in the dark at 2-8˚C. For long term storage a temperature of -20˚C is recommended for the lyophilized vaccine. Protect from light. The diluent should not be frozen, but should be kept cool.

6.5 Nature and contents of container

For 1, 2 & 5 Dose: Amber colored tubular type I vial, 16.5 x 35 mm vial, 13 mm slotted, Grey Bromo butyl Rubber Stopper and 13 mm Flip off Aluminum Cap

For 10 Dose: Amber colored tubular type I vial, 16.5 x 50 mm in height with 13 mm slotted, Grey, Bromo butyl Rubber Stopper and 13 mm Flip off Aluminum Cap Diluent Container: Clear, transparent, OPC Type I Glass ampoule

6.6 Special precautions for disposal and other handling

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

7. MARKETING AUTHORISATION HOLDER

SERUM INSTITUTE OF INDIA PVT. LTD.

212/2, Hadapsar, Pune 411028, INDIA

8. MARKETING AUTHORISATION NUMBER(S)

12566

9. DATE OF FIRST AUTHORISATION/RENEWAL OF THE AUTHORISATION

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10. DATE OF REVISION OF THE TEXT

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