MEASLES AND RUBELLA VIRUS VACCINE LIVE U.S.P. (Freeze-Dried)

DESCRIPTION
The vaccine is prepared from the live, attenuated strains of Edmonston-Zagreb measles virus and Wistar RA 27/3 rubella virus. Both measles and rubella viruses are propagated on human diploid cells (HDC). The vaccine is lyophilized and is provided with diluent. The product has the appearance of a yellowish-white dry cake. The vaccine meets the requirements of U.S.P. and WHO when tested by the methods outlined in U.S.P. and WHO, TRS 840(1994).

POTENCY
Each single human dose when reconstituted in a volume of 0.5 ml. contains not less than 1000 $CCID_{50}$ of measles virus and 1000 $CCID_{50}$ of rubella virus.

INDICATIONS
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).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 diluent supplied (Sterile water for injection) 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 upper arm in older children. If the vaccine is not used immediately then it should be stored in the dark at 2° 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 vaccine vial monitor (see figure), if present would have been removed on reconstitution.
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. Water for injection 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.

ADVERSE REACTIONS
The type and rate of severe adverse reactions do not differ significantly from the measles, mum s 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 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 MR 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. Anaphylactic reactions are also rare.
Clinical experience has exceptionally recorded isolated reactions involving the CNS. These more serious reactions have however, not been directly linked to vaccination.

DRUG INTERACTIONS
Due to the risk of inactivation, the rubella 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.

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. 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.
DO NOT ADMINISTER THE VACCINE DURING PREGNANCY, CAUTION VACCINEES NOT TO CONCEIVE FOR 28 DAYS PERIOD FOLLOWING VACCINATION.

HIV INFECTION
Measles and Rubella virus vaccine live may be used in children with known or suspected HIV infection. Although the data are limited and further studies are being encouraged, there is no evidence to date of any increased rate of adverse reactions using this or other measles and rubella vaccines in symptomatic or asymptomatic HIV-infected children. The vaccine should be avoided in other cell-mediated immune deficiency states.

RECOMMENDED STORAGE
IT IS IMPORTANT TO PROTECT BOTH THE LYOPHILIZED AND RECONSTITUTED VACCINE FROM THE LIGHT. The vaccine should be stored in the dark at a temperature between 2° and 8°C. For long term storage a temperature of -20°C is recommended for the lyophilised vaccine. The diluent should not be frozen, but should be kept cool.

SHELF LIFE
24 months from the date of last satisfactory potency test, if stored in a dark place at a temperature between 2° and 8°C.

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)

THE VACCINE VIAL MONITOR

Inner square lighter than outer circle. **If the expiry date has not passed, USE the vaccine.**
At a later time, inner square still lighter than outer circle. **If the expiry date has not passed, USE the vaccine.**
Discard point:
Inner square matches colour of outer circle.
DO NOT use the vaccine.
Beyond the discard point:
Inner square darker than outer ring.
DO NOT use the vaccine.

Vaccine Vial Monitors (VVMs) are part of the label on Measles and Rubella Virus Vaccine Live U.S.P. supplied through Serum Institute of India Ltd. The colour dot which appears on the label of the vial is a VVM. This is a time-temperature sensitive dot that provides an indications of the cumulative heat to which the vial has been exposed. It warns the end user when exposure to heat is likely to have degraded the vaccine beyond an acceptable level.
The interpretation of the VVM is simple. Focus on the central square. Its colour will change progressively. As long as the colour of this square is lighter than the colour of the ring, then the vaccine can be used. As soon as the colour of the central square is the same colour as the ring or of a darker colour than the ring, then the vial should be discarded.

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 (0.1-0.5ml of 1:1000 injection) given s/c or i/m. Single dose should not exceed 1 mg (1ml). For infants and children the recommended dose of adrenaline is 0.01mg/kg (0.01ml/kg of 1:1000 injection). Single paediatric dose should not exceed 0.5mg (0.5ml). 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 vaccines should remain under observation for not less than 30 minutes for possibility of occurrence of rapid allergic reactions. Efcorlin hydrochloride and antihistaminics should also be available in addition to supportive measures such as oxygen inhalation.

Manufactured by:
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Protection from birth onwards