

MERUVAX II®**PRODUCT INFORMATION**

(Rubella Virus Vaccine, Live, MSD)

Wistar RA 27/3 Strain

DESCRIPTION

MERUVAX II (Rubella Virus Vaccine, Live, MSD) is a live virus vaccine for immunisation against rubella (German measles).

MERUVAX II is a sterile lyophilised preparation of the Wistar Institute RA 27/3 strain of live attenuated rubella virus. The virus was adapted to and propagated in human diploid cell (WI-38) culture.

The reconstituted vaccine is for subcutaneous administration. When reconstituted as directed, the dose for injection is 0.5 mL and contains not less than the equivalent of 1,000 TCID₅₀ (tissue culture infectious doses) of the U.S. Reference Rubella Virus. Each dose also contains approximately 25 µg of neomycin and 3 mg of human serum albumin. The product contains no preservative. Sorbitol and hydrolysed gelatin are added as stabilisers.

The manufacture of this product includes exposure to bovine derived materials. No evidence exists that any case of vCJD (considered to be the human form of bovine spongiform encephalopathy) has resulted from the administration of any vaccine product.

CLINICAL PHARMACOLOGY

MERUVAX II produces a modified, non-communicable rubella infection in susceptible persons.

Extensive clinical trials of rubella virus vaccines, prepared using RA 27/3 strain rubella virus, have shown that a single injection of the vaccine induces rubella haemagglutination-inhibiting (HI) antibodies in 97% or more of susceptible persons. The RA 27/3 rubella strain elicits higher immediate post-vaccination HI, complement-fixing and neutralising antibody levels than other strains of rubella vaccine and has been shown to induce a broader profile of circulating antibodies including anti-theta and anti-iota precipitating antibodies. The RA 27/3 rubella strain immunologically simulates natural infection closely. The broad profile of antibodies produced by RA 27/3 strain rubella virus vaccine appears to correlate with resistance to subclinical reinfection with the wild virus.

Vaccine induced antibody levels have been shown to persist for at least ten years without substantial decline. If the present pattern continues, it will provide a basis for the expectation that immunity following vaccination will be permanent. However, continued surveillance will be required to demonstrate this point.

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INDICATIONS AND USAGE

Immunisation against Rubella (German Measles)

1. **Children between 12-15 months of age and puberty.**

Notes: (i) It is not recommended for infants younger than 12 months (because they may retain maternal rubella neutralising antibodies that may interfere with the immune response), unless such immunisation is considered essential in view of logistic difficulties e.g. in geographically isolated locations.

(ii) Previously unimmunised children of susceptible pregnant women should receive live attenuated rubella vaccine, because an immunised child will be less likely to acquire wild-type rubella and introduce the virus into the household.

2. **Adolescent and adult males.**

As an adjunctive measure in preventing or controlling outbreaks of rubella in circumscribed population groups (e.g. military bases and schools).

3. **Susceptible non-pregnant adolescent and adult females of child bearing age.** (see Contra-indications, Precautions-Use in Pregnancy).

Notes: (i) Women of child bearing age should be advised not to become pregnant for three months after vaccination and should be informed of the reason for this precaution.

(ii) It is recommended that rubella susceptibility be determined by serological testing prior to immunisation. If immune, as evidenced by a specific rubella antibody titre of 1:8 or greater (haemagglutination-inhibition test), vaccination is unnecessary.

(iii) Postpubertal females should be informed of the frequent occurrence of generally self-limited arthralgia and/or arthritis beginning 2 to 4 weeks after vaccination (see ADVERSE REACTIONS).

4. **Postpartum Women**

Note: It has been found convenient in many instances to vaccinate rubella-susceptible women in the immediate postpartum period (see Nursing Mothers).

Revaccination

Children vaccinated when younger than 12 months of age should be revaccinated. Based on available evidence, there is no reason to routinely revaccinate persons who were vaccinated originally when 12 months of age or older. However, persons should be revaccinated if there is evidence to suggest that initial immunisation was ineffective.

Use with Other Vaccines

Routine administration of DTP (diphtheria, tetanus, pertussis) and/or OPV (oral polio-virus vaccine) concomitantly with measles, mumps and rubella vaccines is not recommended because there are insufficient data relating to the simultaneous administration of these antigens. However, the American Academy of Paediatrics has noted that in some circumstances, particularly when the patient may not return, some practitioners prefer to administer all these antigens on a single day. If done, separate sites and syringes should be used for DTP and MERUVAX II.

MERUVAX II should not be given less than one month before or after administration of other virus vaccines.

CONTRAINDICATIONS

Hypersensitivity to any component of the vaccine, including gelatin.

Do not give MERUVAX II to pregnant females; the possible effects of the vaccine on foetal development are unknown at this time. If vaccination of postpubertal females is undertaken, pregnancy should be excluded and avoided for three months following vaccination. (See PRECAUTIONS, Pregnancy).

Anaphylactic or anaphylactoid reactions to neomycin (each dose of reconstituted vaccine contains approximately 25 µg of neomycin). A history of contact dermatitis to neomycin is not a contraindication; however, the possibility of a flare up of skin lesions should be borne in mind.

Any febrile respiratory illness or other active febrile infection.

Active untreated tuberculosis.

Patients receiving immunosuppressive therapy. (This contraindication does not apply to patients who are receiving corticosteroids as replacement therapy, e.g. for Addison's disease.)

Individuals with blood dyscrasias, leukaemia, lymphomas of any type, or other malignant neoplasms affecting the bone marrow or lymphatic systems.

Primary and acquired immunodeficiency states, including patients who are immunosuppressed in association with AIDS or other clinical manifestations of infection with human immunodeficiency viruses, cellular immune deficiencies, hypogammaglobulinaemic and dysgammaglobulinaemic states.

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

PRECAUTIONS

General

Adequate treatment provisions including adrenaline, should be available for immediate use should an anaphylactic or anaphylactoid reaction occur.

Due caution should be employed in administration of MERUVAX II to persons with individual or family histories of convulsions, a history of cerebral injury or any other condition in which stress due to fever should be avoided. the physician should be alert to the temperature elevation which may occur following vaccination (see ADVERSE REACTIONS).

Thrombocytopaenia

Individuals with current thrombocytopaenia may develop more severe thrombocytopaenia following vaccination. In addition, individuals who experienced thrombocytopaenia with the first dose of M-M-R II (or its component vaccines) may develop thrombocytopaenia with repeat doses. Serologic status may be evaluated to determine whether or not additional doses of vaccine are needed. the potential risk to benefit ratio should be carefully evaluated before considering vaccination in such cases (see ADVERSE REACTIONS).

Other

Excretion of small amounts of the live attenuated rubella virus from the nose or throat has occurred in the majority of susceptible individuals 7-28 days after vaccination. There is no confirmed evidence to indicate that such virus is transmitted to susceptible persons who are in contact with the vaccinated individuals. Consequently, transmission through close personal contact is a theoretical possibility. However, transmission of the vaccine virus to infants via breast milk has been documented (see Nursing Mothers).

There is no evidence that live rubella virus vaccine given after exposure to wild-type rubella virus will prevent illness. There is, however, no contraindication to vaccinating children already exposed to wild-type rubella.

Vaccination should be deferred for at least three months following blood or plasma transfusions, or administration of human immune serum globulin. However, susceptible postpartum patients who received blood products may receive MERUVAX II prior to discharge provided that a repeat HI titre is drawn 6-8 weeks after vaccination to ensure seroconversion. Similarly, although studies with other live rubella virus vaccines suggest that MERUVAX II may be given in the immediate postpartum period to those non-immune women who have received anti-Rho (D) globulin (human) without interfering with vaccine effectiveness, a follow-up post-vaccination HI titre should also be determined.

Congenital malformations do occur in up to seven percent of all live births. Their chance appearance after vaccination should be borne in mind. A history of rubella illness is not reliable enough to exclude individuals from immunisation with MERUVAX II.

It has been reported that attenuated rubella 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 MERUVAX II.

This product contains albumin, a derivative of human blood. Due to effective donor screening and product manufacturing processes, there is an extremely remote risk for transmission of known and unknown viral diseases.

In addition, virus removal and inactivation procedures are included in the manufacturing process. Current Good Manufacturing Practices are applied in the manufacture of this product and are effective against enveloped viruses such as HIV (human immunodeficiency virus), hepatitis B and hepatitis C viruses, and the non-enveloped virus hepatitis A. They are also known to have some effect on the removal of the non-enveloped virus, parvovirus B 19.

Although there is a theoretical risk for transmission of Creutzfeldt-Jakob disease (CJD), no cases of transmission have ever been identified that were associated with albumin. There is also the possibility that other known or unknown infectious agents may be present in such products.

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

USE IN PREGNANCY (Category B2)

Women of child-bearing age should be tested for rubella antibodies prior to pregnancy. All seronegative women, provided they are not pregnant, should be offered rubella vaccine. Those administering the vaccine should be careful to instruct women to whom it is given that they should not become pregnant for at least two full menstrual cycles. However, to date, there have not been any rubella-like birth defects in the live born infants (about 400) of seronegative mothers vaccinated during or just before pregnancy. Based on this experience, rubella vaccination during pregnancy need not be the reason to recommend interruption of pregnancy. The final decision must be made by the patient and her physician.

Currently available live virus vaccines have not caused teratogenic effects in humans. Caution needs to be exercised as live virus vaccines have been shown to cross the placenta and infect the foetus. Some live virus vaccines have caused birth defects in animals. (The NH&MRC publication " Immunisation Procedures " should be consulted for more comprehensive information.)

Nursing Mothers

Recent studies have shown that lactating postpartum women immunised with live attenuated rubella vaccine may secrete the virus in breast milk and transmit it to breast-fed infants. Caution should be exercised when MERUVAX II is administered to a nursing woman.

Paediatric Use

Safety and effectiveness of rubella vaccine in infants below the age of 12 months have not been established.

Drug Interactions

Administration of immune globulins concurrently with MERUVAX II may interfere with the expected immune response. Vaccination should be deferred for 3 months or longer following administration of immune globulin (human) and blood or plasma transfusions.

ADVERSE REACTIONS

Patients may complain of burning and/or stinging of short duration at the injection site.

Symptoms of the same kind as those seen following wild-type rubella may occur after vaccination. These include regional lymphadenopathy, urticaria, anaphylaxis and anaphylactoid reactions as well as related phenomena such as angioneurotic oedema (including peripheral or facial oedema) in individuals with or without an allergic history; rash, erythema multiforme, Stevens-Johnson syndrome, pruritis (reported rarely), malaise, sore throat, cough, fever, headache, dizziness, nausea, vomiting, diarrhoea, polyneuritis, and arthralgia and/or arthritis (usually transient and sometimes chronic). Local pain, wheal and flare, induration, and erythema may occur at the site of injection. Syncope and irritability have been reported. Reactions are usually mild and transient.

Moderate fever (38.3 - 39.4°C) occurs occasionally, and high fever (over 39.4°C) occurs less commonly.

Arthralgia and/or arthritis (usually transient and rarely chronic), and polyneuritis are features of wild-type rubella and vary in frequency and severity with age and sex, being greatest in adult females and least in prepubertal children. Chronic arthritis has been associated with wild-type rubella infection and has been related to persistent virus and/or viral antigen isolated from body tissues. Only rarely have vaccine recipients developed chronic joint symptoms.

Following vaccination in children, reactions in joints are uncommon and generally of brief duration. In women, incidence rates for arthritis and arthralgia are generally higher than those seen in children (children: 0.3%; women: 12-20%) and the reactions tend to be more marked and of longer duration. Symptoms may persist for a matter of months or on rare occasions for years. In adolescent girls, the reactions appear to be intermediate in incidence between those seen in children and in adult women. Even in older women (35 - 45 years), these reactions are generally well tolerated and rarely interfere with normal activities. Myalgia and paraesthesia have been reported rarely after administration of MERUVAX II.

Nervous system reactions such as convulsions have occurred rarely.

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

Cardiovascular reactions such as vasculitis have been reported rarely.

Isolated reports of polyneuropathy including Guillain-Barre syndrome have been reported after immunisation with rubella containing vaccines.

Clinical experience with live rubella vaccines thus far indicates that encephalitis and other nervous system reactions have occurred very rarely in subjects who were given the vaccines, but a cause and effect relationship has not been established.

In view of the decreases in platelet counts that have been reported, thrombocytopaenic purpura is a theoretical hazard.

Death from various, and in some cases, unknown, causes has been reported rarely following vaccination with measles, mumps and rubella vaccines; however, a causal relationship has not been established.

Post-marketing surveillance indicates that serious adverse events such as encephalitis and encephalopathy continue to be rarely reported.

DOSAGE AND ADMINISTRATION

FOR SUBCUTANEOUS ADMINISTRATION - **Do not inject intravenously**

The dosage of vaccine is the same for all persons. Inject the total volume of the single dose vial (about 0.5 mL) of reconstituted vaccine subcutaneously, preferably into the outer aspect of the upper arm. **Do not give immune globulin (IG) concurrently with MERUVAX II.**

To ensure that there is no loss of potency during shipment, the vaccine must be maintained at a temperature of 2-8°C.

Before reconstitution, store MERUVAX II at 2-8°C. **Protect from light.**

CAUTION: A sterile syringe free of preservatives, antiseptics, and detergents should be used for each injection and/or reconstitution of the vaccine because these substances may inactivate the live virus vaccine. A 25 gauge, 5/8" (16 mm) needle is recommended.

To reconstitute, use only the diluent supplied, since it is free of preservatives or other antiviral substances which might inactivate the vaccine.

First withdraw the entire volume of diluent into the syringe to be used for reconstitution. Inject all the diluent in the syringe into the vial of lyophilised vaccine, and agitate to mix thoroughly. Withdraw the entire contents into a syringe and inject the total volume of restored vaccine subcutaneously.

It is important to use a separate sterile syringe and needle for each individual patient to prevent transmission of hepatitis B and other infectious agents from one person to another.

Each dose contains not less than the equivalent of 1,000 TCID₅₀ of the U.S. Reference Rubella Virus.

Parenteral drug products should be inspected visually for particulate matter and discoloration prior to administration. MERUVAX II, when reconstituted, is clear yellow.

Storage

It is recommended that the vaccine be used as soon as possible after reconstitution. Protect vaccine from light at all times, since such exposure may inactivate the virus. Store reconstituted vaccine in the vaccine vial in a dark place at 2-8°C and discard if not used within eight hours.

HOW SUPPLIED

No. 4747 - MERUVAX II is supplied as a single-dose vial of lyophilised vaccine, with diluent.

MANUFACTURER/DISTRIBUTOR

Distributed for:
Merck Sharp & Dohme (Australia) Pty. Limited
54-68 Ferndell St., Granville, N.S.W. 2142

by
CSL Biotherapies Pty Ltd
45 Poplar Rd., Parkville, Vic. 3052

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