1. NAME OF THE MEDICINAL PRODUCT

Rubella Vaccine (Live) I.P.
Brand name: R-VAC

2. QUALITATIVE AND QUANTITATIVE COMPOSITION

R-Vac (Rubella Vaccine (Live) I.P.) freeze dried is prepared using Wistar RA 27/3 strain Rubella vaccine virus. This vaccine virus is propagated on human diploid cells (HDC). 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 contains bubbles and/or indentations. The vaccine meets the requirement of I.P. and WHO when tested by the methods outlined in I.P. and WHO TRS 840 (1994).

Each single human dose when reconstituted in a volume of 0.5 ml. contains not less than 1000 $CCID_{50}$ of Rubella live virus particles. Stability data has shown that the vaccine retains the potency of 1000 $CCID_{50}$ per dose after 1 week at 37ºC.

3. PHARMACEUTICAL FORM

Injectable, Freeze-dried powder for injection

4. CLINICAL PARTICULARS

4.1 Indications

R-VAC is indicated for:
1) Immunization against Rubella in persons from 12 months of age to puberty

2) Vaccination of adolescent and adult males may be a useful procedure in preventing or controlling outbreaks of rubella in circumscribed population groups.

3) Non-pregnant adolescent and adult females: Immunization of susceptible non-pregnant adolescent and adult females of child bearing age with live attenuated Rubella virus vaccine is indicated if certain precautions are observed. Vaccinating susceptible post-pubertal females confers individual protection against subsequently acquiring rubella infection during pregnancy, which in turn prevents infections of foetus and consequent congenital rubella injury. Women of child bearing age should be advised not to become pregnant for two months after vaccination.

4) Post-partum Woman: It has been found convenient in many instances to vaccinate rubella susceptible women in the immediate post-partum period.

5) Revaccination: Children first 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 immunization was ineffective. Rubella vaccine can be safely and effectively given simultaneously with DTP, DT, Td, TT, BCG, Polio vaccine (OPV and IPV), Haemophilus influenzae type b and Hepatitis B or yellow fever vaccines or vitamin A supplementation (WHO Model Insert – Rubella Vaccine, Weekly Epid. Record (2011, 86: 301-316) Clarke et al 2016, Zepp et al 2007).

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) 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 of Rubella vaccine should be administered deep subcutaneously 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 - 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 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 Rubella 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 diluents 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: Since the effect of the live rubella vaccine on the fetus is not known, it is contraindicated in pregnancy. Rubella vaccine should not be administered to women known to be pregnant because of risks to the fetus from administration of these live virus vaccines cannot be excluded for theoretical reasons. Women should be counseled to avoid becoming pregnant for 28 days after vaccination with rubella vaccine. 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, leukemia, severe anemia and other severe diseases of the blood system, severe impairment of renal function, decompensated heart disease, following administration of gammaglobulin or blood transfusions.
  The vaccine is contraindicated in persons who are severely immunocompromised as a result of a congenital immune disorder, 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

- Individuals receiving corticosteroids, other immuno-suppressive drugs or undergoing radio-therapy may not develop an optimal immune response.
- Low grade fever, mild respiratory infection or diarrhoea and other minor illness should not be considered as contraindication. It is particularly important to immunize children with malnutrition.
- Asymptomatic HIV-positive persons can be immunized.
- Children with malignant disease or who have had a bone marrow transplant should be immunized against rubella six (6) months after immunosuppressant treatment is stopped. Vaccination should be postponed if the potential vaccinee has a serious illness.
- Persons with active tuberculosis should not be vaccinated until treatment has been established.
- 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.

4.5 Interaction with other medicinal products and other forms of Interaction

Due to the risk of inactivation, the 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.

Rubella vaccine can be safely and effectively given simultaneously with DTP, DT, Td, TT, BCG, Polio vaccine (OPV and IPV), Haemophilus influenzae type b and Hepatitis B or yellow fever vaccines or vitamin A supplementation.
Concomitant vaccines should be given by separate injections.

4.6 Pregnancy and lactation

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

Reactions are generally mild and transient. Rubella vaccine may cause mild pain and tenderness at the injection site within 24 hours of 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 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.
Following adverse events in clinical trials were reported irrespective of causal relationship to vaccine.

Local Symptoms:
Pain, redness, swelling, tenderness.
General symptoms:
Mild to moderate fever
Skin:
Rash
Haemopoietic system and Lymphatic System: Thrombocytopenia.
Musculoskeletal System:
Arthralgia, myalgia
Anaphylactic reactions can also occur rarely. In susceptible individuals the vaccine may very rarely cause allergic reactions like urticaria, pruritis and allergic rash within 24 hours of vaccination.

4.9 Overdose

No case of overdose has been reported.

5. PHARMACOLOGICAL PROPERTIES

5.1 Pharmacodynamic properties

Pharmacotherapeutic group: Viral vaccine,
Rubella, live attenuated, ATC code: J07BJ01

SIIPL's Rubella vaccine is highly immunogenic and induces immune response in 80-100% vaccinated individuals as observed in clinical studies.

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 product.

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

S.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 *GS*6740, 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 (White colour)

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	3 ml	Height 75 mm

	Point Cut (OPC) mechanism		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, Maharashtra, INDIA.
Telephone: ++ 91-20- 26993900
Fax: ++ 91- 20-26993924 / 26993921
Website: www.seruminstitute.com

8. MARKETING AUTHORISATION NUMBER(S)

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

Rubella Vaccine (Live) I.P Permission No MF/BIO/20/000066 in Form 46

9.DATE OF FIRST AUTHORISATION/RENEWAL OF THE AUTHORISATION

Date of First Authorization: 11th August, 1992
Date of Renewal of the Authorization: 27th August 2020

Date: 31 December 2022