1. NAME OF THE MEDICINAL PRODUCT

Measles, Mumps and Rubella Vaccine (Live) I.P. (Freeze Dried)

2. QUALITATIVE AND QUANTITATIVE COMPOSITION

Each dose of 0.5 ml after reconstitution contains:

Live Attenuated Measles Virus (Edmonston Zagreb Strain) (Propagated on Human Diploid Cells)	NLT 1000 $CCID_{50}$
Live Attenuated Mumps Virus (Hoshino Strain): (Propagated on Chick Fibroblast Cells)	NLT 5000 $CCID_{50}$
Live Attenuated Rubella Virus (RA 27/3 strain) (Propagated on Human Diploid Cells)	NLT 1000 $CCID_{50}$

Diluent for reconstitution: Sterile Water for Injections I.P.

3. PHARMACEUTICAL FORM

- Freeze dried vaccine for subcutaneous injection upon reconstitution.

4. CLINICAL PARTICULARS

4.1 Therapeutic indications

ZyVac® MMR is indicated for prevention of Measles, Mumps and Rubella virus infections.

4.2 Posology and method of administration

Measles, Mumps and Rubella Vaccine (Live) I.P. (Freeze Dried) has to be diluted with the diluent provided before administration. Single dose of 0.5 ml should be administered as subcutaneous injection in the anterolateral aspect of thigh or the upper arm taking aseptic precautions.

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.

Steps for preparation:

A) Breaking of ampoule, to be done in the axis and over the cut.

- Hold the body of the ampule facing the colored dot (the side of the crack on the neck part).
- Put the thumb of dominant hand on the ampule head and hold tight on the opposite side with index finger.
- The dot of ampoule must be covered by thumb.
- Snap off the head of the ampoule by pushing it to the opposite side. Apply constant force to avoid uneven breakage.
- Withdraw the entire content of supplied diluent from the ampoule into a syringe.

B) Reconstitution of Lyophilized Vaccine

- Pierce the bung of the vial with the needle and gently inject the diluent into the vial.
- Detach the syringe leaving the needle in vial bung. Wait for 15 seconds.
- Revolve the vial gently between palms till the lyophilized material become a solution. Avoid shaking the vial to avoid frothing effect.
- Invert the vial, withdraw the reconstituted solution into the syringe. Use new needle and administer.

4.3 Contraindications

ZyVac® MMR should not be administered during the following conditions:

- Subjects with known hypersensitivity to egg protein, gelatin or to any other component of the vaccine.
- Pregnancy, Furthermore, pregnancy should be avoided for 1 month following vaccination

- Leukaemia, lymphomatoses and other Malignant diseases
- Severe febrile diseases
- 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.
- History of febrile convulsions or impairment of CNS.

4.4 Special warnings and precautions for use

The vaccine should be administered by subcutaneous route only.

Alcohol and other disinfecting agents must be allowed to evaporate from the skin before injection of the vaccine since they may inactivate the virus. In rare cases anaphylactic shock may occur in susceptible individual and for such emergency 1:1000 adrenaline injection should be kept 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 injections) 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 injections). Single paediatric dose should not exceed 0.5mg (0.5 ml).

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. Antihistaminic 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

Immune globulin (IG) should not to be given concomitantly with Measles, Mumps and Rubella Vaccine (Live) I.P. (Freeze Dried). Administration of immune globulins concomitantly with Measles, Mumps and Rubella Vaccine (Live) I.P. (Freeze Dried) may interfere with the expected immune response. Vaccination should be deferred for at least 3

months following blood or plasma transfusions, or administration of human immune serum globulin. Administration of measles, mumps or rubella antibody-containing blood products, including immune globulin preparations, should be avoided within 1 month after a dose of Measles, Mumps and Rubella Vaccine (Live) I.P. (Freeze Dried) unless considered to be essential.

If administration of other live virus vaccines is required, Measles, Mumps and Rubella Vaccine (Live) I.P. (Freeze Dried) should be given concomitantly at separate injection sites, or one month before or after administration of other live virus vaccines.

It has been reported that live attenuated measles, mumps and rubella virus vaccine may result in a temporary depression of tuberculin skin sensitivity. Therefore, if a tuberculin test is to be done, it should be administered either any time before, simultaneously with, or 4 to 6 weeks after vaccination with Measles, Mumps and Rubella Vaccine (Live) I.P. (Freeze Dried).

4.6 Special Population

The safety and effectiveness is not established in pregnant women and in lactating mothers. It is not known whether this vaccine is excreted in human milk.

4.7 Effects on ability to drive and use machines

No studies on the effect of ZyVac® MMR 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, 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 paraesthesia 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

ZyVac® MMR is a live attenuated viral vaccine which consists of Edmonston Zagreb strain of Measles virus propagated in MRC-5 cells, Hoshino strain of Mumps virus propagated on Chick Fibroblast Cells and RA 27/3 strain of rubella virus propagated on Human Diploid Cells. The vaccine when administered subcutaneously in a dose of 0.5 ml confers significant protection against measles, mumps and rubella based on the production of antibodies. Immunity appears 4 to 6 weeks after vaccination.

5.1 PHARMACODYNAMICPROPERTIES

The immunogenicity of ZyVac® MMR has been evaluated in the clinical trials conducted in India.

Phase II clinical trial: The study was conducted in a total of 123 healthy paediatric subjects aged 15-18 months. Among the 116 subjects evaluated for immunogenicity in this study, the seroconversion rate in subjects seronegative at baseline was 100% for measles and mumps component and 98.9% for the rubella component.

Phase III clinical trial: This was a randomized non-inferiority study conducted in a total of 328 healthy paediatric subjects aged 15-18 months. Among the subjects evaluated for immunogenicity in this study, the seroconversion rate in subjects seronegative at baseline was 99.1% for measles, 86.6% for mumps and 94.2% for rubella. These immunogenicity results were non-inferior to the WHO pre-qualified MMR vaccine used as comparator in this study.

5.2 PHARMACOKINETIC PROPERTIES

Evaluation of pharmacokinetic properties is not required for vaccines.

5.3 Preclinical safety data

5.3.1 Animal Toxicology & Pharmacology:

Non-clinical data reveal no special hazard for humans based on conventional single-dose and repeated-dose toxicity studies.

6. PHARMACEUTICAL PARTICULARS

6.1 List of excipients

In the formulation of Measles, Mumps and Rubella Vaccine (Live) I.P. (Freeze Dried), all the active ingredients are formulated with Stabilizer 176 and diluent Medium 199. The Stabilizer 176 contains following excipients: Gelatin, D-Sorbitol, Lactose monohydrate, Lactalbumin hydrolysate, Calcium gluconate, L-Alanine, L-Histidine and Tricine. pH of the Stabilizer 176 is adjusted with Sodium hydroxide.

6.2 Incompatibilities

This vaccine must not be mixed with other medicinal products.

6.3 Shelf life

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

6.4 Special precautions for storage

Store at 2°C to 8°C before and after reconstitution.
Do not freeze after reconstitution.
The diluent should not be frozen, but should be kept cool
Keep the vial in the outer carton in order to protect from light
For Single Dose: Use immediately after reconstitution.
For Multi dose: Use within 6 hour after reconstitution

6.5 Nature and contents of container

Nature and contents of container for Single dose (0.5 ml) Vials

2R Amber glass vial – USP type I with 13 mm Bromo Butyl Rubber Stopper and 13 mm Aluminium Flip Off Seals.

Nature and contents of container for Multi dose (5.0 ml, 10 dose) vial

5.0 mL Amber glass vial – USP type I with 13 mm Bromo Butyl Rubber Stopper and 13 mm Aluminium Flip Off Seals.

6.6 Special precautions for disposal

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

7. Details of manufacturer

Zydus Lifesciences Limited
Plot Survey No. 23, 25/P, 37, 40/P, 42 to 47, 49 & 50
Sarkhej- Bavla N. H. No. 8A, Opp. Ramdev Masala,
Village: Changodar, Taluka: Sanand,
Dist. Ahmedabad – 382 213, Gujarat

8. MARKETING AUTHORISATION NUMBER(S)

Permission No. MF-104/2016

9. DATE OF FIRST AUTHORISATION

30th June, 2016 and amendment dated 11th August 2016.

SmPC updated on: 26/12/2023