SUMMARY OF PRODUCT CHARACTERISTICS

MEBELLA™

[ATC Code: J07BD53]

December 2023

Manufactured by

HUMAN BIOLOGICALS INSTITUTE
(A Division of Indian Immunologicals Ltd.)
Rakshapuram, Gachibowli post,
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SUMMARY OF PRODUCT CHARACTERISTICS

1. NAME OF THE MEDICINAL PRODUCT

Brand Name: Mebella™

Generic Name: Measles and Rubella Vaccine (Live) I.P.

2. QUALITATIVE AND QUANTITATIVE COMPOSITION

Composition:

Each dose of 0.5 mL in vial lyophilized vaccine contains:
Measles virus [AIK-C strain] $\geq 10^3$ $CCID_{50}$ per single human dose
Rubella virus [RA-27/3 strain] $\geq 10^3$ $CCID_{50}$ per single human dose

(For list of excipients, see section 6.1)

3. PHARMACEUTICAL FORM

Lyophilized vaccine to be reconstituted with Sterile Water for Injection (for Subcutaneous Injection).

4. CLINICAL PARTICULARS

4.1 Therapeutic indications

- For active immunization in children of 9 months of age and older against Measles and Rubella.

4.2 Posology and method of administration:

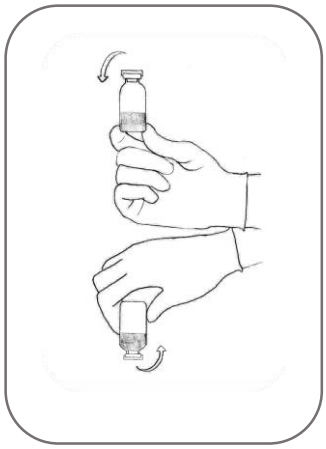
Posology:

A single dose consists of 0.5 mL of the reconstituted vaccine.
It is administered to children above 9 months of age as per recommended vaccination schedule.

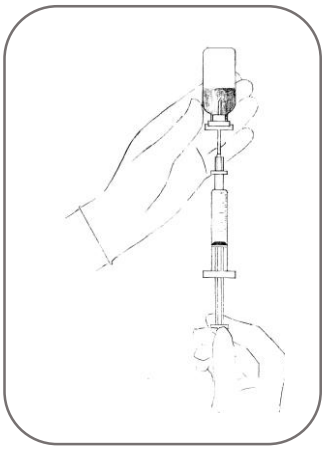
Administration:

A sterile disposable syringe and needle should be used for each administration. Prior to administration, the lyophilized vaccine has to be reconstituted only with the diluent supplied along with it. Diluent of 0.5 mL has to be used for single dose vial and 2.5 mL for 5 dose multi-dose vial. The lyophilized vaccine is easily dissolved in the diluent on gentle shaking. A single dose of 0.5 mL of reconstituted vaccine has to be withdrawn into a syringe and administered subcutaneously in anterolateral aspect of upper thigh in infants and toddlers and upper arm in older children and adults.

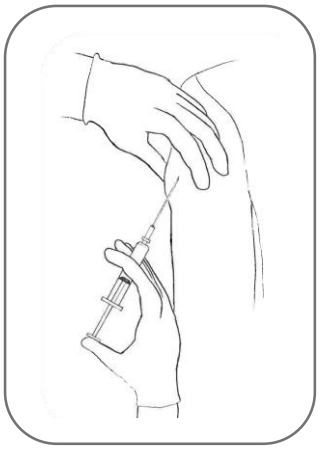
If the vaccine is not used immediately after reconstitution, it can be used within six hours, provided it is stored between +2°C to +8°C. Any amount left should be discarded after six hours of reconstitution or at the end of the vaccination session whichever is earlier.



Reconstitution with diluent & mixing before withdrawal into syringe



Withdrawal of the vaccine into the syringe before administration



Subcutaneous Administration

4.3 Contraindications:

- Vaccination with Measles and Rubella Vaccine (Live) should be avoided in any persons having high fever (>102°F / 38-39°C) or serious disease.
- Vaccination with Measles and Rubella Vaccine (Live) is contraindicated in Pregnancy. Also, pregnancy should be avoided for 1 month following vaccination.
- Persons with a history of an anaphylactic reaction to any component of the Measles and Rubella Vaccine (Live) vaccine should not receive this vaccine.
- Persons who are severely immune compromised as a result of congenital disease, HIV infection (full blown AIDS), malignant disease or treatment with high dose steroids, alkylating agents or antimetabolites, receiving immunosuppressive therapeutic medications/ radiations should not be vaccinated with Measles and Rubella Vaccine (Live).
- Diseases and disorders of the central nervous system.

4.4 Special warnings and special precautions for use:

Warnings:

- Infants from 9 to 12 months of age vaccinated with a measles-containing vaccine during measles outbreaks or for other reasons may fail to respond to the vaccine due to the presence of circulating antibodies of maternal origin and/or immaturity of the immune system
- Individuals with current thrombocytopenia may develop more severe thrombocytopenia following vaccination. In addition, individuals who experienced thrombocytopenia with the first dose of the vaccine may develop thrombocytopenia 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.

Precautions:

- *Only the diluent supplied along with the vaccine vial should be used for reconstitution*.
- The vaccinee should be observed for 30 to 60 minutes after administration of vaccine for any immediate reactions. This would help in prompt management of the adverse reaction, if any, and can be potentially reversed with proper and timely treatment.
- For anaphylactic reactions, adrenaline/ epinephrine (1 in1000) may be used. 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 (0.5mL).
- Antihistamines, hydrocortisone, IV fluids and other appropriate medications should also be used as per requirement.
- *Care should be taken to ensure that injection does not enter into a blood vessel.*

4.5 Interaction with other medicinal products and other forms of interaction:

- Routine vaccination should be deferred, if possible, in patients who are receiving Immunosuppressive therapies including radiation, corticosteroids, antimetabolites, alkylating agents and cytotoxic drugs as they may reduce the immune response to vaccines.
- Administration of immunoglobulins or other antibody-containing blood products may interfere with the immune response of the vaccine. Following vaccination with Measles and Rubella Vaccine (Live), administration of such blood products should be avoided for 2 weeks, if possible.
- This vaccine can be administered as a booster dose in subjects who have previously received any other measles/ rubella/ measles and rubella/MMR vaccine.
- Data on concomitant administration of Measles and Rubella Vaccine (Live) and other vaccines are not available.
- It has been reported that live measles and rubella virus vaccines may result in a temporary depression of tuberculin skin sensitivity. Therefore, if a tuberculin test is to be done, it should be administered either some time before or 4 to 6 weeks after vaccination with Measles and Rubella Vaccine (Live).

4.6 Fertility pregnancy and Lactation

This vaccine is contraindicated in Pregnant and Lactating women.

4.7 Effects on ability to drive and use machines

There has been no reported case of any effect of administration of Measles and Rubella Vaccine (Live) on driving or using machines.

4.8 Undesirable effects:

Measles and Rubella Vaccine (Live) is generally well tolerated. The following adverse events have been observed in clinical trials involving Measles and Rubella Vaccine (Live):

Local (at the injection site) reactions: pain, tenderness, erythema (redness) and swelling.

Systemic reactions: fever (pyrexia), myalgia (body pain), upper respiratory tract infection, boils over body.

The following additional adverse events have been documented involving use of similar live Measles and Rubella vaccines as per published literatures:

Local (at the injection site) reactions: Induration, rash.

Systemic reactions: Arthritis, arthralgia, thrombocytopenia, purpura, regional lymphadenopathy, leukocytosis, rash, paresthesia, allergic reactions including anaphylaxis

4.9 Overdose:

There has been no report of overdose with Measles and Rubella Vaccine (Live).

5. PHARMACOLOGICAL PROPERTIES:

Mechanism of Action:

Measles and Rubella Vaccine (Live) is intended to be used for prophylaxis against Measles and Rubella infection. After administration, the vaccine triggers the production of specific antibodies against Measles and Rubella in the body. These antibodies provide immunity against infection caused by Measles and Rubella virus.

5.1 Pharmacodynamic properties

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Administration of Measles and Rubella Vaccine (Live) stimulates the immune system of the body. The immune response thus elicited includes production of protective antibodies against Measles and Rubella in the body. The humoral immune response is considered seroprotective when anti-measles antibody (IgG) titre of ≥ 200 mIU/ mL and anti-rubella antibody (IgG) titre of ≥ 10 IU/mL are achieved.

In an open label Phase I study conducted in India, the safety and immunogenicity of the vaccine was evaluated when administered as a single dose in two groups of healthy subjects: 33 subjects in age group of 19 to 49 years (Group A) and 22 subjects in the age group of 12 years to below 19 years (Group B). No Serious adverse event (SAE) was reported in the study. Among the local adverse events, pain at the injection site (12.7%) and swelling at the injection site (3.6%) were the only local adverse events that were reported in the study. Among the systemic adverse events, fever (7.3%) was the only adverse event reported in both the groups. The severity of all the adverse events reported were mild. None of the adverse events were of moderate or severe category. There was overall 100% seroprotection for all the subjects of both the groups for both measles and rubella components. A rise in GMT was observed for both measles and rubella components in both the groups after vaccination. For Measles component, the GMT increased from 981.5 mIU/mL (Pre-vaccination) to 2062.2 mIU/ mL (Post-vaccination). Similarly for rubella component, the GMT significantly increased from 109.0 IU/mL (Pre-vaccination) to 185.3 IU/mL (Post-vaccination).

In Phase II/III Clinical trial conducted in India, immunogenicity and safety of the vaccine were studied when administered to four age groups of healthy subjects: 148 subjects in the age group of 18- 49 years (Group A), 148 subjects from 2 years to below 18 years of age (Group B), 148 subjects from 12 months to below 24 months of age (Group C) and 148 subjects from 9 months to below 12 months of age (Group D). The overall Seroprotection rate post vaccination for measles component for Test vaccine was 99.31% whereas the same for the rubella component was 100%. There was a significant rise in Geometric mean titres post vaccination in comparison to pre-vaccination titres for both measles and rubella components for all the age groups. The overall post vaccination GMT titre for measles component was 1495.58 mIU/mL whereas the same for rubella component was 123.87 IU/mL. No Serious adverse event

(SAE) was reported during the study. Among the Local adverse events, Injection site Erythema was present in 0.2% subjects, Injection site Pain in 3.5% subjects, Injection site Tenderness in 0.2% subject, Injection site Swelling in 1.7% subjects. Among the Systemic adverse events, Fever in 3.7% subjects , Body Pain was present in 0.2% subjects, Upper Respiratory Tract Infection in 0.2% subjects and Boils over body in 0.2% subjects. All the adverse events were either of mild or moderate severity.

5.2 Pharmacokinetic properties

Not applicable

5.3 Preclinical safety data:

Preclinical toxicology studies conducted for Measles and Rubella Vaccine (Live) concluded that the vaccine is safe for use at the recommended human dose.

6. PHARMACEUTICAL PARTICULARS

6.1 List of Excipients

D-Sorbitol, Gelatin hydrolysate, L-Alanine, L-Arginine HCl, Lactalbumin hydrolysate and Maltose monohydrate, WFI.

6.2 Incompatibilities

The vaccine should not be mixed with any other product other than the diluent supplied along with it for administration.

6.3 Shelf life

24 months when stored at + 2°C to + 8°C.

6.4 Special precaution for Storage

- Keep out of reach of Children.
- Protect from light.
- Store and transport between +2°C and +8°C. However, storage temperature of -20°C for vaccine vial is recommendeded for long term storage.
- DO NOT FREEZE THE DILUENT.
- Discard the diluent ampoule if frozen.
- Do not keep the vaccine and the diluent along with other medicinal product including other vaccine(s) that could create confusion and lead to admixture.

- In case of vaccine vials with vaccine vial monitor (VVM) the following has to be checked for decision regarding use/ discard of the vial:

The vaccine vial monitor (VVM), has not reached the discard point. if:

✓ Inner Square lighter than outer circle.
If the expiry date has not been passed USE the vaccine.

✓ At a later time, inner square still lighter than outer circle
If the expiry date has not been passed USE the vaccine.

The vaccine vial monitor (VVM), has reached the discard point, if:

× Inner Square matches colour of outer circle
DO NOT use the vaccine.

The vaccine vial monitor (VVM), has crossed the discard point, if:

× Inner Square is darker than outer ring.

DO NOT use the vaccine.

6.5 Nature and contents of the container:

Measles and Rubella Vaccine (Live) is supplied as lyophilized powder in a amber coloured glass vial. Each vaccine vial is supplied along with a separate clear glass ampoule containing diluent (water for injection) for reconstitution.

6.6 Special precautions for disposal and other handling:

A)Disposal:

As per applicable Biomedical Waste Disposal guidelines/ rules.

B) Other guidelines:

- Use a new sterile syringe and needle for every administration.
- Alcohol and other disinfecting agents must be allowed to evaporate from skin before injection of vaccine.
- 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, the diluent or reconstituted vaccine must be discarded.

7 MARKETING AUTHORISATION HOLDER

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Hyderabad-500 032, Telangana,india.
Web:www.indimmune.com

8 MARKETING AUTHORISATION NUMBER

The Marketing Authorization Number is country specific. In India, the country of origin, the Marketing Authorization Number is: **02/RR/AP/2005/V/R**

9 DATE OF FIRST AUTHORISATION

Date of First Authorization in India, the country of origin: March 2023.

10 DATE OF COMPILATION OF THE TEXT

December 2023.