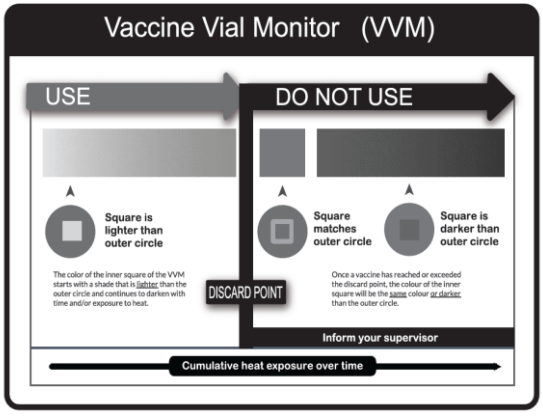
Presentation:
5 dose Vial along with diluent (2.5mL)
10 dose Vial along with diluent (5mL)

Presentation available with or without vaccine vial monitor.



VVM is a label containing a heat- sensitive material which is placed on a Flip-off Seal to register cumulative heat exposure over time. The colour dot appears on the VVM label in square element is a time - temperature sensitive dot that provides an indication 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 ofthe 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.

References:

1. WHO model pack insert
2. Data on Biological E. Limited's file
3. WHO position paper - Measles Vaccines (August 2009)

5xxx.01 ENG

For use only of a Registered Medical Practitioner or a Hospital or a Laboratory.

Manufactured by: *Biological E. Limited*
Regd. office Address: 18/1 & 3, Azamabad,
Hyderabad, Telangana - 500 020, INDIA.
Web: www.biologicale.com

Manufacturing site address:

SEZ-Unit, Sy.No 549, 550, 552 to 556,
Kolthur Village - 500 078, Shameerpet,
Medchal-Malkajgiri district, Telangana, India.

Measles Vaccine (Live) (Attenuated, Freeze Dried)

Description:

Measles vaccine is prepared from the live, attenuated strains of Measles virus (CAM-70 Tanabe strain).

Measles virus is propagated in chicken embryo fibroblast (CEF) cells. The vaccine is lyophilized preparation with physical appearance of a white to light yellow compact cake. The vaccine is provided with diluent. The vaccine meets requirements of IP and WHO.

Composition:

Each reconstituted dose of 0.5 mL contains:
Measles virus (CAM-70 strain),
propagated in chicken embryo fibroblast cells ≥1000 $CCID_{50}$

Reconstitute the vaccine vial with the diluent (0.9% w/v Sodium Chloride Injection) supplied.

Pharmaceutical Form:

Lyophilized Powder for Subcutaneous Injection upon reconstitution.

CLINICAL PARTICULARS:

Therapeutic indications:

For active immunization against measles in 9 - 12 months healthy infants at risk. 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.

Posology:

In countries where the incidence and mortality from measles is high in the first year of life, the recommended age for vaccination against measles is at 9 months of age (270 days) or shortly after. In countries where infection occurs later in life (due to sustained high vaccination coverage), the age of vaccination can be moved to 12-15 months. It is recommended that all children have two (2) opportunities for immunization with a measles-containing vaccine to reduce the number both of unvaccinated children and of those who are vaccinated but fail to respond to the vaccine (primary vaccination failures). The second dose of measles vaccine may be provided as early as one (1) month following the first dose through routine or supplemental immunization activities.

Method of Administration:

Inject a single dose of 0.5mL Measles vaccine subcutaneously. The preferred site of injection is the upper arm (fatty tissue over triceps) or in front of thigh (fatty tissue over antero-lateral thigh muscle). The lyophilized vial must be reconstituted by adding the entire contents of the supplied diluent to the vaccine vial. The vaccine pellet should be completely dissolved in the diluent. Following reconstitution, the vaccine should be inspected visually for any foreign particulate matter prior to administration. If observed, the vaccine must be discarded.

The reconstituted vaccine should be used within six (6) hours. Any opened vials remaining at the end of an immunization session or six hours after reconstitution should be discarded.

The vaccine is supplied along with the diluent (0.9% w/v Sodium Chloride Injection). Only the diluent supplied along with the vaccine should be used to reconstitute the vaccine. Using an incorrect diluent will result in damage to the vaccine and/or serious reactions to those receiving the vaccine. Diluent must not be frozen but must be cooled between +2°C and +8°C before reconstitution.

Instructions for Use:

A sterile needle and sterile syringe must be used for the reconstitution of the vaccine and aseptic techniques should be followed.

Draw the diluent into Syringe, 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, after 15 seconds remove the needle. Rotate the vial gently between your palms till the material dissolves. Avoid shaking the vial as this would cause frothing. Withdraw the reconstituted solution into the syringe, now ready for administration.

Contraindications & warnings:

A previous allergic reaction to measles and measles containing vaccine is a contraindication. Persons with a history of an anaphylactic reaction to any components of the vaccine should not be vaccinated. Apart from these, there are few contraindications to the administration of Measles vaccine. It is particularly important to immunize children with malnutrition. Low-grade fever, mild respiratory infections or diarrhoea, and other minor illnesses should not be considered as contraindications. On theoretical ground measles vaccine should also be avoided in pregnancy. The vaccine must not be given to a pregnant woman and that woman should not become pregnant within two months after having the vaccine.

Immune deficiency:

Children with known or suspected HIV infection are at increased risk of severe measles and should be offered measles vaccine as early as possible. The standard WHO recommendation for children at high risk of contracting measles is to immunize with measles vaccine at six (6) months of age, followed by an extra dose at nine (9) months. The vaccine is contraindicated in 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 antimetabolites, or in persons who are receiving immunosuppressive therapeutic radiation.

Clinical Trial Experience:

Adverse Reactions:

The safety and immunogenicity of Measles component is established in the clinical trials conducted with BE's Measles and Rubella Vaccine conducted in India.

Side effects following Measles vaccination are mostly mild and transient, and are similar in frequency and severity to those following administration of each of the single antigen products.

In a Phase I clinical trial, the most common treatment emergent adverse events (AEs) were pyrexia (16.67%), injection site pain (12.5%), injection site swelling (12.5%) injection site erythema (8.33%), cough (4.17%) and nasopharyngitis (4.17%). Vital signs and physical examination results observed did not indicate any safety issues.

In a Phase II/III non-inferiority clinical trial the most frequently reported AEs were Pyrexia 19 (6.33%), Injection site pain 15 (5.00%), Irritability 11 (3.67%), Injection site swelling 10 (3.33%), Injection site erythema 10 (3.33%) and Crying 9 (3.00%) in General disorders and administration site conditions; Cough 6 (2.00%) in Respiratory, thoracic and mediastinal disorders; and Nasopharyngitis 4 (1.33%) in infections and infestations. There were no clinically significant differences in the mean change for vital signs (temperature, heart rate and respiratory rate) from screening visit to subsequent visits.

In a Phase IV, post marketing clinical trial, the most frequently reported AEs were Injection site pain (4.7%), Pyrexia (2.20%), Injection site erythema (1.60%), Injection site swelling (1.40%) and postvaccinal irritability (0.90%). Vital signs, physical examinations and systemic examinations did not indicate any safety issues of concern.

Most of the local and systemic AEs reported were either mild or moderate in their intensity. The most commonly observed AEs were in line with the expected AE profile as seen with other available Measles and Rubella containing combination vaccines.

Anaphylactic reactions are also rare but have the potential to be fatal. 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. 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 (0.01 ml/kg of 1:1000 injection). Single paediatric dose should not exceed 0.5 mg (0.5 ml). This will help in tackling the anaphylactic shock/reaction effectively.

The use of intravenous (IV) adrenaline (epinephrine) is hazardous and should only be considered in extreme emergency in subjects with profound shock that is immediately life-threatening. Only dilute adrenaline (at least 1:10,000) will be used, and the injection given slowly. Because of the possibility of delayed reactions, subjects who have had an anaphylactic reaction will be retained in hospital, even though they may appear to have made a full recovery. The use of an appropriate sized airway for resuscitation is only advised in the hands of properly trained and competent health professional, and only in unconscious subjects.

Hydrocortisone and antihistaminics should also be available in addition to supportive measures such as oxygen inhalation. These should be considered, however, in the further management of anaphylaxis by appropriately trained staff.

Immune response:

In a Phase II/III non-inferiority clinical trial, overall 600 infants aged between 9-12 months were equally randomised into one of the two treatment groups. All 300 subjects in test vaccine arm received BE's MR vaccine and all 300 subjects in control vaccine arm received comparator vaccine. The proportion of subjects seroconverted in BE's MR vaccine and comparator vaccine groups for Measles were 82.83% (246/297) and 86.01% (252/293) respectively There was no statistically significant difference in proportion of subjects seroconverted between groups at Day 42 (p-value 0.3083 for Measles)

The primary analysis of anti-Measles antibody titres at Day 42 showed geometric mean titres (GMT) of 372.64 and 337.73 in BE's MR vaccine group and comparator vaccine group respectively. There is no statistically significant difference in geometric mean titres (GMT) between the groups as the p-value (0.3083) derived using independent sample t-test is not less than 0.05.

Based on the evaluation of safety and immunogenicity of Measles component as part of BE's MR vaccine clinical trials, no separate clinical studies were conducted with Measles Vaccine (Monovalent).

Pre-clinical Safety Data:

Single dose toxicity studies in Mice, Rats and repeat dose toxicity studies in Rats and Rabbits were conducted. Based on the toxicity studies conducted, it is concluded that the vaccine formulation did not produce any adverse effects. Immunogenicity studies were also conducted with the vaccine in Rats and Rabbits. Based on the immunogenicity studies, the vaccine found to be immunogenic.

Shelf life:

24 months from date of manufacture

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

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 2-8ºC. The diluent should not be frozen, but should be kept cool.