Rotavirus Vaccine, Live Attenuated (Oral) Liquid

DESCRIPTION

Rotavirus Vaccine, Live Attenuated (Oral), Liquid supplied by Serum Institute of India Pvt. Ltd. is a Liquid Bovine Human Reassortant Rotavirus-Pentavalent Vaccine (LBRV-PV). The vaccine constitutes five viruses (Human and Bovine reassortant strains) of serotype G1, G2, G3, G4, and G9. All these strains constitute VP7 gene of respective serotype from human strains reassorted with bovine (UK) rotavirus. Each strain is propagated in VERO cells individually; and all five strains are blended before filling.

Rotavirus Vaccine, Live Attenuated (Oral), Liquid is available as ready to use liquid formulation and the product has the appearance of yellowish translucent liquid with possible presence of inherent product aggregates. The vaccine contains no preservatives. Rotavirus Vaccine, Live Attenuated (Oral), Liquid is for oral administration and not for injection. The vaccine conforms to I.P. and World Health Organization (W.H.O.) requirements.

COMPOSITION

Each dose of 2 ml contains:

Live Attenuated Bovine - Human Rotavirus Reassortant [G1, G2, G3, G4 and G9]* $\geq 10^{5.6}$ FFU / Serotype.

*Grown on vero cells.

Excipients :Citric Acid Anhydrous, Potassium Phosphate Dibasic Anhydrous, Sucrose, Hydrolyzed Gelatin, Zinc Chloride, Calcium Chloride Dihydrate, Sodium citrate tribasic dihydrate, Eagle's MEM (Minimum Essential Medium) with Hank's Salts, Glutamine, Sodium Bicarbonate and Water for injection.

This vaccine contains no Preservatives.

Dose : 2 ml - 1 dose by oral administration.

INDICATION

Rotavirus Vaccine, Live Attenuated (Oral), Liquid is indicated for active immunization of healthy infants from the age of 6 weeks for the prevention of gastroenteritis due to rotavirus infection when administered as a 3-dose series. The three dose regimen should be completed by one year of age.

CONTRAINDICATIONS

Hypersensitivity to any component of the vaccine is a contraindication to vaccine. Individuals who develop symptoms suggestive of hypersensitivity after receiving a dose of Rotavirus Vaccine, Live Attenuated (Oral), Liquid should not receive further doses. Infants with a history of uncorrected congenital malformation of the gastrointestinal tract that would predispose the infant for intussusception should not receive vaccine. Individuals with Severe Combined Immunodeficiency Disease (SCID) should not receive vaccine as cases of gastroenteritis associated with other live rotavirus vaccines have been reported in infants with SCID. History of intussusception (IS) is a contraindication to vaccine administration.

WARNINGS and PRECAUTIONS

No safety or efficacy data of Rotavirus Vaccine, Live Attenuated (Oral), Liquid is available in immunocompromised infants, infants infected with HIV or infants with chronic gastroenteritis. Administration of Rotavirus Vaccine, Live Attenuated (Oral), Liquid may be considered with caution in immunocompromised infants and infants in close contact with immunodeficient persons if in the opinion of the physician the benefit far outweigh the risks of vaccine. Similarly, acute infection or febrile illness may be a reason for delaying the administration of Rotavirus Vaccine, Live Attenuated (Oral), Liquid, if in the opinion of the physician the benefits far outweigh the risks of vaccine. Low-grade fever and mild upper respiratory tract infection are not contraindications to Rotavirus Vaccine, Live Attenuated (Oral), Liquid.

Available published data shows a small increased incidence of intussusception (IS) following other live oral Rotavirus vaccines especially after the first dose. The safety data from the clinical trials of Rotavirus Vaccine, Live Attenuated (Oral) (already licensed lyophilized formulation of BRV-PV) did not show any increased risk of IS when compared with placebo. In Phase III trial, no intussusception was reported in Rotavirus Vaccine, Live Attenuated (Oral), Liquid and Rotavirus Vaccine, Live Attenuated (Oral) groups. However, health care providers should carefully evaluate cases with symptoms suggestive of IS.

Similar to other rotavirus vaccines, vaccination with Rotavirus Vaccine, Live Attenuated (Oral), Liquid may not protect all vaccine recipients against rotavirus infection. Also, Rotavirus Vaccine, Live Attenuated (Oral), Liquid will not provide protection against gastroenteritis caused by the other pathogens.

Drug Interactions

Immunosuppressive therapies including irradiation, antimetabolites, alkylating agents, cytotoxic drugs and corticosteroids (used in greater than minimal doses), may reduce the immune response to vaccines.

Rotavirus Vaccine, Live Attenuated (Oral), Liquid can be administered concomitantly with other vaccines of the infant immunization programme, including combined diphtheria, tetanus toxoid and pertussis vaccine (DTP), inactivated poliovirus vaccine (IPV), oral polio vaccine (OPV), H. influenzae type b conjugate (Hib), hepatitis B vaccine. No interaction studies have been performed with Rotavirus Vaccine, Live Attenuated (Oral), Liquid in infants with other medicinal products.

In phase 2/3 study of Rotavirus Vaccine, Live Attenuated (Oral), Liquid, three doses of either Rotavirus Vaccine, Live Attenuated (Oral), Liquid or Rotavirus Vaccine, Live Attenuated (Oral), (Freeze-Dried) were administered 4 weeks apart (minimum interval of 4 weeks and maximum of 6 weeks). All subjects received concomitantly other UIP vaccines as per the national immunization schedule (DTwP-HepB-Hib, bOPV, IPV). Other than UIP, OPV was also administered during national / sub-national immunization days; BCG and Pneumococcal vaccines were also allowed during the study period.

Pregnancy

Rotavirus Vaccine, Live Attenuated (Oral), Liquid is not indicated for adults, including women of child-bearing age and should not be administered to pregnant females. Animal reproduction studies have not been conducted with Rotavirus Vaccine, Live Attenuated (Oral), Liquid.

ADVERSE REACTIONS

In the phase III trial of Rotavirus Vaccine, Live Attenuated (Oral), no differences were detected between Rotavirus Vaccine, Live Attenuated (Oral) and placebo groups in the post vaccination rates of solicited adverse events within 7 days of each dose of vaccine. Similarly, in the phase III trial of Rotavirus Vaccine, Live Attenuated (Oral), Liquid, no differences were detected between Rotavirus Vaccine, Live Attenuated (Oral), Liquid and Rotavirus Vaccine, Live Attenuated (Oral) groups in the post-vaccination rates of solicited adverse events within 7 days of each dose of vaccine. These events in decreasing order of frequency were:

Fever [64.6% in Rotavirus Vaccine, Live Attenuated (Oral), Liquid group and 64.6% in Rotavirus Vaccine, Live Attenuated (Oral) group], irritability [51.5% in Rotavirus Vaccine, Live Attenuated (Oral), Liquid group and 50.5% in Rotavirus Vaccine, Live Attenuated (Oral) group)], decreased appetite [31.9% in Rotavirus Vaccine, Live Attenuated (Oral), Liquid group and 31.6 % in Rotavirus Vaccine, Live Attenuated (Oral) group], decreased activity level [23.2% in Rotavirus Vaccine, Live Attenuated (Oral), Liquid group and 22.3% in Rotavirus Vaccine, Live Attenuated (Oral)], vomiting [17.9% in Rotavirus Vaccine, Live Attenuated (Oral), Liquid group and 13.8 % in Rotavirus Vaccine, Live Attenuated (Oral)] and diarrhea [12.1% in Rotavirus Vaccine, Live Attenuated (Oral), Liquid group and 13.8% in Rotavirus Vaccine, Live Attenuated (Oral) group]. The incidence of all solicited events was similar in Rotavirus Vaccine, Live Attenuated (Oral), Liquid and Rotavirus Vaccine, Live Attenuated (Oral) groups. Most of these events were of short duration and predominately mild (74% of episodes) in severity. It should be noted that in the phase 3 study, Rotavirus Vaccine, Live Attenuated (Oral), Liquid and Rotavirus Vaccine, Live Attenuated (Oral) were administered to all children concomitantly with DTwP vaccine, which is known to cause a level of reactogenicity similar to that observed in this study.

The occurrence of unsolicited adverse events was monitored throughout the phase 3 trial and the incidence was similar in both the groups. The most frequent serious adverse events (SAE) observed included bronchiolitis, lower respiratory tract infection and gastroenteritis. Only one SAE of gastroenteritis that occurred within 7 days post-vaccination in Rotavirus Vaccine, Live Attenuated (Oral) group was considered to be causally related.

No death as well as intussusception case was reported in this study.

Further, in Phase III trial of Rotavirus Vaccine, Live Attenuated (Oral), total thirteen cases of intussusception were diagnosed; 6 occurred in the Rotavirus Vaccine, Live Attenuated (Oral) arm and 7 in the placebo arm. None occurred within 28 days of receiving a dose of Rotavirus Vaccine, Live Attenuated (Oral) or placebo. None were related to study vaccination or led to discontinuations from the study.

DOSAGE AND ADMINISTRATION

Rotavirus Vaccine, Live Attenuated (Oral), Liquid is for ORAL ADMINISTRATION ONLY AND MUST NOT BE ADMINISTERED PARENTERALLY.

Dosage:

Rotavirus Vaccine, Live Attenuated (Oral), Liquid should be administered as a 3-dose regimen, 4 weeks apart, beginning at 6 weeks of age. The three dose regimen should be completed by one year of age. Rotavirus Vaccine, Live Attenuated (Oral), Liquid may be co-administered with other routine childhood immunizations (i.e., Diphtheria, Tetanus and Pertussis [DTwP], Hepatitis B vaccine, H. influenzae type b (Hib) vaccine, inactivated polio vaccine (IPV) and Oral Polio Vaccine [OPV]). Because of the typical age distribution of rotavirus gastroenteritis, rotavirus vaccination of children > 24 months of age is not recommended. Based on recommendations from the World Health Organization, if the routine childhood immunizations are initiated later than 6 weeks of age and/or at a longer dose interval than 4-weeks, Rotavirus Vaccine, Live Attenuated (Oral), Liquid can still be administered, by itself or concomitantly with DTwP. There are no restrictions on the infant's consumption of food or liquid, including breast milk, either before or after vaccination with Rotavirus Vaccine, Live Attenuated (Oral), Liquid.

It is recommended that infants who receive Rotavirus Vaccine, Live Attenuated (Oral), Liquid as the first dose should complete the three dose series with Rotavirus Vaccine, Live Attenuated (Oral), Liquid. There is no data on safety, immunogenicity or efficacy of Rotavirus Vaccine, Live Attenuated (Oral), Liquid when administered interchangeably with other available rotavirus vaccines.

In case that an incomplete dose is administered (the baby spits up or regurgitates most of the vaccine), a single replacement dose may be administered at the same vaccination visit*. The baby may continue to receive the remaining doses as per schedule.

*Physician's discretion is advised

Dosage administration:

Each single oral dose of Rotavirus Vaccine, Live Attenuated (Oral), Liquid is 2 ml in volume. The vaccine is available as ready to use vial. If the integrity of the vaccine vial has been compromised, that particular vial must be discarded. The content of vial should be inspected visually for any foreign particulate matter and/or abnormal physical appearance prior to administration. In the event of either being observed, discard the vaccine. Vaccine must be used immediately. If not used immediately, it can be held for a period of maximum 6 hours, provided, a syringe* is used to cap the opening of the vial adapter and the entire assembly is stored at 2 to 8°C.

* Use fresh syringe for administration of each dose. The vaccine vial monitor (see figure), for this type of vaccine is attached to the vial cap and should be discarded when the vaccine is being used. Any unused vaccine or waste material should be disposed-off in accordance with local requirements.

The vaccine must not be mixed with other medicinal products.

For administration of vaccine orally refer section "Instructions for use".

STORAGE

Rotavirus Vaccine, Live Attenuated (Oral), Liquid must be stored between +2°C to +8°C. Protect from light. DO NOT FREEZE.

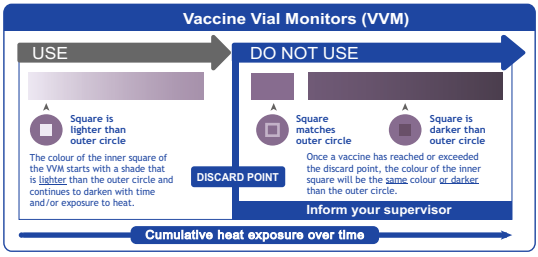
SHELF LIFE

24 months. Do not use after expiry date.

PRESENTATION

2 ml - 1 dose vial + 1 adapter and sterile disposable syringe.
4 ml - 2 doses vial + 1 adapter and 2 sterile disposable syringes.

THE VACCINE VIAL MONITOR (VVM) (Optional)



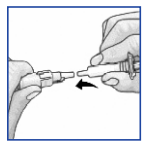
Vaccine Vial Monitors (VVMs) are on the cap of Rotavirus Vaccine, Live Attenuated (Oral), Liquid supplied through Serum Institute of India Pvt. Ltd. This is a time-temperature sensitive dot that provides an indication of the cumulative heat to which the vial has been exposed. It warns the end user when 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 of the outer circle, then the vaccine can be used. As soon as the colour of the central square is the same colour as the outer circle or of a darker colour than the outer circle, then the vial should be discarded.

INSTRUCTIONS FOR USE

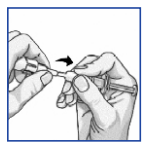
To administer the vaccine orally:

1. Remove plastic cap from the vial containing vaccine.

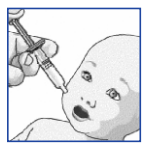


2. Fit the vial adapter on the vaccine vial. Connect the syringe to the vial adapter.

3. While holding the plunger down, turn syringe with vial upside down. Pull back the plunger to withdraw single dose (2 ml) into the syringe.



4. Remove the syringe from the vial adapter. The vaccine is ready for administration.



5. Administer the entire content of the syringe orally (on the inside of the cheek). The child should be seated in a reclining position. Do not inject.

Multidose vial: Leave the vial adapter on the vaccine vial. Use a fresh syringe for second dose after withdrawal and administration of first dose.

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Protection from birth onwards
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