SERUM INSTITUTE OF INDIA PVT. LTD.
Cyrus Poonawalla Group

Corporate Plant
Format

Title	Artwork Format		
Format No.	2002-0001-F0003-000		
Effective Date	09/11/2020	**Page No.**	1 of 2

Rotavirus Vaccine, Live Attenuated (Oral)

Freeze-Dried

DESCRIPTION

Rotavirus Vaccine, Live Attenuated (Oral) supplied by Serum Institute of India Pvt. Ltd. is a pentavalent vaccine. 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 and then freeze-dried. The vaccine is for protection from any severe rotavirus infection.
Rotavirus vaccine is available as a vial of freeze-dried vaccine to be reconstituted with a liquid diluent in a vial containing antacid (Citrate bicarbonate buffer). Vaccine is to be reconstituted with the help of adapter and syringe just prior to oral administration.
The vaccine or diluents contains no preservatives. The vaccine is for oral administration and not for injection.
The vaccine conforms to the World Health Organization (W.H.O.) requirements.

COMPOSITION

Each dose of 2.5 ml contains :
Live Attenuated Bovine - Human Rotavirus Reassortant
[G1, G2, G3, G4 and G9]* $\geqslant 10^{5.6}$ FFU / Serotype
Reconstitute with Diluent for Rotavirus Vaccine.
Diluent is a sterile solution (Citrate Bicarbonate Buffer) prepared using
9.6 mg /ml citric acid monohydrate and 25.6 mg/ml sodium bicarbonate.
* Grown on vero cells.
Excipients:
Eagle's MEM (Minimum Essential Medium) with Hank's Salts, Glutamine and Sodium bicarbonate. Sucrose and Glycine.

INDICATIONS

SII Rotavirus Vaccine, Live Attenuated, Oral (Freeze-Dried) 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.

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) 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) is available in immunocompromised infants, infants infected with HIV or infants with chronic gastroenteritis. Administration of Rotavirus Vaccine, Live Attenuated (Oral) 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). Low-grade fever and mild upper respiratory tract infection are not contraindications to Rotavirus Vaccine, Live Attenuated (Oral).
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) did not show any increased risk of IS. 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) may not protect all vaccine recipients against rotavirus infection. Also, Rotavirus Vaccine, Live Attenuated (Oral) 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) 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) vaccine and hepatitis B vaccine. No interaction studies have been performed with Rotavirus Vaccine, Live Attenuated (Oral) in infants with other medicinal products.

Pregnancy

Animal reproduction studies have not been conducted with Rotavirus Vaccine, Live Attenuated (Oral). It is also not known whether Rotavirus Vaccine, Live Attenuated (Oral) can cause fetal harm when administered to a pregnant woman or can affect reproduction capacity. Rotavirus Vaccine, Live Attenuated (Oral) is not indicated for adults including women of child-bearing age and should not be administered to pregnant females.

Lactation

Rotavirus Vaccine, Live Attenuated (Oral) is not intended for use in adults. There are no data of its use during pregnancy and lactation.

Effects on Ability to Drive and Use Machine

Not relevant.

Preclinical Safety Data

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

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. These events in decreasing order of frequency were : Fever (68.2% in the Rotavirus Vaccine, Live Attenuated (Oral) group, 69.7% in the placebo group), irritability (42.6% in the Rotavirus Vaccine, Live Attenuated (Oral) group, 36.1% in the placebo group), decreased appetite (20.4% in the Rotavirus Vaccine, Live Attenuated (Oral) group, 20.0% in the placebo group), decreased activity level (18.8% in the Rotavirus Vaccine, Live Attenuated (Oral) group, 17.1% in the placebo group), vomiting (17.0% in the Rotavirus Vaccine, Live Attenuated (Oral) group, 16.9% in the placebo group) and diarrhea (8.4% in the Rotavirus Vaccine, Live Attenuated (Oral) group, 10% in the placebo group). Except for irritability, the incidence of all solicited events was similar in Rotavirus Vaccine, Live Attenuated (Oral) and placebo groups. Most of these events were of short duration and predominately mild (98% of episodes) in severity. It should be noted that in the phase 3 efficacy study, Rotavirus Vaccine, Live Attenuated (Oral) and placebo 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 efficacy trial. The most frequent serious adverse events observed included gastroenteritis, lower respiratory tract infection, bronchiolitis, bronchopneumonia, pyrexia and pneumonia. Except for 11 cases of gastroenteritis that occurred within 7 days post-vaccination, none of the SAEs observed were considered to be related to study products. Of the 11 gastroenteritis cases, 6 participants had received Rotavirus Vaccine, Live Attenuated (Oral) and 5 had received Placebo. However, out of these 11, only one tested positive for rotavirus antigen in stool by ELISA.
A total of seven cases of intussusception occurred until time of primary analysis of which four were in the Rotavirus Vaccine, Live Attenuated (Oral) group and three in the Placebo group. None of the cases occurred within 28 days of receiving a dose of Rotavirus Vaccine, Live Attenuated (Oral) or Placebo. All cases of intussusception were causally unrelated to study vaccination.

DOSAGE AND ADMINISTRATION

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

Dosage:

Rotavirus Vaccine, Live Attenuated (Oral) should be administered as a 3-dose regimen, 4 weeks apart, beginning at 6 weeks of age, course should be completed before 32 weeks of age. 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) can still be administered, by itself or concomitantly with DTP, inactivated poliovirus vaccine (IPV), oral poliovirus vaccine (OPV), H. influenzae type b conjugate (Hib) vaccine, and hepatitis B vaccine. 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).
It is recommended that infants who receive Rotavirus Vaccine, Live Attenuated (Oral) as the first dose should complete the three dose series with Rotavirus Vaccine, Live Attenuated (Oral). There is no data on safety, immunogenicity or efficacy of Rotavirus Vaccine, Live Attenuated (Oral) 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) is 2.5 ml in volume. The administration of a single dose vaccine requires one vial of freeze-dried vaccine, one vial of citrate bicarbonate buffer, one adapter and syringe(s) for vaccine reconstitution and administration. Only the specific buffer diluent provided must be used for reconstitution. If the integrity of either the vaccine or buffer diluent vial has been compromised, that particular vial must be discarded. The content of vial containing buffered diluent should be inspected visually for any foreign particulate matter and/or abnormal physical appearance prior to reconstitution. Reconstituted vaccine may contain inherent product aggregates. The vaccine must not be mixed with other medicinal products. Reconstituted 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.
In the event of either being observed, discard the vaccine. The vaccine must not be mixed with other medicinal products. Any unused vaccine or waste material should be disposed of in accordance with local requirements.
For Reconstitution instructions for Rotavirus Vaccine, Live Attenuated (Oral) refer "Instructions for use and handling".

PHARMACODYNAMIC PROPERTIES

Rota virus, pentavalent, live, reassorted, ATC code J07BH02.
Rotavirus Vaccine, Live Attenuated (Oral) has been developed to mimic the immunologic responses stimulated by natural infection. It is assumed that vaccine virus replicates in the small intestine and induces immunity. The immunologic mechanism by which Rotavirus Vaccine, Live Attenuated (Oral) protects against rotavirus gastro-enteritis is not entirely understood. It is thought that IgA antibodies generated against Rotavirus Vaccine, Live Attenuated (Oral) reflect a local immune response. Though there is no serological correlate of protection, a Phase II randomized, double- blind, placebo controlled study assessed the serum IgA response to Rotavirus Vaccine, Live Attenuated (Oral) in 60 healthy infants. Three doses of the $10^{5.6}$ FFU/serotype formulation induced a significant immune response. The seroconversion rate at 28 days post dose 3 was 60% among vaccine recipients and 7.69%among placeborecipients ($p < 0.05$). The seroconversion rates indicated that the vaccine is immunogenic in infants. These results are similar to those reported in India for other licensed rotavirus vaccines.

PHARMACOKINETIC PROPERTIES

Evaluation of pharmacokinetic properties is not applicable for vaccines.

OVER DOSE AND TREATMENT

No cases of overdose have been reported.

STORAGE

Rotavirus Vaccine, Live Attenuated (Oral) should be stored below + 25°C.
The diluent should be stored below + 30°C and should not be frozen,
but should be kept cool.
Keep medicine out of reach of children.

SHELF LIFE

30 months. Do not use after expiry date.

PRESENTATION

50 x 1 dose

Revision date: 19.11.2021

Manufactured and released by:
SERUM INSTITUTE OF INDIA PVT. LTD.
212/2, Hadapsar, Pune 411028, INDIA
Protection from birth onwards

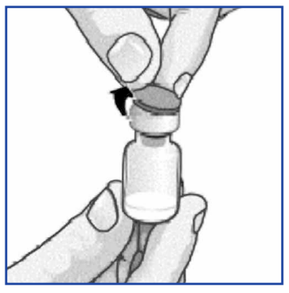
P. R. Holder:
SM Pharmaceuticals Sdn. Bhd.
Lot 88, Sungai Petani Industrial Estate,
08000, Sungai Petani, Kedah, Malaysia

200XXXXX/0

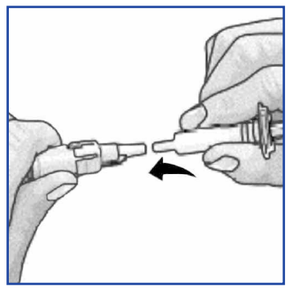
Reason for issue: New			Specification: Printed on bible 40 gsm.	
Customer: Malaysia	Store below + 25°C			
Product: **Rotavirus Vaccine, Live Attenuated (Oral)**	1 dose		Colour: C M Y K Pantone 220 C and Pantone 072 C	
Item Code number: 200XXXXX/0		Specification No.:		Artwork made to: 100%
Supercedes Item Code:			Dimensions: 353 x 292 mm	
PACKAGING DEVELOPMENT	QUALITY CONTROL	REGULATORY AFFAIRS	MEDICAL DEPARTMENT	QUALITY ASSURANCE

File Name: E:\Packaging artworks as on 090212\Artworks SII Pvt Ltd 231015\Insert\Malaysia\Rotavirus Vaccine (Oral), generic, 25°C, 1 dose, Eng Insert.cdr Date: 19.11.2021

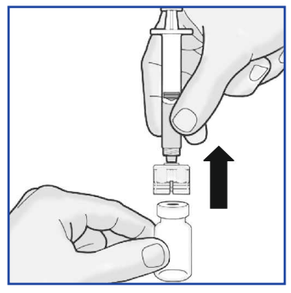
Instructions for use and handling



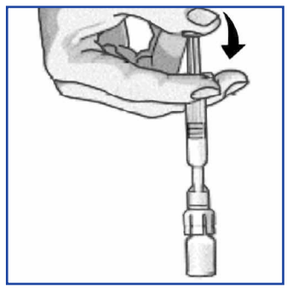
1. Remove plastic caps from the vials containing diluent and freeze-dried powder.



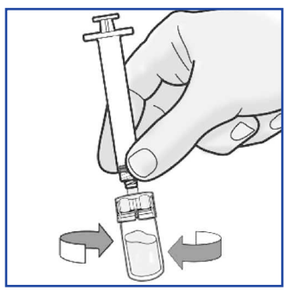
2. Fit the vial adapter on the diluent vial. Connect the syringe to the vial adapter. Withdraw the entire diluent into the syringe.



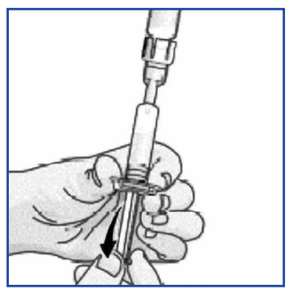
3. Disconnect the vial adapter and the attached syringe from the diluent vial.



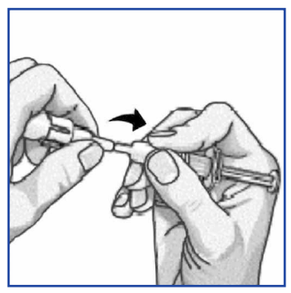
4. Fit the vial adapter with the syringe on to the vaccine vial. Inject the entire contents of the syringe into the vial containing the freeze-dried powder.



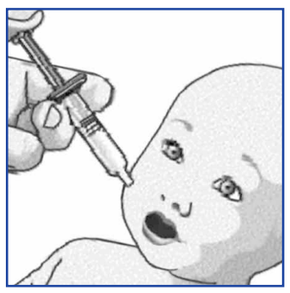
5. While holding the syringe, gently swirl until the solution is clear. Do not shake. The reconstituted vaccine will appear as pinkish to yellowish liquid.



6. While holding the plunger down, turn syringe with vial upside down. Pull back the plunger to withdraw single dose (2.5 ml) mixture back into the syringe.



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



8. 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.

Reason for issue: New			Specification: Printed on bible 40 gsm.	
Customer: Malaysia	Store below + 25°C			
Product: **Rotavirus Vaccine, Live Attenuated (Oral)**	1 dose		Colour: C M Y K Pantone 220 C and Pantone 072 C	
Item Code number: 200XXXXX/0		Specification No.:		Artwork made to: 100%
Supercedes Item Code:			Dimensions: 353 x 292 mm	
PACKAGING DEVELOPMENT	QUALITY CONTROL	REGULATORY AFFAIRS	MEDICAL DEPARTMENT	QUALITY ASSURANCE

File Name: E:\Packaging artworks as on 090212\Artworks SII Pvt Ltd 231015\Insert\Malaysia\Rotavirus Vaccine (Oral), generic, 25°C, 1 dose, Eng Insert.cdr Date: 19.11.2021