SUMMARY OF PRODUCT CHARACTERISTICS

ROTASIIL – Liquid

1. NAME OF THE MEDICINAL PRODUCT

ROTASIIL-Liquid,
Rotavirus Vaccine, Live Attenuated, (Oral) (Liquid) 1 Dose

2. QUALITATIVE AND QUANTITATIVE 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.

Each single oral dose of ROTASIIL-Liquid is 2.0 ml in volume. The vaccine is supplied as ready to use either one plastic ampoule or a strip of five plastic ampoules of ROTASIIL-Liquid. This vaccine contains no preservatives.

3. PHARMACEUTICAL FORM

Liquid, ready to use formulation for oral administration.
Yellowish translucent liquid with possible presence of inherent product aggregates.

4. CLINICAL PARTICULARS

4.1 Therapeutic indications

ROTASIIL-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.

4.2 Posology and method of administration

ROTASIIL-Liquid is for ORAL ADMINISTRATION ONLY AND MUST NOT ADMINISTERED PARENTERALLY.

Dosage:

ROTASIIL-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. ROTASIIL-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, ROTASIIL-Liquid can still be coadministered with DTwP. There are no restrictions on the infant's consumption of food or liquid, including breast milk, either before or after vaccination with ROTASIIL-Liquid.

It is recommended that infants who receive ROTASIIL-Liquid as the first dose should complete the three dose series with ROTASIIL-Liquid. There is no data on safety, immunogenicity or efficacy of ROTASIIL-Liquid when administered interchangeably with other available rotavirus vaccines.

In case, 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 ROTASIIL-Liquid is 2 ml in volume. The vaccine is available as ready to use either one plastic ampoule or a strip of five plastic ampoules of ROTASIIL-Liquid. If the integrity of the vaccine ampoule has been compromised, that particular ampoule must be discarded. The content of ampoule 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. The vaccine is dispensed as a single dose and is for one time use only. 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.

Instructions for ROTASIIL-Liquid administration:

- Clear the fluid from the dispensing tip by tapping the ampoule and holding it vertically.

- Open the dosing ampoule by easy twist motion.
- Administer the complete dose (2.0 ml) by gently squeezing the ampoule into baby's mouth toward the inner cheek until dosing tube is empty.

4.3 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 ROTASIIL-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.

4.4 Special warnings and precautions for use

No safety or efficacy data of ROTASIIL-Liquid is available in immunocompromised infants, infants infected with HIV or infants with chronic gastroenteritis. Administration of ROTASIIL-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 ROTASIIL-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 ROTASIIL-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) (Freeze-Dried) (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 ROTASIIL-Liquid and ROTAVIRUS VACCINE, LIVE ATTENUATED (ORAL) (Freeze-Dried) groups. However, health care providers should carefully evaluate cases with symptoms suggestive of IS.

Similar to other rotavirus vaccines, vaccination with ROTASIIL-Liquid may not protect all vaccine recipients against rotavirus infection. Also, ROTASIIL-Liquid will not provide protection against gastroenteritis caused by the other pathogens.

4.5 Interaction with other medicinal products and other forms of interaction

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

ROTASIIL-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 ROTASIIL-Liquid in infants with other medicinal products.

In phase 2/3 study of ROTASIIL-Liquid, three doses of either ROTASIIL-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.

4.6 Fertility, pregnancy and lactation

ROTASIIL-Liquid is not indicated for adults, including women of child-bearing age and should not be administered to pregnant or lactating females. Animal reproduction studies have not been conducted with ROTASIIL-Liquid.

4.7 Effects on ability to drive and use machines

Effect of ROTASIIL-Liquid on ability to drive and use machines is not known. However, ROTASIIL-Liquid is indicated for use in infant population and hence, this is not applicable.

4.8 Undesirable effects

In the phase III trial of ROTAVIRUS VACCINE, LIVE ATTENUATED (ORAL) (Freeze-Dried), no differences were detected between ROTAVIRUS VACCINE, LIVE ATTENUATED (ORAL) (Freeze-Dried) 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 ROTASIIL-Liquid, no differences were detected between ROTASIIL-Liquid and ROTAVIRUS VACCINE, LIVE ATTENUATED (ORAL) (Freeze-Dried) 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 ROTASIIL-Liquid group and 66.8% in ROTAVIRUS VACCINE, LIVE ATTENUATED (ORAL) (Freeze-Dried) group], irritability [51.5% in ROTASIIL-Liquid group and 50.5% in ROTAVIRUS VACCINE, LIVE ATTENUATED (ORAL) (Freeze-Dried) group], decreased appetite [31.9% in ROTASIIL-Liquid group and 31.6 % in ROTAVIRUS VACCINE, LIVE

ATTENUATED (ORAL) (Freeze-Dried) group], decreased activity level [23.2% in ROTASIIL-Liquid group and 22.3% in ROTAVIRUS VACCINE, LIVE ATTENUATED (ORAL) (Freeze-Dried) group], vomiting [17.9% in ROTASIIL-Liquid group and 13.8 % in ROTAVIRUS VACCINE, LIVE ATTENUATED (ORAL) (Freeze-Dried) group] and diarrhea [12.1% in ROTASIIL-Liquid group and 13.8% in ROTAVIRUS VACCINE, LIVE ATTENUATED (ORAL) (Freeze-Dried) group]. The incidence of all solicited events was similar in ROTASIIL-Liquid and ROTAVIRUS VACCINE, LIVE ATTENUATED (ORAL) (Freeze-Dried) 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, ROTASIIL-Liquid and ROTAVIRUS VACCINE, LIVE ATTENUATED (ORAL) (Freeze-Dried) 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) (Freeze-Dried) 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) (Freeze-Dried), total thirteen cases of intussusception were diagnosed; 6 occurred in the ROTAVIRUS VACCINE, LIVE ATTENUATED (ORAL) (Freeze-Dried) arm and 7 in the placebo arm. None occurred within 28 days of receiving a dose of ROTAVIRUS VACCINE, LIVE ATTENUATED (ORAL) (Freeze-Dried) or placebo. None were related to study vaccination or led to discontinuations from the study.

4.9 Overdose

No case of overdose has been reported.

5. PHARMACOLOGICAL PROPERTIES

5.1 Pharmacodynamic properties

The immune response to natural rotavirus infection is not completely defined. It is known that prior exposure to rotavirus provides incomplete protection from the virus and therefore, infants and children can be reinfected from year to year. Natural infection, however, may provide some protection from severe diarrhea during subsequent infections. This may result from a virus specific immune response generated at the intestinal mucosal surface. ROTASIIL-Liquid 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 ROTASIIL-Liquid protects against rotavirus gastroenteritis is not entirely understood. It is thought that IgA antibodies generated against ROTASIIL – Liquid reflect a local immune response. A Phase III study with ROTAVIRUS VACCINE, LIVE ATTENUATED (ORAL) (Freeze-Dried) assessed the immune response of ROTASIIL-Liquid in 1500 healthy infants. The seropositivity rates post dose 3 were 60.41% and 52.75% for ROTASIIL-Liquid and ROTAVIRUS VACCINE, LIVE ATTENUATED (ORAL) (Freeze-Dried) respectively. The seropositivity rates indicated that the vaccine is immunogenic in infants. These results are similar to those reported in India for other licensed rotavirus vaccines.

5.2 Pharmacokinetic properties

Evaluation of pharmacokinetic properties is not applicable for vaccines.

5.3 Preclinical safety data

SIIPL conducted single- and repeated-dose toxicity studies of liquid rotavirus vaccine in rodents (Wistar rats) and non-rodents (New Zealand white rabbits) by oral gavage administrations. These studies were conducted with a hexavalent vaccine which included G1, G2, G3, G4, G8 and G9 reassortants. Single dose studies included 60 rats and 18 rabbits in three groups while repeated dose studies included 70 rats in four groups and 18 rabbits in three groups. The vaccine in single and repeated-dose toxicity studies in both the species had no effects on their general health. There were no changes in body temperature, cumulative net body weight gains and hematological, clinical chemistry and urinalysis parameters in animals of either sex. No gross or microscopic histopathological changes were detected in all the organs studied.

The results of these studies showed that liquid rotavirus vaccine is well tolerated in Wistar rats and New Zealand white rabbits, even at more than five times of human dose.

6. PHARMACEUTICAL PARTICULARS

6.1 List of Excipients

Minimum Essential Medium (MEM) with Hank’s Salt, Sodium Bicarbonate, Glutamine, Hydrolysed Gelatin, Sucrose, Zinc Chloride, Calcium Chloride, Citirc Acid, Potassium Phosphate dibasic anhydrous, Sodium Citrate tri basic dihydrate, Water for Injection.

6.2 Incompatibilities

Under no circumstances should Rotavirus Vaccine, Live Attenuated (Oral) be mixed with any other medicinal products.

6.3 Shelf-life

24 months. Do not use after expiry date.

6.4 Special Precautions for Storage

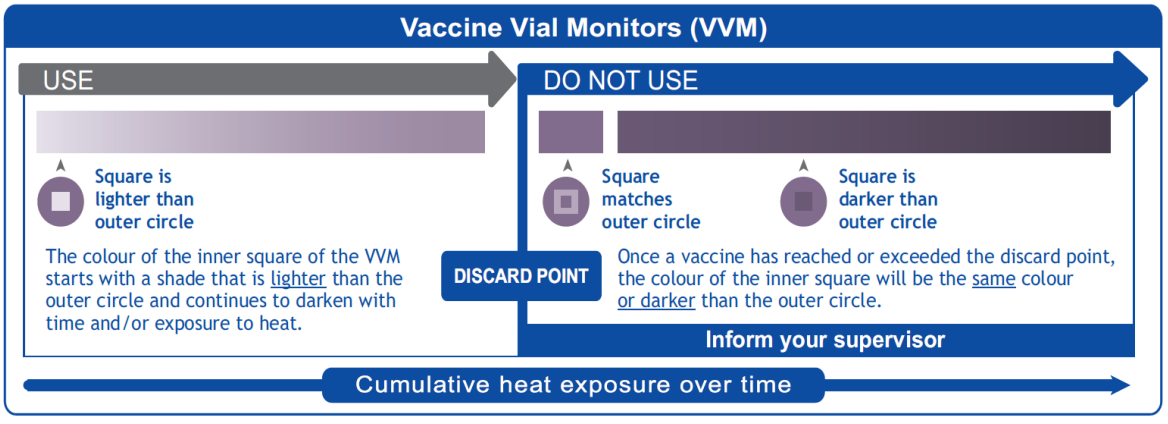
ROTASIIL-Liquid should be stored between + 2°C to + 8°C. Protect from light.
DO NOT FREEZE.

6.5 Nature and Contents of Container

Single plastic ampoule with a twist off, non-re-sealable, cap containing 2 ml Vaccine.

Strip of 5 plastic ampoules, each individual ampoule (as above) detachable from the strip, 10 such strips presented in a pack

THE VACCINE VIAL MONITOR (VVM) (Optional)



Vaccine Vial Monitors (VVMs) are part of the label on ROTASIIL-Liquid supplied through Serum Institute of India Pvt. Ltd. The colour dot which appears on the label of the ampoule is a VVM. This is a time-temperature sensitive dot that provides an indication of the cumulative heat to which the ampoule 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 inner 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 inner square is the same colour as the outer circle or of a darker colour than the outer circle, then the ampoule should be discarded.

6.6 Instructions for Use, Handling and Disposal

No special requirements.
Any unused product or waste material should be disposed of in accordance with local requirements.

7. MARKETING AUTHORISATION HOLDER

MASU CO., LTD.
Bangkok, Thailand.
Tel. 0-2556-1710-14

Manufactured by

SERUM INSTITUTE OF INDIA PVT. LTD.

212/2, Hadapsar, Pune 411028, INDIA

Protection from birth onwards

8. MARKETING AUTHORISATION NUMBER (S)

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9. DATE OF AUTHORISATION

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10. DATE OF REVISION OF THE TEXT

27 March 2023