Summary of Product Characteristics for Pharmaceutical Products

1. NAME OF THE MEDICINAL PRODUCT

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

2. QUALITATIVE AND QUANTITATIVE COMPOSITION

Each dose of 2 mL contains :
Live Attenuated Bovine-Human Rotavirus Reassortant [G1, G2, G3, G4 and G9]* ≥ 105.6 FFU / serotype.
* Grown on vero cells.

Each single oral dose of Rotavirus Vaccine, Live Attenuated, (Oral) (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 Rotavirus Vaccine, Live Attenuated, (Oral) (Liquid). This vaccine contains no preservatives.

3. PHARMACEUTICAL FORM

Liquid, ready to use formulation for oral administration.

4. CLINICAL PARTICULARS

4.1 Therapeutic indications

Rotavirus Vaccine, Live Attenuated, (Oral) 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

Rotavirus Vaccine, Live Attenuated (Oral) is for ORAL ADMINISTRATION ONLY AND MUST NOT 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]). 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 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 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, 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 either one plastic ampoule or a strip of five plastic ampoules of Rotavirus Vaccine, Live Attenuated (Oral) (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 of in accordance with local requirements. The vaccine must not be mixed with other medicinal products.
Instructions for Rotavirus Vaccine, Live Attenuated (Oral) (Liquid) administration:

- The appropriate dosing ampoule to be chosen.
- Remove the dosing ampoule from the kit.
- Hold the ampoule in left hand in vertical position and remove the upper rectangular part by twisting with right hand. Care need to be taken while twisting the tube; the vaccine should not be spilled out.
- 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 of vaccine. 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 benefits outweigh risks of vaccine. Similarly, acute infection or febrile illness may be reason for delaying the administration of ROTASIIL - Liquid. 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 ROTASIIL (already licensed lyophilized formulation) did not show any increased risk of IS when compared with placebo. In Phase III trial, no intussusception was reported in ROTASIIL
- Liquid and ROTASIIL 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 poliovirus vaccine (OPV), H. influenzae type b conjugate (Hib) vaccine, and hepatitis B vaccine.

No interaction studies have been performed with ROTASIIL - Liquid in infants with other medicinal products.

4.6 Pregnancy

ROTASIIL - 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 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 ROTASIIL, no differences were detected between ROTASIIL 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 ROTASIIL groups in the post-vaccination rates of solicited adverse events within 7 days of each dose of vaccine. Following adverse reactions have been reported during the phase III clinical trial of ROTASIIL - Liquid. Within each frequency grouping, undesirable effects irrespective of causal relationship to vaccine are presented below.

General disorders and administration site conditions:

Very common (≥1/10): Fever, irritability and decreased activity level.

Gastrointestinal disorders:

Very common (≥1/10): Decreased appetite, vomiting and diarrhea.

Common (≥1/100 and < 1/10): Gastroenteritis, abdominal pain, constipation and flatulence.

Uncommon (≥1/1000 and < 1/100): Abdominal discomfort.

Infections and infestations:

Common (≥1/100 and < 1/10): Bronchiolitis and respiratory tract infections.

The number of subjects who had one or more IAE in the 30 minute observation period, after any dose out of three doses was 17 in the ROTASIIL - Liquid group and none in the ROTASIIL group. The 17 IAEs in ROTASIIL - Liquid groups were of vomiting among at least 3246 doses (0.52%) of ROTASIIL - Liquid administered. All these events were observed within 5 minutes of administration. There was no recurrence of these symptoms after subsequent doses. All events were mild in severity and brief in duration. Neither of the event required hospitalization or any other treatment. The events were assessed as related. Further, no acute hypersensitivity reactionwas reported.

The solicited adverse events recorded within the 7 days post-vaccination were generally mild to moderate in intensity. A solicited adverse event was experienced by at least 862 (76.9%) subjects in the ROTASIIL - Liquid groups and 289 (76.9%) subjects in the ROTASIIL group. Fever was the most commonly reported solicited event in both, the combined ROTASIIL - Liquid (64.6%) and ROTASIIL (66.8%) groups (overall 65.1% of subjects). All subjects received other Universal Immunization Programme (UIP) vaccination as per the national immunization schedule (DTwPHepB- Hib, bOPV, IPV). DTwP-HepB-Hib is known to cause fever, irritability, decreased appetite, decreased activity, etc., in a high proportion of recipients and therefore a portion of the systemic solicited adverse events may be attributed to concomitant use of these vaccines. No statistically significant differences in incidence of solicited adverse events (overall and by dose) were observed during pairwise comparison between the three lots of the ROTASIIL – Liquid vaccines ($p>0.05$ for all pairs). The proportion of subjects with solicited AEs remained same for all three doses combined data of ROTASIIL - Liquid and ROTASIIL. Most subjects reporting solicited events experienced mild (85.48 %) to moderate (13.76 %) events.

Unsolicited adverse events were analyzed through 28 days' post last dose. A total of 934 subjects (62.39%) experienced 2177 unsolicited events during the specified period. The incidence of unsolicited AEs was similar in both the groups, with 1608 events in the ROTASIIL – Liquid combined group and 569 events in the ROTASIIL group. The most frequently reported unsolicited symptom was respiratory tract infection 193 (17.2%) subjects in the ROTASIIL - Liquid combined group and 66 (17.6%) subjects in the ROTASIIL group. Other common events included upper respiratory tract infection and injection site pain at DTwP-HepB-Hib injection site. The majority of events were mild to moderate and the incidence of grade 3 or higher unsolicited AEs was similar for the two groups. All the events were considered to be unrelated to the Investigational Products.

A total of 34 subjects (2.27%) reported 35 SAEs during the specified period. The proportions of subjects with SAEs in the study groups were similar with 22 (2.0%) subjects reporting 22 events in the ROTASIIL - Liquid Combined group and 12 (3.2%) subjects reporting 13 events in the ROTASIIL group. The most frequently reported SAE was bronchiolitis which occurred in 5 (0.4%) subjects in the ROTASIIL - Liquid combined group and in 2 (0.5%) subjects in the ROTASIIL group. Other common events included lower respiratory tract infection, and Gastroenteritis. Except for one SAE of gastroenteritis in ROTASIIL group, none of the SAEs were causally related to study vaccines. No intussusception cases and deaths were reported in this study.

Reporting of suspected adverse reactions

Reporting suspected adverse reactions after authorisation of the medicinal product is important. It allows continued monitoring of the benefit/risk balance of the medicinal product. Healthcare professionals are asked to report any suspected adverse reactions via the PPB website https://pv.pharmacyboardkenya.org.

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 ROTASIIL 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 ROTASIIL 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

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

6.2 Incompatibilities

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

6.3Shelflife

24 months.

6.4 Special precautions for storage

Rotavirus Vaccine, Live Attenuated (Oral) (Liquid) should be stored between + 2°C to + 8°C. Do not use after expiry date.

6.5 Nature and contents of container

Single plastic ampoule with a twist off, non-re-sealable, cap containing 2 ml Vaccine. Presented as a unit pack (private / trade market).
Strip of 5 plastic ampoules, each individual ampoule (as above) detachable from the strip, 10 such strips presented in a pack (pack of 50 – for EPI markets).

6.6 Special precautions for disposal and other handling

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

7. MARKETING AUTHORISATION HOLDER

Serum Institute Of India Pvt. Ltd.
212/2, Hadapsar, Pune 411028, India

8. MARKETING AUTHORISATION NUMBER(S)

H2021/CTD8690/18621

9. DATE OF FIRST AUTHORISATION/RENEWAL OF THE AUTHORISATION

2019

10. DATE OF REVISION OF THE TEXT

12/2024