PUBLIC ASSESSMENT SUMMARY REPORT

ROTAVAC 5D®, Rotavirus Vaccine (Live, Oral)

Bharat Biotech International Ltd., India

What is ROTAVAC 5D®, Rotavirus Vaccine (Live, Oral)?

ROTAVAC 5D®, Rotavirus Vaccine (Live, Oral), is a monovalent vaccine containing suspension of live attenuated rotavirus strain 116E propagated in Vero cells.
Rotaviruses are classified in a dual classification system based on two proteins on the surface of the virus into G and P types. Based on this nomenclature, Rotavirus 116E is classified as G9P [11].
A single human dose of ROTAVAC 5D® is 0.5 mL containing not less than [NLT] $10^{5.0}$ FFU [Focus Forming Unit] of live rotavirus 116E.

The vaccine is available as a vial of sterile liquid for oral use.

ROTAVAC 5D®, Rotavirus Vaccine (Live, Oral), is presented in USP type l glass vials and available with two presentations: Single Dose (0.5 mL) and multi-Dose (2.5 mL).
A semi-transparent gamma irradiated pink low-density polyethylene (LDPE) moulded dropper with a cap, packed in a plastic sachet is provided along with the vaccine vial.

The vaccine consists of the following composition per 0.5 mL (5 Drops) with a pH range: 6.50 to 7.50.

Components	Quantity
Active Ingredients Vero cell derived Rotavirus 116E bulk, Live attenuated	$\geq 10^{5.0}$ FFU/Dose
Excipients:	
Neomycin Sulphate BP	15 µg
Kanamycin Acid Sulphate BP	15 µg
Sucrose BP	0.25 gms
Trehalose BP	2.5 mg
Lactalbumin Hydrolyslate (LAH)	2.5 mg
Human Albumin BP	0.35 %
Potassium Di-Hydrogen Orthophosphate BP	1.65 mg
Di-Potassium Hydrogen Orthophosphate BP	10 mg
Tri-Sodium Citrate Di-hydrate BP	7.75 mg
Water for Injections BP	Quantity sufficient

The vaccine contains no preservatives. Once opened, multi-dose vials should be kept at +2°C to +8°C, with the LDPE dropper and cap and should be used within 28 days.

The oral vaccine vial bears a Vaccine Vial Monitor (VVM) type 7. The VVM7 dot is a part of the Label of the vaccine vial.

What is ROTAVAC 5D®, Rotavirus Vaccine (Live, Oral), used for?

ROTAVAC 5D® is indicated for active immunization of infants from the age of 6 weeks for the prevention of gastroenteritis due to rotavirus infection when administered as a 3-dose regimen. The vaccine is for prophylactic use only.
The upper age limit for the 3-dose primary schedule of Rotavirus vaccine should be administered to children by the age of 8 months (34 weeks) (Centre for Disease Control and Prevention).

How is ROTAVAC 5D®, Rotavirus Vaccine (Live, Oral) used?

ROTAVAC 5D® is for oral administration only *and must not be administrated parenterally.*

Care should be taken not to contaminate the multi-dose dropper of the vaccine with saliva of the babies.
Multi Dose Vials of **ROTAVAC 5D®** from which one or more doses of vaccine have been removed during an immunization session may be used in subsequent immunization sessions for up to a maximum of 28 days after opening, provided that all of the following conditions are met (as described in the WHO policy statement: Multi-Dose Vial Policy (MDVP), Revision 2014 WHO/IVB/14.07.

- Once opened, multi-dose vials should be kept between +2°C and + 8°C
- The vaccine is approved for use for up to 28 days after opening of the vial, as determined by WHO. (https://extranet.who.int/pqweb/vaccines/list-prequalified-vaccines)
- The expiry date of the vaccine has not passed.
- The vaccine vial has been, and will continue to be, stored at the recommended temperature with the dropper and cap in place; furthermore, the vaccine vial monitor is visible on the vaccine label and is not past its discard point, and the vaccine has not been damaged by freezing.

It is recommended that infants who receive **ROTAVAC 5D®** as the first dose should complete the 3-dose regimen with **ROTAVAC 5D®** There is no data on safety, immunogenicity or efficacy when **ROTAVAC 5D®** is administered interchangeably with other rotavirus vaccines.

What are the vaccine characteristics?

The **ROTAVAC 5D®**, Rotavirus Vaccine (Live, Oral) vaccine is pale yellow coloured sterile liquid for oral use. The Vaccine should be stored at 2 to 8°C with shelf-life of 24 months. During the immunization session, the Vaccine should be used with the LDPE dropper provided with the Vaccine.

Who is the regulatory authority responsible for its oversight vis a vis WHO?

Drugs Controller General of India (DCGI)/Central Drugs Standard Control Organization (CDSCO).

How ROTAVAC 5D®, Rotavirus Vaccine (Live, Oral), has been studied from the clinical point of view?

ROTAVAC 5D® is an alternative formulation of the WHO Pre-qualified ROTAVAC® vaccine manufactured by the Bharat Biotech International Limited (BBIL). **ROTAVAC 5D®** contains the same rotavirus strain (116E) as in ROTAVAC® and developed as a liquid formulation which is stable at 2-8°C (5±3°C) storage temperature for 24 months, thus offering an affordable and better vaccine against rotaviral diarrhoea for programmatic use in the field.

The clinical development of **ROTAVAC 5D®** was based on the prototype vaccine, ROTAVAC®, which share the same drug substance. About twenty clinical studies were conducted most of which were on the parental vaccine, which evaluated safety, immunogenicity, efficacy, EPI vaccines interference, non-inferiority, etc. in North America, Asia, and Africa. In a Phase 3 study, ROTAVAC® vaccine was assessed for its efficacy in 6800 healthy infants and found to be safe and efficacious against rotaviral gastroenteritis.

ROTAVAC 5D®, was further evaluated in 5 human clinical trials in Asia and Africa for safety, immunogenicity, non-inferiority, lot to lot consistency, etc. Specifically **ROTAVAC 5D®**, was successfully evaluated for non-inferiority against ROTAVAC® and ROTARIX.
Specifically, as it relates to **ROTAVAC 5D®**, a Phase 3 immunobridging study was conducted to compare the **ROTAVAC 5D®** vaccine with pre-existing WHO pre-qualified ROTAVAC® vaccine. A total of 360 healthy infants ages 6-8 weeks were enrolled and randomized to receive both the vaccines **ROTAVAC 5D®** and ROTAVAC® in 3:1 ratio. The results of the study revealed that **ROTAVAC 5D®** vaccine induces a similar immune response as its reference vaccine without any safety concerns. A Phase 4 study was conducted to assess the **ROTAVAC 5D®** vaccine lot consistency and non-interference with EPI vaccine and the results were reported that the vaccine lots are inducing similar immune response and non-interfere with the EPI vaccines when they were co-administered. In a Phase 2b clinical study **ROTAVAC 5D®** vaccine was demonstrated to be immunologically non-inferior to the licensed and WHO pre-qualified ROTAVAC® and ROTARIX vaccines when administered orally along with routine EPI vaccines in Zambian infants. Both BBIL vaccines, **ROTAVAC 5D®** and ROTAVAC®, had acceptable safety profile and were well tolerated by Zambian infants when co-administered with routine EPI vaccines.

Other information about evaluation of ROTAVAC 5D®, Rotavirus Vaccine (Live, Oral):

As part of the prequalification process for **ROTAVAC 5D®,** Rotavirus Vaccine (Live, Oral), dossier was reviewed by WHO and a site inspection was conducted from 27 February-3 March 2017 and found in compliance with WHO published recommendations.

WHO has conducted independent testing of **ROTAVAC 5D®,** Rotavirus Vaccine (Live, Oral) batches, for critical release parameters in contracted laboratories qualified by WHO for the purpose, and results obtained were in compliance with the quality specifications of the product.

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