



FAQ ON THE USE OF ROTAVIRUS VACCINES:

RotaSIIIL (Serum Institute of India)
and RotaVac (Bharat Biotech)

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Which rotavirus vaccines are in the global market and prequalified by WHO?

There are four WHO prequalified vaccines:

- RotaTeq (Merck), 2008;
- Rotarix (GSK), 2009;
- RotaSILL (Serum Institute of India), 2018;
- RotaVac (Bharat Biotech), 2018.



What are the indications, dosage, and administration of these four rotavirus vaccines?

RotaTeq is a human and bovine reassortant rotavirus-pentavalent vaccine, containing G1, G2, G3, G4, and P1A[8] and is indicated for the prevention of rotavirus gastroenteritis in infants and children caused by types G1, G2, G3, G4, and G9 when administered as a 3-dose series. Each dose is 2 mL for oral use. The vaccination series consists of three ready-to-use liquid doses of RotaTeq administered orally starting at 6–12 weeks of age, with the subsequent doses administered at 4- to 10-week intervals.

Rotarix is a monovalent human G1P[8] rotavirus vaccine indicated for the prevention of rotavirus gastroenteritis caused by G1 and non-G1 types (G3, G4, and G9) when administered as a 2-dose series. Each dose is 1 mL administered orally only. Administer first dose to infants beginning at 6 weeks of age. Administer second dose after an interval of at least four weeks.

RotaSILL is a liquid human and bovine reassortant rotavirus-pentavalent vaccine. The vaccine is indicated for the prevention of rotavirus gastroenteritis in infants and children caused by serotypes G1, G2, G3, G4, and G9. RotaSILL should be administered as a 3-dose regimen, administered orally four weeks apart beginning at 6 weeks of age. Each dose of RotaSILL Lyophilized is 2.5 mL and RotaSILL Liquid 2.0 mL. RotaSILL Lyophilized reconstituted vaccine must be used immediately. If not used immediately, it can be held for a maximum period of six hours, provided that a syringe is used to cap the opening of the vial adapter and the entire assembly is stored at 2–8 °C.

RotaVac is a monovalent vaccine derived from a single Indian neonatal strain of human rotavirus classified as G9P[11] and is indicated for the prevention of rotavirus gastroenteritis in infants and children caused by types G1, G2, G3, G4, and G9. It is administered as a 3-dose series of 0.5 mL, administered orally four weeks apart starting at 6 weeks of age. It is available in five-dose or ten-dose glass vial with dose dropper.



Characteristics of currently WHO-prequalified, live, oral rotavirus vaccines

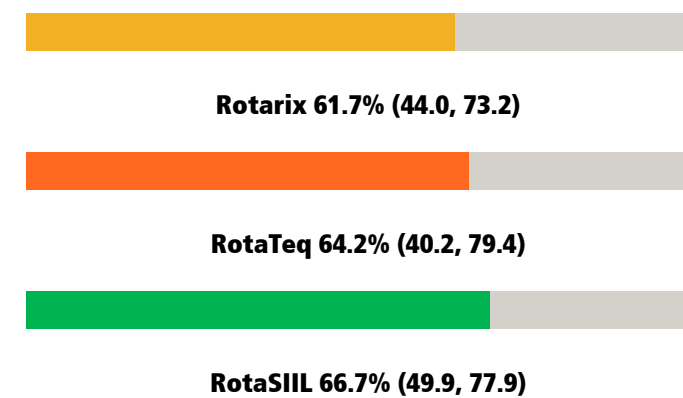
Product	Manufacturer	Doses	Composition	Formulation/storage	Presentation
Rotarix	GSK	2	G1P[8]	Liquid 2–8 °C for 36 months	One-dose plastic tube Strip of five single-dose plastic tubes
RotaTeq	Merck	3	G1, G2, G3, G4, P[8]	Liquid 2–8 °C for 24 months	One-dose plastic tube
RotaVac	Bharat Biotech	3	G9P[11]	Frozen liquid <20 °C long-term 2–8 °C for 7 months	Five-dose or 10-dose glass vial, with dose dropper
RotaSILL	Serum Institute of India	3	G1, G2, G3, G4, G9	Lyophilized <25 °C for 30 months The diluent should not be frozen but should be kept cool.	One-dose or two-dose glass vial, with vial of diluent, adapter, and syringe One-dose ampoule
				Liquid 2–8 °C for 24 months	



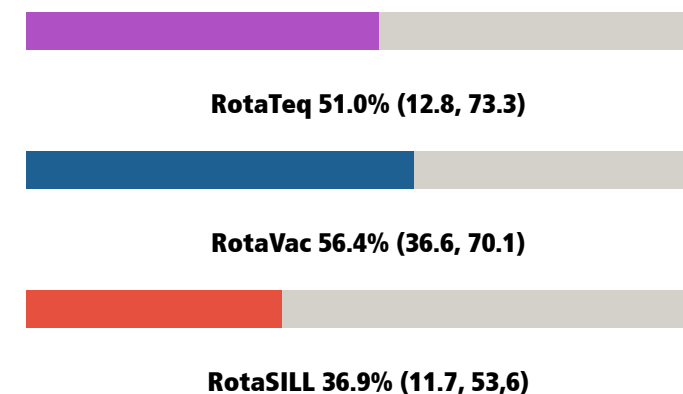
What is the efficacy of these vaccines?

In low-income countries, vaccine efficacy can be lower than in industrialized settings, similar to other live oral vaccines. Even with this lower efficacy, a greater reduction in absolute numbers of severe gastroenteritis cases and deaths was seen, due to the higher background rotavirus disease incidence.

RotaTeq evaluations in Finland, United States of America, and other countries evidenced efficacy of 98%; 95% CI (88.3, 100), and Rotarix in Latin America and Finland 84.7% (71.1, 92.4). The efficacy rates against severe rotavirus gastroenteritis in the first year of life in six African countries (Ghana, Kenya, Malawi, Mali, Niger, and South Africa) are:



The efficacy rates in three Asian countries are:



What is the impact and effectiveness of these vaccines?

According to WHO, all four vaccines are considered highly effective in preventing severe gastrointestinal disease.

For RotaTeq and Rotarix, both impact and effectiveness data are available from multiple countries and regions as they have been used for more than a decade.

According to a literature review including observational, post-licensure studies with laboratory-confirmed rotavirus as the endpoint published in 2006–2019, Rotarix vaccine effectiveness (VE) against laboratory-confirmed rotavirus among children <12 months old was 86%; 95% CI (81, 90), 77% (66, 85), and 63% (54, 70) in the low, medium, and high mortality strata, respectively. VE among children age 12–23 months ranged from 87% to 54%. RotaTeq VE among children <12 months old was 86% (76, 92) and 66% (51, 76) in the low and high strata, respectively. RotaTeq VE was 84% (79, 89) among children age 12–23 months in the low stratum. There was no substantial heterogeneity (I² range 0–36%). Median VEs in the low stratum were similar between Rotarix (83%; IQR 78, 91), RotaTeq (85%; IQR 81, 92), mixed series (86%; IQR 70, 91), and non-product specific (89%; IQR 75, 91). Rotavirus vaccines were effective in preventing rotavirus diarrhea, with a gradient in performance by child mortality.

Regarding the impact and effectiveness of RotaVac in India, sentinel surveillance has been conducted to monitor trends in acute gastroenteritis among children <5 years following roll-out in initial states. Vaccine effectiveness was evaluated using a test-negative case control design using the surveillance platform. Declines were observed in the number and proportion of acute diarrhea hospitalizations among children <5 years of age following RotaVac introduction. Preliminary vaccine effectiveness estimates are like the efficacy from clinical trials.

In 2018, Palestine switched from Rotarix to RotaVac and the same trend for diarrhea is being observed.

Studies are ongoing to evaluate the effectiveness of RotaSILL.



Are these vaccines safe?

Yes, all the rotavirus vaccines are safe.

WHO has highlighted that the benefits of rotavirus vaccination with RotaTaq and Rotarix against severe diarrhea and death from rotavirus infection far exceed the risk of intussusception. Data from RotaVac and RotaSIIIL have shown that intussusception risks among vaccinated groups were not higher than the placebo group.

The RotaVac clinical trial was not of sufficient size to detect increased risk of intussusception following vaccination, but several post-marketing evaluations for RotaVac have been conducted: active sentinel surveillance in early-introducing states in India's Universal Immunization Program (UIP) by CMC Vellore/THSTI; an early roll-out in three areas by the Society of Applied Studies was published (Vaccine June 2020); and an INCLEN Intussusception Network Surveillance Study is finalizing its analysis.

The phase III clinical trials for both RotaVac and RotaSIIIL reported zero cases of intussusception in the first month following any dose of vaccine or placebo. Post-licensure safety monitoring will also continue to be important as new vaccines are adopted more widely.

RotaVac was rolled out in India's UIP, beginning with four states in 2016, using the schedule of three doses at 6, 10, and 14 weeks of age. The first dose can be given up to 1 year of age. Active sentinel surveillance for intussusception has been conducted in 28 hospitals in nine early-introducing states using a common protocol for comparability across sites/countries, which allowed pooling of data for analysis. The risk of intussusception following vaccination was analyzed using the self-controlled case-series method. No increased risk of intussusception

following RotaVac administration in Indian infants was found. This finding is like those of other rotavirus vaccines in low income, high burden settings. Differential risk of intussusception by setting could be due to a range of factors, including age at vaccination, immune response to vaccination, or concomitant administration of the oral polio vaccine.

Similar data are also being generated outside India, in early-introducing countries in Africa.



Which countries have been using RotaVac and RotaSIIIL?

Currently, approximately 60% of the Indian birth cohort receives RotaVac and 40% receives RotaSIIIL. Globally, Palestine switched from Rotarix to RotaVac in 2018, while Benin (2019), Ghana, and Nigeria (2020) have introduced RotaVac; Congo and São Tomé and Príncipe will introduce it in 2021. Regarding RotaSIIIL, Burkina Faso and the Democratic Republic of the Congo introduced it in 2019.



How much is the cost of each rotavirus vaccine?

The availability and prices of the rotavirus vaccines can be found on the PAHO Revolving Fund website: <https://www.paho.org/en/revolvingfund>

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