RotaTeq®
[Rotavirus Vaccine, Live, Oral, Pentavalent]
Circular Number 9714300

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MERCK & CO., INC.
Whitehouse Station, NJ 08889, USA

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DESCRIPTION

RotaTeq* is a live, oral pentavalent vaccine that contains 5 live reassortant rotaviruses. The rotavirus parent strains of the reassortants were isolated from human and bovine hosts. Four reassortant rotaviruses express one of the outer capsid proteins (G1, G2, G3, or G4) from the human rotavirus parent strain and the attachment protein (P7) from the bovine rotavirus parent strain. The fifth reassortant virus expresses the attachment protein, P1A (genotype P[8]), hereafter referred to as P1[8], from the human rotavirus parent strain and the outer capsid protein G6 from the bovine rotavirus parent strain (see Table 1).

Table 1

Name of Reassortant	Human Rotavirus Parent Strains and Outer Surface Protein Compositions	Bovine Rotavirus Parent Strain and Outer Surface Protein Composition	Reassortant Outer Surface Protein Composition (Human Rotavirus Component in Bold)	Minimum Dose Levels (10^6 infectious units)
G1	WI79 - G1, P1[8]	WC3 - G6, P7[5]	**G1**, P7[5]	2.2
G2	SC2 - G2, P2[6]		**G2**, P7[5]	2.8
G3	WI78 - G3, P1[8]		**G3**, P7[5]	2.2
G4	BrB - G4, P2[6]		**G4**, P7[5]	2.0
P1[8]	WI79 - G1, P1[8]		G6, **P1[8]**	2.3

The reassortants are propagated in Vero cells using standard cell culture techniques in the absence of antifungal agents.

The reassortants are suspended in a buffered stabilizer solution. Each vaccine dose contains sucrose, sodium citrate, sodium phosphate monobasic monohydrate, sodium hydroxide, polysorbate 80, cell culture media, and trace amounts of fetal bovine serum. There are no preservatives or thimerosal present.

RotaTeq is a pale yellow clear liquid that may have a pink tint.

CLINICAL PHARMACOLOGY

Rotavirus is a leading cause of severe acute gastroenteritis in infants and young children, with over 95% of these children infected by the time they are 5 years old.[1] The most severe cases occur among infants and young children between 6 months and 24 months of age.[2]

Mechanism of Action

The exact immunologic mechanism by which RotaTeq protects against rotavirus gastroenteritis is unknown (see CLINICAL STUDIES, *Immunogenicity*). RotaTeq is a live viral vaccine that replicates in the small intestine and induces immunity.

CLINICAL STUDIES

Overall, 72,324 infants were randomized in 3 placebo-controlled, phase 3 studies conducted in 11 countries on 3 continents. The data demonstrating the efficacy of RotaTeq in preventing rotavirus gastroenteritis come from 6,983 of these infants from the US (including Navajo and White Mountain Apache Nations) and Finland who were enrolled in 2 of these studies: the Rotavirus Efficacy and Safety Trial (REST) and Study 007. The third trial, Study 009, provided clinical evidence supporting the consistency of manufacture and contributed data to the overall safety evaluation.

The racial distribution of the efficacy subset was as follows: White (RotaTeq 68%, placebo 69%); Hispanic-American (RotaTeq 10%, placebo 9%); Black (2% in both groups); Multiracial (RotaTeq 4%, placebo 5%); Asian (<1% in both groups); Native American (RotaTeq 15%, placebo 14%), and Other (<1% in both groups). The gender distribution was 52% male and 48% female in both vaccination groups.

The efficacy evaluations in these studies included: 1) Prevention of any grade of severity of rotavirus gastroenteritis; 2) Prevention of severe rotavirus gastroenteritis, as defined by a clinical scoring system; and 3) Reduction in hospitalizations due to rotavirus gastroenteritis.

The vaccine was given as a three-dose series to healthy infants with the first dose administered between 6 and 12 weeks of age and followed by two additional doses administered at 4- to 10-week intervals. The age of infants receiving the third dose was 32 weeks of age or less. Oral polio vaccine administration was not permitted; however, other childhood vaccines could be concomitantly administered. Breast-feeding was permitted in all studies.

The case definition for rotavirus gastroenteritis used to determine vaccine efficacy required that a subject meet both of the following clinical and laboratory criteria: (1) greater than or equal to 3 watery or looser-than-normal stools within a 24-hour period and/or forceful vomiting; and (2) rotavirus antigen detection by enzyme immunoassay (EIA) in a stool specimen taken within 14 days of onset of symptoms. The severity of rotavirus acute gastroenteritis was determined by a clinical scoring system that took into account the intensity and duration of symptoms of fever, vomiting, diarrhea, and behavioral changes.

The primary efficacy analyses included cases of rotavirus gastroenteritis caused by serotypes G1, G2, G3, and G4 that occurred at least 14 days after the third dose through the first rotavirus season post vaccination.

Analyses were also done to evaluate the efficacy of RotaTeq against rotavirus gastroenteritis caused by serotypes G1, G2, G3, and G4 at any time following the first dose through the first rotavirus season postvaccination among infants who received at least one vaccination (Intent-to-treat, ITT).

Rotavirus Efficacy and Safety Trial

Primary efficacy against any grade of severity of rotavirus gastroenteritis caused by naturally occurring serotypes G1, G2, G3, or G4 through the first rotavirus season after vaccination was 74.0% (95% CI: 66.8, 79.9) and the ITT efficacy was 60.0% (95% CI: 51.5, 67.1). Primary efficacy against severe rotavirus gastroenteritis caused by naturally occurring serotypes G1, G2, G3, or G4 through the first rotavirus season after vaccination was 98.0% (95% CI: 88.3, 100.0), and ITT efficacy was 96.4%, (95% CI: 86.4, 99.6). See Table 2.

Table 2
Efficacy of RotaTeq against any grade of severity of and severe* G1-4 rotavirus gastroenteritis through the first rotavirus season postvaccination in REST

	Per Protocol		Intent-to-Treat[1]	
	RotaTeq	Placebo	RotaTeq	Placebo
Subjects vaccinated	2,834	2,839	2,834	2,839
Gastroenteritis cases				
Any grade of severity	82	315	150	371
Severe*	1	51	2	55
Efficacy estimate % and (95% confidence interval)				
Any grade of severity	74.0 (66.8, 79.9)		60.0 (51.5, 67.1)	
Severe*	98.0 (88.3, 100.0)		96.4 (86.4, 99.6)	

* Severe gastroenteritis defined by a clinical scoring system based on the intensity and duration of symptoms of fever, vomiting, diarrhea, and behavioral changes
[1] ITT analysis includes all subjects in the efficacy cohort who received at least one dose of vaccine.

The efficacy of RotaTeq against severe disease was also demonstrated by a reduction in hospitalizations for rotavirus gastroenteritis among all subjects enrolled in REST. RotaTeq reduced hospitalizations for rotavirus gastroenteritis caused by serotypes G1, G2, G3, and G4 through the first two years after the third dose by 95.8% (95% CI: 90.5, 98.2). The ITT efficacy in reducing hospitalizations was 94.7% (95% CI: 89.3, 97.3) as shown in Table 3.

Table 3
Efficacy of RotaTeq in reducing G1-4 rotavirus-related hospitalizations in REST

	Per Protocol		Intent-to-Treat*	
	RotaTeq	Placebo	RotaTeq	Placebo
Subjects vaccinated	34,035	34,003	34,035	34,003
Number of hospitalizations	6	144	10	187
Efficacy estimate % and (95% confidence interval)	95.8 (90.5, 98.2)		94.7 (89.3, 97.3)	

* ITT analysis includes all subjects who received at least one dose of vaccine.

Study 007

Primary efficacy against any grade of severity of rotavirus gastroenteritis caused by naturally occurring serotypes G1, G2, G3, or G4 through the first rotavirus season after vaccination was 72.5% (95% CI: 50.6, 85.6) and the ITT efficacy was 58.4% (95% CI: 33.8, 74.5). Primary efficacy against severe rotavirus gastroenteritis caused by naturally occurring serotypes G1, G2, G3, or G4 through the first rotavirus season after vaccination was 100% (95% CI: 13.0, 100.0) and ITT efficacy against severe rotavirus disease was 100%, (95% CI: 30.9, 100.0) as shown in Table 4.

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Table 4
Efficacy of RotaTeq against any grade of severity of and severe* G1-4 rotavirus gastroenteritis through the first rotavirus season postvaccination in Study 007

	Per Protocol		Intent-to-Treat[1]	
	RotaTeq	Placebo	RotaTeq	Placebo
Subjects vaccinated	650	660	650	660
Gastroenteritis cases				
Any grade of severity	15	54	27	64
Severe*	0	6	0	7
Efficacy estimate % and (95% confidence interval)				
Any grade of severity	72.5 (50.6, 85.6)		58.4 (33.8, 74.5)	
Severe*	100.0 (13.0, 100.0)		100.0 (30.9, 100.0)	

* Severe gastroenteritis defined by a clinical scoring system based on the intensity and duration of symptoms of fever, vomiting, diarrhea, and behavioral change
[1] ITT analysis includes all subjects in the efficacy cohort who received at least one dose of vaccine.

Multiple Rotavirus Seasons

The efficacy of RotaTeq through a second rotavirus season was evaluated in a single study (REST). Efficacy against any grade of severity of rotavirus gastroenteritis caused by rotavirus serotypes G1, G2, G3, and G4 through the two rotavirus seasons after vaccination was 71.3% (95% CI: 64.7, 76.9). The efficacy of RotaTeq in preventing cases occurring only during the second rotavirus season postvaccination was 62.6% (95% CI: 44.3, 75.4). The efficacy of RotaTeq beyond the second season postvaccination was not evaluated.

Rotavirus Gastroenteritis Regardless of Serotype

The rotavirus serotypes identified in the efficacy subset of REST and Study 007 were G1, P1[8]; G2, P1[4]; G3, P1[8]; G4, P1[8]; and G9, P1[8].

In REST, the efficacy of RotaTeq against any grade of severity of naturally occurring rotavirus gastroenteritis regardless of serotype was 71.8% (95% CI: 64.5, 77.8) and efficacy against severe rotavirus disease was 98.0% (95% CI: 88.3, 99.9). The ITT efficacy starting at dose 1 was 51.0% (95% CI: 41.7, 58.9) for any grade of severity of rotavirus disease and was 96.4% (95% CI: 86.4, 99.6) for severe rotavirus disease.

In Study 007, the primary efficacy of RotaTeq against any grade of severity of rotavirus gastroenteritis regardless of serotype was 72.7% (95% CI: 51.9, 85.4) and efficacy against severe rotavirus disease was 100% (95% CI: 12.7, 100). The ITT efficacy starting at dose 1 was 48.0% (95% CI: 21.6, 66.1) for any grade of severity of rotavirus disease and was 100% (95% CI: 31.0, 100.0) for severe rotavirus disease.

Rotavirus Gastroenteritis By Serotype

The efficacy against any grade of severity of rotavirus gastroenteritis by serotype in REST is shown in Table 5.

Table 5
Serotype-specific efficacy of RotaTeq against any grade of severity of rotavirus gastroenteritis among infants in REST through the first rotavirus season postvaccination (Per Protocol)

	Number of cases		
Serotype identified by PCR	RotaTeq (N=2,834)	Placebo (N=2,839)	% Efficacy (95% Confidence Interval)
Serotypes present in RotaTeq			
G1, P1[8]	72	286	74.9 (67.3, 80.9)
G2, P1[4]	6	17	63.4 (2.6, 88.2)
G3, P1[8]	1	6	NS
G4, P1[8]	3	6	NS
Serotypes not present in RotaTeq			
G9, P1[8]	1	3	NS
Unidentified*	11	15	NS

N=number vaccinated
NS=not significant

* Includes rotavirus antigen-positive samples in which the specific serotype could not be identified by PCR

Immunogenicity

A relationship between antibody responses to RotaTeq and protection against rotavirus gastroenteritis has not been established. In phase 3 studies, 92.9% to 100% of 439 recipients of RotaTeq achieved a 3-fold or more rise in serum anti-rotavirus IgA after a three-dose regimen when compared to 12.3%-20.0% of 397 placebo recipients.

INDICATIONS AND USAGE

RotaTeq is indicated for the prevention of rotavirus gastroenteritis in infants and children caused by the serotypes G1, G2, G3, and G4 when administered as a 3-dose series to infants between the ages of 6 to 32 weeks. The first dose of RotaTeq should be administered between 6 and 12 weeks of age (see DOSAGE AND ADMINISTRATION).

CONTRAINDICATIONS

A demonstrated history of hypersensitivity to any component of the vaccine.

Infants who develop symptoms suggestive of hypersensitivity after receiving a dose of RotaTeq should not receive further doses of RotaTeq.

PRECAUTIONS

General

Prior to administration of RotaTeq, the health care provider should determine the current health status and previous vaccination history of the infant, including whether there has been a reaction to a previous dose of RotaTeq or other rotavirus vaccine.

Febrile illness may be reason for delaying use of RotaTeq except when, in the opinion of the physician, withholding the vaccine entails a greater risk. Low-grade fever (<100.5°F [38.1°C]) itself and mild upper respiratory infection do not preclude vaccination with RotaTeq.

The level of protection provided by only one or two doses of RotaTeq was not studied in clinical trials.

As with any vaccine, vaccination with RotaTeq may not result in complete protection in all recipients.

Regarding post-exposure prophylaxis, no clinical data are available for RotaTeq when administered after exposure to rotavirus.

Intussusception

Following administration of a previously licensed live rhesus rotavirus-based vaccine, an increased risk of intussusception was observed.[3] In REST (n=69,625), the data did not show an increased risk of intussusception for RotaTeq when compared to placebo. See ADVERSE REACTIONS, *Intussusception*.

Immunocompromised Populations

No safety or efficacy data are available for the administration of RotaTeq to infants who are potentially immunocompromised including:

- Infants with blood dyscrasias, leukemia, lymphomas of any type, or other malignant neoplasms affecting the bone marrow or lymphatic system.
- Infants on immunosuppressive therapy (including high-dose systemic corticosteroids). RotaTeq may be administered to infants who are being treated with topical corticosteroids or inhaled steroids.
- Infants with primary and acquired immunodeficiency states, including HIV/AIDS or other clinical manifestations of infection with human immunodeficiency viruses; cellular immune deficiencies; and hypogammaglobulinemic and dysgammaglobulinemic states. There are insufficient data from the clinical trials to support administration of RotaTeq to infants with indeterminate HIV status who are born to mothers with HIV/AIDS.
- Infants who have received a blood transfusion or blood products, including immunoglobulins within 42 days.

No safety or efficacy data are available for administration of RotaTeq to infants with a history of gastrointestinal disorders including infants with active acute gastrointestinal illness, infants with chronic diarrhea and failure to thrive, and infants with a history of congenital abdominal disorders, abdominal surgery, and intussusception. Therefore, caution is advised when considering administration of RotaTeq to these infants.

Shedding and Transmission

Shedding was evaluated among a subset of subjects in REST 4 to 6 days after each dose and among all subjects who submitted a stool antigen rotavirus positive sample at any time. RotaTeq was shed in the stools of 32 of 360 [8.9%, 95% CI (6.2%, 12.3%)] vaccine recipients tested after dose 1; 0 of 249 [0.0%, 95% CI (0.0%, 1.5%)] vaccine recipients tested after dose 2; and in 1 of 385 [0.3%, 95% CI (<0.1%, 1.4%)] vaccine recipients after dose 3. In phase 3 studies, shedding was observed as early as 1 day and as late as 15 days after a dose. Transmission was not evaluated.

Caution is advised when considering whether to administer RotaTeq to individuals with immunodeficient close contacts such as:

- individuals with malignancies or who are otherwise immunocompromised; or
- individuals receiving immunosuppressive therapy.

There is a theoretical risk that the live virus vaccine can be transmitted to non-vaccinated contacts. The potential risk of transmission of vaccine virus should be weighed against the risk of acquiring and transmitting natural rotavirus.

Information for Parents/Guardians

Parents or guardians should be given a copy of the required vaccine information and be given the "Patient Information" appended to this insert. Parents and/or guardians should be encouraged to read the patient information that describes the

benefits and risks associated with the vaccine and ask any questions they may have during the visit.

Drug Interactions

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

For administration of RotaTeq with other vaccines, see DOSAGE AND ADMINISTRATION, *Use with Other Vaccines*.

Carcinogenesis, Mutagenesis, Impairment of Fertility

RotaTeq has not been evaluated for its carcinogenic or mutagenic potential or its potential to impair fertility.

Pediatric Use

Safety and efficacy have not been established in infants less than 6 weeks of age or greater than 32 weeks of age.

Data are available from clinical studies to support the use of RotaTeq in pre-term infants according to their age in weeks since birth (see ADVERSE REACTIONS, *Safety in Pre-Term Infants*).

Data are available from clinical studies to support the use of RotaTeq in infants with controlled gastroesophageal reflux disease.

ADVERSE REACTIONS

71,725 infants were evaluated in 3 placebo-controlled clinical trials including 36,165 infants in the group that received RotaTeq and 35,560 infants in the group that received placebo. Parents/guardians were contacted on days 7, 14, and 42 after each dose regarding intussusception and any other serious adverse events. The racial distribution was as follows: White (69% in both groups); Hispanic-American (14% in both groups); Black (8% in both groups); Multiracial (5% in both groups); Asian (2% in both groups); Native American (RotaTeq 2%, placebo 1%), and Other (<1% in both groups). The gender distribution was 51% male and 49% female in both vaccination groups.

Because clinical trials are conducted under conditions that may not be typical of those observed in clinical practice, the adverse reaction rates presented below may not be reflective of those observed in clinical practice.

Serious Adverse Events

Serious adverse events occurred in 2.4% of recipients of RotaTeq when compared to 2.6% of placebo recipients within the 42-day period of a dose in the phase 3 clinical studies of RotaTeq. The most frequently reported serious adverse events for RotaTeq compared to placebo were:

bronchiolitis	(0.6% RotaTeq vs. 0.7% Placebo),
gastroenteritis	(0.2% RotaTeq vs. 0.3% Placebo),
pneumonia	(0.2% RotaTeq vs. 0.2% Placebo),
fever	(0.1% RotaTeq vs. 0.1% Placebo), and
urinary tract infection	(0.1% RotaTeq vs. 0.1% Placebo).

Deaths

Across the clinical studies, 52 deaths were reported. There were 25 deaths in the RotaTeq recipients compared to 27 deaths in the placebo recipients. The most commonly reported cause of death was sudden infant death syndrome, which was observed in 8 recipients of RotaTeq and 9 placebo recipients.

Intussusception

In REST, 34,837 vaccine recipients and 34,788 placebo recipients were monitored by active surveillance to identify potential cases of intussusception at 7, 14, and 42 days after each dose, and every 6 weeks thereafter for 1 year after the first dose.

For the primary safety outcome, cases of intussusception occurring within 42 days of any dose, there were 6 cases among RotaTeq recipients and 5 cases among placebo recipients (see Table 6). The data did not suggest an increased risk of intussusception relative to placebo.

Table 6
Confirmed cases of intussusception in recipients of RotaTeq as compared with placebo recipients during REST

	RotaTeq (n=34,837)	Placebo (n=34,788)
Confirmed intussusception cases within 42 days of any dose	6	5
Relative risk (95% CI)[1]	1.6 (0.4, 6.4)	
Confirmed intussusception cases within 365 days of dose 1	13	15
Relative risk (95% CI)	0.9 (0.4, 1.9)	

[1] Relative risk and 95% confidence interval based upon group sequential design stopping criteria employed in REST.

Among vaccine recipients, there were no confirmed cases of intussusception within the 42-day period after the first dose, which was the period of highest risk for the rhesus rotavirus-based product (see Table 7).

Table 7
Intussusception cases by day range in relation to dose in REST

	Dose 1		Dose 2		Dose 3		Any Dose	
Day Range	RotaTeq	Placebo	RotaTeq	Placebo	RotaTeq	Placebo	RotaTeq	Placebo
1-7	0	0	1	0	0	0	1	0
1-14	0	0	1	0	0	1	1	1
1-21	0	0	3	0	0	1	3	1
1-42	0	1	4	1	2	3	6	5

All of the children who developed intussusception recovered without sequelae with the exception of a 9-month-old male who developed intussusception 98 days after dose 3 and died of post-operative sepsis. There was a single case of intussusception among 2,470 recipients of RotaTeq in a 7-month-old male in the phase 1 and 2 studies (716 placebo recipients).

Seizures

All seizures reported in the phase 3 trials of RotaTeq (by vaccination group and interval after dose) are shown in Table 8.

Table 8
Seizures reported by day range in relation to any dose in the phase 3 trials of RotaTeq

Day range	1-7	1-14	1-42
RotaTeq	10	15	33
Placebo	5	8	24

Seizures reported as serious adverse experiences occurred in <0.1% (27/36,150) of vaccine and <0.1% (18/35,536) of placebo recipients (not significant). Ten febrile seizures were reported as serious adverse experiences, 5 were observed in vaccine recipients and 5 in placebo recipients.

Most Common Adverse Events

Solicited Adverse Events

Detailed safety information was collected from 11,711 infants (6,138 recipients of RotaTeq) which included a subset of subjects in REST and all subjects from Studies 007 and 009 (Detailed Safety Cohort). A Vaccination Report Card was used by parents/guardians to record the child's temperature and any episodes of diarrhea and vomiting on a daily basis during the first week following each vaccination. Table 9 summarizes the frequencies of these adverse events and irritability.

Table 9
Solicited adverse experiences within the first week after doses 1, 2, and 3 (Detailed Safety Cohort)

Adverse experience	Dose 1		Dose 2		Dose 3	
	RotaTeq	Placebo	RotaTeq	Placebo	RotaTeq	Placebo
Elevated temperature	n=5,616 17.1%	n=5,077 16.2%	n=5,215 20.0%	n=4,725 19.4%	n=4,865 18.2%	n=4,382 17.6%
	n=6,130	n=5,560	n=5,703	n=5,173	n=5,496	n=4,989
Vomiting	6.7%	5.4%	5.0%	4.4%	3.6%	3.2%
Diarrhea	10.4%	9.1%	8.6%	6.4%	6.1%	5.4%
Irritability	7.1%	7.1%	6.0%	6.5%	4.3%	4.5%

* Temperature ≥100.5°F [38.1°C] rectal equivalent obtained by adding 1 degree F to otic and oral temperatures and 2 degrees F to axillary temperatures

Other Adverse Events

Parents/guardians of the 11,711 infants were also asked to report the presence of other events on the Vaccination Report Card for 42 days after each dose.

Fever was observed at similar rates in vaccine (N=6,138) and placebo (N=5,573) recipients (42.6% vs. 42.8%). Adverse events that occurred at a statistically higher incidence (i.e., 2-sided p-value <0.05) within the 42 days of any dose among recipients of RotaTeq as compared with placebo recipients are shown in Table 10.

Table 10
Adverse events that occurred at a statistically higher incidence within 42 days of any dose among recipients of RotaTeq as compared with placebo recipients

Adverse event	RotaTeq N=6,138 n (%)	Placebo N=5,573 n (%)
Diarrhea	1,479 (24.1%)	1,186 (21.3%)
Vomiting	929 (15.2%)	758 (13.6%)
Otitis media	887 (14.5%)	[illegible]
Nasopharyngitis	422 (6.9%)	325 (5.8%)
Bronchospasm	66 (1.1%)	40 (0.7%)

Safety in Pre-Term Infants

RotaTeq or placebo was administered to 2,070 pre-term infants (25 to 36 weeks gestational age, median 34 weeks) according to their age in weeks since birth in REST. All pre-term infants were followed for serious adverse experiences; a subset of 308 infants was monitored for all adverse experiences. There were 4 deaths throughout the study, 2 among vaccine recipients (1 SIDS and

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Patient Information

RotaTeq®* (pronounced "RŌ-tuh-tek") rotavirus vaccine, live, oral, pentavalent

You should read this information before your child receives the RotaTeq vaccine and ask your child's doctor any questions you may have. Your child will need 3 doses of the vaccine over the course of a few months. So read the leaflet before your child receives each dose of the vaccine in case any of the information about the vaccine changes. This leaflet is a summary of certain information about the vaccine. If you would like additional information, your health care provider can give you more complete information about this vaccine that is written for health care professionals. This leaflet does not take the place of talking with your child's doctor.

What is RotaTeq and How Does it Work?

RotaTeq is a vaccine that can help protect your child from getting a virus infection that can cause fever, vomiting, and diarrhea. The vaccine is given by mouth at 3 different times, each about one to two months apart. Nearly all children become infected with the rotavirus by the time they are 5 years old.

RotaTeq helps protect against diarrhea and vomiting only if they are caused by the rotavirus. It does not protect against diarrhea and vomiting that are caused by anything else.

RotaTeq may not fully protect all children that get the vaccine, and if your child already has the virus it will not help them.

What are the Symptoms of a Rotavirus Infection?

Infection with the Rotavirus is the most common cause of severe diarrhea in infants. Sometimes the diarrhea and vomiting can be severe and lead to the loss of body fluids (dehydration) and even to death.

Signs that your infant is dehydrated include:

- Sleepiness
- Dry mouth and tongue
- Fussiness
- Dry diaper for several hours

If your infant shows signs that they are dehydrated, you should call the doctor immediately.

What should I tell the doctor before my child gets RotaTeq?

There are some things your doctor should know before your child gets the vaccine. You should tell your doctor if your child:

- Has any illness with fever. A mild fever or cold by itself is not a reason to delay taking the vaccination.
- Has diarrhea or has been vomiting.
- Has not been gaining weight.
- Is not growing as expected.
- Has a blood disorder.
- Has any type of cancer.
- Has a weak immune system because of a disease (this includes HIV/AIDS).
- Gets treatment or takes medicines that may weaken the immune system (such as high doses of steroids) or has received a blood transfusion or blood products within the past 42 days.
- Was born with gastrointestinal problems, or has had a blockage or abdominal surgery.
- Has regular close contact with a member of the family or household who has a weakened immune system. For example, a person in the house with cancer or one who is taking medicines that may weaken their immune system.

Who should not receive RotaTeq?

Your child should not get the vaccine if:

- He or she had an allergic reaction after getting a dose of this vaccine.
- He or she is allergic to any of the ingredients of the vaccine. A list of ingredients can be found at the end of this leaflet.

What are the possible side effects of RotaTeq?

The most common side effects reported after taking RotaTeq were diarrhea, vomiting, fever, runny nose and sore throat, wheezing or coughing, and ear infection.

These are NOT all the possible side effects of RotaTeq. You can ask your doctor or health care provider for a more complete list.

If your child develops sudden abdominal pain; vomiting, blood in their stools or other changes in their bowel movements, it may be a sign of a serious problem. **You should call the doctor immediately.**

If your child seems to be having any side effects that are not mentioned in this leaflet, please call your doctor or other healthcare provider. If the condition continues or worsens, you should seek medical attention.

You, as a parent or guardian may also report any adverse reactions to your child's health care provider or directly to the Vaccine Adverse Event Reporting System (VAERS). The VAERS toll-free number is 1-800-822-7967 or report on line to www.vaers.hhs.gov.

Can RotaTeq be given with other vaccines?

Your child may get RotaTeq at the same time as other childhood vaccines.

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How is RotaTeq given?

The vaccine is given by mouth. Your child will receive 3 doses of the vaccine. The first dose is given when your child is 6 to 12 weeks of age, the second dose is given 4 to 10 weeks later and the third dose is given 4 to 10 weeks after the second dose. The last (third) dose should be given to your child by 32 weeks of age.

Your health care provider will gently squeeze the vaccine into your child's mouth (see Figure 1). Your infant may spit out some or all of it. If this happens, the dose does not need to be given again during that visit.

Figure 1:

What do I do if my child misses a dose of RotaTeq?

All 3 doses of the vaccine should be given to your child by 32 weeks of age. Your health care provider will tell you when your child should come for the follow-up doses. It is important to keep those appointments. If you forget or are not able to go back at the planned time, ask your health care provider for advice.

What else should I know about RotaTeq?

This leaflet gives a summary of certain information about the vaccine. If you have any questions or concerns about RotaTeq, talk to your health care provider. You can also visit www.rotateq.com.

What are the ingredients in RotaTeq?

Active Ingredient: 5 live rotavirus strains (G1, G2, G3, G4, and P1).

Inactive Ingredients: sucrose, sodium citrate, sodium phosphate monobasic monohydrate, sodium hydroxide, polysorbate 80 and also fetal bovine serum.

Rx only

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1 motor vehicle accident) and 2 among placebo recipients (1 SIDS and 1 unknown cause). No cases of intussusception were reported. Serious adverse experiences occurred in 5.5% of vaccine and 5.8% of placebo recipients. The most common serious adverse experience was bronchiolitis, which occurred in 1.4% of vaccine and 2.0% of placebo recipients. Parents/guardians were asked to record the child's temperature and any episodes of vomiting and diarrhea daily for the first week following vaccination. The frequencies of these adverse experiences and irritability within the week after dose 1 are summarized in Table 11.

Table 11
Solicited adverse experiences within the first week of doses 1, 2, and 3 among pre-term infants

	Dose 1		Dose 2		Dose 3	
Adverse event	RotaTeq	Placebo	RotaTeq	Placebo	RotaTeq	Placebo
	N=127	N=133	N=124	N=121	N=115	N=108
Elevated temperature	18.1%	17.3%	25.0%	28.1%	14.8%	20.4%
	N=154	N=154	N=137	N=137	N=135	N=129
Vomiting	5.8%	7.8%	2.9%	2.2%	4.4%	4.7%
Diarrhea	6.5%	5.8%	7.3%	7.3%	3.7%	3.9%
Irritability	3.9%	5.2%	2.9%	4.4%	8.1%	5.4%

*Temperature ≥100.5°F [38.1°C] rectal equivalent obtained by adding 1 degree F to otic and oral temperatures and 2 degrees F to axillary temperatures

Reporting Adverse Events

Parents or guardians should be instructed to report any adverse reactions to their health care provider. The US Department of Health and Human Services has established a Vaccine Adverse Event Reporting System (VAERS) to accept all reports of suspected adverse events after the administration of any vaccine, including but not limited to the reporting of events required by the National Childhood Vaccine Injury Act of 1986. For information or a copy of the vaccine reporting form, call the VAERS toll-free number at 1-800-822-7967 or report on line to www.vaers.hhs.gov.[4]

DOSAGE AND ADMINISTRATION

FOR ORAL USE ONLY. NOT FOR INJECTION.

The vaccination series consists of three ready-to-use liquid doses of RotaTeq administered orally starting at 6 to 12 weeks of age, with the subsequent doses administered at 4- to 10-week intervals. The third dose should not be given after 32 weeks of age (see CLINICAL STUDIES).

There are no restrictions on the infant's consumption of food or liquid, including breast milk, either before or after vaccination with RotaTeq.

Do not mix the RotaTeq vaccine with any other vaccines or solutions. Do not reconstitute or dilute (see *INSTRUCTIONS FOR USE*).

Each dose is supplied in a container consisting of a squeezable plastic, latex-free dosing tube with a twist-off cap, allowing for direct oral administration. The dosing tube is contained in a pouch (see *INSTRUCTIONS FOR USE*).

Use with Other Vaccines

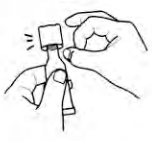
In clinical trials, RotaTeq was routinely administered concomitantly with diphtheria and tetanus toxoids and acellular pertussis (DTaP), inactivated poliovirus vaccine (IPV), *H. influenzae* type b conjugate vaccine (Hib), hepatitis B vaccine, and pneumococcal conjugate vaccine (see CLINICAL STUDIES). The safety data available are in the ADVERSE REACTIONS section.

There was no evidence for reduced antibody responses to the diphtheria or tetanus toxoid components of DTaP or to the other vaccines that were concomitantly administered with RotaTeq. However, insufficient immunogenicity data are available to confirm lack of interference of immune responses when RotaTeq is concomitantly administered with childhood vaccines to prevent pertussis.

INSTRUCTIONS FOR USE

To administer the vaccine:

Tear open the pouch and remove the dosing tube.



Clear the fluid from the dispensing tip by holding tube vertically and tapping cap.

Open the dosing tube in 2 easy motions:

1. Puncture the dispensing tip by screwing cap ***clockwise*** until it becomes tight.

2. Remove cap by turning it ***counterclockwise***.

Administer dose by gently squeezing liquid into infant's mouth toward the inner cheek until dosing tube is empty. (A residual drop may remain in the tip of the tube.)

If for any reason an incomplete dose is administered (e.g., infant spits or regurgitates the vaccine), a replacement dose is not recommended, since such dosing was not studied in the clinical trials. The infant should continue to receive any remaining doses in the recommended series.

Discard the empty tube and cap in approved biological waste containers according to local regulations.

HOW SUPPLIED

No. 4047 — RotaTeq, 2 mL, a suspension for oral use, is a pale yellow clear liquid that may have a pink tint. It is supplied as follows:

NDC 0006-4047-31 package of 1 individually pouched single-dose tube

NDC 0006-4047-41 package of 10 individually pouched single-dose tubes.

Storage

Store and transport refrigerated at 2-8°C (36-46°F). RotaTeq should be administered as soon as possible after being removed from refrigeration. For information regarding stability under conditions other than those recommended, call 1-800-MERCK-90.

Protect from light.

RotaTeq should be discarded in approved biological waste containers according to local regulations.

The product must be used before the expiration date.

REFERENCES

1. Parashar UD et al. Global illness and deaths caused by rotavirus disease in children. Emerg Infect Dis 2003;9(5):565-572.
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3. Murphy TV, Gargiullo PM, Massoudi MS et al. Intussusception among infants given an oral rotavirus vaccine. N Engl J Med 2001;344:564-572.
4. Centers for Disease Control and Prevention. General recommendations on immunization: recommendations of the Advisory Committee on Immunization Practices (ACIP) and the American Academy of Family Physicians (AAFP). MMWR 2002;51(RR-2):1-35.

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