ANNEX I

SUMMARY OF PRODUCT CHARACTERISTICS

1. NAME OF THE MEDICINAL PRODUCT

Rotarix **oral** suspension in pre-filled **oral** applicator
Rotarix **oral** suspension in squeezable tube
Rotarix **oral** suspension in multi-monodose (5 single dose) squeezable tube presentation connected by a bar
Rotavirus vaccine, live

2. QUALITATIVE AND QUANTITATIVE COMPOSITION

1 dose (1.5 mL) contains:

Human rotavirus RIX4414 strain (live, attenuated)* not less than $10^{6.0}$ $CCID_{50}$

*Produced on Vero cells

Excipients with known effect:
This product contains 1 073 mg of sucrose, 32 mg of sodium, 10 micrograms of glucose and 0.15 microgram of phenylalanine per dose (see section 4.4).

For the full list of excipients, see section 6.1.

3. PHARMACEUTICAL FORM

Oral suspension.
Rotarix is a clear and colourless liquid.

4. CLINICAL PARTICULARS

4.1 Therapeutic indications

Rotarix is indicated for the active immunisation of infants aged 6 to 24 weeks for prevention of gastro-enteritis due to rotavirus infection (see sections 4.2, 4.4 and 5.1).

The use of Rotarix should be based on official recommendations.

4.2 Posology and method of administration

Posology

The vaccination course consists of two doses. The first dose may be administered from the age of 6 weeks. There should be an interval of at least 4 weeks between doses. The vaccination course should preferably be given before 16 weeks of age, but must be completed by the age of 24 weeks.

Rotarix may be given with the same posology to preterm infants born after at least 27 weeks of gestational age (see sections 4.8 and 5.1).

In clinical trials, spitting or regurgitation of the vaccine has rarely been observed and, under such circumstances, a replacement dose was not given. However, in the unlikely event that an infant spits out or regurgitates most of the vaccine dose, a single replacement dose may be given at the same vaccination visit.

It is recommended that infants who receive a first dose of Rotarix complete the 2-dose regimen with Rotarix. There are no data on safety, immunogenicity or efficacy when Rotarix is administered for the

first dose and another rotavirus vaccine is administered for the second dose or vice versa.

Paediatric population

Rotarix should not be used in children over 24 weeks of age.

Method of administration

Rotarix is for **oral** use only.

Rotarix should under no circumstances be injected.

For instructions for administration, see section 6.6.

4.3 Contraindications

Hypersensitivity to the active substance or to any of the excipients listed in section 6.1.

Hypersensitivity after previous administration of rotavirus vaccines.

History of intussusception.

Individuals with uncorrected congenital malformation of the gastrointestinal tract that would predispose for intussusception.

Individuals with Severe Combined Immunodeficiency (SCID) disorder (see section 4.8).

Administration of Rotarix should be postponed in individuals suffering from acute severe febrile illness. The presence of a minor infection is not a contra-indication for immunisation.

The administration of Rotarix should be postponed in individuals suffering from diarrhoea or vomiting.

4.4 Special warnings and precautions for use

It is good clinical practice that vaccination should be preceded by a review of the medical history especially with regard to the contraindications and by a clinical examination.

Appropriate medical treatment should always be readily available in case of an anaphylactic event following the administration of the vaccine (see section 4.8).

There are no data on the safety and efficacy of Rotarix in infants with gastrointestinal illnesses or growth retardation. Administration of Rotarix may be considered with caution in such infants when, in the opinion of the physician, withholding the vaccine entails a greater risk.

As a precaution, healthcare professionals should follow-up on any symptoms indicative of intussusception (severe abdominal pain, persistent vomiting, bloody stools, abdominal bloating and/or high fever) since data from observational safety studies indicate an increased risk of intussusception, mostly within 7 days after rotavirus vaccination (see section 4.8). Parents/guardians should be advised to promptly report such symptoms to their healthcare provider.

For individuals with a predisposition for intussusception, see section 4.3.

Asymptomatic and mildly symptomatic HIV infections are not expected to affect the safety or efficacy of Rotarix. A clinical study in a limited number of asymptomatic or mildly symptomatic HIV positive infants showed no apparent safety problems (see section 4.8).

Administration of Rotarix to infants who have known or suspected immunodeficiency, including *in utero* exposure to an immunosuppressive treatment, should be based on careful consideration of potential benefits and risks.

Excretion of the vaccine virus in the stools is known to occur after vaccination with peak excretion around the 7th day. Viral antigen particles detected by ELISA were found in 50% of stools after the first dose of Rotarix lyophilised formulation and 4% of stools after the second dose. When these stools were tested for the presence of live vaccine strain, only 17% were positive. In two comparative controlled trials, vaccine shedding after vaccination with Rotarix liquid formulation was comparable to that observed after vaccination with Rotarix lyophilised formulation.

Cases of transmission of this excreted vaccine virus to seronegative contacts of vaccinees have been observed without causing any clinical symptom.

Rotarix should be administered with caution to individuals with immunodeficient close contacts, such as individuals with malignancies, or who are otherwise immunocompromised or individuals receiving immunosuppressive therapy.

Contacts of recent vaccinees should observe personal hygiene (e.g. wash their hands after changing child's nappies).

The potential risk of apnoea and the need for respiratory monitoring for 48-72h should be considered when administering the primary immunisation series to very premature infants (born ≤ 28 weeks of gestation) and particularly for those with a previous history of respiratory immaturity.

As the benefit of the vaccination is high in this group of infants, vaccination should not be withheld or delayed.

A protective immune response may not be elicited in all vaccinees (see section 5.1).

The extent of protection that Rotarix might provide against other rotavirus strains that have not been circulating in clinical trials is currently unknown. Clinical studies from which efficacy data were derived were conducted in Europe, Central and South America, Africa and Asia (see section 5.1).

Rotarix does not protect against gastro-enteritis due to other pathogens than rotavirus.

No data are available on the use of Rotarix for post-exposure prophylaxis.

Rotarix should under no circumstances be injected.

Excipients

This vaccine contains sucrose and glucose as excipients. Patients with rare hereditary problems of fructose intolerance, glucose-galactose malabsorption or sucrase-isomaltase insufficiency should not take this vaccine.

This vaccine contains 0.15 microgram phenylalanine in each dose. Phenylalanine may be harmful for patients with phenylketonuria (PKU).

This vaccine contains 32 mg sodium in each dose.

Traceability

In order to improve the traceability of biological medicinal products, the name and the batch number of the administered product should be clearly recorded.

4.5 Interaction with other medicinal products and other forms of interaction

Rotarix can be given concomitantly with any of the following monovalent or combination vaccines [including hexavalent vaccines (DTPa-HBV-IPV/Hib)]: diphtheria-tetanus-whole cell pertussis vaccine (DTPw), diphtheria-tetanus-acellular pertussis vaccine (DTPa), *Haemophilus influenzae* type b vaccine (Hib), inactivated polio vaccine (IPV), hepatitis B vaccine (HBV), pneumococcal conjugate vaccine and meningococcal serogroup C conjugate vaccine. Clinical studies demonstrated that the immune responses and the safety profiles of the administered vaccines were unaffected.

Concomitant administration of Rotarix and oral polio vaccine (OPV) does not affect the immune response to the polio antigens. Although concomitant administration of OPV may slightly reduce the immune response to rotavirus vaccine, clinical protection against severe rotavirus gastro-enteritis was shown to be maintained in a clinical trial involving more than 4 200 participants who received Rotarix concomitantly with OPV.

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

4.6 Fertility, pregnancy and lactation

Rotarix is not intended for use in adults. There are no data on the use of Rotarix during pregnancy and lactation.

Based on evidence generated in clinical trials, breast-feeding does not reduce the protection against rotavirus gastro-enteritis afforded by Rotarix. Therefore, breast-feeding may be continued during the vaccination schedule.

4.7 Effects on ability to drive and use machines

Not relevant.

4.8 Undesirable effects

Summary of the safety profile

The safety profile presented below is based on data from clinical trials conducted with either the lyophilised or the liquid formulation of Rotarix.
In a total of four clinical trials, approximately 3 800 doses of Rotarix liquid formulation were administered to approximately 1 900 infants. Those trials have shown that the safety profile of the liquid formulation is comparable to the lyophilised formulation.

In a total of twenty-three clinical trials, approximately 106 000 doses of Rotarix (lyophilised or liquid formulation) were administered to approximately 51 000 infants.

In three placebo-controlled clinical trials (Finland, India and Bangladesh), in which Rotarix was administered alone (administration of routine paediatric vaccines was staggered), the incidence and severity of the solicited events (collected 8 days post-vaccination), diarrhoea, vomiting, loss of appetite, fever, irritability and cough/runny nose were not significantly different in the group receiving Rotarix when compared to the group receiving placebo. No increase in the incidence or severity of these events was seen with the second dose.

In a pooled analysis from seventeen placebo-controlled clinical trials (Europe, North America, Latin America, Asia, Africa) including trials in which Rotarix was co-administered with routine paediatric vaccines (see section 4.5), the following adverse reactions (collected 31 days post-vaccination) were considered as possibly related to vaccination.

Tabulated list of adverse reactions

Adverse reactions reported from clinical studies, post-marketing surveillance and spontaneous reporting are listed according to the following frequency:

Frequencies are reported as:
Very common (≥ 1/10)
Common (≥ 1/100 to < 1/10)
Uncommon (≥ 1/1 000 to < 1/100)
Rare (≥ 1/10 000 to < 1/1 000)
Very rare (< 1/10 000)
Not known (cannot be estimated from the available data)

System Organ Class	Frequency	Adverse reactions
Immune system disorders	Not known	Anaphylactic reaction[1]
Gastrointestinal disorders	Common	Diarrhoea
	Uncommon	Abdominal pain, flatulence
	Very rare	Intussusception (see section 4.4)
	Not known	Haematochezia[1]
	Not known	Gastroenteritis with vaccine viral shedding in infants with Severe Combined Immunodeficiency (SCID) disorder[1]
Skin and subcutaneous tissue disorders	Uncommon	Dermatitis
	Very rare	Urticaria
General disorders and administration site conditions	Common	Irritability
Respiratory, thoracic and mediastinal disorders	Not known	Apnoea in very premature infants (≤ 28 weeks of gestation)[1] (see section 4.4)

[1]Adverse reaction from spontaneous reporting.

Description of selected adverse reactions

Intussusception

Data from observational safety studies performed in several countries indicate that rotavirus vaccines carry an increased risk of intussusception, mostly within 7 days of vaccination. Up to 6 additional cases per 100 000 infants have been observed in these countries against a background incidence of 25 to 101 per 100 000 infants (less than one year of age) per year, respectively.
There is limited evidence of a smaller increased risk following the second dose.
It remains unclear whether rotavirus vaccines affect the overall incidence of intussusception based on longer periods of follow-up (see section 4.4).

Other special populations

Safety in preterm infants

In a clinical study, 670 pre-term infants from 27 to 36 weeks of gestational age were administered Rotarix lyophilised formulation and 339 received placebo. The first dose was administered from 6 weeks after birth. Serious adverse events were observed in 5.1% of recipients of Rotarix as

compared with 6.8% of placebo recipients. Similar rates of other adverse events were observed in Rotarix and placebo recipients. No cases of intussusception were reported.

Safety in infants with human immunodeficiency (HIV) infection

In a clinical study, 100 infants with HIV infection were administered Rotarix lyophilised formulation or placebo. The safety profile was similar between Rotarix and placebo recipients.

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 national reporting system listed in Appendix V.

4.9 Overdose

Some cases of overdose have been reported. In general, the adverse event profile reported in these cases was similar to that observed after administration of the recommended dose of Rotarix.

5. PHARMACOLOGICAL PROPERTIES

5.1 Pharmacodynamic properties

Pharmaco-therapeutic group: rotavirus diarrhoea vaccines, ATC code: J07BH01

Protective efficacy of the lyophilised formulation

In clinical trials, efficacy was demonstrated against gastro-enteritis due to rotavirus of the most common genotypes G1P[8], G2P[4], G3P[8], G4P[8] and G9P[8]. In addition, efficacy against uncommon rotavirus genotypes G8P[4] (severe gastro-enteritis) and G12P[6] (any gastro-enteritis) has been demonstrated. These strains are circulating worldwide.

Clinical studies have been conducted in Europe, Latin America, Africa and Asia to evaluate the protective efficacy of Rotarix against any and severe rotavirus gastro-enteritis (RVGE).

Severity of gastro-enteritis was defined according to two different criteria:
- the Vesikari 20-point scale, which evaluates the full clinical picture of rotavirus gastro-enteritis by taking into account the severity and duration of diarrhoea and vomiting, the severity of fever and dehydration as well as the need for treatment

or
- the clinical case definition based on World Health Organization (WHO) criteria

Clinical protection was assessed in the ATP cohort for efficacy, which includes all participants from the ATP cohort for safety who entered into the concerned efficacy follow-up period.

Protective efficacy in Europe

A clinical study performed in Europe evaluated Rotarix given according to different European schedules (2, 3 months; 2, 4 months; 3, 4 months; 3, 5 months) in 4 000 participants.

After two doses of Rotarix, the protective vaccine efficacy observed during the first and second year of life is presented in the following table:

	1st year of life Rotarix N=2 572 Placebo N=1 302		2nd year of life Rotarix N=2 554 Placebo N=1 294	
Vaccine efficacy (%) against any and severe rotavirus gastro-enteritis [95% CI]				
Genotype	**Any severity**	**Severe†**	**Any severity**	**Severe†**
G1P[8]	95.6 [87.9;98.8]	96.4 [85.7;99.6]	82.7 [67.8;91.3]	96.5 [86.2;99.6]
G2P[4]	62.0* [<0.0;94.4]	74.7* [<0.0;99.6]	57.1 [<0.0;82.6]	89.9 [9.4;99.8]
G3P[8]	89.9 [9.5;99.8]	100 [44.8;100]	79.7 [<0.0;98.1]	83.1* [<0.0;99.7]
G4P[8]	88.3 [57.5;97.9]	100 [64.9;100]	69.6* [<0.0;95.3]	87.3 [<0.0;99.7]
G9P[8]	75.6 [51.1;88.5]	94.7 [77.9;99.4]	70.5 [50.7;82.8]	76.8 [50.8;89.7]
Strains with P[8] genotype	88.2 [80.8;93.0]	96.5 [90.6;99.1]	75.7 [65.0;83.4]	87.5 [77.8;93.4]
Circulating rotavirus strains	87.1 [79.6;92.1]	95.8 [89.6;98.7]	71.9 [61.2;79.8]	85.6 [75.8;91.9]
Vaccine efficacy (%) against rotavirus gastro-enteritis requiring medical attention [95% CI]				
Circulating rotavirus strains	91.8 [84;96.3]		76.2 [63.0;85.0]	
Vaccine efficacy (%) against hospitalisation due to rotavirus gastro-enteritis [95% CI]				
Circulating rotavirus strains	100 [81.8;100]		92.2 [65.6;99.1]	

† Severe gastro-enteritis was defined as a score ≥11 on the Vesikari scale

* Not statistically significant ($p \geq 0.05$). These data should be interpreted with caution.

Vaccine efficacy during the first year of life progressively increased with increasing disease severity, reaching 100% (95% CI: 84.7;100) for Vesikari scores ≥ 17.

Protective efficacy in Latin America

A clinical study performed in Latin America evaluated Rotarix in more than 20 000 participants. Severity of gastro-enteritis (GE) was defined according to WHO criteria. The protective vaccine efficacy against severe rotavirus (RV) gastro-enteritis requiring hospitalisation and/or rehydration therapy in a medical facility and the genotype specific vaccine efficacy after two doses of Rotarix are presented in the table below:

Genotype	**Severe rotavirus gastro-enteritis† (1st year of life)** Rotarix N=9 009 Placebo N=8 858	**Severe rotavirus gastro-enteritis† (2nd year of life)** Rotarix N=7 175 Placebo N=7 062
	Efficacy (%) [95% CI]	**Efficacy (%) [95% CI]**
All RVGE	84.7 [71.7;92.4]	79.0 [66.4;87.4]
G1P[8]	91.8 [74.1;98.4]	72.4 [34.5;89.9]
G3P[8]	87.7	71.9*

	[8.3;99.7]	[<0.0;97.1]
G4P[8]	50.8#* [<0.0;99.2]	63.1 [0.7;88.2]
G9P[8]	90.6 [61.7;98.9]	87.7 [72.9;95.3]
Strains with P[8] genotype	90.9 [79.2;96.8]	79.5 [67.0;87.9]

† Severe rotavirus gastro-enteritis was defined as an episode of diarrhoea with or without vomiting that required hospitalisation and/or re-hydration therapy in a medical facility (WHO criteria)

* Not statistically significant ($p \geq 0.05$). These data should be interpreted with caution

The numbers of cases, on which the estimates of efficacy against G4P[8] were based, were very small (1 case in the Rotarix group and 2 cases in the placebo group)

A pooled analysis of five efficacy studies*, showed a 71.4% (95% CI: 20.1;91.1) efficacy against severe rotavirus gastro-enteritis (Vesikari score ≥ 11) caused by rotavirus G2P[4] genotype during the first year of life.

* In these studies, the point estimates and confidence intervals were respectively: 100% (95% CI: -1 858.0;100), 100% (95% CI: 21.1;100), 45.4% (95% CI: -81.5;86.6), 74.7% (95% CI: -386.2;99.6). No point estimate was available for the remaining study.

Protective efficacy in Africa

A clinical study performed in Africa (Rotarix: N = 2 974; placebo: N = 1 443) evaluated Rotarix given at approximately 10 and 14 weeks of age (2 doses) or 6, 10 and 14 weeks of age (3 doses). The vaccine efficacy against severe rotavirus gastro-enteritis during the first year of life was 61.2% (95% CI: 44.0;73.2). The protective vaccine efficacy (pooled doses) observed against any and severe rotavirus gastro-enteritis is presented in the following table:

Genotype	**Any rotavirus gastro-enteritis** Rotarix N=2 974 Placebo N=1 443	**Severe rotavirus gastro-enteritis†** Rotarix N=2 974 Placebo N=1 443
	Efficacy (%) **[95% CI]**	**Efficacy (%)** **[95% CI]**
G1P[8]	68.3 [53.6;78.5]	56.6 [11.8;78.8]
G2P[4]	49.3 [4.6;73.0]	83.8 [9.6;98.4]
G3P[8]	43.4* [<0.0;83.7]	51.5* [<0.0;96.5]
G8P[4]	38.7* [<0.0;67.8]	63.6 [5.9;86.5]
G9P[8]	41.8* [<0.0;72.3]	56.9* [<0.0;85.5]
G12P[6]	48.0 [9.7;70.0]	55.5* [<0.0; 82.2]
Strains with P[4] genotype	39.3 [7.7;59.9]	70.9 [37.5;87.0]
Strains with P[6] genotype	46.6 [9.4;68.4]	55.2* [<0.0;81.3]
Strains with P[8] genotype	61.0 [47.3;71.2]	59.1 [32.8;75.3]

† Severe gastro-enteritis was defined as a score ≥ 11 on the Vesikari scale

* Not statistically significant ($p \geq 0.05$). These data should be interpreted with caution.

Sustained efficacy up to 3 years of age in Asia

A clinical study conducted in Asia (Hong Kong, Singapore and Taiwan) (Total vaccinated cohort: Rotarix: N = 5 359; placebo: N = 5 349) evaluated Rotarix given according to different schedules (2, 4 months of age; 3, 4 months of age).

During the first year, significantly fewer participants in the Rotarix group reported severe rotavirus gastro-enteritis caused by the circulating wild-type RV compared to the placebo group from 2 weeks after Dose 2 up to one year of age (0.0% versus 0.3%), with a vaccine efficacy of 100% (95% CI: 72.2;100).

The protective vaccine efficacy after two doses of Rotarix observed against severe rotavirus gastro-enteritis up to 2 years of age is presented in the following table:

	Efficacy up to 2 years of age Rotarix N= 5 263 Placebo N= 5 256
Vaccine efficacy (%) against severe rotavirus gastro-enteritis [95% CI]	
Genotype	Severe†
G1P[8]	100 [80.8;100]
G2P[4]	100* [<0.0;100]
G3P[8]	94.5 [64.9;99.9]
G9P[8]	91.7 [43.8;99.8]
Strains with P[8] genotype	95.8 [83.8;99.5]
Circulating rotavirus strains	96.1 [85.1;99.5]
Vaccine efficacy (%) against rotavirus gastro-enteritis requiring hospitalisation and/or rehydration therapy in a medical facility [95% CI]	
Circulating rotavirus strains	94.2 [82.2;98.8]

† Severe gastro-enteritis was defined as a score ≥ 11 on the Vesikari scale

* Not statistically significant (p ≥ 0.05). These data should be interpreted with caution.

During the third year of life, there were no cases of severe RV gastro-enteritis in the Rotarix group (N=4 222) versus 13 (0.3%) in the placebo group (N=4 185). Vaccine efficacy was 100% (95% CI: 67.5; 100). The severe RV gastro-enteritis cases were due to RV strains G1P[8], G2P[4], G3P[8] and G9P[8]. The incidence of severe RV gastro-enteritis associated with the individual genotypes was too small to allow calculation of efficacy. The efficacy against severe RV gastro-enteritis requiring hospitalisation was 100% (95% CI: 72.4;100).

Protective efficacy of the liquid formulation

Since the immune response observed after 2 doses of Rotarix liquid formulation was comparable to the immune response observed after 2 doses of Rotarix lyophilised formulation, the levels of vaccine efficacy observed with the lyophilised formulation can be extrapolated to the liquid formulation.

Immune response

The immunologic mechanism by which Rotarix protects against rotavirus gastro-enteritis is not completely understood. A relationship between antibody responses to rotavirus vaccination and protection against rotavirus gastro-enteritis has not been established.

The following table shows the percentage of participants initially seronegative for rotavirus (IgA antibody titres < 20 U/mL) (by ELISA) with serum anti-rotavirus IgA antibody titres ≥ 20 U/mL one to two months after the second dose of vaccine or placebo as observed in different studies with Rotarix lyophilised formulation.

Schedule	Studies conducted in	Vaccine		Placebo	
		N	% ≥ 20 U/mL [95% CI]	N	% ≥ 20 U/mL [95% CI]
2, 3 months	France, Germany	239	82.8 [77.5;87.4]	127	8.7 [4.4;15.0]
2, 4 months	Spain	186	85.5 [79.6;90.2]	89	12.4 [6.3;21.0]
3, 5 months	Finland, Italy	180	94.4 [90.0;97.3]	114	3.5 [1.0;8.7]
3, 4 months	Czech Republic	182	84.6 [78.5;89.5]	90	2.2 [0.3;7.8]
2, 3 to 4 months	Latin America; 11 countries	393	77.9% [73.8;81.6]	341	15.1% [11.7;19.0]
10, 14 weeks and 6, 10, 14 weeks (Pooled)	South Africa, Malawi	221	58.4 [51.6;64.9]	111	22.5 [15.1;31.4]

In three comparative controlled trials, the immune response elicited by Rotarix liquid formulation was comparable to the one elicited by Rotarix lyophilised formulation.

Immune response in preterm infants

In a clinical study conducted in preterm infants, born after at least 27 weeks of gestational age, the immunogenicity of Rotarix was assessed in a subset of 147 participants and showed that Rotarix is immunogenic in this population; 85.7% (95% CI: 79.0;90.9) of participants achieved serum anti-rotavirus IgA antibody titres ≥ 20 U/mL (by ELISA) one month after the second dose of vaccine.

Effectiveness

In observational studies, vaccine effectiveness was demonstrated against severe gastro-enteritis leading to hospitalisation due to rotavirus of common genotypes G1P[8], G2P[4], G3P[8], G4P[8] and G9P[8] as well as the less common rotavirus genotypes G9P[4] and G9P[6]. All of these strains are circulating worldwide.

Effectiveness after 2 doses in preventing RVGE leading to hospitalisation

Countries Period	Age range	N(1) (cases/controls)	Strains	Effectiveness % [95% CI]
High Income countries				
Belgium 2008-2010(2)	< 4 yrs	160/198	All	90 [81;95]
	3-11 m			91 [75;97]
	< 4 yrs	41/53	G1P[8]	95 [78;99]
	< 4 yrs	80/103	G2P[4]	85 [64;94]
	3-11 m			83 [22;96](3)
	< 4 yrs	12/13	G3P[8]	87* [<0;98](3)
	< 4 yrs	16/17	G4P[8]	90 [19;99](3)
Singapore 2008-2010(2)	< 5 yrs	136/272	All	84 [32;96]
		89/89	G1P[8]	91 [30;99]
Taiwan 2009-2011	< 3 yrs	184/1 623(4)	All	92 [75;98]
			G1P[8]	95 [69;100]

US 2010-2011	< 2 yrs	85/1 062[5]	All G1P[8] G2P[4]	85 [73;92] 88 [68;95] 88 [68;95]
	8-11 m		All	89 [48;98]
US 2009-2011	< 5 yrs	74/255[4]	All	68 [34;85]
Middle Income Countries				
Bolivia 2010-2011	< 3 yrs 6-11 m	300/974	All	77 [65;84][6] 77 [51;89]
	< 3 yrs 6-11 m		G9P[8]	85 [69;93] 90 [65;97]
	< 3 yrs		G3P[8] G2P[4] G9P[6]	93 [70;98] 69 [14;89] 87 [19;98]
Brazil 2008-2011	< 2 yrs	115/1 481	All G1P[8] G2P[4]	72 [44;85][6] 89 [78;95] 76 [64;84]
Brazil 2008-2009[2]	< 3 yrs 3-11 m	249/249[5]	All	76 [58;86] 96 [68;99]
	< 3 yrs 3-11 m	222/222[5]	G2P[4]	75 [57;86] 95 [66;99][3]
El Salvador 2007-2009	< 2 yrs 6-11 m	251/770[5]	All	76 [64;84][6] 83 [68;91]
Guatemala 2012-2013	< 4 yrs	NA[7]	All	63 [23;82]
Mexico 2010	< 2 yrs	9/17[5]	G9P[4]	94 [16;100]
Low Income Countries				
Malawi 2012-2014	< 2 yrs	81/286[5]	All	63 [23;83]

m: months
yrs: years
* Not statistically significant ($p \geq 0.05$). These data should be interpreted with caution.
(1) The number of fully vaccinated (2 doses) and unvaccinated cases and controls is given.
(2) GSK sponsored studies
(3) Data from a post-hoc analysis
(4) Vaccine effectiveness was calculated using rotavirus-negative hospital control participants (estimates from Taiwan were calculated using combined rotavirus-negative hospital control and non-diarrhoea hospital control participants).
(5) Vaccine effectiveness was calculated using neighbourhood controls.
(6) In participants who did not receive the full course of vaccination, the effectiveness after one dose ranged from 51% (95% CI: 26;67, El Salvador) to 60% (95% CI: 37;75, Brazil).
(7) NA: Not available. Vaccine effectiveness estimate is based on 41 fully vaccinated cases and 175 fully vaccinated controls.

Impact on mortality[§]

Impact studies with Rotarix conducted in Panama, Brazil and Mexico showed a decrease in all-cause diarrhoea mortality ranging from 17% to 73% in children less than 5 years of age, within 2 to 4 years after vaccine introduction.

Impact on hospitalisation[§]

In a retrospective database study in Belgium conducted in children 5 years of age and younger, the direct and indirect impact of Rotarix vaccination on rotavirus-related hospitalisation ranged from 64% (95% CI: 49;76) to 80% (95% CI: 77;83) two years after vaccine introduction. Similar studies in

Armenia, Australia, Brazil, Canada, El Salvador and Zambia showed a reduction of 45 to 93% between 2 and 4 years after vaccine introduction.

In addition, nine impact studies on all-cause diarrhoea hospitalisation conducted in Africa and Latin America showed a reduction of 14% to 57% between 2 and 5 years after vaccine introduction.

[§]NOTE: Impact studies are meant to establish a temporal relationship but not a causal relationship between the disease and vaccination. Natural fluctuations of the incidence of the disease may also influence the observed temporal effect.

5.2 Pharmacokinetic properties

Not applicable.

5.3 Preclinical safety data

Non-clinical data reveal no special hazard for humans based on conventional studies of repeated dose toxicity.

6. PHARMACEUTICAL PARTICULARS

6.1 List of excipients

Sucrose
Di-sodium Adipate
Dulbecco's Modified Eagle Medium (DMEM) (containing phenylalanine, sodium, glucose, and other substances)
Sterile water

6.2 Incompatibilities

In the absence of compatibility studies, this medicinal product must not be mixed with other medicinal products.

6.3 Shelf life

- Pre-filled oral applicator: 3 years
- Squeezable tube fitted with a membrane and a tube cap: 3 years
- Multi-monodose (5 single dose) squeezable tube presentation connected by a bar: 2 years

The vaccine should be used immediately after opening.

6.4 Special precautions for storage

Store in a refrigerator (2°C – 8°C).
Do not freeze.

Store in the original package in order to protect from light.

6.5 Nature and contents of container

Pre-filled oral applicator
1.5 mL of **oral** suspension in a pre-filled **oral** applicator (type I glass) with a plunger stopper (butyl rubber) and a protective rubber tip cap (styrene butadiene rubber), in pack sizes of 1, 5, 10 or 25.

The tip cap and plunger stopper of the **oral** applicator are made with synthetic rubber.

Squeezable tube
1.5 mL of **oral** suspension in a squeezable tube (polyethylene) fitted with a membrane and a tube cap (polypropylene), in pack sizes of 1, 10 or 50.

Multi-monodose (5 single dose) squeezable tube presentation connected by a bar
1.5 mL of **oral** suspension in a squeezable tube (polyethylene) presented in a multi-monodose (5 single dose) squeezable tube presentation connected by a bar, in pack size of 50 tubes.

Not all pack sizes may be marketed.

6.6 Special precautions for disposal and other handling

The vaccine is presented as a clear, colourless liquid, free of visible particles, for **oral** administration.

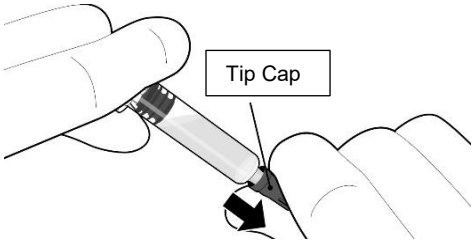
The vaccine is ready to use (no reconstitution or dilution is required).
The vaccine is to be administered **orally** without mixing with any other vaccines or solutions.

The vaccine should be inspected visually for any foreign particulate matter and/or abnormal physical appearance. In the event of either being observed, discard the vaccine.

Any unused medicinal product or waste material should be disposed of in accordance with local requirements.

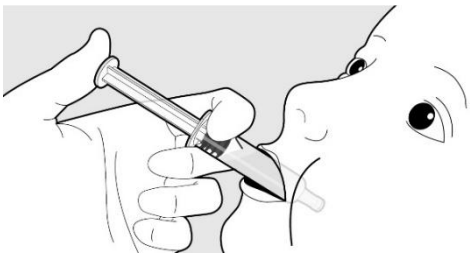
Instructions for administration of the vaccine in a pre-filled oral applicator:

Please read the instructions for use all the way through before starting to give the vaccine.



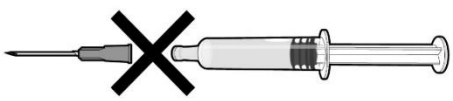
Remove the protective Tip Cap from the **oral** applicator.

Do not pull the **oral** applicator plunger out of the barrel. If it happens, do not administer the vaccine.



For **oral administration only**.

Have the infant seated in a reclining position. Place the **oral** applicator towards the inner cheek. Administer the entire contents of the **oral** applicator into the infant's mouth.



Do not inject.

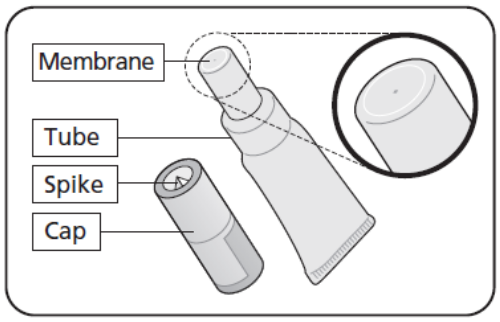
Discard the empty **oral** applicator and tip cap in approved biological waste containers according to local regulations.

Instructions for administration of the vaccine in a squeezable tube:

Please read the instructions for use all the way through before starting to give the vaccine.

A What you need to do before giving Rotarix

- Check the expiry date.
- Check the tube has not been damaged nor is already open.
- Check the liquid is clear and colourless, without any particles in it.



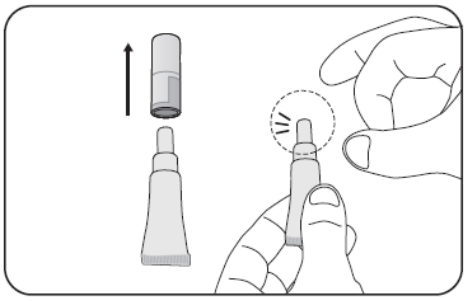
If you notice anything abnormal, do not use the vaccine.

- This vaccine is given orally - straight from the tube.
- It is ready to use - you do not need to mix it with anything.

B Get the tube ready

1. Pull off the cap

- Keep the cap – you need this to pierce the membrane.
- Hold the tube upright.

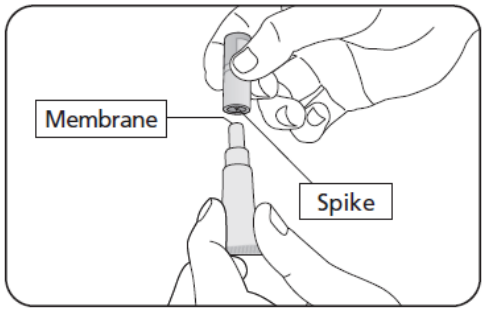


2. Repeatedly flick the top of the tube until it is clear of any liquid

- Clear any liquid from the thinnest section of the tube by flicking just below the membrane.

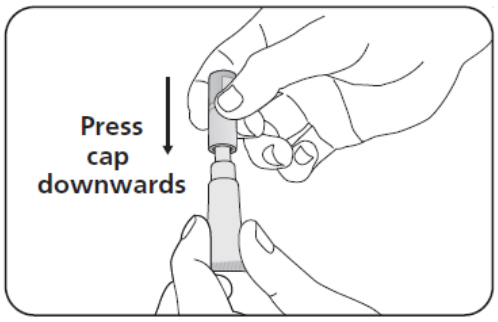
3. Position the cap to open the tube

- Keep the tube held upright.
- Hold the side of tube
- There is a small spike inside the top of the cap - in the centre.
- Turn the cap upside down (180°).



4. To open the tube

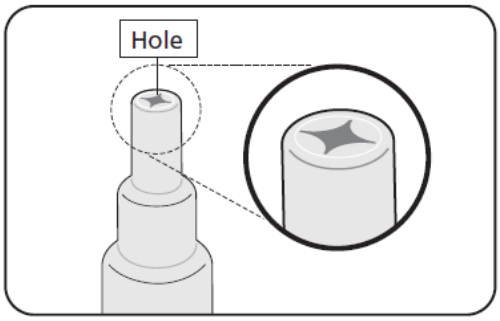
- You do not need to twist. Press the cap down to pierce the membrane.
- Then lift off the cap.



C Check the tube has opened correctly

1. Check the membrane has been pierced

- There should be a hole at the top of the tube.

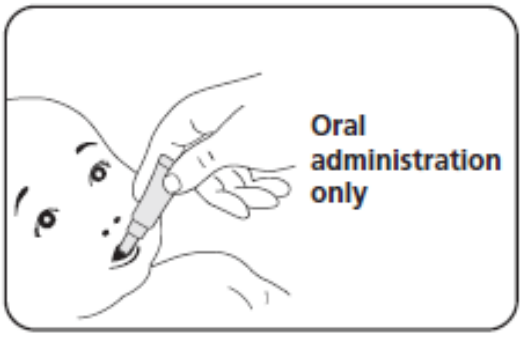


2. What to do if the membrane has not been pierced

- If the membrane has not been pierced return to section B and repeat steps 2, 3 and 4.

D Give the vaccine

- Once the tube is open check the liquid is clear, without any particles in it.
  If you notice anything abnormal, do not use the vaccine.
- Give the vaccine straight away.



1. Position the child to give the vaccine

- Seat the child leaning slightly backwards.

2. Administer the vaccine

- Squeeze the liquid gently into the side of the child's mouth - towards the inside of their cheek.
- You may need to squeeze the tube a few times to get all of the vaccine out - it is okay if a drop remains in the tip of the tube.

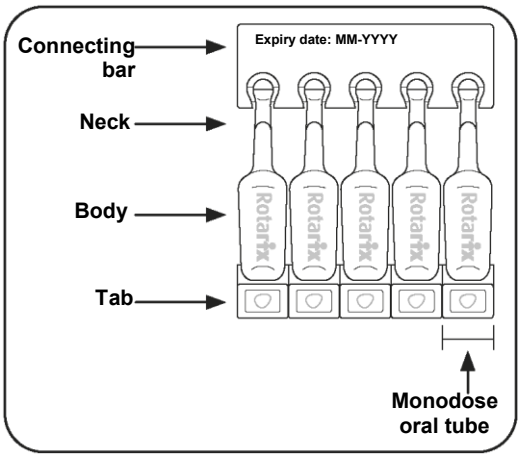
Discard the empty tube and cap in approved biological waste containers according to local regulations.

<u>Instructions for administration of the vaccine in a multi-monodose (5 single dose) squeezable tube presentation connected by a bar:</u>

Please read the instructions for use all the way through before starting to give the vaccine.

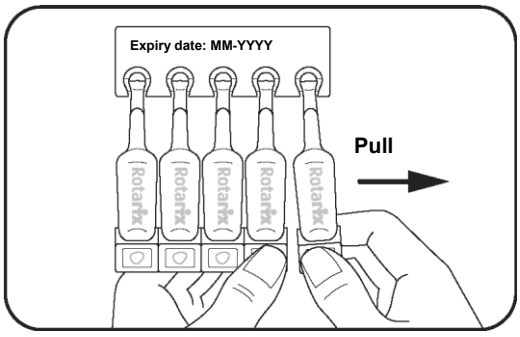
- This vaccine is given orally straight from an individual tube.
- One oral tube delivers one dose of vaccine.
- This vaccine is ready to use - do not mix it with anything else.

A. What you need to do before giving Rotarix

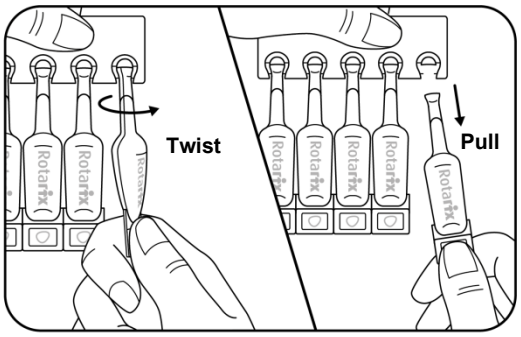


1. Check the expiry date on the connecting bar.
2. Check the liquid in the oral tubes is clear, colourless and free from any particles.
   - **Do not use any of the oral tubes on the connecting bar if you notice anything unusual.**
3. Check that each individual oral tube is not damaged and is still sealed.
   - **Do not use the affected oral tube if you notice anything unusual.**

B. Get the oral tube ready

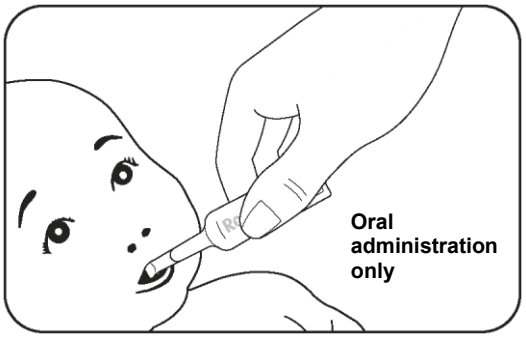


1. To separate one oral tube from the others starting at one end:
   a) Hold the tab of one of the end oral tubes to separate it from the others.
   b) With your other hand, hold the tab of the oral tube next to it.
   c) Pull the tab and tear it away from the oral tube next to it.



2. To open the separated oral tube:
   d) Keep the separated oral tube held upright.
   e) Hold the tab of the separated oral tube in one hand and the connecting bar in the other hand. **Do not hold the body of the oral tube, you may squeeze out some of the vaccine.**
   f) Twist the separated oral tube.
   g) Pull it from the connecting bar.

C. Give the vaccine orally immediately after opening

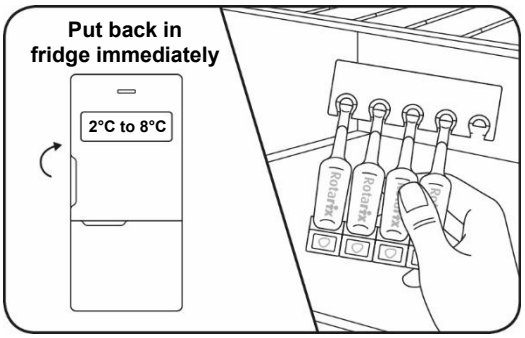


1. To position the child to receive the vaccine:
   - Seat the child leaning slightly backwards.

2. To administer the vaccine orally:
   - Squeeze the liquid gently into the side of the child's mouth, towards the inside of their cheek.
   - You may need to squeeze the oral tube a few times to get all of the vaccine out - it is okay if a drop stays in the oral tube.

D. Store remaining doses in the fridge immediately

Unused oral tubes that are still attached to the connecting bar must be put back in the fridge immediately after an oral tube has been used. This is so that the unused oral tubes can be used for the next vaccination.



Discard the used oral tubes in approved biological waste containers according to local regulations.

7. MARKETING AUTHORISATION HOLDER

GlaxoSmithKline Biologicals SA
Rue de l'Institut 89
B-1330 Rixensart, Belgium

8. MARKETING AUTHORISATION NUMBER(S)

Pre-filled oral applicator
EU/1/05/330/005
EU/1/05/330/006
EU/1/05/330/007
EU/1/05/330/008

Squeezable tube
EU/1/05/330/009
EU/1/05/330/010
EU/1/05/330/011

Multi-monodose (5-single dose) squeezable tube presentation connected by a bar
EU/1/05/330/012

9. DATE OF FIRST AUTHORISATION/RENEWAL OF THE AUTHORISATION

Date of first authorisation: 21 February 2006
Date of latest renewal: 14 January 2016

10. DATE OF REVISION OF THE TEXT

Detailed information on this medicinal product is available on the website of the European Medicines Agency https://www.ema.europa.eu.

ANNEX II

A. MANUFACTURER(S) OF THE BIOLOGICAL ACTIVE SUBSTANCE(S) AND MANUFACTURER(S) RESPONSIBLE FOR BATCH RELEASE

B. CONDITIONS OR RESTRICTIONS REGARDING SUPPLY AND USE

C. OTHER CONDITIONS AND REQUIREMENTS OF THE MARKETING AUTHORISATION

D. CONDITIONS OR RESTRICTIONS WITH REGARD TO THE SAFE AND EFFECTIVE USE OF THE MEDICINAL PRODUCT

A. MANUFACTURER(S) OF THE BIOLOGICAL ACTIVE SUBSTANCE(S) AND MANUFACTURER(S) RESPONSIBLE FOR BATCH RELEASE

Name and address of the manufacturer(s) of the biological active substance(s)

GlaxoSmithKline Biologicals SA
Parc de la Noire Epine
Rue Fleming, 20
1300 Wavre Belgium

Name and address of the manufacturer(s) responsible for batch release

GlaxoSmithKline Biologicals SA
Rue de l'Institut 89
1330 Rixensart
Belgium

B. CONDITIONS OR RESTRICTIONS REGARDING SUPPLY AND USE

Medicinal product subject to medical prescription.

Official batch release:

In accordance with Article 114 of Directive 2001/83/EC, the official batch release will be undertaken by a state laboratory or a laboratory designated for that purpose.

C. OTHER CONDITIONS AND REQUIREMENTS OF THE MARKETING AUTHORISATION

- **Periodic safety update reports (PSURs)**

The requirements for submission of PSURs for this medicinal product are set out in the list of Union reference dates (EURD list) provided for under Article 107c(7) of Directive 2001/83/EC and any subsequent updates published on the European medicines web-portal.

D. CONDITIONS OR RESTRICTIONS WITH REGARD TO THE SAFE AND EFFECTIVE USE OF THE MEDICINAL PRODUCT

- **Risk management plan (RMP)**

The marketing authorisation holder (MAH) shall perform the required pharmacovigilance activities and interventions detailed in the agreed RMP presented in Module 1.8.2. of the marketing authorisation and any agreed subsequent updates of the RMP.

An updated RMP should be submitted:

- At the request of the European Medicines Agency;
- Whenever the risk management system is modified, especially as the result of new information being received that may lead to a significant change to the benefit/risk profile or as the result of an important (pharmacovigilance or risk minimisation) milestone being reached.

ANNEX III

LABELLING AND PACKAGE LEAFLET

A. LABELLING

PARTICULARS TO APPEAR ON THE OUTER PACKAGING
PRE-FILLED ORAL APPLICATOR, PACK SIZE OF 1, 5, 10 OR 25

1. NAME OF THE MEDICINAL PRODUCT

Rotarix **oral** suspension in pre-filled **oral** applicator
rotavirus vaccine, live

2. STATEMENT OF ACTIVE SUBSTANCE(S)

1 dose (1.5 mL) contains:

Human rotavirus RIX4414 strain (live, attenuated) not less than $10^{6.0}$ $CCID_{50}$

3. LIST OF EXCIPIENTS

Sucrose, sodium, glucose, phenylalanine

See the package leaflet for further information

4. PHARMACEUTICAL FORM AND CONTENTS

Oral suspension in pre-filled **oral** applicator
1 pre-filled **oral** applicator
1 dose (1.5 mL)

5 pre-filled **oral** applicators
5 x 1 dose (1.5 mL)

10 pre-filled **oral** applicators
10 x 1 dose (1.5 mL)

25 pre-filled **oral** applicators
25 x 1 dose (1.5 mL)

5. METHOD AND ROUTE(S) OF ADMINISTRATION

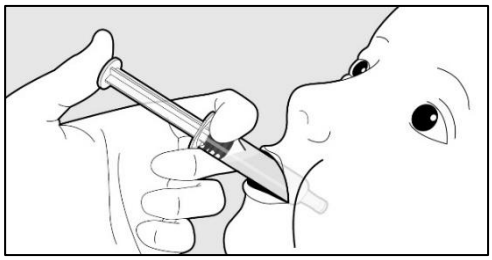
Oral use
Do not inject!
Read the package leaflet before use

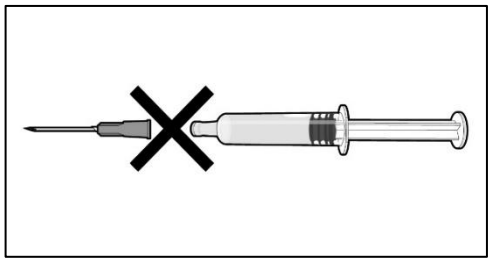
6. SPECIAL WARNING THAT THE MEDICINAL PRODUCT MUST BE STORED OUT OF THE SIGHT AND REACH OF CHILDREN

Keep out of the sight and reach of children

7. OTHER SPECIAL WARNING(S), IF NECESSARY

Ready to use
No reconstitution required





8. EXPIRY DATE

EXP {MM/YYYY}

9. SPECIAL STORAGE CONDITIONS

Store in a refrigerator
Do not freeze
Store in the original package in order to protect from light

10. SPECIAL PRECAUTIONS FOR DISPOSAL OF UNUSED MEDICINAL PRODUCTS OR WASTE MATERIALS DERIVED FROM SUCH MEDICINAL PRODUCTS, IF APPROPRIATE

11. NAME AND ADDRESS OF THE MARKETING AUTHORISATION HOLDER

GlaxoSmithKline Biologicals SA
Rue de l'Institut 89
B-1330 Rixensart, Belgium

12. MARKETING AUTHORISATION NUMBER(S)

EU/1/05/330/005 – pack of 1 pre-filled **oral** applicator
EU/1/05/330/006 – pack of 5 pre-filled **oral** applicators
EU/1/05/330/007 – pack of 10 pre-filled **oral** applicators
EU/1/05/330/008 – pack of 25 pre-filled **oral** applicators

13. BATCH NUMBER

Lot

14. GENERAL CLASSIFICATION FOR SUPPLY

15. INSTRUCTIONS ON USE

16. INFORMATION IN BRAILLE

Justification for not including Braille accepted

17. UNIQUE IDENTIFIER – 2D BARCODE

2D barcode carrying the unique identifier included.

18. UNIQUE IDENTIFIER - HUMAN READABLE DATA

PC
SN
NN

PARTICULARS TO APPEAR ON THE OUTER PACKAGING
TUBE, PACK SIZES OF 1, 10 OR 50

1. NAME OF THE MEDICINAL PRODUCT

Rotarix **oral** suspension
rotavirus vaccine, live

2. STATEMENT OF ACTIVE SUBSTANCE(S)

1 dose (1.5 mL) contains:

Human rotavirus RIX4414 strain (live, attenuated) not less than $10^{6.0}$ $CCID_{50}$

3. LIST OF EXCIPIENTS

Sucrose, sodium, glucose, phenylalanine
See the package leaflet for further information

4. PHARMACEUTICAL FORM AND CONTENTS

Oral suspension
1 tube
1 dose (1.5 mL)

10 tubes
10 x 1 dose (1.5 mL)

50 tubes
50 x 1 dose (1.5 mL)

5. METHOD AND ROUTE(S) OF ADMINISTRATION

Oral use
Do not inject!
Read the package leaflet before use

6. SPECIAL WARNING THAT THE MEDICINAL PRODUCT MUST BE STORED OUT OF THE SIGHT AND REACH OF CHILDREN

Keep out of the sight and reach of children

7. OTHER SPECIAL WARNING(S), IF NECESSARY

Read the instructions before administration of the vaccine.

This vaccine is intended for **oral administration only**.

8. EXPIRY DATE

EXP {MM/YYYY}

9. SPECIAL STORAGE CONDITIONS

Store in a refrigerator
Do not freeze
Store in the original package in order to protect from light

10. SPECIAL PRECAUTIONS FOR DISPOSAL OF UNUSED MEDICINAL PRODUCTS OR WASTE MATERIALS DERIVED FROM SUCH MEDICINAL PRODUCTS, IF APPROPRIATE

11. NAME AND ADDRESS OF THE MARKETING AUTHORISATION HOLDER

GlaxoSmithKline Biologicals SA
Rue de l'Institut 89
B-1330 Rixensart, Belgium

12. MARKETING AUTHORISATION NUMBER(S)

EU/1/05/330/009 – pack of 1 tube
EU/1/05/330/010 – pack of 10 tubes
EU/1/05/330/011 – pack of 50 tubes

13. BATCH NUMBER

Lot

14. GENERAL CLASSIFICATION FOR SUPPLY

15. INSTRUCTIONS ON USE

16. INFORMATION IN BRAILLE

Justification for not including Braille accepted

17. UNIQUE IDENTIFIER – 2D BARCODE

2D barcode carrying the unique identifier included.

18. UNIQUE IDENTIFIER - HUMAN READABLE DATA

PC
SN
NN

PARTICULARS TO APPEAR ON THE OUTER PACKAGING
MULTI-MONODOSE (5 SINGLE DOSE) SQUEEZABLE TUBE PRESENTATION CONNECTED BY A BAR, PACK SIZE OF 50 TUBES

1. NAME OF THE MEDICINAL PRODUCT

Rotarix **oral** suspension
rotavirus vaccine, live

2. STATEMENT OF ACTIVE SUBSTANCE(S)

1 dose (1.5 mL) contains:

Human rotavirus RIX4414 strain (live, attenuated) not less than $10^{6.0}$ $CCID_{50}$

3. LIST OF EXCIPIENTS

Sucrose, sodium, glucose, phenylalanine
See the package leaflet for further information

4. PHARMACEUTICAL FORM AND CONTENTS

Oral suspension

50 tubes
10 x 5 single dose tubes connected by a bar
1 dose (1.5 mL)

5. METHOD AND ROUTE(S) OF ADMINISTRATION

Oral use
Do not inject!
Read the package leaflet before use.

6. SPECIAL WARNING THAT THE MEDICINAL PRODUCT MUST BE STORED OUT OF THE SIGHT AND REACH OF CHILDREN

Keep out of the sight and reach of children.

7. OTHER SPECIAL WARNING(S), IF NECESSARY

Read the instructions before administration of the vaccine.

This vaccine is intended for **oral administration only**.

8. EXPIRY DATE

EXP {MM/YYYY}

9. SPECIAL STORAGE CONDITIONS

Store in a refrigerator.
Do not freeze.
Store in the original package in order to protect from light.

10. SPECIAL PRECAUTIONS FOR DISPOSAL OF UNUSED MEDICINAL PRODUCTS OR WASTE MATERIALS DERIVED FROM SUCH MEDICINAL PRODUCTS, IF APPROPRIATE

Dispose of in accordance with local regulations.

11. NAME AND ADDRESS OF THE MARKETING AUTHORISATION HOLDER

GlaxoSmithKline Biologicals SA
Rue de l'Institut 89
B-1330 Rixensart, Belgium

12. MARKETING AUTHORISATION NUMBER(S)

EU/1/05/330/012 – pack of 50 tubes

13. BATCH NUMBER

Lot

14. GENERAL CLASSIFICATION FOR SUPPLY

15. INSTRUCTIONS ON USE

16. INFORMATION IN BRAILLE

Justification for not including Braille accepted

17. UNIQUE IDENTIFIER – 2D BARCODE

2D barcode carrying the unique identifier included.

18. UNIQUE IDENTIFIER - HUMAN READABLE DATA

PC
SN
NN

MINIMUM PARTICULARS TO APPEAR ON SMALL IMMEDIATE PACKAGING UNITS
PRE-FILLED ORAL APPLICATOR

1. NAME OF THE MEDICINAL PRODUCT AND ROUTE(S) OF ADMINISTRATION

Rotarix
Oral suspension
rotavirus vaccine, live
Oral use

2. METHOD OF ADMINISTRATION

3. EXPIRY DATE

EXP

4. BATCH NUMBER

Lot

5. CONTENTS BY WEIGHT, BY VOLUME OR BY UNIT

1 dose (1.5 mL)

6. OTHER

MINIMUM PARTICULARS TO APPEAR ON SMALL IMMEDIATE PACKAGING UNITS
TUBE

1. NAME OF THE MEDICINAL PRODUCT AND ROUTE(S) OF ADMINISTRATION

Rotarix
Oral suspension
rotavirus vaccine, live
Oral use

2. METHOD OF ADMINISTRATION

3. EXPIRY DATE

EXP

4. BATCH NUMBER

Lot

5. CONTENTS BY WEIGHT, BY VOLUME OR BY UNIT

1 dose (1.5 mL)

6. OTHER

MINIMUM PARTICULARS TO APPEAR ON SMALL IMMEDIATE PACKAGING UNITS MULTI-MONODOSE (5 SINGLE DOSE) SQUEEZABLE TUBE PRESENTATION CONNECTED BY A BAR

1. NAME OF THE MEDICINAL PRODUCT AND ROUTE(S) OF ADMINISTRATION

Rotarix
Oral suspension
rotavirus vaccine, live
Oral use

2. METHOD OF ADMINISTRATION

3. EXPIRY DATE

EXP

4. BATCH NUMBER

Lot

5. CONTENTS BY WEIGHT, BY VOLUME OR BY UNIT

5 single dose tubes
1 dose (1.5 mL)

6. OTHER

B. PACKAGE LEAFLET

Package leaflet: Information for the user

Rotarix oral suspension in pre-filled oral applicator
rotavirus vaccine, live

Read all of this leaflet carefully before your child receives this vaccine because it contains important information for you.
- Keep this leaflet. You may need to read it again.
- If you have any further questions, ask your doctor or pharmacist.
- This vaccine has been prescribed for your child only. Do not pass it on to others.
- If you get any side effects, talk to your doctor or pharmacist. This includes any possible side effects not listed in this leaflet. See section 4.

What is in this leaflet

1. What Rotarix is and what it is used for
2. What you need to know before your child receives Rotarix
3. How Rotarix is given
4. Possible side effects
5. How to store Rotarix
6. Contents of the pack and other information

1. What Rotarix is and what it is used for

Rotarix is a viral vaccine, containing live, attenuated human rotavirus, that helps to protect your child, from the age of 6 weeks, against gastro-enteritis (diarrhoea and vomiting) caused by rotavirus infection.

How Rotarix works

Rotavirus infection is the most common cause of severe diarrhoea in infants and young children. Rotavirus is easily spread from hand-to-mouth due to contact with stools from an infected person. Most children with rotavirus diarrhoea recover on their own. However, some children become very ill with severe vomiting, diarrhoea and life-threatening loss of fluids that requires hospitalisation.

When a person is given the vaccine, the immune system (the body's natural defences) will make antibodies against the most commonly occurring types of rotavirus. These antibodies protect against disease caused by these types of rotavirus.

As with all vaccines, Rotarix may not completely protect all people who are vaccinated against the rotavirus infections it is intended to prevent.

2. What you need to know before your child receives Rotarix

Rotarix should not be given
- if your child has previously had any allergic reaction to rotavirus vaccines or any of the other ingredients of this vaccine (listed in section 6). Signs of an allergic reaction may include itchy skin rash, shortness of breath and swelling of the face or tongue.
- if your child has previously had intussusception (a bowel obstruction in which one segment of bowel becomes enfolded within another segment).
- if your child was born with a malformation of the gut that could lead to intussusception.
- if your child has a rare inherited illness which affects their immune system called Severe Combined Immunodeficiency (SCID).
- if your child has a severe infection with a high temperature. It might be necessary to postpone the vaccination until recovery. A minor infection such as a cold should not be a problem, but talk to your doctor first.

- if your child has diarrhoea or is vomiting. It might be necessary to postpone the vaccination until recovery.

Warnings and precautions
Talk to your doctor/health care professional before your child receives Rotarix if:
- he/she has a close contact such as a household member who has a weakened immune system, e.g., a person with cancer or who is taking medicines that may weaken the immune system.
- he/she has any disorder of the gastrointestinal system.
- he/she has not been gaining weight and growing as expected.
- he/she has any disease or is taking any medicine which reduces his/her resistance to infection or if his/her mother has taken during pregnancy any medicine that may weaken the immune system.

After your child has received Rotarix, contact a doctor/health care professional right away if your child experiences severe stomach pain, persistent vomiting, blood in stools, a swollen belly and/or high fever (see also section 4 “Possible side effects”).

As always, please take care to wash your hands thoroughly after changing soiled nappies.

Other medicines and Rotarix
Tell your doctor if your child is taking, has recently taken or might take any other medicines or has recently received any other vaccine.

Rotarix may be given at the same time your child receives other normally recommended vaccines, such as diphtheria, tetanus, pertussis (whooping cough), *Haemophilus influenzae* type b, oral or inactivated polio, hepatitis B vaccines as well as pneumococcal and meningococcal serogroup C conjugate vaccines.

Rotarix with food and drink
There are no restrictions on your child’s consumption of food or liquids, either before or after vaccination.

Breast-feeding
Based on evidence generated in clinical trials, breast-feeding does not reduce the protection against rotavirus gastro-enteritis afforded by Rotarix. Therefore, breast-feeding may be continued during the vaccination schedule.

Rotarix contains sucrose, glucose, phenylalanine and sodium
If you have been told by your doctor that the child being vaccinated has an intolerance to some sugars, contact your doctor before your child receives this vaccine.

This vaccine contains 0.15 microgram phenylalanine in each dose. Phenylalanine may be harmful if your child has phenylketonuria (PKU), a rare genetic disorder in which phenylalanine builds up because the body cannot remove it properly.

This vaccine contains 32 mg sodium (main component of cooking/table salt) in each dose.

3. How Rotarix is given

The doctor or nurse will administer the recommended dose of Rotarix to your child. The vaccine (1.5 mL liquid) will be given **orally**. Under no circumstance should this vaccine be administered by injection.

Your child will receive two doses of the vaccine. Each dose will be given on a separate occasion with an interval of at least 4 weeks between the two doses. The first dose may be given from the age of 6 weeks. The two doses of the vaccine must have been given by the age of 24 weeks, although they should preferably have been given before 16 weeks of age.

Rotarix may be given according to the same vaccination course to infants who were born prematurely, provided that the pregnancy had lasted at least 27 weeks.

In case your child spits out or regurgitates most of the vaccine dose, a single replacement dose may be given at the same vaccination visit.

When Rotarix is given to your child for the first dose, it is recommended that your child also receives Rotarix (and not another rotavirus vaccine) for the second dose.

It is important that you follow the instructions of your doctor or nurse regarding return visits. If you forget to go back to your doctor at the scheduled time, ask your doctor for advice.

4. Possible side effects

Like all medicines, this vaccine can cause side effects, although not everybody gets them.

Contact a doctor/health care professional right away if your child experiences one of the following symptoms:

- Allergic reactions (frequency cannot be estimated from the available data), which may be severe (anaphylaxis), and may include: shortness of breath or allergic swelling that may affect the face, lips, tongue or throat.
- Intussusception (part of the intestine gets blocked or twisted) (frequency very rare). The signs may include severe stomach pain, persistent vomiting, blood in stools, a swollen belly and/or high fever.

The following other side effects may happen with this vaccine:

♦ Common (These may occur with up to 1 in 10 doses of the vaccine):
- diarrhoea
- irritability

♦ Uncommon (These may occur with up to 1 in 100 doses of the vaccine):
- abdominal pain (see also above for signs of very rare side effects of intussusception)
- flatulence
- inflammation of the skin

♦ Side effects that have been reported during marketed use of Rotarix include:
- Very rare: hives (urticaria)
- blood in stools
- in babies born very prematurely (at or before 28 weeks of gestation) longer gaps than normal between breaths may occur for 2-3 days after vaccination.
- children with a rare inherited illness called Severe Combined Immunodeficiency (SCID) may have an inflamed stomach or gut (gastroenteritis) and pass the vaccine virus in their stools. The signs of gastroenteritis may include feeling sick, being sick, stomach cramps or diarrhoea.

Reporting of side effects
If your child gets any of the side effects, talk to your doctor or pharmacist. This includes any possible side effects not listed in this leaflet. You can also report side effects directly via the national reporting system listed in Appendix V. By reporting side effects you can help provide more information on the safety of this medicine.

5. How to store Rotarix

Keep this vaccine out of the sight and reach of children.

Do not use this vaccine after the expiry date which is stated on the carton. The expiry date refers to the last day of that month.

Store in a refrigerator (2 °C – 8 °C).
Do not freeze.
Store in the original package in order to protect from light.

The vaccine should be used immediately after opening.

Do not throw away any medicines via wastewater or household waste. Ask your pharmacist how to throw away medicines your child no longer uses. These measures will help to protect the environment.

6. Contents of the pack and other information

What Rotarix contains

- The active substances are:

  Human rotavirus RIX4414 strain (live, attenuated)* not less than $10^{6.0}$ $CCID_{50}$

  *Produced on Vero cells

- The other ingredients in Rotarix are: sucrose , Di-sodium Adipate, Dulbecco's Modified Eagle Medium (DMEM) (containing phenylalanine, sodium, glucose, and other substances), sterile water, (see also section 2, "Rotarix contains sucrose, glucose, phenylalanine and sodium")

What Rotarix looks like and contents of the pack

Oral suspension in pre-filled **oral** applicator.

Rotarix is supplied as clear and colourless liquid in a single dose pre-filled **oral** applicator (1.5 mL).

Rotarix is available in a pack of 1, 5, 10 or 25.

Not all pack sizes may be marketed.

Marketing Authorisation Holder and Manufacturer

GlaxoSmithKline Biologicals SA
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This leaflet was last revised in.

Other sources of information

Detailed information on this medicine is available on the European Medicines Agency web site: https://www.ema.europa.eu.

The following information is intended for healthcare professionals only:

The vaccine is presented as a clear, colourless liquid, free of visible particles, for **oral** administration.

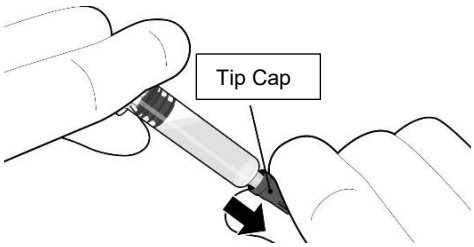
The vaccine is ready to use (no reconstitution or dilution is required).
The vaccine is to be administered **orally** without mixing with any other vaccines or solutions.

The vaccine should be inspected visually for any foreign particulate matter and/or abnormal physical appearance. In the event of either being observed, discard the vaccine.

Any unused vaccine or waste material should be disposed of in accordance with local requirements.

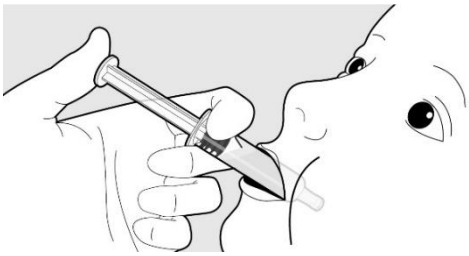
Instructions for administration of the vaccine:

Please read the instructions for use all the way through before starting to give the vaccine.



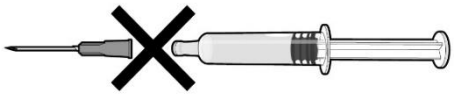
Remove the protective Tip Cap from the **oral** applicator.

Do not pull the **oral** applicator plunger out of the barrel. If it happens, do not administer the vaccine.



For **oral administration only**.

Have the infant seated in a reclining position. Place the **oral** applicator towards the inner cheek. Administer the entire contents of the **oral** applicator into the infant's mouth.



Do not inject.

Discard the empty **oral** applicator and tip cap in approved biological waste containers according to local regulations.

Package leaflet: Information for the user

Rotarix oral suspension in squeezable tube
rotavirus vaccine, live

Read all of this leaflet carefully before your child receives this vaccine because it contains important information for you.
- Keep this leaflet. You may need to read it again.
- If you have any further questions, ask your doctor or pharmacist.
- This vaccine has been prescribed for your child only. Do not pass it on to others.
- If you get any side effects, talk to your doctor or pharmacist. This includes any possible side effects not listed in this leaflet. See section 4.

What is in this leaflet

1. What Rotarix is and what it is used for
2. What you need to know before your child receives Rotarix
3. How Rotarix is given
4. Possible side effects
5. How to store Rotarix
6. Contents of the pack and other information

1. What Rotarix is and what it is used for

Rotarix is a viral vaccine, containing live, attenuated human rotavirus, that helps to protect your child, from the age of 6 weeks, against gastro-enteritis (diarrhoea and vomiting) caused by rotavirus infection.

How Rotarix works

Rotavirus infection is the most common cause of severe diarrhoea in infants and young children. Rotavirus is easily spread from hand-to-mouth due to contact with stools from an infected person. Most children with rotavirus diarrhoea recover on their own. However, some children become very ill with severe vomiting, diarrhoea and life-threatening loss of fluids that requires hospitalisation.

When a person is given the vaccine, the immune system (the body's natural defences) will make antibodies against the most commonly occurring types of rotavirus. These antibodies protect against disease caused by these types of rotavirus.

As with all vaccines, Rotarix may not completely protect all people who are vaccinated against the rotavirus infections it is intended to prevent.

2. What you need to know before your child receives Rotarix

Rotarix should not be given
- if your child has previously had any allergic reaction to rotavirus vaccines or any of the other ingredients of this vaccine (listed in section 6). Signs of an allergic reaction may include itchy skin rash, shortness of breath and swelling of the face or tongue.
- if your child has previously had intussusception (a bowel obstruction in which one segment of bowel becomes enfolded within another segment).
- if your child was born with a malformation of the gut that could lead to intussusception.
- if your child has a rare inherited illness which affects their immune system called Severe Combined Immunodeficiency (SCID).
- if your child has a severe infection with a high temperature. It might be necessary to postpone the vaccination until recovery. A minor infection such as a cold should not be a problem, but talk to your doctor first.

- if your child has diarrhoea or is vomiting. It might be necessary to postpone the vaccination until recovery.

Warnings and precautions
Talk to your doctor/health care professional before your child receives Rotarix if:
- he/she has a close contact such as a household member who has a weakened immune system, e.g., a person with cancer or who is taking medicines that may weaken the immune system.
- he/she has any disorder of the gastrointestinal system.
- he/she has not been gaining weight and growing as expected.
- he/she has any disease or is taking any medicine which reduces his/her resistance to infection or if his/her mother has taken during pregnancy any medicine that may weaken the immune system.

After your child has received Rotarix, contact a doctor/health care professional right away if your child experiences severe stomach pain, persistent vomiting, blood in stools, a swollen belly and/or high fever (see also section 4 “Possible side effects”).

As always, please take care to wash your hands thoroughly after changing soiled nappies.

Other medicines and Rotarix
Tell your doctor if your child is taking, has recently taken or might take any other medicines or has recently received any other vaccine.

Rotarix may be given at the same time your child receives other normally recommended vaccines, such as diphtheria, tetanus, pertussis (whooping cough), *Haemophilus influenzae* type b, oral or inactivated polio, hepatitis B vaccines as well as pneumococcal and meningococcal serogroup C conjugate vaccines.

Rotarix with food and drink
There are no restrictions on your child’s consumption of food or liquids, either before or after vaccination.

Breast-feeding
Based on evidence generated in clinical trials, breast-feeding does not reduce the protection against rotavirus gastro-enteritis afforded by Rotarix. Therefore, breast-feeding may be continued during the vaccination schedule.

Rotarix contains sucrose, glucose, phenylalanine and sodium
If you have been told by your doctor that the child being vaccinated has an intolerance to some sugars, contact your doctor before your child receives this vaccine.

This vaccine contains 0.15 microgram phenylalanine in each dose. Phenylalanine may be harmful if your child has phenylketonuria (PKU), a rare genetic disorder in which phenylalanine builds up because the body cannot remove it properly.

This vaccine contains 32 mg sodium (main component of cooking/table salt) in each dose.

3. How Rotarix is given

The doctor or nurse will administer the recommended dose of Rotarix to your child. The vaccine (1.5 mL liquid) will be given **orally**. Under no circumstance should this vaccine be administered by injection.

Your child will receive two doses of the vaccine. Each dose will be given on a separate occasion with an interval of at least 4 weeks between the two doses. The first dose may be given from the age of 6 weeks. The two doses of the vaccine must have been given by the age of 24 weeks, although they should preferably have been given before 16 weeks of age.

Rotarix may be given according to the same vaccination course to infants who were born prematurely, provided that the pregnancy had lasted at least 27 weeks.

In case your child spits out or regurgitates most of the vaccine dose, a single replacement dose may be given at the same vaccination visit.

When Rotarix is given to your child for the first dose, it is recommended that your child also receives Rotarix (and not another rotavirus vaccine) for the second dose.

It is important that you follow the instructions of your doctor or nurse regarding return visits. If you forget to go back to your doctor at the scheduled time, ask your doctor for advice.

4. Possible side effects

Like all medicines, this vaccine can cause side effects, although not everybody gets them.

Contact a doctor/health care professional right away if your child experiences one of the following symptoms:

- Allergic reactions (frequency cannot be estimated from the available data), which may be severe (anaphylaxis), and may include: shortness of breath or allergic swelling that may affect the face, lips, tongue or throat.
- Intussusception (part of the intestine gets blocked or twisted) (frequency very rare). The signs may include severe stomach pain, persistent vomiting, blood in stools, a swollen belly and/or high fever.

The following other side effects may happen with this vaccine:

♦ Common (These may occur with up to 1 in 10 doses of the vaccine):
- diarrhoea
- irritability

♦ Uncommon (These may occur with up to 1 in 100 doses of the vaccine):
- abdominal pain (see also above for signs of very rare side effects of intussusception)
- flatulence
- inflammation of the skin

♦ Side effects that have been reported during marketed use of Rotarix include:
- Very rare: hives (urticaria)
- blood in stools
- in babies born very prematurely (at or before 28 weeks of gestation) longer gaps than normal between breaths may occur for 2-3 days after vaccination.
- children with a rare inherited illness called Severe Combined Immunodeficiency (SCID) may have an inflamed stomach or gut (gastroenteritis) and pass the vaccine virus in their stools. The signs of gastroenteritis may include feeling sick, being sick, stomach cramps or diarrhoea.

Reporting of side effects
If your child gets any of the side effects, talk to your doctor or pharmacist. This includes any possible side effects not listed in this leaflet. You can also report side effects directly via the national reporting system listed in Appendix V. By reporting side effects you can help provide more information on the safety of this medicine.

5. How to store Rotarix

Keep this vaccine out of the sight and reach of children.

Do not use this vaccine after the expiry date which is stated on the carton. The expiry date refers to the last day of that month.

Store in a refrigerator (2 °C – 8 °C).
Do not freeze.
Store in the original package in order to protect from light.

The vaccine should be used immediately after opening.

Do not throw away any medicines via wastewater or household waste. Ask your pharmacist how to throw away medicines your child no longer uses. These measures will help to protect the environment.

6. Contents of the pack and other information

What Rotarix contains

- The active substances are:

  Human rotavirus RIX4414 strain (live, attenuated)* not less than $10^{6.0}$ $CCID_{50}$

  *Produced on Vero cells

- The other ingredients in Rotarix are: sucrose, Di-sodium Adipate, Dulbecco's Modified Eagle Medium (DMEM) (containing phenylalanine, sodium, glucose, and other substances), sterile water, (see also section 2, "Rotarix contains sucrose, glucose, phenylalanine and sodium")

What Rotarix looks like and contents of the pack

Oral suspension.

Rotarix is supplied as clear and colourless liquid in a single dose squeezable tube (1.5 mL).

Rotarix is available in a pack of 1, 10 or 50.

Not all pack sizes may be marketed.

Marketing Authorisation Holder and Manufacturer

GlaxoSmithKline Biologicals SA
Rue de l'Institut 89
B-1330 Rixensart
Belgium

For any information about this medicine, please contact the local representative of the Marketing Authorisation Holder:

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Other sources of information

Detailed information on this medicine is available on the European Medicines Agency web site: https://www.ema.europa.eu.

The following information is intended for healthcare professionals only:

The vaccine is presented as a clear, colourless liquid, free of visible particles, for **oral** administration.

The vaccine is ready to use (no reconstitution or dilution is required).
The vaccine is to be administered **orally** without mixing with any other vaccines or solutions.

The vaccine should be inspected visually for any foreign particulate matter and/or abnormal physical appearance. In the event of either being observed, discard the vaccine.

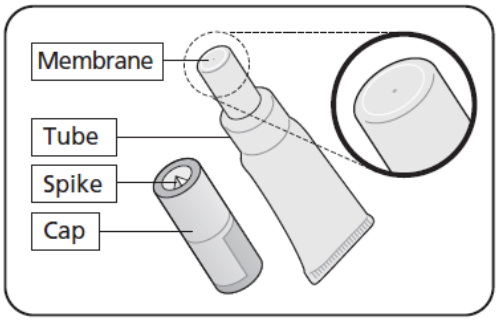
Any unused vaccine or waste material should be disposed of in accordance with local requirements.

Instructions for administration of the vaccine:

Please read the instructions for use all the way through before starting to give the vaccine.

A What you need to do before giving Rotarix

- Check the expiry date.
- Check the tube has not been damaged nor is already open.
- Check the liquid is clear and colourless, without any particles in it.



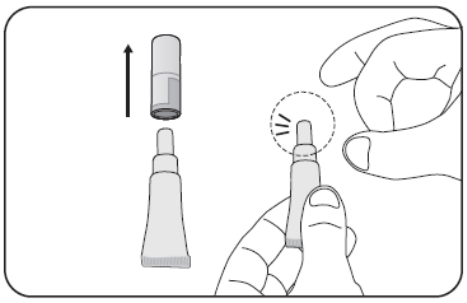
If you notice anything abnormal, do not use the vaccine.

- This vaccine is given orally - straight from the tube.
- It is ready to use - you do not need to mix it with anything.

B Get the tube ready

1. Pull off the cap

- Keep the cap – you need this to pierce the membrane.
- Hold the tube upright.

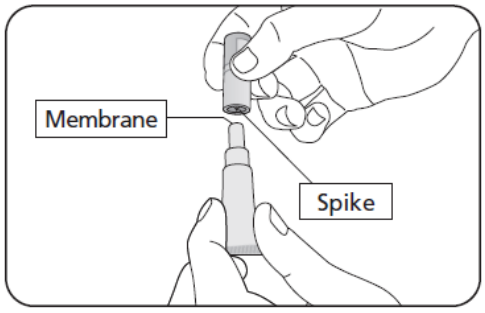


2. Repeatedly flick the top of the tube until it is clear of any liquid

- Clear any liquid from the thinnest section of the tube by flicking just below the membrane.

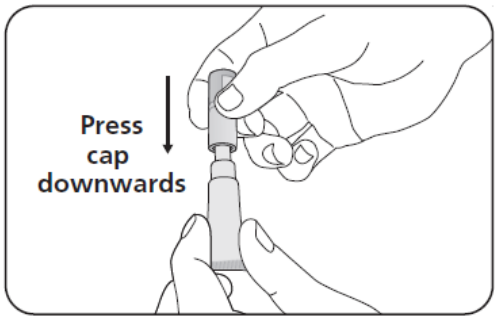
3. Position the cap to open the tube

- Keep the tube held upright.
- Hold the side of tube
- There is a small spike inside the top of the cap - in the centre.
- Turn the cap upside down (180°).



4. To open the tube

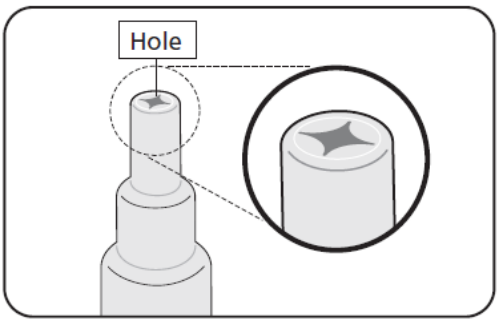
- You do not need to twist. Press the cap down to pierce the membrane.
- Then lift off the cap.



C Check the tube has opened correctly

1. Check the membrane has been pierced

- There should be a hole at the top of the tube.

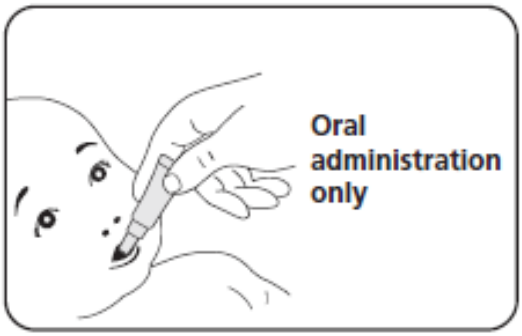


2. What to do if the membrane has not been pierced

- If the membrane has not been pierced return to section B and repeat steps 2, 3 and 4.

D Give the vaccine

- Once the tube is open check the liquid is clear, without any particles in it.
  If you notice anything abnormal, do not use the vaccine.
- Give the vaccine straight away.



1. Position the child to give the vaccine

- Seat the child leaning slightly backwards.

2. Administer the vaccine

- Squeeze the liquid gently into the side of the child's mouth - towards the inside of their cheek.
- You may need to squeeze the tube a few times to get all of the vaccine out - it is okay if a drop remains in the tip of the tube.

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

Package leaflet: Information for the user

Rotarix oral suspension in multi-monodose (5 single dose) squeezable tube presentation connected by a bar
rotavirus vaccine, live

Read all of this leaflet carefully before your child receives this vaccine because it contains important information for you.
- Keep this leaflet. You may need to read it again.
- If you have any further questions, ask your doctor or pharmacist.
- This vaccine has been prescribed for your child only. Do not pass it on to others.
- If you get any side effects, talk to your doctor or pharmacist. This includes any possible side effects not listed in this leaflet. See section 4.

What is in this leaflet

1. What Rotarix is and what it is used for
2. What you need to know before your child receives Rotarix
3. How Rotarix is given
4. Possible side effects
5. How to store Rotarix
6. Contents of the pack and other information

1. What Rotarix is and what it is used for

Rotarix is a viral vaccine, containing live, attenuated human rotavirus, that helps to protect your child, from the age of 6 weeks, against gastro-enteritis (diarrhoea and vomiting) caused by rotavirus infection.

How Rotarix works

Rotavirus infection is the most common cause of severe diarrhoea in infants and young children. Rotavirus is easily spread from hand-to-mouth due to contact with stools from an infected person. Most children with rotavirus diarrhoea recover on their own. However, some children become very ill with severe vomiting, diarrhoea and life-threatening loss of fluids that requires hospitalisation.

When a person is given the vaccine, the immune system (the body's natural defences) will make antibodies against the most commonly occurring types of rotavirus. These antibodies protect against disease caused by these types of rotavirus.

As with all vaccines, Rotarix may not completely protect all people who are vaccinated against the rotavirus infections it is intended to prevent.

2. What you need to know before your child receives Rotarix

Rotarix should not be given
- if your child has previously had any allergic reaction to rotavirus vaccines or any of the other ingredients of this vaccine (listed in section 6). Signs of an allergic reaction may include itchy skin rash, shortness of breath and swelling of the face or tongue.
- if your child has previously had intussusception (a bowel obstruction in which one segment of bowel becomes enfolded within another segment).
- if your child was born with a malformation of the gut that could lead to intussusception.
- if your child has a rare inherited illness which affects their immune system called Severe Combined Immunodeficiency (SCID).
- if your child has a severe infection with a high temperature. It might be necessary to postpone the vaccination until recovery. A minor infection such as a cold should not be a problem, but talk to your doctor first.

- if your child has diarrhoea or is vomiting. It might be necessary to postpone the vaccination until recovery.

Warnings and precautions
Talk to your doctor/health care professional before your child receives Rotarix if:
- he/she has a close contact such as a household member who has a weakened immune system, e.g., a person with cancer or who is taking medicines that may weaken the immune system.
- he/she has any disorder of the gastrointestinal system.
- he/she has not been gaining weight and growing as expected.
- he/she has any disease or is taking any medicine which reduces his/her resistance to infection or if his/her mother has taken during pregnancy any medicine that may weaken the immune system.

After your child has received Rotarix, contact a doctor/health care professional right away if your child experiences severe stomach pain, persistent vomiting, blood in stools, a swollen belly and/or high fever (see also section 4 “Possible side effects”).

As always, please take care to wash your hands thoroughly after changing soiled nappies.

Other medicines and Rotarix
Tell your doctor if your child is taking, has recently taken or might take any other medicines or has recently received any other vaccine.

Rotarix may be given at the same time your child receives other normally recommended vaccines, such as diphtheria, tetanus, pertussis (whooping cough), *Haemophilus influenzae* type b, oral or inactivated polio, hepatitis B vaccines as well as pneumococcal and meningococcal serogroup C conjugate vaccines.

Rotarix with food and drink
There are no restrictions on your child’s consumption of food or liquids, either before or after vaccination.

Breast-feeding
Based on evidence generated in clinical trials, breast-feeding does not reduce the protection against rotavirus gastro-enteritis afforded by Rotarix. Therefore, breast-feeding may be continued during the vaccination schedule.

Rotarix contains sucrose, glucose, phenylalanine and sodium
If you have been told by your doctor that the child being vaccinated has an intolerance to some sugars, contact your doctor before your child receives this vaccine.

This vaccine contains 0.15 microgram phenylalanine in each dose. Phenylalanine may be harmful if your child has phenylketonuria (PKU), a rare genetic disorder in which phenylalanine builds up because the body cannot remove it properly.

This vaccine contains 32 mg sodium (main component of cooking/table salt) in each dose.

3. How Rotarix is given

The doctor or nurse will administer the recommended dose of Rotarix to your child. The vaccine (1.5 mL liquid) will be given **orally**. Under no circumstance should this vaccine be administered by injection.

Your child will receive two doses of the vaccine. Each dose will be given on a separate occasion with an interval of at least 4 weeks between the two doses. The first dose may be given from the age of 6 weeks. The two doses of the vaccine must have been given by the age of 24 weeks, although they should preferably have been given before 16 weeks of age.

Rotarix may be given according to the same vaccination course to infants who were born prematurely, provided that the pregnancy had lasted at least 27 weeks.

In case your child spits out or regurgitates most of the vaccine dose, a single replacement dose may be given at the same vaccination visit.

When Rotarix is given to your child for the first dose, it is recommended that your child also receives Rotarix (and not another rotavirus vaccine) for the second dose.

It is important that you follow the instructions of your doctor or nurse regarding return visits. If you forget to go back to your doctor at the scheduled time, ask your doctor for advice.

4. Possible side effects

Like all medicines, this vaccine can cause side effects, although not everybody gets them.

Contact a doctor/health care professional right away if your child experiences one of the following symptoms:

- Allergic reactions (frequency cannot be estimated from the available data), which may be severe (anaphylaxis), and may include: shortness of breath or allergic swelling that may affect the face, lips, tongue or throat.
- Intussusception (part of the intestine gets blocked or twisted) (frequency very rare). The signs may include severe stomach pain, persistent vomiting, blood in stools, a swollen belly and/or high fever.

The following other side effects may happen with this vaccine:

♦ Common (These may occur with up to 1 in 10 doses of the vaccine):
- diarrhoea
- irritability

♦ Uncommon (These may occur with up to 1 in 100 doses of the vaccine):
- abdominal pain (see also above for signs of very rare side effects of intussusception)
- flatulence
- inflammation of the skin

♦ Side effects that have been reported during marketed use of Rotarix include:
- Very rare: hives (urticaria)
- blood in stools
- in babies born very prematurely (at or before 28 weeks of gestation) longer gaps than normal between breaths may occur for 2-3 days after vaccination.
- children with a rare inherited illness called Severe Combined Immunodeficiency (SCID) may have an inflamed stomach or gut (gastroenteritis) and pass the vaccine virus in their stools. The signs of gastroenteritis may include feeling sick, being sick, stomach cramps or diarrhoea.

Reporting of side effects
If your child gets any of the side effects, talk to your doctor or pharmacist. This includes any possible side effects not listed in this leaflet. You can also report side effects directly via the national reporting system listed in Appendix V. By reporting side effects you can help provide more information on the safety of this medicine.

5. How to store Rotarix

Keep this vaccine out of the sight and reach of children.

Do not use this vaccine after the expiry date which is stated on the carton. The expiry date refers to the last day of that month.

Store in a refrigerator (2 °C – 8 °C).
Do not freeze.
Store in the original package in order to protect from light.

The vaccine should be used immediately after opening.

Do not throw away any medicines via wastewater or household waste. Ask your pharmacist how to throw away medicines your child no longer uses. These measures will help to protect the environment.

6. Contents of the pack and other information

What Rotarix contains

- The active substances are:

  Human rotavirus RIX4414 strain (live, attenuated)* not less than $10^{6.0}$ $CCID_{50}$

  *Produced on Vero cells

- The other ingredients in Rotarix are: sucrose , Di-sodium Adipate, Dulbecco's Modified Eagle Medium (DMEM) (containing phenylalanine, sodium, glucose and other substances), sterile water, (see also section 2, "Rotarix contains sucrose, glucose, phenylalanine and sodium")

What Rotarix looks like and contents of the pack

Oral suspension.

Rotarix is supplied as clear and colourless liquid in 5 single dose squeezable tubes (5 x 1.5 mL) connected by a bar.

Rotarix is available in a pack of 50 tubes.

Not all pack sizes may be marketed.

Marketing Authorisation Holder and Manufacturer

GlaxoSmithKline Biologicals SA
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This leaflet was last revised in.

Other sources of information

Detailed information on this medicine is available on the European Medicines Agency web site: https://www.ema.europa.eu.

The following information is intended for healthcare professionals only:

The vaccine is presented as a clear, colourless liquid, free of visible particles, for **oral** administration.

The vaccine is ready to use (no reconstitution or dilution is required).
The vaccine is to be administered **orally** without mixing with any other vaccines or solutions.

The vaccine should be inspected visually for any foreign particulate matter and/or abnormal physical appearance. In the event of either being observed, discard the vaccine.

Any unused vaccine or waste material should be disposed of in accordance with local requirements.

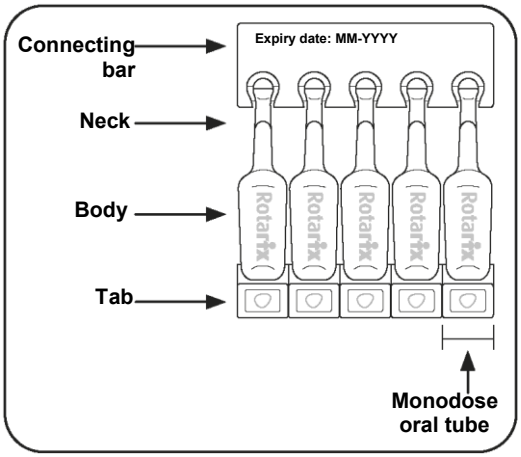
Instructions for administration of the vaccine:

Please read the instructions for use all the way through before starting to give the vaccine.

- This vaccine is given orally straight from an individual tube.
- One oral tube delivers one dose of vaccine.
- This vaccine is ready to use - do not mix it with anything else.

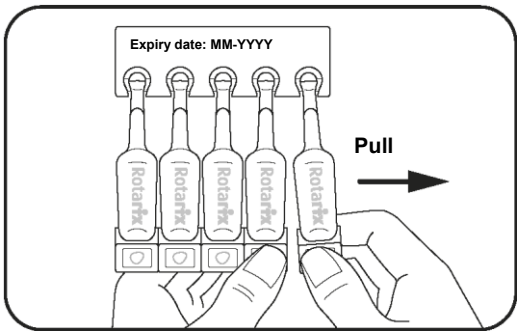
A. What you need to do before giving Rotarix

1. Check the expiry date on the connecting bar.
2. Check the liquid in the oral tubes is clear, colourless and free from any particles.
   - **Do not use any of the oral tubes on the connecting bar if you notice anything unusual.**
3. Check that each individual oral tube is not damaged and is still sealed.
   - **Do not use the affected oral tube if you notice anything unusual.**

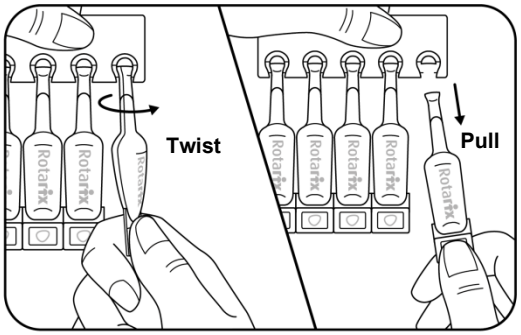


B. Get the oral tube ready

1. To separate one oral tube from the others starting at one end:
   a) Hold the tab of one of the end oral tubes to separate it from the others.
   b) With your other hand, hold the tab of the oral tube next to it.
   c) Pull the tab and tear it away from the oral tube next to it.



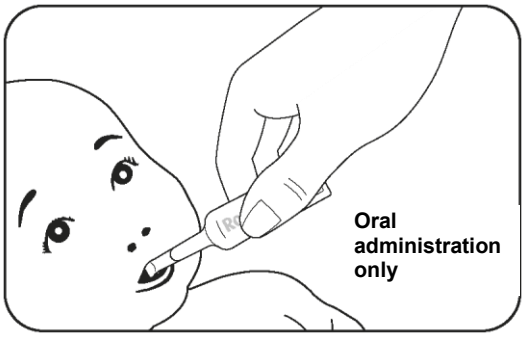
2. To open the separated oral tube:
   d) Keep the separated oral tube held upright.
   e) Hold the tab of the separated oral tube in one hand and the connecting bar in the other hand. **Do not hold the body of the oral tube, you may squeeze out some of the vaccine.**
   f) Twist the separated oral tube.
   g) Pull it from the connecting bar.



C. Give the vaccine orally immediately after opening

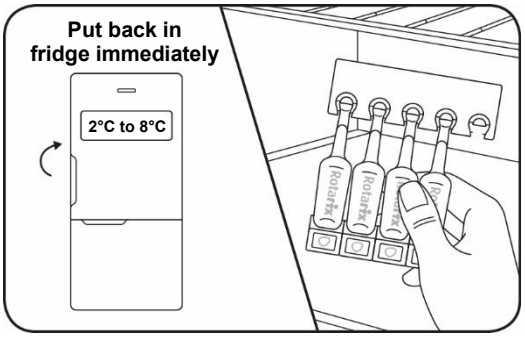
1. To position the child to receive the vaccine:
   - Seat the child leaning slightly backwards.

2. To administer the vaccine orally:
   - Squeeze the liquid gently into the side of the child's mouth, towards the inside of their cheek.
   - You may need to squeeze the oral tube a few times to get all of the vaccine out - it is okay if a drop stays in the oral tube.



D. Store remaining doses in the fridge immediately

Unused oral tubes that are still attached to the connecting bar must be put back in the fridge immediately after an oral tube has been used. This is so that the unused oral tubes can be used for the next vaccination.



Discard the used oral tubes in approved biological waste containers according to local regulations.