

ANNEX I
SUMMARY OF PRODUCT CHARACTERISTICS

1. NAME OF THE MEDICINAL PRODUCT

Rotarix, powder and solvent for oral suspension
Rotavirus vaccine, live

2. QUALITATIVE AND QUANTITATIVE COMPOSITION

After reconstitution, 1 dose (1 ml) contains:

Human rotavirus RIX4414 strain (live attenuated)* not less than $10^{6.0}$ CCID₅₀

*Produced on Vero cells

For a full list of excipients, see section 6.1.

3. PHARMACEUTICAL FORM

Powder and solvent for oral suspension.

The powder is white.

The solvent is a turbid liquid with a slow settling white deposit and a colourless supernatant.

4. CLINICAL PARTICULARS

4.1 Therapeutic indications

Rotarix is indicated for the active immunisation of infants from the age of 6 weeks for prevention of gastro-enteritis due to rotavirus infection (see section 4.2).

In clinical trials, efficacy was demonstrated against gastro-enteritis due to rotavirus of types G1P[8], G3P[8] and G9P[8] (see sections 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.

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.

Method of administration

Rotarix is for oral use only.

ROTARIX SHOULD UNDER NO CIRCUMSTANCES BE INJECTED.

4.3 Contraindications

Hypersensitivity to the active substance or to any of the excipients.

Hypersensitivity after previous administration of rotavirus vaccines.

Previous history of intussusception.

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

Infants who have known or suspected immunodeficiency. Asymptomatic HIV infection is not expected to affect the safety or efficacy of Rotarix. However, in the absence of sufficient data, administration of Rotarix to asymptomatic HIV subjects is not recommended.

Administration of Rotarix should be postponed in subjects 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 subjects 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.

The vaccine contains 9 mg of sucrose as an excipient. This amount is too low to cause adverse events in patients with rare hereditary problems such as fructose intolerance, glucose-galactose malabsorption or sucrase-isomaltase insufficiency.

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.

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 and 4% of stools after the second dose. When these stools were tested for the presence of live vaccine strain, only 17% were positive.

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).

Limited data in 140 premature children indicate that Rotarix can be given to premature children, however a lower immune response may be observed and the level of clinical protection remains unknown.

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

In clinical trials, efficacy was demonstrated against gastro-enteritis due to rotavirus of types G1P[8], G3P[8] and G9P[8]. There are insufficient data at this time to determine whether Rotarix can protect against infection with other G types. Clinical studies from which efficacy data were derived were conducted in Finland and Central and South America (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.

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) and pneumococcal 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 there is currently no evidence that clinical protection against severe rotavirus gastro-enteritis would be affected. The immune response to Rotarix is unaffected when OPV is administered two weeks apart from Rotarix.

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

4.6 Pregnancy and lactation

Rotarix is not intended for use in adults. Thus human data on use during pregnancy or lactation are not available and animal reproduction studies have not been performed.

There is no evidence available to suggest that breast-feeding would 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

In a total of eleven placebo-controlled clinical trials, approximately 77,800 doses of Rotarix were administered to approximately 40,200 infants.

In two clinical trials (Finland), Rotarix was administered alone (administration of routine paediatric vaccines was staggered). The incidence of diarrhoea, vomiting, loss of appetite, fever and irritability was not different in the group receiving Rotarix when compared to the group receiving placebo. No increase in the incidence or severity of these reactions was seen with the second dose.

In the remaining nine trials (Finland, Czech Republic, Canada, USA, Brazil, Mexico, Venezuela, Panama, Columbia, Peru, Singapore, South-Africa), Rotarix was co-administered with routine

paediatric vaccines (see section 4.5). The adverse reaction profile observed in these subjects was similar to the adverse reaction profile observed in subjects receiving the same paediatric vaccines and placebo.

The occurrence of adverse reactions was actively monitored up to 14 days after vaccination.

Adverse reactions are listed below per system organ class and frequency.

Frequencies are reported as:

Very common ($\geq 1/10$)

Common ($\geq 1/100, < 1/10$)

Uncommon ($\geq 1/1,000, < 1/100$)

Rare ($\geq 1/10,000, < 1/1,000$)

Infections and infestations

Rare: upper respiratory tract infection

Psychiatric disorders

Very common: irritability

Uncommon: crying, sleep disorder

Nervous system disorders

Uncommon: somnolence

Respiratory, thoracic and mediastinal disorders

Rare: hoarseness, rhinorrhoea

Gastrointestinal disorders

Very common: loss of appetite

Common: diarrhoea, vomiting, flatulence, abdominal pain, regurgitation of food

Uncommon: constipation

Skin and subcutaneous tissue disorders

Rare: dermatitis, rash

Musculoskeletal and connective tissue disorders

Rare: muscle cramp

General disorders and administration site conditions

Common: fever, fatigue

The risk of intussusception has been evaluated in a large safety trial conducted in Latin America and Finland where 63,225 subjects were enrolled. This trial gave evidence of no increased risk of intussusception in the Rotarix group when compared with the placebo group as shown in the table below.

Intussusception within 31 days after administration of:	Rotarix N=31,673	Placebo N=31,552	Relative risk (95% CI)
First dose	1	2	0.50 (0.07;3.80)
Second dose	5	5	0.99 (0.31;3.21)

CI: confidence interval

4.9 Overdose

No case of overdose has been reported.

5. PHARMACOLOGICAL PROPERTIES

5.1 Pharmacodynamic properties

Pharmaco-therapeutic group: viral vaccines, ATC code: J07BH01

Protective efficacy

Clinical studies have been conducted in Finland and Latin America to evaluate the protective efficacy of Rotarix against any and severe rotavirus gastro-enteritis.

A clinical study performed in Finland evaluated a formulation with a lower viral titre ($10^{5.3}$ CCID₅₀/dose) than the commercial formulation in approximately 400 subjects. Severity of gastro-enteritis was defined according to 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. After two doses of Rotarix, the protective vaccine efficacy during the first year of life was 90% (95% CI: 10.3;99.8) against severe gastro-enteritis (Vesikari score ≥ 11) and 73% (95% CI: 27.1;90.9) against any rotavirus gastro-enteritis. Protective efficacy of Rotarix during the second year of life was 83% (95% CI: 7.2;98.4) and 73% (95% CI: 19.9;91.8) against severe and any gastro-enteritis respectively.

The type specific vaccine efficacy observed against severe gastro-enteritis (Vesikari score ≥ 11) caused by G1P[8] was 87% (95% CI: 24.8;99.7) and against any gastro-enteritis caused by G1P[8] was 68% (95% CI: 9.8;89.5).

A clinical study performed in Latin America evaluated the commercial formulation (viral titre of $10^{6.5}$ CCID₅₀/dose) in more than 20,000 subjects. The observed vaccine efficacy against severe rotavirus gastro-enteritis requiring hospitalisation and/or rehydration therapy in a medical facility was 84.7% (95% CI: 71.7;92.4). The type specific vaccine efficacy observed against severe gastro-enteritis was 91.8% (95% CI: 74.1;98.4) for G1P[8], 87.7% (95% CI: 8.3;99.7) for G3P[8], 90.6% (95% CI: 61.7;98.9) for G9P[8] and 90.9% (95% CI: 79.2;96.8) for strains with P8 genotype.

A pooled analysis of three efficacy studies*, showed a point estimate of 67% (95% CI: 14.8;87.1) for efficacy against severe gastro-enteritis (Vesikari score ≥ 11) caused by rotavirus G2P[4] type, suggesting efficacy against this type.

* In these studies, the point estimates and confidence intervals were respectively: 100% (95%CI: -1858.0;100), 100% (95%CI: 21.1;100) and 45.4% (95%CI: -81.5;86.6).

Immune response

The immunologic mechanism by which Rotarix protects against rotavirus gastroenteritis is not completely understood. A relationship between antibody responses to rotavirus vaccination and protection against rotavirus gastroenteritis has not been established. The following table shows the percentage of subjects with serum anti-rotavirus IgA antibody titers ≥ 20 U/ml (by ELISA) after the second dose of vaccine or placebo as observed in different studies.

Study conducted in	Schedule	Viral titer	Vaccine	Placebo
Finland	2, 4 months	$10^{5.3}$ CCID ₅₀ /dose [†]	83.6%	1.7%
Finland	3, 5 months	$10^{6.5}$ CCID ₅₀ /dose [‡]	94.8%	3.7%
Czech Republic	3, 4 months	$10^{6.5}$ CCID ₅₀ /dose [‡]	84.5%	2.0%
Latin America	2, 3 to 4 months	$10^{6.5}$ CCID ₅₀ /dose [‡]	77.9%	15.1%

[†] Formulation with a lower viral titre than the commercial formulation

[‡] Commercial formulation

5.2 Pharmacokinetic properties

Evaluation of pharmacokinetic properties is not required for vaccines.

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

Powder

Sucrose

Dextran

Sorbitol

Amino acids

Dulbecco's Modified Eagle Medium (DMEM)

Solvent

Calcium carbonate

Xanthan gum

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

3 years.

After reconstitution:

After reconstitution, the vaccine contained in the syringe should be administered promptly.

In case of temporary storage of the reconstituted vaccine outside the refrigerator, experimental data have shown that the reconstituted vaccine is stable when stored at ambient temperature (18-25°C) for 24 hours. These data are not recommendations for storage.

If the reconstituted vaccine is not used within 24 hours, it should be discarded.

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.

In case of temporary storage of the powder and the solvent outside the refrigerator, experimental data have shown that the powder as well as the solvent are stable when stored at temperatures up to 37°C for 1 week. These data are not recommendations for storage.

For storage conditions of the reconstituted product, see section 6.3.

6.5 Nature and contents of container

1 dose of powder in a vial (type I glass) with a stopper (rubber butyl)

1 ml of solvent in pre-filled syringe (type I glass) with a plunger stopper and a protective tip cap (rubber butyl).

Transfer adapter for reconstitution (1/dose)

in the following pack sizes:

- pack size of 1 vial of powder plus 1 pre-filled syringe of solvent
- pack size of 5 vials of powder plus 5 pre-filled syringes of solvent
- pack size of 10 vials of powder plus 10 pre-filled syringes of solvent
- pack size of 25 vials of powder plus 25 pre-filled syringes of solvent

Not all pack sizes may be marketed.

6.6 Special precautions for disposal

A white deposit and clear supernatant is observed upon storage of the syringe containing the solvent. The solvent should be inspected visually both before and after shaking for any foreign particulate matter and/or abnormal physical appearance prior to reconstitution.

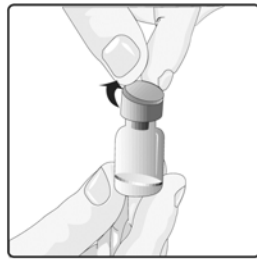
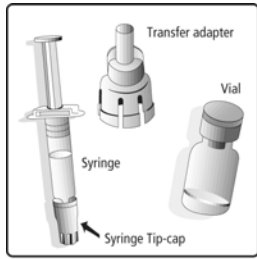
The reconstituted vaccine is slightly more turbid than the solvent and is milky white in appearance.

The reconstituted vaccine should also be inspected visually for any foreign particulate matter and/or abnormal physical appearance prior to administration. In the event of either being observed, discard the vaccine. Any unused vaccine or waste material should be disposed of in accordance with local requirements.

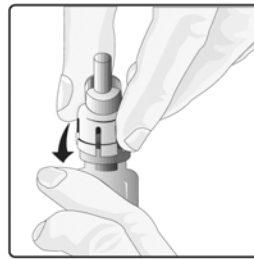
Instructions for reconstitution and administration of the vaccine:

1. Remove the plastic cover from the vial containing the powder.
2. Connect the transfer adapter onto the vial by pushing it downwards until the transfer adapter is properly and securely placed.
3. Shake the syringe containing the solvent vigorously. The shaken suspension will appear as a turbid liquid with a slow settling white deposit.
4. Remove the protective tip cap from the syringe.
5. Connect the syringe into the transfer adapter by pushing it firmly on this device.
6. Inject the entire content of the syringe into the vial containing the powder.
7. With the syringe still attached, shake the vial and examine it for complete suspension of the powder. The reconstituted vaccine will appear more turbid than the solvent alone. This appearance is normal.
8. Withdraw the entire mixture back into the syringe.
9. Remove the syringe from the transfer adapter.
10. This vaccine is for **oral administration only**. The child should be seated in a reclining position. Administer the entire content of the syringe **ORALLY** (by administering the entire content of the syringe on the inside of the cheek). **Do not inject.**

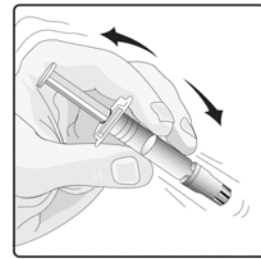
If the reconstituted vaccine is to be stored temporarily before administration, replace the protective tip cap on the syringe. The syringe containing the reconstituted vaccine should be shaken gently again before **ORAL** administration. **Do not inject.**



1. Remove the plastic cover from the vial containing the lyophilised powder.



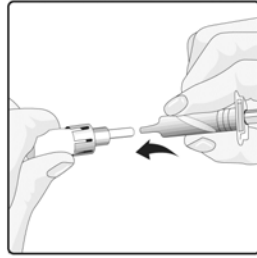
2. Connect the transfer adapter onto the vial by pushing it downwards until the transfer adapter is positioned securely on the top of the vial.



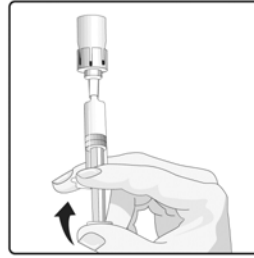
3. Shake the syringe containing the suspension vigorously. The shaken suspension will appear as a turbid liquid with a slow settling white deposit.



4. Remove the protective tip cap from the syringe.



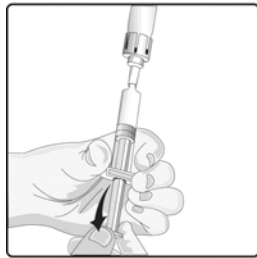
5. Connect the syringe into the transfer adapter by pushing it firmly on this device.



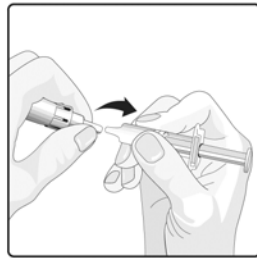
6. Inject the entire content of the syringe into the vial containing the lyophilised powder.



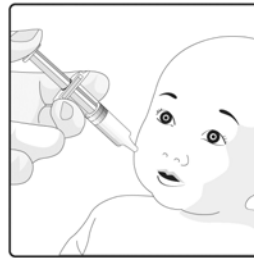
7. With the syringe still attached, shake the vial and examine it for complete suspension of the powder. The reconstituted vaccine will appear turbid. This appearance is normal.



8. Withdraw the entire mixture back into the syringe.



9. Remove the syringe from the transfer adapter.



10. Administer the entire content of the syringe orally (on the inside of the cheek). The child should be seated in a reclining position. Do not inject.

7. MARKETING AUTHORISATION HOLDER

GlaxoSmithKline Biologicals s.a.
Rue de l'Institut 89
B-1330 Rixensart, Belgium

8. MARKETING AUTHORISATION NUMBER(S)

9. DATE OF FIRST AUTHORISATION/RENEWAL OF THE AUTHORISATION

10. DATE OF REVISION OF THE TEXT

ANNEX II

- A. MANUFACTURER(S) OF THE BIOLOGICAL ACTIVE
SUBSTANCE(S) AND MANUFACTURING
AUTHORISATION HOLDER(S) RESPONSIBLE FOR
BATCH RELEASE**

- B. CONDITIONS OF THE MARKETING AUTHORISATION**

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

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

GlaxoSmithKline Biologicals s.a.
Rue de l'Institut 89
1330 Rixensart
Belgium

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

GlaxoSmithKline Biologicals s.a.
Rue de l'Institut 89
1330 Rixensart
Belgium

B. CONDITIONS OF THE MARKETING AUTHORISATION

• **CONDITIONS OR RESTRICTIONS REGARDING SUPPLY AND USE IMPOSED ON
THE MARKETING AUTHORISATION HOLDER**

Medicinal product subject to medical prescription.

• **CONDITIONS OR RESTRICTIONS WITH REGARD TO THE SAFE AND
EFFECTIVE USE OF THE MEDICINAL PRODUCT**

Not applicable.

• **OTHER CONDITIONS**

Official batch release: in accordance with Article 114 Directive 2001/83/EC as amended, the official batch release will be undertaken by a state laboratory or a laboratory designated for that purpose.

ANNEX III
LABELLING AND PACKAGE LEAFLET

A. LABELLING

**PARTICULARS TO APPEAR ON THE OUTER PACKAGING
PACK SIZE OF 1 VIAL WITH 1 SYRINGE AND 1 TRANSFER ADAPTER**

1. NAME OF THE MEDICINAL PRODUCT

Rotarix, powder and solvent for oral suspension
Rotavirus vaccine, live

2. STATEMENT OF ACTIVE SUBSTANCE(S)

After reconstitution, 1 dose (1 ml) contains:

Human rotavirus RIX4414 strain (live attenuated)* not less than $10^{6.0}$ CCID₅₀

*Produced on Vero cells

3. LIST OF EXCIPIENTS

Powder: sucrose, dextran, sorbitol, amino acids, Dulbecco's Modified Eagle Medium (DMEM)

Solvent: calcium carbonate, xanthan gum, sterile water

4. PHARMACEUTICAL FORM AND CONTENTS

Powder and solvent for oral suspension

vial: powder

syringe: solvent

transfer adapter

1 dose (1 ml)

5. METHOD AND ROUTE(S) OF ADMINISTRATION

Oral administration

Do not inject!

Shake before use

Read the package leaflet before use

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

Keep out of the reach and sight of children.

7. OTHER SPECIAL WARNING(S), IF NECESSARY

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 s.a.
Rue de l'Institut 89
B-1330 Rixensart, Belgium

12. MARKETING AUTHORISATION NUMBER(S)

EU/0/00/000/000

13. BATCH NUMBER

Lot

14. GENERAL CLASSIFICATION FOR SUPPLY

Medicinal product subject to medical prescription.

15. INSTRUCTIONS ON USE

16. INFORMATION IN BRAILLE

**PARTICULARS TO APPEAR ON THE OUTER PACKAGING
PACK SIZE OF 5 VIALS WITH 5 SYRINGES AND 5 TRANSFER ADAPTERS**

1. NAME OF THE MEDICINAL PRODUCT

Rotarix, powder and solvent for oral suspension
Rotavirus vaccine, live

2. STATEMENT OF ACTIVE SUBSTANCE(S)

After reconstitution, 1 dose (1 ml) contains:

Human rotavirus RIX4414 strain (live attenuated)* not less than $10^{6.0}$ CCID₅₀

*Produced on Vero cells

3. LIST OF EXCIPIENTS

Powder: sucrose, dextran, sorbitol, amino acids, Dulbecco's Modified Eagle Medium (DMEM)

Solvent: calcium carbonate, xanthan gum, sterile water

4. PHARMACEUTICAL FORM AND CONTENTS

Powder and solvent for oral suspension

vial: powder

syringe: solvent

transfer adapter

5 x 1 dose

1 dose (1 ml)

5. METHOD AND ROUTE(S) OF ADMINISTRATION

Oral administration

Do not inject!

Shake before use

Read the package leaflet before use

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

Keep out of the reach and sight of children.

7. OTHER SPECIAL WARNING(S), IF NECESSARY

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.

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

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EU/0/00/000/000

13. BATCH NUMBER

Lot

14. GENERAL CLASSIFICATION FOR SUPPLY

Medicinal product subject to medical prescription.

15. INSTRUCTIONS ON USE

16. INFORMATION IN BRAILLE

**PARTICULARS TO APPEAR ON THE OUTER PACKAGING
PACK SIZE OF 10 VIALS WITH 10 SYRINGES AND 10 TRANSFER ADAPTERS**

1. NAME OF THE MEDICINAL PRODUCT

Rotarix, powder and solvent for oral suspension
Rotavirus vaccine, live

2. STATEMENT OF ACTIVE SUBSTANCE(S)

After reconstitution, 1 dose (1 ml) contains:

Human rotavirus RIX4414 strain (live attenuated)* not less than $10^{6.0}$ CCID₅₀

*Produced on Vero cells

3. LIST OF EXCIPIENTS

Powder: sucrose, dextran, sorbitol, amino acids, Dulbecco's Modified Eagle Medium (DMEM)

Solvent: calcium carbonate, xanthan gum, sterile water

4. PHARMACEUTICAL FORM AND CONTENTS

Powder and solvent for oral suspension

vial: powder

syringe: solvent

transfer adapter

10 x 1 dose

1 dose (1 ml)

5. METHOD AND ROUTE(S) OF ADMINISTRATION

Oral administration

Do not inject!

Shake before use

Read the package leaflet before use

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

Keep out of the reach and sight of children.

7. OTHER SPECIAL WARNING(S), IF NECESSARY

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.

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

12. MARKETING AUTHORISATION NUMBER(S)

EU/0/00/000/000

13. BATCH NUMBER

Lot

14. GENERAL CLASSIFICATION FOR SUPPLY

Medicinal product subject to medical prescription.

15. INSTRUCTIONS ON USE

16. INFORMATION IN BRAILLE

**PARTICULARS TO APPEAR ON THE OUTER PACKAGING
PACK SIZE OF 25 VIALS WITH 25 SYRINGES AND 25 TRANSFER ADAPTERS**

1. NAME OF THE MEDICINAL PRODUCT

Rotarix, powder and solvent for oral suspension
Rotavirus vaccine, live

2. STATEMENT OF ACTIVE SUBSTANCE(S)

After reconstitution, 1 dose (1 ml) contains:

Human rotavirus RIX4414 strain (live attenuated)* not less than $10^{6.0}$ CCID₅₀

*Produced on Vero cells

3. LIST OF EXCIPIENTS

Powder: sucrose, dextran, sorbitol, amino acids, Dulbecco's Modified Eagle Medium (DMEM)

Solvent: calcium carbonate, xanthan gum, sterile water

4. PHARMACEUTICAL FORM AND CONTENTS

Powder and solvent for oral suspension

vial: powder

syringe: solvent

transfer adapter

25 x 1 dose

1 dose (1 ml)

5. METHOD AND ROUTE(S) OF ADMINISTRATION

Oral administration

Do not inject!

Shake before use

Read the package leaflet before use

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

Keep out of the reach and sight of children.

7. OTHER SPECIAL WARNING(S), IF NECESSARY

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.

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13. BATCH NUMBER

Lot

14. GENERAL CLASSIFICATION FOR SUPPLY

Medicinal product subject to medical prescription.

15. INSTRUCTIONS ON USE

16. INFORMATION IN BRAILLE

**MINIMUM PARTICULARS TO APPEAR ON SMALL IMMEDIATE PACKAGING UNITS
VIAL WITH POWDER TO BE RECONSTITUTED WITH SOLVENT**

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

Rotarix
Powder for oral suspension
Rotavirus vaccine, live
Oral administration

2. METHOD OF ADMINISTRATION

3. EXPIRY DATE

EXP

4. BATCH NUMBER

Lot

5. CONTENTS BY WEIGHT, BY VOLUME OR BY UNIT

1 dose

6. OTHER

**MINIMUM PARTICULARS TO APPEAR ON SMALL IMMEDIATE PACKAGING UNITS
SYRINGE WITH SOLVENT FOR RECONSTITUTION WITH POWDER**

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

Rotarix
Solvent for oral suspension
Rotavirus vaccine, live
Oral administration

2. METHOD OF ADMINISTRATION

3. EXPIRY DATE

EXP

4. BATCH NUMBER

Lot

5. CONTENTS BY WEIGHT, BY VOLUME OR BY UNIT

1 dose (1 ml)

6. OTHER

B. PACKAGE LEAFLET

PACKAGE LEAFLET: INFORMATION FOR THE USER

Rotarix, powder and solvent for oral suspension

Rotavirus vaccine, live

Read all of this leaflet carefully before your child receives this vaccine.

- 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. Do not pass it on to others.
- If any of the side effects gets serious, or if you notice any side effects not listed in this leaflet, please tell your doctor or pharmacist.

In this leaflet:

1. What Rotarix is and what it is used for
2. Before your child receives Rotarix
3. How Rotarix is given
4. Possible side effects
5. How to store Rotarix
6. Further information

1. WHAT ROTARIX IS AND WHAT IT IS USED FOR

Pharmaco-therapeutic group: viral vaccines, ATC code: J07BH01

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

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. Rotavirus infections are responsible for hundreds of thousands of deaths worldwide every year especially in developing countries, where nutrition and health care are not optimal.

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. BEFORE YOUR CHILD RECEIVES ROTARIX

Rotarix should not be given:

- if your child has previously had any allergic reaction to rotavirus vaccines or any component contained in Rotarix. The active substances and other ingredients in Rotarix are listed at the end of the leaflet. 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 gastrointestinal system that would predispose for intussusception.
- if your child has any disease which reduces his/her resistance to infection.

- 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.

Take special care with Rotarix

Excretion of the live vaccine virus in the stools of vaccinated children is known to occur after vaccination, especially around the 7th day. Persons in contact with recent vaccinated children should wash their hands after changing the child's nappies.

Rotarix should be given with caution to children in close contacts with individuals having any disease or receiving any medicine which may reduce his/her resistance to infection.

A lower immune response (reduced ability of the body to respond to the vaccine) may be observed when Rotarix is given to premature children.

Rotarix should be given with caution to children with disorders of the stomach or intestines or children with growth retardation.

Using other vaccines

Please tell your doctor if your child is taking or has recently taken any other medicines, including medicines obtained without a prescription or has recently received any other vaccine.

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

Using 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

There is no evidence available to suggest that breast-feeding would reduce the protection against rotavirus gastro-enteritis afforded by Rotarix. Therefore, breast-feeding may be continued during the vaccination schedule.

Important information about some of the ingredients of Rotarix

If you have been told by your doctor that the child being vaccinated has an intolerance to some sugars, contact your doctor before using this vaccine.

3. HOW ROTARIX IS GIVEN

The doctor or nurse will administer the recommended dose of Rotarix to your child. The vaccine (1 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.

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, Rotarix can cause side effects, although not everybody gets them.

Side effects that occurred during clinical trials with Rotarix were as follows:

- ◆ Very common (side effects which may occur in equal or more than 1 per 10 doses of vaccine):
 - loss of appetite
 - irritability
- ◆ Common (side effects which may occur in less than 1 per 10 but equal or more than 1 per 100 doses of vaccine):
 - fever, fatigue
 - diarrhoea, vomiting, regurgitation of food, flatulence, abdominal pain
- ◆ Uncommon (side effects which may occur in less than 1 per 100 but equal or more than 1 per 1,000 doses of vaccine):
 - crying
 - sleep disorder, sleepiness
 - constipation
- ◆ Rare (side effects which may occur in less than 1 per 1,000 but equal or more than 1 per 10,000 doses of vaccine):
 - upper respiratory tract infection, hoarseness, runny nose
 - dermatitis, rash
 - muscle cramp

If any of the side effects gets serious, or if you notice any side effects not listed in this leaflet, please tell your doctor or pharmacist.

5. HOW TO STORE ROTARIX

Keep out of the reach and sight of children.

Do not use Rotarix 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.

After reconstitution, the vaccine contained in the syringe should be administered promptly. If the reconstituted vaccine is not used within 24 hours, it should be discarded.

Medicines should not be disposed of via wastewater or household waste. Ask your pharmacist how to dispose of medicines no longer required. These measures will help to protect the environment.

6. FURTHER INFORMATION

What Rotarix contains

- The active substances are:

Human rotavirus RIX4414 strain (live attenuated)*	not less than 10 ^{6.0} CCID ₅₀
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 *Produced on Vero cells
- The other ingredients in Rotarix are:
 - Powder: sucrose, dextran, sorbitol, amino acids, Dulbecco's Modified Eagle Medium (DMEM)
 - Solvent: calcium carbonate, xanthan gum, sterile water

What Rotarix looks like and contents of the pack

Powder and solvent for oral suspension

Rotarix is supplied as a whitish powder in a single dose glass vial and a separate pre-filled syringe of solvent which contains a slow settling white deposit and a colourless supernatant. There is also a transfer adapter which allows easy transfer of the solvent into the vial containing the powder for mixing the different components of the vaccine.

Both components must be mixed together before your child receives the vaccine. The mixed vaccine will appear more turbid than the solvent alone.

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

Not all pack sizes may be marketed.

Marketing Authorisation Holder and Manufacturer

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This leaflet was last approved in

Detailed information on this medicine is available on the European Medicines Agency (EMA) web site: <http://www.emea.eu.int/>.

The following information is intended for medical or healthcare professionals only:

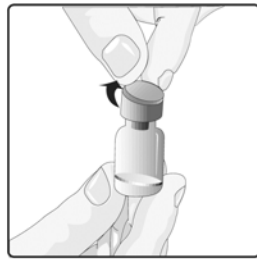
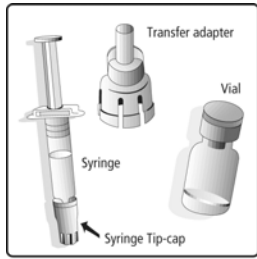
A white deposit and clear supernatant is observed upon storage of the syringe containing the solvent. The solvent should be inspected visually both before and after shaking for any foreign particulate matter and/or abnormal physical appearance prior to reconstitution.

The reconstituted vaccine is slightly more turbid than the solvent and is milky white in appearance. The reconstituted vaccine should also be inspected visually for any foreign particulate matter and/or abnormal physical appearance prior to administration. In the event of either being observed, discard the vaccine. Any unused vaccine or waste material should be disposed of in accordance with local requirements.

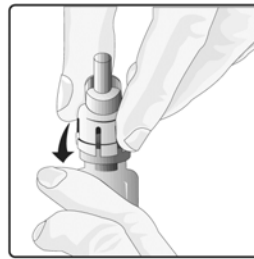
Instructions for reconstitution and administration of the vaccine:

1. Remove the plastic cover from the vial containing the powder.
2. Connect the transfer adapter onto the vial by pushing it downwards until the transfer adapter is properly and securely placed.
3. Shake the syringe containing the solvent vigorously. The shaken suspension will appear as a turbid liquid with a slow settling white deposit.
4. Remove the protective tip cap from the syringe.
5. Connect the syringe into the transfer adapter by pushing it firmly on this device.
6. Inject the entire content of the syringe into the vial containing the powder.
7. With the syringe still attached, shake the vial and examine it for complete suspension of the powder. The reconstituted vaccine will appear more turbid than the solvent alone. This appearance is normal.
8. Withdraw the entire mixture back into the syringe.
9. Remove the syringe from the transfer adapter.
10. This vaccine is for **oral administration only**. The child should be seated in a reclining position. Administer the entire content of the syringe **ORALLY** (by administering the entire content of the syringe on the inside of the cheek). **Do not inject.**

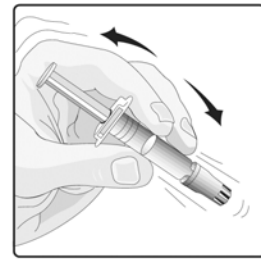
If the reconstituted vaccine is to be stored temporarily before administration, replace the protective tip cap on the syringe. The syringe containing the reconstituted vaccine should be shaken gently again before **ORAL** administration. **Do not inject.**



1. Remove the plastic cover from the vial containing the lyophilised powder.



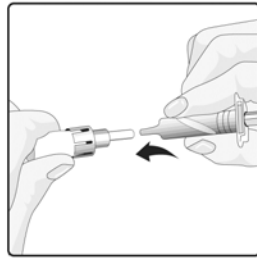
2. Connect the transfer adapter onto the vial by pushing it downwards until the transfer adapter is positioned securely on the top of the vial.



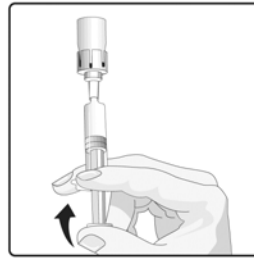
3. Shake the syringe containing the suspension vigorously. The shaken suspension will appear as a turbid liquid with a slow settling white deposit.



4. Remove the protective tip cap from the syringe.



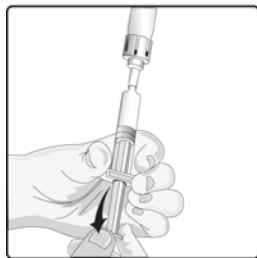
5. Connect the syringe into the transfer adapter by pushing it firmly on this device.



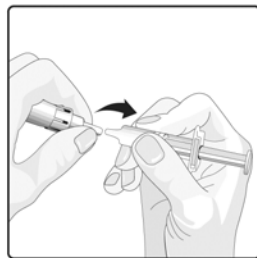
6. Inject the entire content of the syringe into the vial containing the lyophilised powder.



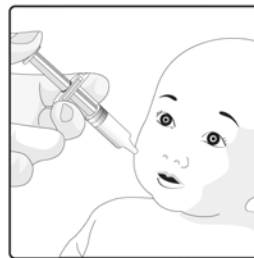
7. With the syringe still attached, shake the vial and examine it for complete suspension of the powder. The reconstituted vaccine will appear turbid. This appearance is normal.



8. Withdraw the entire mixture back into the syringe.



9. Remove the syringe from the transfer adapter.



10. Administer the entire content of the syringe orally (on the inside of the cheek). The child should be seated in a reclining position. **Do not inject.**