Rotavirus - Vaccine characteristics, content, dosage, administration, and storage

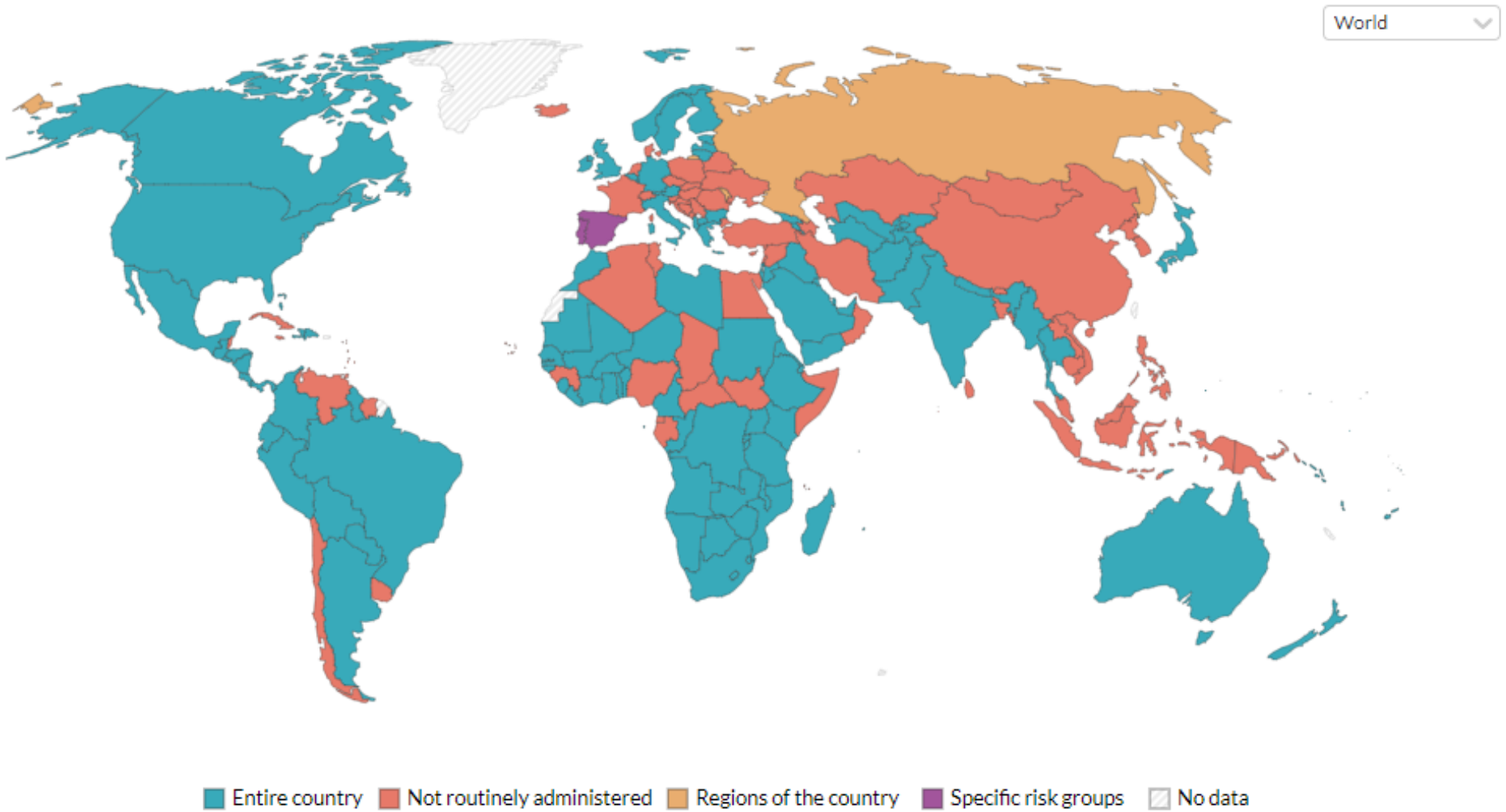
Burden of Rotavirus infection in Iran

- 54% of cases of watery diarrhea in children under 5 years old who are hospitalized are due to this virus.
- Incidence of rotavirus diarrhea in the country is equal to 93,000 per 100,000 children under 5 years old annually.
- The incidence of severe infections leading to hospitalization of children is equal to 2,800 cases per 100,000 children under 5 years old.
- The annual number of new cases of disease caused by rotavirus diarrhea in Iran is equal to 5.5 million, which rises to 172,000 cases for severe cases of the disease among children under 5 years old, leading to approximately 50 deaths.

Which countries include rotavirus vaccines in their vaccination schedules?, 2021

This shows which countries provide and recommend rotavirus vaccines through routine services. People may still be able to receive the vaccine if it's not in the routine schedule – it might be optional or available commercially.

Our World in Data



Source: WHO and UNICEF (2021)
Note: Rotavirus vaccines became available for the first time in 2006.

OurWorldInData.org/vaccination • CC BY

2006 2021

Expected impact of Rotavirus vaccine introduction in Iran

- Based on internal studies rotavirus disease, without the implementation of the vaccination program, the number of cases of rotavirus disease in Iran during two 10-year periods in children under 5 years old is equal to 64,464,813 cases, of which 62.5 million cases are non-severe diarrhea and Nearly 2 million cases of severe diarrhea will result in hospitalization.

- In the same period of time, 39.5 million cases of diarrhea, 1.7 million cases of hospitalization and 300 cases of death due to the disease can be prevented by using the vaccine.

Overview:

- Rotavirus vaccines:
  - live, oral, attenuated rotavirus strains
  - human and/or animal origin that replicate in the human intestine to elicit an immune response.
- The first 2 rotavirus vaccines prequalified by WHO were:
  - **RotaTeq** (Merck & Co. Inc., Whitehouse Station, NJ, USA) in 2008, and
  - **Rotarix** (GlaxoSmithKline Biologicals, Rixensart, Belgium) in 2009.
- In 2018, 2 additional vaccines were prequalified by WHO:
  - **Rotavac** (Bharat Biotech International Ltd, India) and
  - **ROTASIIL** (Serum Institute of India, India).

RotaTeq:

- a pentavalent - contains 5 re-assortant rotaviruses developed from human and bovine (WC3, a G6P[5] strain)
- available in one presentation:
  - a single-dose (2 mL) squeezable plastic tube with a twist-off cap.
- Storage at 2–8 °C and protected from light.
- No VVMs - have a shelf life of 2 years.
- Following removal from refrigeration, the vaccine should be used as soon as possible.
- Recommended schedule is 3 oral doses given 4 – 10 weeks apart beginning at 6–12 weeks of age; the series should be completed by the age of 32 weeks

Rotarix:

- a **monovalent** vaccine originating from a G1P[8] strain that was isolated from a case of infantile gastroenteritis.
- available as a ready-to-use liquid formulation with 2 presentations:
  - a single-dose squeezable plastic tube, and
  - a multi-monodose presentation with a strip of 5 single-dose plastic tubes.
- Storage - should be kept at 2–8 °C, protected from light, and should not be frozen.
- The vaccine has a VVM7, and a shelf life of 2 years.
- The vaccine should be used immediately after opening.
- Recommended schedule –
  - 2 oral doses given 4 weeks apart beginning at 6 weeks of age;
  - the series should be given before 16 weeks.

Rotavac:

- a **monovalent** vaccine containing rotavirus strain 116E grown in Vero cells.
- Liquid, in frozen form
- available in 2 presentations:
  - 5-dose and 10-dose glass vials with oral droppers.
- Storage:
  - at -20 °C and has a shelf life of 5 years.
  - at 2–8 °C until the discard point of the VVM2 within 6 months after thawing or for 6 months for presentations with no VVM2.
- It should be fully thawed until liquid prior to administration and
- once opened, should be kept at 2–8 °C and should be discarded 6 hours after opening or at the end of the immunization session, whichever comes first.
- Recommended schedule is 3 oral doses given 4 weeks apart beginning at 6 weeks of age; the series should be completed before the age of 8 months.

ROTASIIL:

- a **pentavalent** vaccine containing 5 single gene (VP7) substitution re-assortants between human strains G1, G2, G3, G4, G9 and the bovine United Kingdom strain (a G6P[5] strain).
- available in 3 different formulations:
  - **Liquid, lyophilized, and thermostable lyophilized,**
- **ROTASIIL-liquid:**
  - available as a ready-to-use liquid formulation with 1 presentation: a single-dose squeezable plastic tube.
  - Each dose contains 2 mL.
  - Storage at 2–8 °C, protected from light, and should not be frozen.
  - The vaccine tube has a VVM7 and a shelf life of 24 months.

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- available as a ready-to-use liquid formulation with 1 presentation: a single-dose squeezable plastic tube.
- Each dose contains 2 mL.
- Storage at 2–8 °C, protected from light, and should not be frozen.
- The vaccine tube has a VVM7 and a shelf life of 24 months.

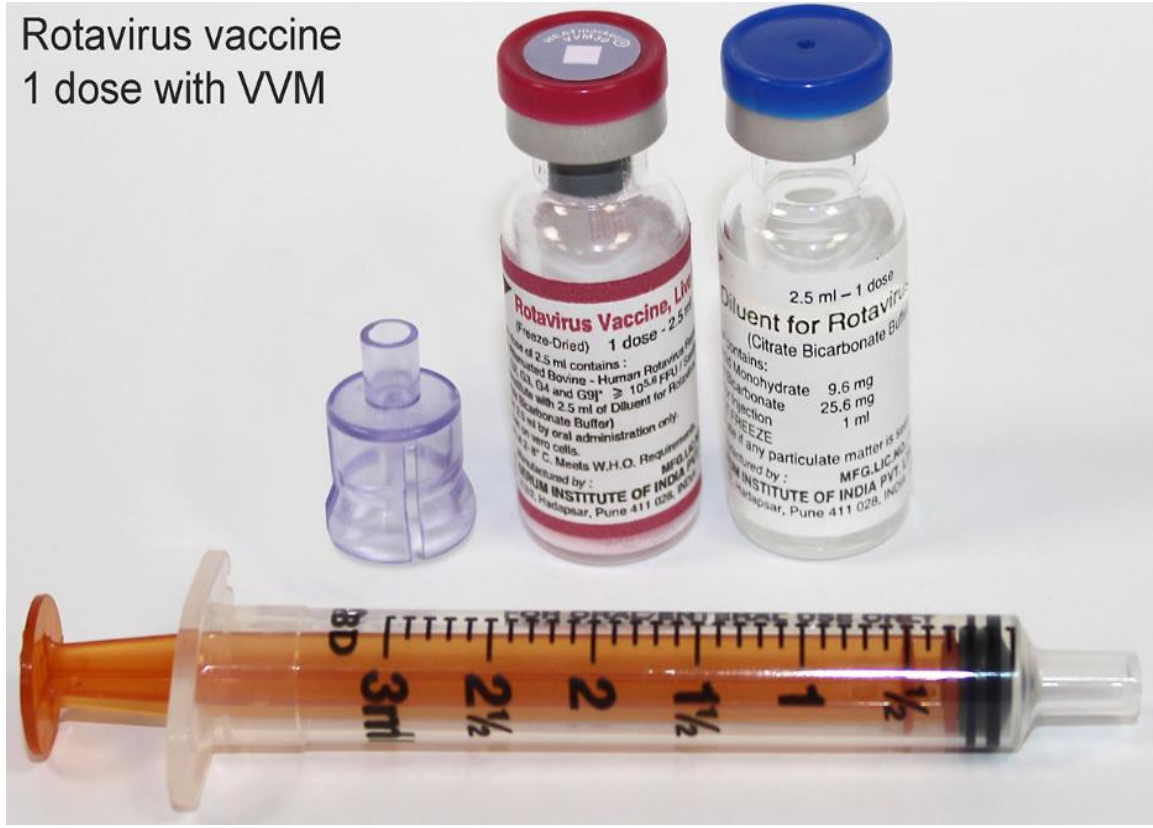
ROTASIIL-liquid, 1 Dose/Vial

Product description

Pharmaceutical Form:	Liquid: ready to use
Presentation:	Plastic Tube
Number of Doses:	1
Diluent:	Not Applicable
Route of Administration:	Oral
Shelf Life:	24 months
Storage Temperature:	2-8°C
Vaccine Vial Monitor:	Type 7
Secondary Packaging:	Carton of 50 plastic ampoules (50 doses). [Dimensions: 15.5 x 7.8 x 8.3 cm]
Tertiary Packaging:	Box containing 2000 plastic ampoules (2000 doses).[Dimensions: 52.5 x 52.5 x 72.5 cm]
Multidose Vial Policy:	Not Applicable.
Vaccine Preservative:	none
Cold Chain Volume:	20.06 cm3/dose (in secondary packaging)

The lyophilized version:

- a lyophilized powder that is reconstituted with a buffered diluent of citrated sodium bicarbonate.
- available in 2 presentations:
  - a 1-dose vial with a 2.5 mL diluent vial, or
  - a 2-dose vial with a 5 mL diluent vial.
- The vaccine vial should be stored at 2–8 °C; the diluent should not be frozen but should be kept cool in either dry storage or fridge.
- The vaccine vial has a VVM30 and a shelf life of 30 months.



Rotasiil lyophilized, 1 Dose/Vial

Product description

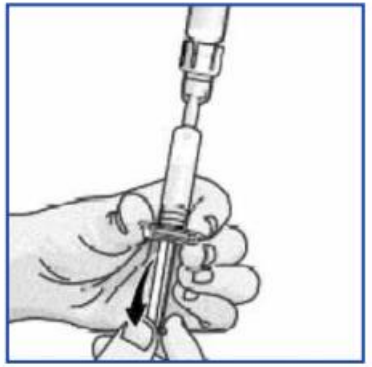
Pharmaceutical Form:	Lyophilised active component to be reconstituted with excipient diluent before use
Presentation:	Two vial set (active + excipient)
Number of Doses:	1
Diluent:	Citrate bicarbonate buffer
Route of Administration:	Oral
Shelf Life:	30 months
Storage Temperature:	2-8°C
Vaccine Vial Monitor:	Type 30
Secondary Packaging:	Active: Carton of 50 vials(50 doses) [Dimensions: 5.0 x 9.5 x 18.5 cm]; Diluent: Carton of 50 vials [Dimensions: 5.0 x 9.5 x 18.5 cm].
Tertiary Packaging:	Active: Box containing 24 cartons of 50 vials (1200 vials/ 1200 doses) [Dimensions: 36 x 48 x 60 cm]; Diluent: Box containing 1200 vials/1200 doses [Dimensions: 24.6 x 32.5 x 40.5 cm].
Multidose Vial Policy:	Not Applicable.
Vaccine Preservative:	none
Cold Chain Volume:	Active and diluent: 17.57 cm3/dose (in secondary packaging)

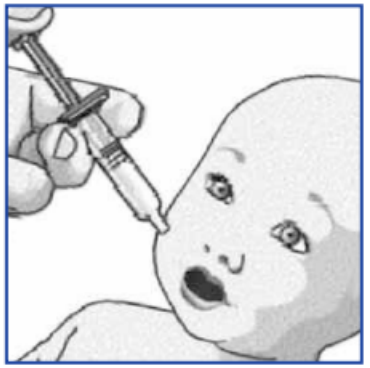
INSTRUCTIONS FOR USE

To administer the vaccine orally

1

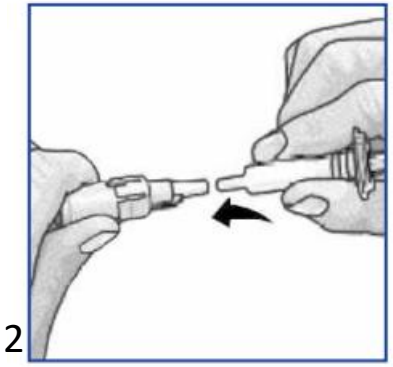
3





5. 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.

2



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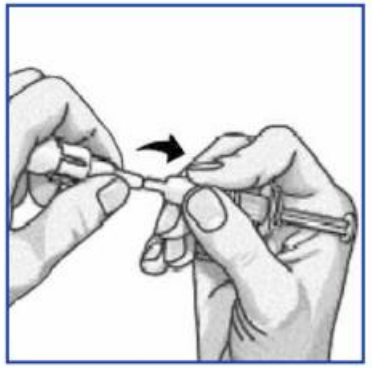

Multidose vial: Leave the vial adapter on the vaccine vial. Use a fresh syringe for second dose after withdrawal and administration of first dose.

- **A thermostable version: ROTASIIL Thermo.**
  - available in 2 presentations:
    - a 1-dose vial with a 2.5 mL diluent vial, or
    - a 2-dose vial with a 5 mL diluent vial.
  - may be stored at temperatures up to 25 ºC (WHO recommends storage below 25 ºC at all times)
  - The vaccine vial has a VVM250 and a shelf life of 30 months (2.5 yrs).
  - If not, the VVM will reach the end point for use before the vaccine reaches the end of the approved shelf life.
  - The diluent should not be frozen but should be kept cool in either dry storage or a refrigerator.
  - During transportation, short-term excursions of temperature up to 37 ºC for a period not exceeding 1 week does not impact the vaccine.
  - reconstituted vaccine should be used immediately.
  - If not used immediately, it can be held for a maximum of 6 hours, provided that a syringe is used to cap the opening of the vial adapter and the entire assembly is stored at 2–8 °C.

- **Schedule:**
  - Recommended schedule is 3 oral doses given 4 weeks apart beginning at 6 weeks of age;
  - the series should be completed during the first 8 months of life.

ROTASIIL Thermo, 2 Dose/Vial

Product description

Pharmaceutical Form:	Lyophilised active component to be reconstituted with excipient diluent before use
Presentation:	Two vial set (active + excipient)
Number of Doses:	2
Diluent:	Citrate bicarbonate buffer
Route of Administration:	Oral
Shelf Life:	30 months
Storage Temperature:	25°C
Vaccine Vial Monitor:	Type +250
Secondary Packaging:	Active: Carton of 50 vials (100 doses) [Dimensions: 6.0 x 9.5 x 18.5 cm]; Diluent: Carton of 50 vials (100 doses) [Dimensions: 6.0 x 9.5 x 18.5 cm].
Tertiary Packaging:	Active: Box containing 24 cartons of 1200 vials (2400 doses) [Dimensions: 41 x 48 x 60 cm]: Diluent: Box containing 1200 vials (2400 doses) [Dimensions: 28.6 x 32.5 x 40.5 cm].
Multidose Vial Policy:	WHO recommends that opened vials of this vaccine should be discarded 6 hours after opening or at the end of the immunization session, whichever comes first.
Vaccine Preservative:	none
Cold Chain Volume:	Active and diluent: 10.54 cm3/dose (in secondary packaging)

Efficacy, effectiveness, impact, and duration of protection

- **Vaccine efficacy:**
- A recent Cochrane review of the 4 WHO prequalified rotavirus vaccines showed that vaccine efficacy against severe RVGE was higher for **low-mortality strata** countries than for high-mortality strata countries.
- Based on –
  - 11 RCTs of RotaTeq,
  - 15 RCTs of Rotarix,
  - 1 RCT of Rotavac, and
  - 2 RCTs of ROTASIIL,
  - this review showed protection against severe RVGE after 1 and/or 2 years of follow-up with modest waning over the period of observation, ranging from:
  - 90%–95% in low-mortality strata countries
  - 44%–70% efficacy in high-mortality strata countries.
- A sub-analysis of **high-mortality countries** in Africa and Asia showed that the 4 vaccines had comparable vaccine efficacy against severe RVGE at 1 year of follow-up, ranging from 48% to 57%.

Vaccine effectiveness

- Rotarix and RotaTeq - vaccine effectiveness against lab-confirmed severe RVGE among children aged 12–23 months was:
  - 84%–86% in low-mortality countries,
  - 54% in medium-mortality countries (Rotarix only), and
  - 58% in high-mortality countries (Rotarix only).
- case-control studies of RVGE-related health-care encounters - Rotarix and RotaTeq reduced RVGE-related health-care encounters by:
  - 79%–83% in low-mortality countries,
  - 58% in medium-mortality countries (Rotarix only), and
  - 48%–69% in high-mortality countries.
- There were no observational studies assessing the effectiveness of **ROTASIIL or Rotavac** on laboratory-confirmed rotavirus or RVGE-related health-care encounters.
- Data from case-control studies show that **Rotarix and RotaTeq** are more effective when the full course is given, but some protection may also be achieved following an incomplete vaccination series.
- Additionally, a meta-analysis of data from middle- and high-income countries showed that Rotarix and RotaTeq have similar effectiveness against homotypic and heterotypic rotavirus strains.

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Vaccine impact:

- The global impact of rotavirus vaccine is evident from the 40% reduction in rotavirus prevalence following the introduction of vaccine documented by an analysis of data from 69 countries participating in the Global Rotavirus Surveillance Network (GRSN), as well as from studies showing reductions in rotavirus hospitalizations, all cause acute gastroenteritis hospitalizations, and gastroenteritis mortality in a variety of countries.

- A recent systematic review of observational studies on rotavirus vaccine impact from 47 countries across different child mortality strata reported median relative reductions of 59% (interquartile range [IQR], 46–74) in rotavirus hospitalizations, 36% (IQR, 23–47) in acute gastroenteritis hospitalizations, and 36% (IQR, 28–46) in acute gastroenteritis mortality among children aged <5 years after rotavirus vaccine introductions

Duration of protection

- A recent meta-regression analysis of RCTs of rotavirus vaccines given in an infant schedule examined pooled estimates of efficacy against severe RVGE at both 2 weeks and 12 months following the last vaccine dose.
- In **low- and medium-mortality settings**, the pooled efficacy estimates were high at the 2-week time point (82%–98%) and provided durable protection at 12 months (77%–94%).
- In high-mortality settings, the pooled efficacy was lower at 2 weeks (66%) and waned more rapidly to 44% by 12 months.
- Efficacy trials in high-income settings with Rotarix and RotaTeq that extended follow-up demonstrated high protection against severe disease during the third year of life.
- As described above, in high-mortality settings, the level of protection from rotavirus vaccines likely wanes.

Vaccine interchangeability

- A study in the United States of America found that 3-dose series that included both Rotarix and RotaTeq products were well tolerated and induced immune responses comparable to those induced by a series containing a single product alone.
- Vaccine effectiveness studies in the United States have also demonstrated high vaccine effectiveness from series that contained both Rotarix and RotaTeq products, similar to that obtained with single product series.
- No other data are available on series that contain both Rotarix and RotaTeq or the newer WHO-prequalified rotavirus vaccines.

Pneumosil, 5 Dose/Vial

Product description

Pharmaceutical Form:	Liquid: ready to use
Presentation:	Vial
Number of Doses:	5
Diluent:	Not Applicable
Route of Administration:	Intramuscular
Shelf Life:	36 months
Storage Temperature:	2-8°C
Vaccine Vial Monitor:	Type 30
Secondary Packaging:	Carton of 50 vials (250 doses)(35 and 40 mm vial height) [Dimensions: 5.0 x 9.5 x 18.5 cm]
Tertiary Packaging:	Box containing 4 cartons of 300 vials (1200 vials/ 60 000 doses)[Dimensions: 36 x 48 x 60 cm]
Multidose Vial Policy:	WHO recommends that opened vials of this vaccine may be kept for use in subsequent immunization sessions (up to a maximum of 28 days) provided the conditions outlined in the WHO Policy Statement: The use of opened multi-dose vials of vaccine in subsequent immunization sessions are met.
Vaccine Preservative:	thiomersal
Vaccine Preservative Concentration:	0.005%
Cold Chain Volume:	3.515 cm3/dose (in secondary packaging)