Priorix™

1. NAME OF THE MEDICINAL PRODUCT

Priorix™

Measles, mumps and rubella vaccine (live, attenuated).

2. QUALITATIVE AND QUANTITATIVE COMPOSITION

Priorix™ is a lyophilised mixed preparation of the attenuated Schwarz measles, RIT 4385 mumps (derived from Jeryl Lynn strain) and Wistar RA 27/3 rubella strains of viruses, separately obtained by propagation either in chick embryo tissue cultures (mumps and measles) or MRC-5 human diploid cells (rubella).

Priorix™ meets the World Health Organisation requirements for manufacture of biological substances and for measles, mumps and rubella vaccines and combined vaccines (live).

Each 0.5 ml dose of the reconstituted vaccine contains not less than $10^{3.0}$ $CCID_{50}$ of the Schwarz measles, not less than $10^{3.7}$ $CCID_{50}$ of the RIT 4385 mumps, and not less than $10^{3.0}$ $CCID_{50}$ of the Wistar RA 27/3 rubella virus strains.

The powder is white to slightly pink.
The solvent is clear and colourless.

3. PHARMACEUTICAL FORM

Powder and solvent for solution for injection.

4. CLINICAL PARTICULARS

4.1 Therapeutic Indications

Priorix™ is indicated for active immunisation against measles, mumps and rubella.

4.2 Posology and Method of Administration

Posology

Priorix™ is indicated for administration of a first dose from the age of 9 months with a second dose at school age (4-6 years).

Method of administration

Priorix™ is for subcutaneous injection, although it can also be given by intramuscular injection, in the deltoid region or in the anterolateral area of the thigh (see 4.4 Special Warnings and Precautions for Use).

The vaccine should be administered subcutaneously in subjects with bleeding disorders (e.g. thrombocytopenia or any coagulation disorder).For instructions on reconstitution of the medicinal product before administration, see 6.6 Instructions for Use/Handling.

4.3 Contra-indications

Priorix™ is contra-indicated in subjects with known systemic hypersensitivity to neomycin or to any other component of the vaccine (for egg allergy, see 4.4 Special Warnings and Precautions for Use). A history of contact dermatitis to neomycin is not a contra-indication.

Priorix™ is contraindicated in subjects having shown signs of hypersensitivity after previous administration of measles, mumps and/or rubella vaccines.

Priorix™ is contraindicated in subjects with severe humoral or cellular (primary or acquired) immunodeficiency e.g. symptomatic HIV infection (see also 4.4 Special Warnings and Precautions for Use).

Priorix™ is contraindicated in pregnant women. Pregnancy should be avoided for one months after vaccination (see 4.6 Pregnancy and Lactation).

4.4 Special Warnings and Precautions for Use

As with other vaccines, the administration of **Priorix™** should be postponed in subjects suffering from acute severe febrile illness. The presence of a minor infection, however, is not a contra-indication for vaccination.

Syncope (fainting) can occur following, or even before, any vaccination as a psychogenic response to the needle injection. It is important that procedures are in place to avoid injury from faints.

Alcohol and other disinfecting agents must be allowed to evaporate from the skin before injection of the vaccine since they can inactivate the attenuated viruses in the vaccine.

Limited protection against measles may be obtained by vaccination up to 72 hours after exposure to natural measles.

Infants below 12 months of age may not respond sufficiently to the measles component of the vaccine, due to the possible persistence of maternal measles antibodies. This should not preclude the use of the vaccine in younger infants (<12 months) since vaccination may be indicated in some situations such as high-risk areas. In these circumstances revaccination at or after 12 months of age should be considered.

As with all injectable vaccines, appropriate medical treatment and supervision should always be readily available in case of a rare anaphylactic event following the administration of the vaccine.

The measles and mumps components of the vaccine are produced in chick embryo cell culture and may therefore contain traces of egg protein. Persons with a history of anaphylactic, anaphylactoid, or other immediate reactions (e.g. generalised urticaria, swelling of the mouth and throat, difficulty breathing, hypotension, or shock) subsequent to egg ingestion may be at an enhanced risk of immediate-type hypersensitivity reactions after vaccination, although these types of reactions have been shown to be very rare. Individuals who have experienced anaphylaxis after egg ingestion should be vaccinated with extreme caution, with adequate treatment for anaphylaxis on hand should such a reaction occur.

Priorix™ should be given with caution to persons with a history or family history of allergic diseases or those with a history or family history of convulsions.

Transmission of measles and mumps virus from vaccinees to susceptible contacts has never been documented. Pharyngeal excretion of the rubella virus is known to occur about 7 to 28 days after vaccination with peak excretion around the 11th day. However there is no evidence of transmission of this excreted vaccine virus to susceptible contacts.

A limited number of subjects received **Priorix™** intramuscularly. An adequate immune response was obtained for all three components (see 4.2 Posology and Method of Administration).

Priorix™ MUST NOT BE ADMINISTERED INTRAVASCULARLY.

As with any vaccine, a protective immune response may not be elicited in all vaccinees.

Cases of worsening of thrombocytopenia and recurrence of thrombocytopenia in subjects who suffered thrombocytopenia after the first dose have been reported following vaccination with live measles, mumps and rubella vaccines. In such cases, the risk-benefit of immunising with **Priorix™** should be carefully evaluated.

There is limited data on the use of **Priorix™** in immunocompromised subjects, therefore vaccination should be considered with caution and only when, in the opinion of the physician, the benefits outweigh the risks (e.g. asymptomatic HIV subjects).

Immunocompromised subjects who have no contraindication for this vaccination (see 4.3 Contraindications) may not respond as well as immunocompetent subjects, therefore some of these subjects may acquire measles, mumps or rubella despite appropriate vaccine administration. Immunocompromised subjects should be monitored carefully for signs of measles, mumps and rubella.

4.5 Interaction with Other Medicinal Products and Other Forms of Interaction

If tuberculin testing has to be done, it should be carried out before or simultaneously with vaccination since it has been reported that live measles (and possibly mumps) vaccine may cause a temporary depression of tuberculin skin sensitivity. This anergy may last for 4-6 weeks and tuberculin testing should not be performed within that period after vaccination to avoid false negative results.

Clinical studies have demonstrated that **Priorix™** can be given simultaneously with any of the following monovalent or combination vaccines: hexavalent vaccine (DTPa-HBV-IPV/Hib), diphtheria-tetanus-acellular pertussis vaccine (DTPa), reduced antigen diphtheria-tetanus-acellular pertussis vaccine (dTpa), *Haemophilus influenzae* type b vaccine (Hib), inactivated polio vaccine (IPV), hepatitis B vaccine (HBV), hepatitis A vaccine (HAV), meningococcal serogroup B vaccine (MenB), meningococcal serogroup C conjugate vaccine (MenC), meningococcal serogroups A, C, W-135 and Y conjugate vaccine (MenACWY), varicella vaccine and pneumococcal conjugate vaccine (PCV).

In addition, it is generally accepted that measles mumps and rubella combined vaccine may be given at the same time as the oral polio vaccine (OPV) or the diphtheria-tetanus-whole cell pertussis vaccine (DTPw).

If **Priorix™** is to be given at the same time as another injectable vaccine, the vaccines should always be administered at different injection sites.

If **Priorix™** cannot be given at the same time as other live attenuated vaccines, an interval of at least one month should be left between both vaccinations.

In subjects who have received human gammaglobulins or a blood transfusion, vaccination should be delayed for at least three months because of the likelihood of vaccine failure due to passively acquired mumps, measles and rubella antibodies.

Priorix™ may be given as a booster dose in subjects who have previously been vaccinated with another measles mumps and rubella combined vaccine.

4.6 Pregnancy and Lactation

Use in Pregnancy

Pregnant women must not be vaccinated with **Priorix**™.

However, fetal damage has not been documented when measles, mumps or rubella vaccines have been given to pregnant women.

Even if a theoretical risk cannot be excluded, no cases of congenital rubella syndrome have been reported in more than 3,500 susceptible women who were unknowingly in early stages of pregnancy when vaccinated with rubella containing vaccines. Therefore, inadvertent vaccination of unknowingly pregnant women with measles, mumps and rubella containing vaccines should not be a reason for termination of pregnancy.

Pregnancy should be avoided for one month after vaccination. Women who intend to become pregnant should be advised to delay pregnancy.

Use in Lactation

There is no human data regarding use in breast-feeding women. Persons can be vaccinated where the benefit outweighs the risk.

4.7 Effects on Ability to Drive and Use Machine

Not applicable.

4.8 Undesirable Effects

In controlled clinical studies, signs and symptoms were actively monitored during a 42-day follow-up period. The vaccinees were also requested to report any clinical events during the study period.

The safety profile presented below is based on a total of approximately 12,000 subjects administered **Priorix™** in clinical trials.

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)

System Organ Class	**Frequency**	**Adverse events**
Infections and infestations	Uncommon	otitis media
	Common	upper respiratory tract infection
Blood and lymphatic system disorders	Uncommon	lymphadenopathy
Immune system disorders	Rare	allergic reactions
Metabolism and nutrition disorders	Uncommon	anorexia
Psychiatric disorders	Uncommon	nervousness, abnormal crying, insomnia
Nervous system disorders	Rare	febrile convulsions
Eye disorders	Uncommon	conjunctivitis
Respiratory, thoracic and mediastinal disorders	Uncommon	bronchitis, cough
Gastrointestinal disorders	Uncommon	parotid gland enlargement, diarrhoea, vomiting
Skin and subcutaneous tissue disorders	Common	rash
General disorders and administration site conditions	Very common	redness at the injection site, fever ≥38°C (rectal) or ≥37.5°C (axillary/oral)
	Common	pain and swelling at the injection site, fever >39.5°C (rectal) or >39°C (axillary/oral)

In general, the frequency category for adverse reactions was similar for the first and second vaccine doses. The exception to this was pain at the injection site which was “Common” after the first vaccine dose and “Very common” after the second vaccine dose.

During post-marketing surveillance, the following reactions have been reported additionally in temporal association with **Priorix™** vaccination:

System Organ Class	Frequency	Adverse events
Infections and infestations	Rare	meningitis, measles-like syndrome, mumps-like syndrome (including orchitis, epididymitis and parotitis)
Blood and lymphatic system disorders	Rare	thrombocytopenia, thrombocytopenic purpura
Immune system disorders	Rare	anaphylactic reactions
Nervous system disorders	Rare	encephalitis, cerebellitis, cerebellitis like symptoms (including transient gait disturbance and transient ataxia), Guillain Barré syndrome, transverse myelitis, peripheral neuritis
Vascular disorders	Rare	vasculitis (including Henoch Schonlein purpura and Kawasaki syndrome)
Skin and subcutaneous tissue disorders	Rare	erythema multiforme
Musculoskeletal and connective tissue disorders	Rare	arthralgia, arthritis

Accidental intravascular administration may give rise to severe reactions or even shock. Immediate measures depend on the severity of the reaction (see 4.4 Special Warnings and Precautions for Use).

In the comparative studies, a statistically significant lower incidence of local pain, redness and swelling was reported with **Priorix™** compared with the comparator. The incidence of other adverse reactions listed above were similar in both vaccines.

4.9 Overdose

Cases of overdose (up to 2 times the recommended dose) have been reported during post-marketing surveillance. No adverse events have been associated to the overdose.

5. PHARMACOLOGICAL PROPERTIES

5.1 Pharmacodynamic Properties

In clinical studies **Priorix™** has been demonstrated to be highly immunogenic.

Antibodies against measles were detected in 98.0%, against mumps in 96.1% and against rubella in 99.3% of previously seronegative vaccinees.

In comparative studies, antibodies against measles, mumps and rubella were detected in 98.7%, 95.5% and 99.5% of previously seronegative vaccinees who received **Priorix™** compared to 96.9%, 96.9% and 99.5% in the group receiving a commercially available measles mumps and rubella combined vaccine.

Subjects followed up to 12 months following vaccination all remained seropositive for anti-measles and anti-rubella antibodies. 88.4% were still seropositive at month 12 for anti-mumps antibody. This percentage is in line with what was observed for the commercially available measles, mumps and rubella combined vaccine (87%).

5.2 Pharmacokinetic Properties

Evaluation of pharmacokinetic properties is not required for vaccines.

Clinical Studies

See 5.1 Pharmacodynamic Properties

5.3 Preclinical Safety Data

Not applicable.

6. PHARMACEUTICAL PARTICULARS

6.1 List of Excipients

Excipients of the vaccine are: amino acids, lactose, mannitol, sorbitol.

Solvent: Water for injection.

Neomycin sulphate is present as a residual from the manufacturing process.

6.2 Incompatibilities

Priorix™ should not be mixed with other vaccines in the same syringe.

6.3 Shelf Life

The expiry date of the vaccine is indicated on the label and packaging.

6.4 Special Precautions for Storage

Priorix™ should be stored in a refrigerator between 2 ºC and 8 ºC.

The solvent can be stored in the refrigerator or at ambient temperature.

Do not freeze the lyophilised vaccine nor the solvent.

During transport, recommended conditions of storage should be respected, particularly in hot climates.

6.5 Nature and Contents of Container

Priorix™ is presented in a glass vial (type I glass). The sterile solvent is presented in a glass prefilled syringe (type I glass) or in a glass ampoule (type I glass).

6.6 Instructions for Use/Handling

Due to minor variation of its pH, the reconstituted vaccine may vary in colour from clear peach to fuchsia pink without deterioration of the vaccine potency.
The solvent and reconstituted vaccine should be inspected visually for any foreign particulate matter and/or variation of physical aspects prior to administration. In the event of either being observed, discard the solvent or reconstituted vaccine.

Monodose presentation:
Inject the entire content of the vial, using a new needle for administration.

Instructions for reconstitution of the vaccine with solvent presented in ampoules

Priorix™ must be reconstituted by adding the entire contents of the supplied ampoule of solvent to the vial containing the powder. After the addition of the solvent to the powder, the mixture should be well shaken until the powder is completely dissolved in the solvent.

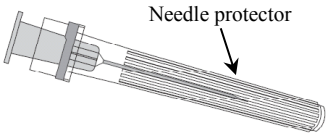
After reconstitution, the vaccine should be used promptly.
A new needle should be used to administer the vaccine.
Withdraw the entire contents of the vial.

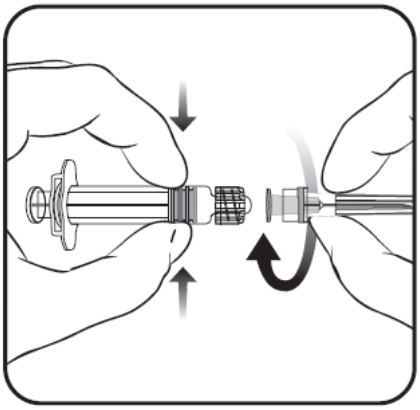
Instructions for reconstitution of the vaccine with the solvent presented in pre-filled syringe

Priorix™ must be reconstituted by adding the entire content of the pre-filled syringe of solvent to the vial containing the powder.

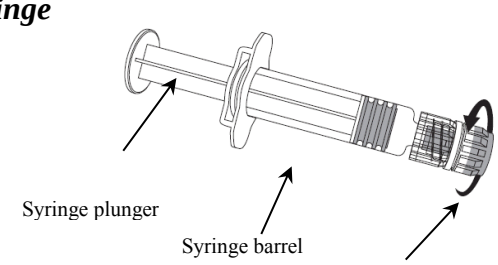
To attach the needle to the syringe, refer to the below drawing. However, the syringe provided with **Priorix™** might be slightly different than the syringe described in the drawing**.**

Needle





Syringe



1. Holding the syringe <u>barrel</u> in one hand (avoid holding the syringe plunger), unscrew the syringe cap by twisting it anticlockwise.
2. To attach the needle to the syringe, twist the needle clockwise into the syringe until you feel it lock. (see picture)
3. Remove the needle protector, which on occasion can be a little stiff.

Add the solvent to the powder. After the addition of the solvent to the powder, the mixture should be well shaken until the powder is completely dissolved in the solvent.

After reconstitution, the vaccine should be used promptly.

A new needle should be used to administer the vaccine.

Withdraw the entire contents of the vial.

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

After reconstitution, the vaccine should be injected immediately. If not used immediately, the reconstituted vaccine must be stored in a refrigerator between 2°C and 8°C and used within:

- 8 hours of reconstitution for the monodose presentation

Not all presentations are available in every country.

7. Marketing Authorisation Holder

GlaxoSmithKline(Thailand) Ltd.

8. Marketing Authorisation Number

2C 13/42 (N)

9. Date of Authorisation

6 August 2001 (unconditional license)

Priorix is trademark of the GSK group of companies.

Version number: GDS14&15/IPI10 / Date of issue: 09/02/2017 © [2017] GSK Group of Companies
Manufacturer: GlaxoSmithKline Biologicals s.a. 89, rue de l'Institut - 1330 Rixensart Belgium Tel: (32) 2 656 81 11 Fax: (32) 2 656 80 00