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PRIORIX™
GlaxoSmithKline

1- Name of the Medicinal Product
Priorix™.

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 MRC5 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 103.0 TCID50 of the Schwarz measles, not less than 103.7 of the RIT 4385 mumps, and not less than 103.0 TCID50 of the Wistar RA 27/3 rubella virus strains.

3 - Pharmaceutical Form
Lyophilised vaccine for reconstitution with the sterile diluent provided.

4 - Clinical Particulars
4.1 Therapeutic indications

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

4.2 Posology and method of administration
Posology

A single 0.5 ml dose of the reconstituted vaccine is recommended.

As vaccination schemes vary from country to country, the advised schedule for each country must be in accordance with the national recommendations.

Method of administration
Priorix™ is for subcutaneous injection, although it can also be given by intramuscular injection. (see section 4.4).

4.3 Contra-indications
Priorix™ is contra-indicated in subjects with known systemic hypersensitivity to neomycin or to any other component of the vaccine. A history of contact dermatitis to neomycin is not a contra-indication. For egg allergy, see section 4.4.

Priorix™ should not be given to subjects with impaired immune responses. These include patients with primary or secondary immunodeficiencies.

However, measles, mumps, rubella combined vaccines can be given to asymptomatic HIV- infected persons without adverse consequences to their illness and may be considered for those who are symptomatic.

It is contra-indicated to administer Priorix™ to pregnant women. Furthermore, pregnancy should be avoided for three months after vaccination (see section 4.6.)

4.4 Special warnings and special 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.

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 section 4.2.)

Priorix™ should under no circumstances be administered intravenously.

4.5 Interaction with other medicaments 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.

Studies have shown that Priorix™ can be administered at the same time as the live attenuated varicella vaccine (Varilrix™) if separate injection sites are used.

Although data on the concomitant administration of Priorix™ and other vaccines are not yet available, 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 inactivated polio vaccine (IPV), the injectable trivalent diphtheria, tetanus and pertussis vaccines (DTPw/DTPa) and Haemophilus influenzae type b (Hib) if separate injection sites are used.

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

Pregnancy

It is contra-indicated to administer Priorix™ to pregnant women. Furthermore, pregnancy should be avoided for three months after vaccination.

Lactation

There are no human data regarding use in breastfeeding women. Persons can be vaccinated where the benefit outweighs the risk.

4.7 Effects on ability to drive and use machines

Not applicable.

4.8 Undesirable effects

Frequencies are reported as:

Very common:	≥10%
Common:	≥1% and <10%
Uncommon:	≥0.1% and <1%
Rare:	≥0.01% and <0.1%

Very rare: <0.01%

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.

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 ≥38oC (rectal) or ≥37.5oC (axillary/oral)

Common: pain and swelling at the injection site, fever >39.5oC (rectal) or >39oC (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:

Infections and infestations:

Meningitis

Blood and lymphatic system disorders:

Thrombocytopenia, thrombocytopenic purpura

Immune system disorders

Anaphylactic reactions

Nervous system disorders:

Transverse myelitis, Guillain Barré syndrome, peripheral neuritis, encephalitis*

Skin and subcutaneous tissue disorders:

Erythema multiforme

Musculoskeletal and connective tissue disorders:

Arthralgia, arthritis

General disorders and administration site conditions:

Kawasaki syndrome

* Encephalitis has been reported with a frequency below 1 per 10 million doses. The risk of encephalitis following administration of the vaccine is far below the risk of encephalitis caused by natural diseases (measles: 1 in 1000 to 2000 cases; rubella: approximately 1 in 6000 cases).

In rare cases a mumps-like condition with an abbreviated incubation period cannot be ruled out. In isolated cases transient, painful swelling of the testicles has been reported after combined mumps, measles, rubella vaccination.

In rare cases a measles-like syndrome has been reported following vaccination with Priorix™.

Accidental intravascular administration may give rise to severe reactions or even shock. Immediate measures depend on the severity of the reaction.(see section 4.4).

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.

5.3 Preclinical safety data
Not applicable.

6 - Pharmaceutical Particulars

6.1 List of excipients
Vaccine: Amino acids, lactose, mannitol, neomycin sulphate, sorbitol.

Diluent: Water for injections.

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 +2oC and +8oC. The diluent can be stored in the refrigerator or at ambient temperature. Do not freeze the lyophilised vaccine nor the diluent. During transport, recommended conditions of storage should be respected, particularly in hot climates.

6.5 Nature and contents of container
Priorix™ is presented as a whitish to slightly pink pellet in a glass vial. The sterile diluent is clear and colourless and presented in a glass prefilled syringe or ampoule. 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.

Monodose and multidose vials/prefilled syringes are made of neutral glass type I, which conforms to European Pharmacopoeia Requirements.

6.6 Instructions for use, handling and disposal (if appropriate)
The diluent 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 diluent or reconstituted vaccine.

The vaccine must be reconstituted by adding the entire contents of the supplied container of diluent to the vial containing the pellet. After the addition of the diluent to the pellet, the mixture should be well shaken until the pellet is completely dissolved in the diluent.

After reconstitution, the vaccine should be injected as soon as possible and not later than 8 hours after reconstitution.

<u>Monodose presentation:</u>

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

<u>Multidose presentation:</u>

When using a multidose vial, each dose should be withdrawn using a sterile needle and syringe under strict aseptic conditions; precautions should be

taken to avoid contamination of the contents. A new needle should be used to administer each individual dose of the vaccine.

For further information, please contact the manufacturer.

Priorix and Varilrix are trademarks.