

SUMMARY OF PRODUCT CHARACTERISTICS

1. NAME OF THE MEDICINAL PRODUCT

Priorix®

Powder and solvent for solution for injection

Measles, Mumps and Rubella vaccine (live)

2. QUALITATIVE AND QUANTITATIVE COMPOSITION

Each 0.5 ml dose of the reconstituted vaccine contains:

- not less than $10^{3.0}$ CCID₅₀* of the Schwarz measles¹
- not less than $10^{3.7}$ CCID₅₀ of the RIT 4385 mumps¹, and
- - not less than $10^{3.0}$ CCID₅₀ of the Wistar RA 27/3 rubella² virus strains.

*CCID₅₀ – Cell Culture Infective Dose 50

¹produced in chick embryo cells

²produced in human diploid (MRC-5) cells

For a full list of excipients, see section 6.1

3. PHARMACEUTICAL FORM

Lyophilised vaccine for reconstitution with the sterile diluent provided.

Before reconstitution, the lyophilised vaccine is a white to slightly pink powder and the diluent is a clear colourless liquid.

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

0.5 ml of the reconstituted vaccine constitutes one dose.

Priorix may be used for both primary immunisation and revaccination of children over 9 months of age, adolescents and adults. For infants in their first year of life see section 4.4. The vaccine should be given according to the recommended schedule.

Priorix may be given to subjects who have previously been vaccinated with other measles, mumps and rubella vaccines.

Children who suffered idiopathic thrombocytopenic purpura (ITP) within 6 weeks of the first dose of MMR (or its component vaccines) should have their serological status evaluated at the time the second dose is due. If serology testing suggests that a child is not fully immune against measles, mumps and rubella then a second dose of MMR is recommended.

Method of administration

Priorix is for subcutaneous injection.

It may also be given by intramuscular injection. A limited number of subjects received Priorix intramuscularly in clinical trials in which an adequate immune response was obtained for all three components.

PRIORIX SHOULD UNDER NO CIRCUMSTANCES BE ADMINISTERED INTRAVASCULARLY.

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.

For instructions on reconstitution of the product before administration refer to section 6.6.

4.3 Contraindications

Priorix is contraindicated in subjects with known systemic hypersensitivity to any component of the vaccine or to neomycin (see also Section 4.4.) A history of contact dermatitis to neomycin is not a contraindication.

Priorix must not be administered to pregnant women. Furthermore, pregnancy must be avoided for one month after vaccination (see Section 4.6).

Priorix should not be given to subjects with impaired immune function. 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.

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 contraindication for vaccination.

4.4 Special warnings and special precautions for use

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.

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

Infants in their first year of life 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 infants from the age of 9 months if this is considered necessary (e.g. due to travel to a region with high prevalence of measles or in outbreak situations). In these circumstances further doses of combined measles, mumps and rubella vaccine should be administered in accordance with official recommendations.

Children who suffered idiopathic thrombocytopenic purpura (ITP) within 6 weeks of the first dose of MMR (or its component vaccines) should have their serological status evaluated at the time the second dose is due. If serology testing suggests that a child is not fully immune against measles, mumps and rubella then a second dose of MMR is recommended.

Transmission of measles 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. Studies have shown that recipients of the Jeryl Lynn strain of mumps virus vaccine do not spread this virus to susceptible contacts and that the virus cannot be isolated from blood, urine or saliva.

As with any vaccine, vaccination with Priorix may not result in complete protection of all vaccinees against the infections it is intended to prevent.

4.5. Interaction with other medicinal products and other forms of interaction

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).

Concomitant vaccines should be given by separate injections into different body sites.

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

If Priorix cannot be given at the same time as other live attenuated vaccines, an interval of 4 weeks should be left between 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. However, if Priorix is being given primarily to achieve protection against rubella, the vaccine may be given within three months of the administration of an immunoglobulin preparation or a blood transfusion. In such instances, serological testing should be performed approximately 8-12 weeks later in order to assess the need for re-immunisation.

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 four to six weeks and tuberculin testing should not be performed within that period after vaccination to avoid false negative results.

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

Priorix is contraindicated in pregnant women. Furthermore, pregnancy should be avoided for one month after vaccination.

Lactation

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

4.7. Effects on ability to drive and use machines

The vaccine is unlikely to produce an effect on the ability to drive and use machines.

4.8. Undesirable effects

Frequencies are reported as:

Very common: $\geq 10\%$

Common: $\geq 1\%$ and $< 10\%$

Uncommon: $\geq 0.1\%$ and $< 1\%$
Rare: $\geq 0.01\%$ and $< 0.1\%$
Very rare: $< 0.01\%$

In controlled clinical studies in children aged from 9 months to 2 years, signs and symptoms were actively monitored during a 42-day follow-up period. Parents/guardians of the vaccinees were also requested to report any adverse 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 $\geq 38^{\circ}\text{C}$ (rectal) or $\geq 37.5^{\circ}\text{C}$ (axillary/oral)

Common: pain and swelling at the injection site, fever $> 39.5^{\circ}\text{C}$ (rectal) or $> 39^{\circ}\text{C}$ (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 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

As in natural rubella infection, arthralgia, or in isolated cases, chronic arthritis as well as myalgia, exanthema and swollen lymph nodes may occur two to four weeks after administration of live rubella vaccines. The incidence of joint reactions increases with the age of the vaccinee. Cases of exudative arthritis are extremely rare.

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

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

In comparative studies with other measles, mumps and rubella vaccines, the incidences of local pain, redness and swelling reported with Priorix were low, while the incidences of other adverse reactions were similar.

* 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 measles-like syndrome has been reported following vaccination with Priorix.

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

Pharmacotherapeutic group: Viral vaccine.
ATC code: J07B D52.

The safety and immunogenicity of Priorix in adolescents and adults has not been specifically studied in clinical trials.

In clinical studies in children aged from 12 months to 2 years Priorix has been demonstrated to be highly immunogenic. Following primary vaccination with a single dose of Priorix in the second year of life antibodies against measles were detected in 98.0%, against mumps in 96.1% and against rubella in 99.3% of previously seronegative vaccinees.

One hundred and fifty five children aged 10 – 22 months at immunisation were followed up for 12 months post 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 other measles, mumps and rubella-combined vaccines (87%).

5.2. Pharmacokinetic properties

Not applicable.

5.3. Preclinical safety data

Not applicable.

6. PHARMACEUTICAL PARTICULARS

6.1 List of excipients

Vaccine:

Lactose

Mannitol

Sorbitol

The vaccine also contains the following amino acids:

L-alanine,

L-arginine,

glycine,

L-histidine

L-isoleucine

L-leucine

L-lysine HCl

L-methionine

L-phenylalanine

L-proline

L-serine

L-threonine,

L-tryptophan

L-tyrosine

L-valine

L-aspartic acid

L-cysteine

L-cystine,

L-hydroxyproline

The vaccine may contain residual amounts of neomycin (25 micrograms maximum).

Diluent: Water for injections.

6.2. Incompatibilities

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

6.3. Shelf-life

The shelf-life of Priorix is two years when the vaccine is stored according to recommendations (see Section 6.4.) The shelf lives of the vaccine and diluent are not identical, therefore their expiry dates are different. The outer carton bears the earlier of the two expiry dates and this date must be respected. The carton and ALL its contents should be discarded on reaching the outer carton expiry date.

6.4. Special precautions for storage

Priorix should be stored in a refrigerator between 2°C and 8°C and protected from light.

Do not freeze.

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 lyophilised pellet in a vial (type I glass) with a stopper (bromobutyl rubber). The sterile diluent is presented in a prefilled syringe (type I glass) with plunger stopper (chlorobutyl rubber) with 2 separate needles or ampoule (type I glass).

Single pack size.

6.6. Instructions for use, handling and disposal

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.

Due to minor variation of its pH, the reconstituted vaccine may vary in colour from clear peach to fuschia pink without deterioration of the vaccine's potency.

Inject the **entire contents** of the vial.

It is normal practice to administer the vaccine immediately after reconstitution with the diluent provided. However, the vaccine may still be used up to 3 hours after reconstitution or to the end of the vaccination session whichever is sooner.

7. MARKETING AUTHORISATION HOLDER

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AUTHORISATION**

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