

## PRODUCT MONOGRAPH

### **PRIORIX**

Combined measles, mumps and rubella vaccine, live, attenuated

Lyophilized powder for injection

Meets WHO requirements

Active immunizing agent against infection by measles, mumps and rubella

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## PRIORIX

Combined measles, mumps and rubella vaccine, live, attenuated

### PART I: HEALTH PROFESSIONAL INFORMATION

#### SUMMARY PRODUCT INFORMATION

Route of Administration	Dosage Form / Strength	Nonmedicinal Ingredients
Subcutaneous or Intramuscular injection	Lyophilized powder for injection / Not less than: $10^{3.0}$ CCID <sub>50</sub> of the Schwarz measles; $10^{3.7}$ CCID <sub>50</sub> of the RIT 4385 mumps; and $10^{3.0}$ CCID <sub>50</sub> of the Wistar RA 27/3 rubella virus strains/ per 0.5 mL dose.	amino acids, lactose, mannitol, sorbitol, and water for injection. Residue: neomycin sulphate

#### DESCRIPTION

PRIORIX is a lyophilized 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<sub>5</sub> human diploid cells (rubella).

#### INDICATIONS AND CLINICAL USE

PRIORIX (combined measles, mumps and rubella vaccine, live, attenuated) is indicated for:

- active immunization against infection by measles, mumps and rubella.

#### Pediatrics:

A single dose is recommended routinely for children on, or as soon as practicable after, their first birthday. Older children who have no documented evidence of having received the vaccine should also be vaccinated.

## CONTRAINDICATIONS

PRIORIX (combined measles, mumps and rubella vaccine, live, attenuated) is contraindicated in:

- subjects with known hypersensitivity to neomycin or to any other component of the vaccine (for egg allergy, see WARNINGS AND PRECAUTIONS). A history of contact dermatitis to neomycin is not a contraindication.
- subjects having shown signs of hypersensitivity after previous administration of measles, mumps and/or rubella vaccines.
- subjects with severe humoral or cellular (primary or acquired) immunodeficiency e.g. symptomatic HIV infection (see also WARNINGS AND PRECAUTIONS).
- pregnant women. Women of child-bearing potential should be advised to avoid pregnancy for one month following vaccination (see also WARNINGS AND PRECAUTIONS).

When other susceptible persons with immune deficiencies are exposed to measles, passive immunization with immune globulin [human (IG)] should be given as soon as possible. It is desirable to immunize close contacts of immunocompromised individuals in order to minimize the risk of exposure of the latter to measles.

## WARNINGS AND PRECAUTIONS

### General

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.

PRIORIX (combined measles, mumps and rubella vaccine, live, attenuated) **must not** be administered intravascularly.

A limited number of subjects received PRIORIX intramuscularly. An adequate immune response was obtained for all three components.

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

Alcohol and other disinfecting agents must be allowed to evaporate from the skin before injection of the vaccine since they may 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.

As with all injectable vaccines, appropriate medical treatment and supervision should 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. generalized 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.

No special precautions are necessary for children with minor egg hypersensitivity who are able to ingest small quantities of egg uneventfully. No special measures are necessary in children who have never been fed eggs before MMR immunization. Prior egg ingestion should not be a prerequisite for MMR immunization.

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 not been documented. Pharyngeal excretion of the rubella virus is known to occur approximately 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.

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.

### **Hematologic**

Individuals with current thrombocytopenia may develop more severe thrombocytopenia following vaccination with measles-mumps-rubella vaccines. In addition, individuals who experienced thrombocytopenia with the first dose of vaccine may develop thrombocytopenia with repeat doses. Serologic status may be evaluated to determine whether or not additional doses of vaccine are needed. The potential risk to benefit ratio should be carefully evaluated before considering vaccination in such cases (see ADVERSE REACTIONS).

## **Immune**

There are 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 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.

## **Special Populations**

**Pregnant Women:** 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.

Women of child-bearing potential should be advised to avoid pregnancy for one month following vaccination. Women who intend to become pregnant should be advised to delay pregnancy.

**Nursing Women:** There are no human data regarding use in breastfeeding women. Nursing mothers may be vaccinated where, in the judgement of the health professional, the benefit outweighs the risk.

**Pediatrics:** 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.

Febrile seizures occasionally follow vaccination, particularly in children who have previously had convulsions or whose sibling or parents have a history of convulsions. However, the risk is low and the benefit of immunizing children greatly outweighs any potential risk associated with febrile seizures.

Under certain conditions, the vaccine may be recommended for children < 1 year of age. When an infant < 12 months of age is at high risk of exposure for measles or is travelling

abroad to an area where measles is common, measles vaccine alone or as MMR may be given as early as 6 months of age.

Under these circumstances, or if vaccine was inappropriately given before the child's first birthday, such children should receive two additional doses of MMR after the first birthday.

Susceptible persons > 12 months of age who are exposed to measles may be protected from disease if measles vaccine is given within 72 hours after exposure. There are no known adverse effects of vaccine given to persons incubating measles. However, immune globulin (IG) given within 6 days after exposure can modify or prevent disease and may be used for this purpose in infants < 12 months of age, persons for whom vaccine is contraindicated or those for whom more than 72 hours but less than 1 week have elapsed since exposure. Unless contraindicated, individuals who receive IG should receive measles vaccine later, at the intervals specified in the Canadian Immunization Guide.

PRIORIX is indicated for most infants infected with the human immunodeficiency virus (HIV) whose immune function at 12 to 15 months of age is compatible with safe MMR vaccination. Consultation with an expert is required in the case of HIV-infected children to determine the presence or absence of significant immunodeficiency in individual cases. Measles revaccination may still be appropriate for HIV-infected persons with moderate immunodeficiency if there is a high risk of measles in the local community or travel to an area where measles is endemic. Consultation with local public health authorities will help determine the local level of measles activity and risk to travellers abroad. Because the response to prior immunization may be impaired, HIV-infected children should receive IG after recognized exposure to measles.

## **ADVERSE REACTIONS**

### **Adverse Drug Reaction Overview**

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%

### **Clinical Trial Adverse Drug Reactions**

*Because clinical trials are conducted under very specific conditions the adverse reaction rates observed in the clinical trials may not reflect the rates observed in practice and should not be compared to the rates in the clinical trials of another drug. Adverse drug reaction information from clinical trials is useful for identifying drug-related adverse events and for approximating rates.*

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.

There were no major study-to-study differences with regards to the frequency of adverse events.

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

**Very Common  $\geq 10\%$**

**General disorders and administration site conditions:** Redness at the injection site, fever  $\geq 38^{\circ}\text{C}$  (rectal) or  $\geq 37.5^{\circ}\text{C}$  (axillary/oral)

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

**Infections and infestations:** Upper respiratory tract infection

**Skin and subcutaneous tissue disorders:** Rash

**General disorders and administration site conditions:** Pain and swelling at the injection site, fever  $> 39.5^{\circ}\text{C}$  (rectal) or  $> 39^{\circ}\text{C}$  (axillary/oral)

**Uncommon  $\geq 0.1\%$  and  $< 1\%$**

**Infections and infestations:** Otitis media

**Blood and lymphatic system disorders:** Lymphadenopathy

**Metabolism and nutrition disorders:** Anorexia

**Psychiatric disorders:** Nervousness, abnormal crying, insomnia

**Eye disorders:** Conjunctivitis

**Respiratory, thoracic and mediastinal disorders:** Bronchitis, cough

**Gastrointestinal disorders:** Parotid gland enlargement, diarrhoea, vomiting

**Rare  $\geq 0.01\%$  and  $< 0.1\%$**

**Immune system disorders:** Allergic reactions

**Nervous system disorders:** Febrile convulsions



There is no difference between the first and second vaccine doses with regard to the frequency category for the adverse reactions, except for pain at the injection site which was "Common" after the first vaccine dose and "Very common" after the second vaccine dose.

Nevertheless, despite being classified in the same frequency category, higher incidences of temperature and rash were observed after the first vaccine dose as compared to the second vaccine dose. Likewise, the incidences of redness and swelling were higher after the second vaccine dose as compared to the first vaccine dose.

A total of 10 serious adverse events that were considered as at least possibly related to vaccination have been reported after the first vaccine dose (N=10,267). None have been reported following the administration of the second vaccine dose (N=1,909).

### **Post-Market Adverse Drug Reactions**

During post-marketing surveillance, the following reactions have been rarely reported additionally in temporal association with PRIORIX vaccination:

**Infections and infestations:** meningitis, measles-like syndrome, mumps-like syndrome (including orchitis, epididymitis and parotitis)

**Blood and lymphatic system disorders:** thrombocytopenia, thrombocytopenic purpura

**Immune system disorders:** anaphylactic reactions

**Nervous system disorders:** encephalitis, cerebellitis, cerebellitis like symptoms (including transient gait disturbance and transient ataxia), Aseptic meningitis, transverse myelitis, Guillain Barré syndrome, peripheral neuritis

**Vascular disorders:** vasculitis (including Henoch Schonlein purpura and Kawasaki syndrome)

**Skin and subcutaneous tissue disorders:** erythema multiforme

**Musculoskeletal and connective tissue disorders:** arthralgia, arthritis

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

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 was similar in both vaccines.

## DRUG INTERACTIONS

### **Administration with Other Vaccines**

Clinical studies have demonstrated that PRIORIX (combined measles, mumps, rubella vaccine, live, attenuated) can be given with any of the following monovalent or combination vaccines: hexavalent vaccines (DTaP-HBV-IPV-Hib), diphtheria-tetanus-acellular pertussis vaccine (DTaP), reduced antigen diphtheria-tetanus-acellular pertussis vaccine (dTAP), *Haemophilus influenzae* type b vaccine (Hib), inactivated polio vaccine (IPV), hepatitis A vaccine (HAV), hepatitis B vaccine (HBV). The immune response to PRIORIX is not decreased by co-administration with any of the following vaccines: BEXSERO [meningococcal serogroup B vaccine], meningococcal serogroup C conjugate vaccine (MenC), meningococcal serogroups A, C, W-135 and Y conjugate vaccine (MenACWY), varicella vaccine and 10-valent pneumococcal conjugate vaccine (PCV).

In addition, although data on the concomitant administration of PRIORIX and oral polio vaccine (OPV) or diphtheria-tetanus-whole cell pertussis vaccine (DTPw) are not yet available, it is generally accepted that measles, mumps and rubella combined vaccine may be given at the same time as these vaccines if they are administered at separate injection sites.

As higher percentages of subjects reported systemic reactions, including fever, change in eating habits, tenderness at the injection site and irritability, following BEXSERO given concomitantly with routine vaccines than after BEXSERO alone, separate vaccinations can be considered when possible.

See Part II CLINICAL TRIALS **Administration of PRIORIX with other vaccines** and Product Monograph of the co-administered vaccine.

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 it is not possible to administer PRIORIX at the same time as other live attenuated vaccines, such as VARILRIX, it is recommended that an interval of at least one month should be left between vaccinations.

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

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

### **Drug-Drug Interactions**

Administration of PRIORIX to subjects who have received human gammaglobulins or a blood transfusion should be delayed for a minimum of three months as there is a possibility of vaccine failure due to passively acquired mumps, measles and rubella antibodies.

According to the Canadian Immunization Guide, if administration of an IG preparation becomes necessary after MMR vaccine or its individual component vaccines have been given, interference can also occur. If the interval between administration of any of these vaccines and subsequent administration of an IG preparation is < 14 days, immunization should be repeated at 3 months or longer, unless serologic test results indicate that antibodies were produced. If the IG product is given more than 14 days after the vaccine, immunization does not have to be repeated.

### **Drug-Food Interactions**

Interactions with food have not been established.

### **Drug-Herb Interactions**

Interactions with herbal products have not been established.

### **Drug-Laboratory Interactions**

If tuberculin testing is required, 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 in order to avoid false negative results.

## **DOSAGE AND ADMINISTRATION**

### **Recommended Dose and Dosage Adjustment**

The Canadian Immunization Guide recommends immunization at 12 months of age, or as soon as practicable thereafter. A second dose of MMR is recommended at least 1 month after the first dose, for the purpose of better measles protection. For convenience, options include giving it with the next scheduled vaccination at 18 months of age or with school entry (4-6 years) vaccinations (depending on the provincial/territorial policy), or at any intervening age that is practicable. The need for a second dose of mumps and rubella vaccine is not established but may benefit (given for convenience as MMR).

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

### **Administration**

It is recommended that PRIORIX (combined measles, mumps and rubella vaccine, live, attenuated) be given by subcutaneous injection, although it may also be given by intramuscular injection, in the deltoid region or in the anterolateral area of the thigh (see

WARNINGS AND PRECAUTIONS). PRIORIX must not be administered intravascularly.

The vaccine should be administered subcutaneously in subjects with bleeding disorders (e.g. thrombocytopenia or any coagulation disorder).

**Directions for Reconstitution**

The diluent (sterile water for injection) 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 as appropriate.

The colour of the reconstituted vaccine may vary from clear peach to fuchsia pink (bright pink) due to minor variations of its pH. This is normal and does not impair the performance of the vaccine. In the event of other variation being observed, discard the vaccine.

**Instructions for reconstitution of the vaccine with diluent presented in ampoules**

Disinfect the neck of the ampoule of sterile diluent and allow to dry. Using a sterile towel, break off the top of the ampoule at the scored line. Using a sterile syringe and needle, withdraw the diluent from the ampoule, ensuring that the point remains immersed throughout the withdrawal.

PRIORIX must be reconstituted by adding the entire content of the supplied ampoule of diluent to the vial containing the powder. Disinfect the rubber stopper of the vial of vaccine and allow to dry. Holding the plunger of the syringe containing the diluent, pierce the center of the rubber stopper of the vial and inject the sterile diluent into the vial containing the lyophilized vaccine. Shake the vial gently until the powder is completely dissolved in the diluent.

After reconstitution, the vaccine should be used promptly.

A new needle should be used to administer the vaccine.

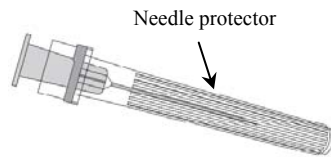
Withdraw the entire contents of the vial.

**Instructions for reconstitution of the vaccine with the diluent presented in pre-filled syringe\***

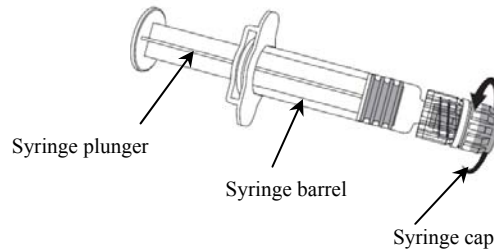
PRIORIX must be reconstituted by adding the entire content of the pre-filled syringe of diluent to the vial containing the powder.

To attach the needle to the syringe, refer to the below drawing.

1. Holding the syringe **barrel** in one hand (avoid holding the syringe plunger), unscrew the syringe cap by twisting it anticlockwise.

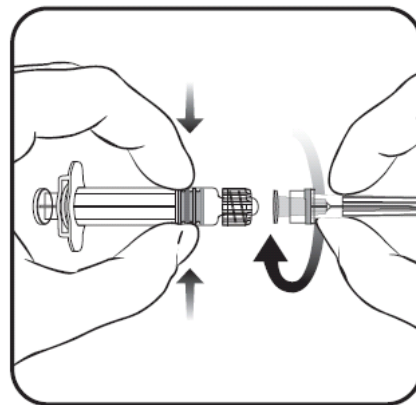


**Needle**



**Syringe**

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.

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

**Note:** The syringe provided with PRIORIX might be slightly different (without screw thread) than the syringe described in the drawing. In that case, the needle should be attached without screwing.

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

Alcohol and other disinfecting agents must be allowed to evaporate from the skin before injection of the vaccine since they may inactivate the virus.

Reconstituted vaccine should be injected promptly, or within 8 hours of reconstitution if it is stored refrigerated (2 to 8°C).

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

*\*Format not available in Canada*

## OVERDOSAGE

For management of a suspected drug overdose, contact your regional Poison Control Centre.

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.

## ACTION AND CLINICAL PHARMACOLOGY

See Part II SCIENTIFIC INFORMATION: CLINICAL TRIALS Section.

### **Duration of Effect**

All subjects followed up to 12 months after vaccination remained seropositive for anti-measles and anti-rubella antibodies. At month 12, 88.4% were still seropositive for anti-mumps antibody. This percentage is comparable to that observed for the commercially available measles, mumps and rubella combined vaccine (87%).

Canadian epidemiological data are available on the Public Health Agency of Canada website:

- Measles: <http://www.phac-aspc.gc.ca/im/vpd-mev/measles-rougeole-eng.php>
- Mumps: <http://www.phac-aspc.gc.ca/im/vpd-mev/mumps-eng.php>
- Rubella: <http://www.phac-aspc.gc.ca/im/vpd-mev/rubella-eng.php>

## STORAGE AND STABILITY

The vaccine should not be used beyond the expiry date stamped on the vial label and outer packaging. The diluent should not be used beyond the expiry date stamped on the syringe\* or ampoule label and outer packaging.

PRIORIX (combined measles, mumps and rubella vaccine, live, attenuated) should be stored in a refrigerator at 2 to 8°C. Do not freeze. Care should be taken to ensure appropriate storage conditions during transport.

The reconstituted vaccine should be administered as soon as possible. It may be kept up to 8 hours in the refrigerator.

Store in the original packaging in order to protect from light.

To conserve refrigerator space, the diluent may be stored separately at room temperature.

*\*Format not available in Canada*

## **DOSAGE FORMS, COMPOSITION AND PACKAGING**

### **Dosage Forms and Packaging**

PRIORIX (combined measles, mumps and rubella vaccine, live, attenuated) is available in packages of 10 vials in the following combinations of lyophilized powder and diluent:

- Boxes of monodose vials of vaccine with 10 ampoules of diluent.

### **Composition**

After reconstitution, 1 dose (0.5 mL) contains:

Live attenuated measles virus <sup>1</sup> (Schwarz strain)	not less than $10^{3.0}$ CCID <sub>50</sub> <sup>3</sup>
Live attenuated mumps virus <sup>1</sup> (RIT 4385 strain, derived from Jeryl Lynn strain)	not less than $10^{3.7}$ CCID <sub>50</sub> <sup>3</sup>
Live attenuated rubella virus <sup>2</sup> (Wistar RA 27/3 strain)	not less than $10^{3.0}$ CCID <sub>50</sub> <sup>3</sup>

<sup>1</sup> produced in chick embryo cells

<sup>2</sup> produced in human diploid (MRC-5) cells

<sup>3</sup> Cell Culture Infective Dose 50%

### **Excipients**

Vaccine: Amino acids, lactose, mannitol and sorbitol.

Diluent: Water for injection.

### **Residue**

Neomycin sulphate

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

## **PART II: SCIENTIFIC INFORMATION**

### **PHARMACEUTICAL INFORMATION**

#### **Drug Substance**

Proper name: combined measles, mumps and rubella vaccine, live, attenuated

#### **Product Characteristics**

PRIORIX (combined measles, mumps and rubella vaccine, live, attenuated) is a whitish to slightly pink coloured cake or powder contained in a glass vial sealed with a rubber stopper. The diluent (sterile water for injection) is clear and colourless. Due to minor variation of its pH, the colour of the reconstituted vaccine may vary from clear peach to fuchsia-pink coloured solution without deterioration of the vaccine potency.

#### **CLINICAL TRIALS**

In clinical studies, PRIORIX (combined measles, mumps and rubella vaccine, live, attenuated) has been demonstrated to be highly immunogenic.

In clinical studies involving 899 subjects, 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 involving 1094 subjects, antibodies against measles, mumps and rubella were detected in 98.7, 95.5 and 99.5% respectively of previously seronegative vaccinees who received PRIORIX compared to 96.9, 96.9 and 99.5% respectively in the group receiving a commercially available measles, mumps and rubella combined vaccine.

Study MeMuRu-OKA-155 was a phase II study evaluating the persistence of measles, mumps and rubella antibodies approximately two years after the initial vaccination study (study MeMuRu-OKA-151). As seen in Table 1 below, the seropositivity rates remained high (ranging from 93.4% to 100%) in subjects in the PRIORIX group who participated in the follow-up study.



**Table 1 Seropositivity rates observed in Study 155**

Antibody	Time point	N	%	95% CI
<b>Measles</b>	Day 42	76	98.7	92.9 to 100
	Year 2	76	93.4	85.3 to 97.8
<b>Mumps</b>	Day 42	72	98.6	92.5 to 100
	Year 2	72	94.4	86.4 to 98.5
<b>Rubella</b>	Day 42	76	100	95.3 to 100
	Year 2	76	100	95.3 to 100

Notes: Seropositivity cut-off levels: Measles ( $\geq 150$  mIU/mL), Mumps ( $\geq 231$  mIU/mL), Rubella ( $\geq 4$  IU/mL)

All subjects were vaccinated on Day 0

N = number of subjects with pre-vaccination results available

% = percentage of subjects with antibody titre within the specified range

95% CI = 95% confidence interval

Day 42: Post-vaccination blood sample obtained 42 days after vaccination

Year 2: Post-vaccination blood sample obtained two years after vaccination

### Administration of PRIORIX with other vaccines

Clinical studies have demonstrated that PRIORIX (combined measles, mumps, rubella vaccine, live, attenuated) can be given simultaneously with any of the following monovalent or combination vaccines: hexavalent vaccines (DTaP-HBV-IPV-Hib), diphtheria-tetanus-acellular pertussis vaccine (DTaP), reduced antigen diphtheria-tetanus-acellular pertussis vaccine (dTAp), *Haemophilus influenzae* type b vaccine (Hib), inactivated polio vaccine (IPV), hepatitis A vaccine (HAV), hepatitis B vaccine (HBV), meningococcal serogroup B vaccine (MenB - BEXSERO), meningococcal serogroup C conjugate vaccine (MenC), meningococcal serogroups A, C, W-135 and Y conjugate vaccine (MenACWY), varicella vaccine and 10-valent pneumococcal conjugate vaccine (PCV).

The data obtained with PRIORIX-TETRA in studies 10Pn-PD-DIT-022, MeMuRu-OKA-013, MenACWY-TT-039, V72P13E1 and MMRV-063 are considered to be extrapolated to PRIORIX since both vaccines have similar active substances and excipients, in particular the measles, mumps and rubella virus antigens, while PRIORIX-TETRA contains additionally the varicella component.

In Study MeMuRu-OKA-013, children who had previously received a complete primary vaccination course against diphtheria, tetanus, pertussis, hepatitis B, polio and *Haemophilus influenzae* type b received INFANRIX HEXA as a booster dose, co-administered with PRIORIX-TETRA. Based on the results, there was no evidence of any clinically relevant interference with the immune response to the measles, mumps and rubella antigens following co-administration with INFANRIX HEXA, and vice versa, except for the pertussis antigen pertactin (PRN), for which a trend of lower seropositivity rate was observed in the concomitant administration group (93.3% versus 98.5% in the DTPa-HBV-IPV-Hib group). However, no significant difference in anti-PRN GMCs was observed.

In studies dTpa-IPV-009 and DTPa-IPV-046, all subjects were seropositive against measles, mumps and rubella after receiving a second dose of PRIORIX co-administered with dTap-IPV (BOOSTRIX-POLIO) or DTaP-IPV (INFANRIX-IPV) vaccines. These responses are consistent with the immune responses towards measles, mumps and rubella antigens observed in other GSK studies performed in children from 15 months to 6 years of age receiving a second dose of PRIORIX vaccine alone [Czajka, 2009, Halperin, 2009]. In addition, no impact on the immune response to dTap-IPV or DTaP-IPV vaccines was observed upon concomitant administration with PRIORIX as compared to the immune responses of these vaccines when administered alone [Sanger, 2007, Lin, 2008, Nilsson, 2005].

Study MMR-157 demonstrated that PRIORIX co-administered with HAV elicited similar immune responses to measles, mumps and rubella antigens as compared to Measles-Mumps-Rubella virus vaccine (MMRII) co-administered with HAV. In addition, the co-administration of PRIORIX with HAV did not impair the immune response to HAV. Study MMR-157 also showed that PRIORIX co-administered with 7-valent pneumococcal conjugate vaccine (PCV) elicits similar immune responses to measles, mumps and rubella antigens as compared to MMRII co-administered with 7-valent PCV. In addition, the co-administration of PRIORIX with 7-valent PCV does not impair the immune response to 7-valent PCV. Study MMR-157 also supports the co-administration of PRIORIX with varicella vaccine, and vice versa.

Study 10PN-PD-DIT-022 assessed the immunogenicity of PRIORIX-TETRA and 10-valent pneumococcal conjugate vaccine (SYNFLORIX) when co-administered with each other. Study 10PN-PD-DIT-022 confirmed that the immunogenicity of PRIORIX-TETRA which includes the measles, mumps and rubella antigens in PRIORIX, is not compromised when co-administered with 10-valent pneumococcal conjugate vaccine and vice versa.

Study V72P13E1 assessed the concomitant use of PRIORIX-TETRA and BEXSERO and demonstrated non-inferiority of the immune response to the PRIORIX components in the PRIORIX-TETRA vaccine in terms of post-vaccination seroconversion rates for anti-measles, anti-mumps and anti-rubella antibodies as compared to the immune response when PRIORIX-TETRA was administered alone. Also, no impact on the immune response to MenB vaccine was observed upon concomitant administration with PRIORIX-TETRA.

Study MenACWY-TT-039 demonstrated non-inferiority of the immune response to the PRIORIX components in the PRIORIX-TETRA vaccine in terms of post-vaccination seroconversion rates for anti-measles, anti-mumps and anti-rubella antibodies when the first dose of PRIORIX-TETRA was administered concomitantly with meningococcal group A, C, W-135 and Y conjugate vaccine (MenACWY-TT - Nimenrix) compared to the immune response when PRIORIX-TETRA was administered alone. Furthermore, there was no impact on the immune response to the antigens in MenACWY-TT conjugate vaccine upon concomitant administration with PRIORIX-TETRA.

Study MMRV-063 demonstrated the non-inferiority of immune response to the PRIORIX components in the PRIORIX-TETRA vaccine in terms of post-vaccination seroconversion rates for anti-measles, anti-mumps and anti-rubella antibodies when the first dose of PRIORIX-TETRA was co-administered with MenC conjugate vaccine (Meningitec) compared to administration of PRIORIX-TETRA alone.

Study Hib-MenC-TT-011, where PRIORIX was co-administered with Hib-MenC vaccine, confirmed the results of study MMRV-063. In both studies MMRV-063 and Hib-MenC-TT-011, there was no impact on the immune response to the antigens in MenC conjugate vaccine upon concomitant administration with PRIORIX-TETRA or PRIORIX.

### **DETAILED PHARMACOLOGY**

Not applicable.

### **MICROBIOLOGY**

Not applicable.

### **TOXICOLOGY**

Not applicable.

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**PART III: CONSUMER INFORMATION**

**PRIORIX**

combined measles, mumps and rubella vaccine, live, attenuated

This leaflet is part III of a three-part "Product Monograph" published for PRIORIX (combined measles, mumps and rubella vaccine, live, attenuated) approved for sale in Canada and is designed specifically for Consumers. This leaflet is a summary and will not tell you everything about PRIORIX. Contact your doctor or pharmacist if you have any questions about the drug.

**ABOUT THIS VACCINE**

**What the vaccine is used for:**

PRIORIX is a vaccine used for protection against measles, mumps and rubella.

**What it does:**

PRIORIX protects your child against measles, mumps and rubella. It works by helping the body to make its own antibodies which protect your child against these diseases. As with all vaccines, PRIORIX may not completely protect all people who are vaccinated.

**When it should not be used:**

PRIORIX

- vaccination should be delayed if you or your child has an infection with a high temperature.
- vaccination should not be received if you think you or your child has previously had an allergic reaction to PRIORIX, neomycin (an antibiotic contained in the vaccine in trace amounts) or any other component contained in this vaccine. Signs of an allergic reaction may include skin rash, shortness of breath and swelling of the face and tongue. If you or your child has had a skin rash (dermatitis) after treatment with neomycin, your child can still be vaccinated with PRIORIX.
- vaccination should not be received if you think your child has previously had an allergic reaction to any vaccine against measles, mumps and rubella
- vaccination should not be received if you or your child's defences against infections (immunity mechanisms) are severely impaired.
- should not be administered to pregnant women. Furthermore, pregnancy should be avoided for one month after vaccination. Breastfeeding women can be vaccinated only where there is a clear need for vaccination. Inadvertent vaccination with PRIORIX

of women who are unaware they are pregnant should not be a reason for termination of pregnancy.

**What the medicinal ingredient is:**

Each 0.5 mL dose of the reconstituted vaccine contains as active ingredients not less than  $10^{3.0}$  CCID<sub>50</sub> of the Schwarz measles, not less than  $10^{3.7}$  CCID<sub>50</sub> of the RIT 4385 mumps, and not less than  $10^{3.0}$  CCID<sub>50</sub> of the Wistar RA 27/3 rubella virus strains.

**What the nonmedicinal ingredients are:**

PRIORIX contains as inactive ingredients: amino acids, lactose, mannitol, sorbitol and water for injection. Residues: Neomycin sulphate.

**What dosage forms it comes in:**

PRIORIX is provided as a freeze-dried vaccine for reconstitution with sterile diluent (water for injection).

**WARNINGS AND PRECAUTIONS**

BEFORE you use PRIORIX talk to your doctor or pharmacist if you or your child:

- has a high temperature (over 38°C), previous allergic reactions to this vaccine, neomycin or any ingredient in the vaccine.
- ever had a severe allergic reaction to eggs or anything that contained eggs.
- has an impaired defence against infections. You or your child should be closely monitored as the responses to the vaccines may not be sufficient to ensure a protection against the illness.
- or somebody else in the family has a history of convulsions or allergic diseases.
- is taking any other medicine or has recently received any other vaccine.
- has any serious health problems.
- has a condition called thrombocytopenia (decreased platelets which may lead to unusual bleeding or bruising).
- is pregnant, or breastfeeding.

As with other vaccines, appropriate medical treatment and supervision should always be readily available in case of rare anaphylactic events (severe allergic reaction that can be life threatening) following the administration of the vaccine.

Fainting can occur following, or even before, any needle injection; therefore, tell the doctor or nurse if you or your child fainted with a previous injection.

## INTERACTIONS WITH THIS VACCINE

In subjects who have received immune globulins or a blood transfusion, vaccination should be delayed for at least three months.

If a tuberculin test (skin test to check for tuberculosis) is to be performed, it should be done either before, at the same time as, or 4 to 6 weeks after vaccination with PRIORIX, otherwise the result of the tuberculin test may not be correct.

PRIORIX can be given at the same time as other vaccines. A different injection site will be used for each vaccine.

## PROPER USE OF THIS VACCINE

In case of drug overdose, contact a health care practitioner, hospital emergency department or regional Poison Control Centre immediately, even if there are no symptoms.

The vaccine must be administered by a health professional.

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

### Usual dose:

PRIORIX will be injected under the skin or into a muscle either in the upper arm or in the outer thigh.

PRIORIX should not be administered intravascularly (into a blood vessel).

Different injectable vaccines should always be administered at different injection sites.

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

### Missed Dose:

Make sure you or your child finishes the complete vaccination course. If not, you or your child may not be fully protected against infection.

## SIDE EFFECTS AND WHAT TO DO ABOUT THEM

Like all vaccines, PRIORIX may occasionally cause unwanted effects.

As with all injectable vaccines, there is a rare risk of allergic reactions. The signs of allergy may include local or widespread skin rash that may be itchy or blistering, swelling

of the eyes and face, difficulty in breathing or swallowing which may lead to collapse. These reactions will usually occur before leaving the doctor's office. However, you should seek immediate treatment in any event.

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

### **Very common: $\geq 10\%$**

- Redness at the injection site
- Fever  $\geq 38^{\circ}\text{C}$  (rectal) or  $\geq 37.5^{\circ}\text{C}$  (axillary/oral)

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

- Upper respiratory tract infection
- Rash
- Pain and swelling at the injection site
- Fever  $> 39.5^{\circ}\text{C}$  (rectal) or  $> 39^{\circ}\text{C}$  (axillary/oral)

### **Uncommon: $\geq 0.1\%$ and $< 1\%$**

- Infection of the middle ear
- Swollen glands in the neck, armpit or groin
- Loss of appetite
- Nervousness, abnormal crying, not being able to sleep (insomnia)
- Discharge with itching of the eyes and crusty eyelids (conjunctivitis)
- Bronchitis, cough
- Swollen glands in the cheek
- Diarrhoea, vomiting

### **Rare: $\geq 0.01\%$ and $< 0.1\%$**

- Allergic reactions
- Seizures with fever

After the marketing of PRIORIX, the following additional side effects have been rarely reported:

- Infection around the brain or spinal cord (meningitis)
- Measles-like symptoms
- Mumps-like symptoms (including transient, painful swelling of the testicles and swollen glands in the neck)
- Bleeding or bruising more easily than normal due to a drop in a type of blood cell called platelets, unusual bleeding or bruising under the skin
- Infection or inflammation of the brain, spinal cord and peripheral nerves resulting in temporary difficulty when walking (unsteadiness) and/or temporary loss of control of bodily movements, inflammation of some nerves, possibly with pins and needles or loss of feeling or normal movement (Guillain-Barré syndrome)

- narrowing or blockage of blood vessels. This may include unusual bleeding or bruising under the skin (Henoch Schonlein purpura) or fever which lasts for more than five days, associated with a rash on the trunk sometimes followed by a peeling of the skin on the hands and fingers, red eyes, lips, throat and tongue (Kawasaki disease)
- Severe condition of the skin that may affect the mouth and other parts of the body
- Joint and muscle pains

If the child develops any other symptom within days following the vaccination, tell the doctor as soon as possible.

*This is not a complete list of side effects. For any unexpected effects while taking PRIORIX, contact your doctor or pharmacist.*

### HOW TO STORE IT

Store your vaccine in a refrigerator at 2 to 8°C.

Do not freeze.

Store in original packaging in order to protect from light.

Store all vaccines out of the reach and sight of children.

The expiry date is shown on the label and packaging. The vaccine should not be used after this date.

### **REPORTING SUSPECTED SIDE EFFECTS**

**To monitor vaccine safety, the Public Health Agency of Canada collects case reports on adverse events following immunization.**

#### **For health care professionals:**

**If a patient experiences an adverse event following immunization, please complete the appropriate Adverse Events following Immunization (AEFI) Form and send it to your local Health Unit in [your province/territory](#).**

#### **For the General Public:**

**Should you experience an adverse event following immunization, please ask your doctor, nurse, or pharmacist to complete the Adverse Events following Immunization (AEFI) Form.**

**If you have any questions or have difficulties contacting your local health unit, please contact Vaccine Safety Section at Public Health Agency of Canada:**

**By toll-free telephone: 1-866-844-0018**

**By toll-free fax: 1-866-844-5931**

**By email: [caefi@phac-aspc.gc.ca](mailto:caefi@phac-aspc.gc.ca)**

**At the following website:**

**<http://www.phac-aspc.gc.ca/im/vs-sv/index-eng.php>**

**By regular mail:**

**The Public Health Agency of Canada**

**Vaccine Safety Section**

**130 Colonnade Road**

**Ottawa, Ontario**

**K1A 0K9 Address Locator 6502A**

**NOTE: Should you require information related to the management of the side effect, please contact your health care provider before notifying the Public Health Agency of Canada. The Public Health Agency of Canada does not provide medical advice.**



**MORE INFORMATION**

This document plus the full product monograph, prepared for health professionals can be found at:

<http://www.gsk.ca>

or by contacting the sponsor,

GlaxoSmithKline Inc.

7333 Mississauga Road

Mississauga, Ontario

L5N 6L4

1-800-387-7374

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