PRIORIX

SCHEDULING STATUS:

S2

1. NAME OF THE MEDICINE:

PRIORIX®

Lyophilised live attenuated vaccine against measles, mumps, and rubella with sterile diluent.

Powder and diluent for solution for injection.

2. QUALITATIVE AND QUANTITATIVE COMPOSITION:

After reconstitution, 1 dose (0,5 ml) contains:

Live attenuated measles virus[a] (Schwarz strain): not less than $10^{3,0}$ $CCID_{50}$[c]

Live attenuated mumps virus[a] (RIT 4385 strain, derived from Jeryl Lynn strain): not less than $10^{3,7}$ $CCID_{50}$[c]

Live attenuated rubella virus[b] (Wistar RA 27/3 strain): not less than $10^{3,0}$ $CCID_{50}$[c]

[a] produced in chick embryo cells

[b] produced in human diploid (MRC-5) cells

[c] Cell Culture Infective Dose 50 %

3. PHARMACEUTICAL FORM:

Vaccine: A whitish to slightly pink coloured cake or powder contained in a 3 ml colourless glass vial with a rubber stopper.

After reconstitution with diluent: Clear peach to fuchsia pink coloured solution.

Diluent: Clear, colourless liquid in sealed 1 ml clear glass self-breakable ampoule or a pre-filled syringe with 2 separate needles.

4. CLINICAL PARTICULARS:

4.1 Therapeutic indications:

PRIORIX is indicated for the active immunisation against measles, mumps and rubella in the second year of life.

It can also be given as a booster at the age of 4-6 years.

4.2 Posology and method of administration:

A single 0,5 ml dose of the reconstituted vaccine is recommended.

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.

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

PRIORIX must not be administered intravascularly.

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

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

4.3 Contraindications:

PRIORIX is contra-indicated:

- In patients with active untreated tuberculosis.

- Individuals with blood dyscrasias, leukaemias, lymphomas of any type or malignant neoplasms affecting bone marrow or lymphatic system.

PRIORIX is contra-indicated in subjects with known hypersensitivity to neomycin or to any other component of the vaccine (for egg allergy, see section 4.4).

A history of contact dermatitis to neomycin is not a contra- indication.

PRIORIX is contra-indicated in subjects having shown signs of hypersensitivity after previous administration of measles, mumps and/or rubella vaccines.

PRIORIX is contra-indicated in subjects with humoral or cellular (primary or acquired) immunodeficiency e.g. symptomatic HIV vaccines (see section4.4).

PRIORIX is contra-indicated in pregnancy (see section 4.6).

Vaccination should be deferred for at least 3 months following plasma or blood transfusions, or administration of human immune serum globulin.

4.4 Special warnings and precautions for use:

PRIORIX must not be administered intravasvularly.

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. 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.

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 reportedfollowing 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 contra-indication for this vaccination (see section 4.3) 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

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.

Appropriate medical treatment including adrenalin and supervision should always be readily available in case of a rare anaphylactic event following the administration of the vaccine.

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.

Excipient Warnings:

PRIORIX contains lactose. Patients with rare hereditary problems of galactose intolerance, the Lapp lactase deficiency or glucose-galactose malabsorption should not be given PRIORIX (see section 6.1).

PRIORIX contains sorbitol. Patients with rare hereditary problems of sorbitol intolerance should not be given PRIORIX.

PRIORIX contains traces of neomycin. The vaccine should not be used in patients with a known hypersensitivity to this antibiotic.

4.5 Interactions with other medicines and other forms of interactions:

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 combined measles, mumps and rubella vaccine may be given at the same time as the oral polio vaccine (OPV) the diphtheria, tetanus and whole cell pertussis vaccines (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 Fertility, pregnancy, and lactation:

Pregnant women must not be vaccinated with PRIORIX (section 4.3). However, foetal 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.

Lactation:

There is little human data regarding use in breastfeeding women. Persons can be vaccinated where the benefit outweighs the risk.

4.7 Effects on the ability to drive and use machines:

Priorix has no or negligible influence on the ability to drive and use machines.

4.8 Undesirable effects:

Summary of the safety profile

The safety profile presented below is based on a total of approximately 12 000 subjects administered PRIORIX in clinical trials. Adverse reactions which might occur following the use of a combined mumps, measles, rubella vaccine correspond to those observed after administration of the monovalent vaccines alone or in combination.

Clinical Trial Data:

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, including isolated reports

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 approximately12 000 subjects administered PRIORIX in clinical trials.

System organ class	**Frequency**	**Adverse reactions**
Infections and infestations	Common	upper respiratory tract infection
	Uncommon	otitis media

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.

Post-marketing Data:

During post-marketing surveillance, the following reactions have been reported additionally following PRIORIX vaccination (as they are reported voluntarily from a population of unknown size, a true estimate of frequency cannot be provided):

System organ class	**Adverse reactions**
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), Guillain Barré syndrome, transverse myelitis, 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 4.2).

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.

Reporting of suspected adverse events:

Reporting suspected adverse reactions after authorisation of the medicine is important.

It allows continued monitoring of the benefit/risk balance of the medicine. Health care provders are asked to report any suspected adverse reactions to SAHPRA via the "6.04 Adverse Drug

Reactions Reporting Form", found online under SAHPRA's publications:
https://www.sahpra.org.za/Publications/Index/8

4.9 Overdose:

Treatment is symptomatic and supportive.

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:

A 30. 2 Antigens

5.1 Pharmacodynamic properties:

PRIORIX has been demonstrated to be immunogenic. Antibodies against measles were detected in 98,0 %, against mumps in 96,1 % and against rubella in 99,3 % of previously seronegative vaccinees

5.2 Pharmacokinetic properties:

An evaluation of pharmacokinetics in vaccines is not necessary.

6. PHARMACEUTICAL PARTICULARS:

6.1 List of Excipients:

Powder: Amino acids, lactose, mannitol, sorbitol.

Diluent: Water for injections.

Residues:

Neomycin sulphate.

6.2 Incompatibilities:

In the absence of compatibility studies, this medicine must not be mixed with other medicines

6.3 Shelf-life:

24 months

6.4 Special precautions for storage:

Store between +2 ºC and +8 ºC. **DO NOT FREEZE.**

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

Keep out of reach of children.

6.5 Nature and contents of container:

Combined lyophilised vaccine in monodose vial and diluent ampoule.

Combined lyophilised vaccine in monodose vial and diluent in pre-filled syringe with 2 separate needles in pack

6.6 Special precautions for disposal and other handling:

The diluent and the reconstituted vaccine should be inspected visually for any foreign particulate matter and/or variation of physical aspects prior to reconstitution or administration. In the event of either being observed, do not use the diluent or the reconstituted vaccine

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

The vaccine must be reconstituted by adding the entire contents of the ampoule of diluent to the vial containing 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. Withdraw the entire contents of the vial.

A new needle should be used to administer the vaccine.

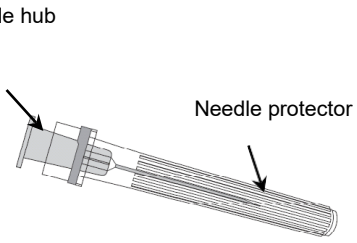
Any unused product or waste material should be disposed of in accordance with local requirements.

Instructions for reconstitution of the vaccine with diluent presented in prefilled syringe:

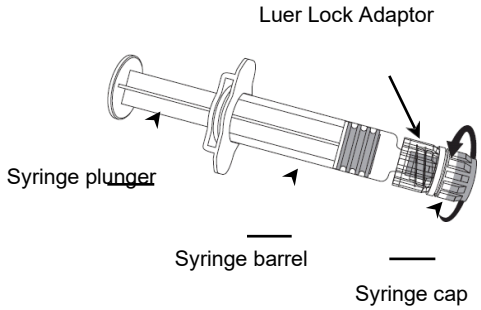
PRIORIX must be reconstituted by adding the entire contents of the pre- filled syringe of diluent to the vial containing the powder.

To attach the needle to the syringe, carefully read the instructions given with pictures 1 and 2. However, the syringe provided with PRIORIX might be slightly different than the syringe illustrated**.**

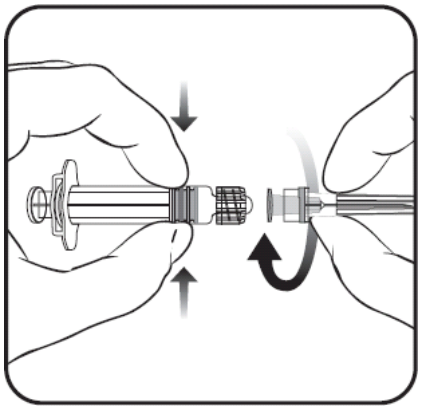
Needle



Syringe



Picture 1



Picture 2

Always hold the syringe by the barrel, not by the syringe plunger or the Luer Lock Adaptor (LLA), and maintain the needle in the axis of the syringe (as illustrated in picture 2). Failure to do this may cause the LLA to become distorted and leak.

During assembly of the syringe, if the LLA comes off, a new vaccine dose (new syringe and vial) should be used.

1. Unscrew the syringe cap by twisting it anticlockwise (as illustrated in picture 1).

2. Attach the needle to the syringe by gently connecting the needle hub into the LLA and rotate a quarter turn clockwise until you feel it lock (as illustrated in picture 2).

3. Remove the needle protector, which may be stiff.

4. Add the diluent to the powder. The mixture should be well shaken until the powder 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.

5. Withdraw the entire contents of the vial.
6. A new needle should be used to administer the vaccine. Unscrew the needle from the syringe and attach the injection needle by repeating step 2 above.

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

7. HOLDER OF CERTIFICATE OF REGISTRATION:

GlaxoSmithKline South Africa (Pty) Ltd

39 Hawkins Avenue

Epping Industria 1, 7460

8. REGISTRATION NUMBER:

33/30.1/0346

Namibia: Reg No 04/30.1/0878	NS1

9. DATE OF FIRST AUTHORISATION/RENEWAL OF THE AUTHORISATION:

Date of registration:

15 June 2001

10. DATE OF REVISION OF TEXT:

Date of most recent revision:

GDS-16

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