PRIORIX

SCHEDULING STATUS:

S2

PROPRIETARY NAME AND DOSAGE FORM:

PRIORIX

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

Powder and diluent for solution for injection.

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 %

Excipients:

Contains sugar (per 0,5 ml: lactose 32 mg, mannitol 8 mg, sorbitol 9 mg).

Powder: Amino acids, lactose, mannitol, sorbitol.

Diluent: Water for injections.

Residues:

Neomycin sulphate.

PHARMACOLOGICAL CLASSIFICATION:

A 30.2 Antigens

PHARMACOLOGICAL ACTION:

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.

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.

CONTRA-INDICATIONS:

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 WARNINGS AND SPECIAL PRECAUTIONS). 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 WARNINGS AND SPECIAL PRECAUTIONS).

PRIORIX is contra-indicated in pregnancy (see PREGNANCY AND LACTATION).

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

WARNINGS AND SPECIAL PRECAUTIONS:

PRIORIX must not be administered intravascularly.

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 reported following vaccination with

live measles, mumps and rubella vaccines. In such cases, the risk-benefit of immunising with PRIORIX should be carefully evaluated.

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

Immunocompromised subjects who have no contra-indication for this vaccination (see CONTRA-INDICATIONS) 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 11^{th} day. However there is no evidence of transmission of this excreted vaccine virus to susceptible contacts.

Excipient Warnings:

PRIORIX contains lactose/fructose. Patients with the rare hereditary conditions of galactose intolerance e.g. galactosaemia, Lapp lactase deficiency, glucose-galactose malabsorption or fructose intolerance should not be given PRIORIX (see COMPOSITION). Lactose may have an effect on the glycaemic control of patients with diabetes mellitus.

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

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.

PREGNANCY AND LACTATION:

Pregnant women must not be vaccinated with PRIORIX (see CONTRA-INDICATIONS).

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.

DOSAGE AND DIRECTIONS FOR USE:

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

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

Use and Handling:

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.

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. 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.

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.

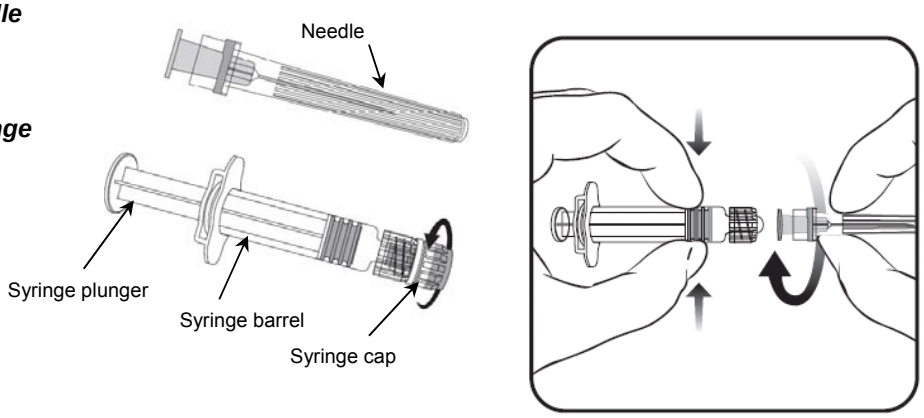
Instructions for reconstitution of the vaccine with diluent presented in prefilled syringe:

PRIORIX must be reconstituted by adding the entire 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. However, the syringe provided with PRIORIX might be slightly different than the syringe described in the drawing.

Needle

Syringe



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

Add the diluent to the 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.

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.

SIDE EFFECTS:

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 approximately 12 000 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	Uncommon	lymphadenopathy

disorders		
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:

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 DOSAGE AND DIRECTIONS FOR USE).

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

KNOWN SYMPTOMS OF OVERDOSAGE AND PARTICULARS OF ITS TREATMENT:

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.

IDENTIFICATION:

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.

PRESENTATION:

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.

STORAGE INSTRUCTIONS:

Store between +2 °C and +8 °C. **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.

REGISTRATION NUMBER:

33/30.1/0346

NAME AND BUSINESS ADDRESS OF THE HOLDER OF THE CERTIFICATE OF REGISTRATION:

GlaxoSmithKline South Africa (Pty) Ltd

39 Hawkins Avenue

Epping Industria 1, 7460

DATE OF PUBLICATION OF THE PACKAGE INSERT:

Date of registration:

15 June 2001

Date of most recent revision:

09 November 2017

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Botswana: Reg No BOT0200530 S2
Namibia: Reg No 04/30.1/0878 NS1

Patient Information Leaflet

SCHEDULING STATUS:

S2

PROPRIETARY NAME, STRENGTH AND PHARMACEUTICAL FORM:

PRIORIX

Powder and diluent for solution for injection.

Read all of this leaflet carefully before you or your child are vaccinated with PRIORIX.

PRIORIX is not for self-medication and must be administered by a healthcare professional.

- Keep this leaflet. You may need to read it again.
- If you have any further questions, please ask your doctor or pharmacist.
- PRIORIX has been prescribed for you or your child only. You should not share medicines with other people. It may harm them, even if their symptoms are the same as yours.

WHAT PRIORIX CONTAINS:

After reconstitution, 1 dose (0,5 ml) of vaccine 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 %

Contains sugar (per 0,5 ml: lactose 32 mg, mannitol 8 mg, sorbitol 9 mg).

The other ingredients are amino acids, lactose, mannitol, neomycin sulphate, sorbitol and water for injections.

WHAT PRIORIX IS USED FOR:

PRIORIX is a vaccine for use from 12 months of age to prevent infections caused by measles, mumps and rubella viruses. It provides protective immunity by encouraging the formation of antibodies against these diseases.

BEFORE YOU ARE GIVEN PRIORIX:

You or your child should not be given PRIORIX:

- if you/your child previously had an allergic reaction to PRIORIX, neomycin (an antibiotic) or to any ingredient contained in this vaccine. The active substances and other ingredients are listed at the beginning of this leaflet. However, if you have had a skin rash (dermatitis) after treatment with neomycin, you can still be vaccinated with PRIORIX
- if you/your child have previously had an allergic reaction to any vaccine against measles, mumps and rubella
- if you/your child have active untreated tuberculosis
- if you/your child have abnormal tumours or growths
- if you/your child have any severe illness, or take any medicine that weakens the immune system
- if you/your child have recently had a blood or plasma transfusion, or been given human immunoglobulin, your doctor may delay vaccination with PRIORIX for at least 3 months.

PRIORIX must not be given during pregnancy. Pregnancy should be avoided for one month following vaccination.

Check with your doctor, if you think any of the above apply to you.

Take special care with PRIORIX:

Your doctor needs to know before you are given PRIORIX, if you or your child:

- have a severe infection with a high temperature (over 38 °C). A minor infection such as a cold should not be a problem, but talk to your doctor first
- have a history or family history of convulsions (fits)
- have a history or family history of allergies
- have ever had a severe allergic reaction to eggs or to anything containing eggs
- have had a side effect after vaccination against measles, mumps or rubella that involved easy bruising or bleeding for longer than usual
- have a weakened immune system. You should be closely monitored as the responses to the vaccines may not be sufficient to ensure protection against the illness
- if your child is below the age of 12 months. Children in their first year of life may not develop a sufficient immune response (body's natural defence reaction) to the measles virus. Your doctor will advise you if additional doses of a measles containing vaccine are needed.

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

Pregnancy and Breastfeeding:

If you are pregnant or breastfeeding your baby, please consult your doctor, pharmacist or other healthcare professional for advice before you are given PRIORIX.

PRIORIX must not be given during pregnancy. It is important that you do not fall pregnant within one month after being vaccinated with PRIORIX. During this time, you should use an effective method of birth control to avoid pregnancy.

Important information about some of the ingredients of PRIORIX:

PRIORIX contains lactose/fructose. Patients with the rare hereditary conditions of lactose/fructose or galactose intolerance should not be given PRIORIX. Lactose may have an effect on the control of your blood sugar if you have diabetes mellitus.

PRIORIX contains traces of neomycin. Tell your doctor if you/your child has had an allergic reaction to this antibiotic.

Taking other medicines with PRIORIX:

Always tell your healthcare professional if you are taking any other medicine. (This includes complementary or traditional medicines.)

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 test may not be correct.

If you or your child has recently had a blood transfusion, or been given human immunoglobulin, your doctor may delay vaccination with PRIORIX for at least 3 months.

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

HOW TO RECEIVE PRIORIX:

Your doctor or nurse will inject the recommended dose of vaccine. If an additional (booster) dose is necessary, the doctor will tell you.

PRIORIX is usually injected under the skin, however can occasionally be injected into the muscle either in the upper arm or in the outer thigh.

The vaccine must never be injected into a vein.

POSSIBLE SIDE EFFECTS:

PRIORIX can have side effects.

Not all side effects reported for PRIORIX are included in this leaflet. Should you/your child's general health worsen, or if you/your child experiences any untoward effects while using PRIORIX, please consult your doctor, pharmacist or other healthcare professional for advice.

Severe allergic reactions may occur. The symptoms include:

- difficulty in breathing or swallowing
- itchy rash of the hands and feet
- swelling of the eyes and face.

Such reactions will usually occur before leaving the doctor's office. However, if your child gets any of these symptoms you should contact a doctor immediately or go the the causualty department at your nearest hospital.

➔ These are all very serious side effects. If you/your child have them, you may have had a serious allergic reaction to PRIORIX. You/your child may need urgent medical attention or hospitalisation.

Frequent side effects include:

- redness at the injection site
- fever greater than or equal to 38 ºC (rectal)
- upper respiratory tract infection
- rash
- pain and swelling at the injection site
- fever greater than or equal to 39,5 ºC (rectal).

Less frequent side effects include:

- 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
- allergic reactions
- seizures with fever.

Other side effects include:

- infection around the brain or spinal cord (meningitis)
- measles-like symptoms
- mumps-like symptoms (including 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, possible 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 a 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, swollen glands in the neck, 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 you notice any side effects not mentioned in this leaflet, please inform your doctor or pharmacist.

STORING AND DISPOSING OF PRIORIX:

Store your vaccine in a refrigerator between +2 °C and +8 °C.

THE VACCINE SHOULD NOT BE FROZEN. Discard if it has been frozen.

Store all medicines out of reach of children.

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

Return all unused medicine to your pharmacist. Do not dispose of unused medicine in drains or sewerage systems (e.g. toilets).

PRESENTATION OF PRIORIX:

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.

IDENTIFICATION OF PRIORIX:

The vaccine is a whitish to slightly pink coloured cake or powder, which after mixing with the diluent is a clear peach to fuchsia pink coloured solution.

The diluent is a clear, colourless liquid.

REGISTRATION NUMBER:

33/30.1/0346

NAME AND ADDRESS OF REGISTRATION HOLDER:

GlaxoSmithKline South Africa (Pty) Ltd

39 Hawkins Avenue

Epping Industria 1, 7460

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