For the use only of Registered Medical Practitioners or a Hospital or a Laboratory

PRIORIX-TETRA

Measles, Mumps, Rubella and Varicella Vaccine (live) Ph. Eur.

1. NAME OF THE MEDICINAL PRODUCT

Measles, Mumps, Rubella and Varicella Vaccine (live) Ph. Eur.

2. QUALITATIVE AND QUANTITATIVE COMPOSITION

Each dose (0.5 ml) of the reconstituted vaccine contains:

Live attenuated measles virus[1] (Schwarz strain)	not less than $10^{3.0}$ $CCID_{50}$[3]
Live attenuated mumps virus[1] (RIT 4385 strain, derived from Jeryl Lynn strain)	not less than $10^{4.4}$ $CCID_{50}$[3]
Live attenuated rubella virus[2] (Wistar RA 27/3 strain)	not less than $10^{3.0}$ $CCID_{50}$[3]
Live attenuated varicella virus[2] (OKA strain)	not less than $10^{3.3}$ PFU[4]
Water for Injections IP	0.5 ml

[1] produced in chick embryo cells
[2] produced in human diploid (MRC-5) cells
[3] Cell Culture Infective Dose 50%
[4] Plaque forming units

This vaccine contains a trace amount of neomycin. See section *4.3 Contraindications*.

Excipient with known effect:
The vaccine contains 14 mg of sorbitol.

For the full list of excipients, see section *6.1 List of excipients*.

3. PHARMACEUTICAL FORM

Powder and solvent for solution for injection.

Before reconstitution, the powder is a white to slightly pink coloured cake and the solvent is a clear colourless liquid.

4. CLINICAL PARTICULARS

4.1 Therapeutic indications

PRIORIX-TETRA is indicated for active immunisation in subjects from the age of 1 year to 12 years of age inclusive against measles, mumps, rubella and varicella (see also *4.4 Special Warnings and precautions for use*).

4.2 Posology and method of administration

Posology

Subjects from the age of 12 months up to and including 12 years of age should receive 2 doses of *PRIORIX-TETRA* to ensure optimal protection against measles, mumps, rubella and varicella (see section *5.1 Pharmacodynamic Properties*). It is preferable to respect an interval of at least 6 weeks between doses. In no circumstances should this interval be less than 4 weeks.

Alternatively, and in accordance with applicable official recommendations*:

- A single dose of *PRIORIX-TETRA* may be administered to children who have already received a single dose of another measles, mumps and rubella (MMR) vaccine and/or a single dose of another varicella vaccine.

- A single dose of *PRIORIX-TETRA* may be administered followed by a single dose of another measles, mumps and rubella (MMR) vaccine and/or a single dose of another varicella vaccine.

** Applicable official recommendations may vary regarding the interval between doses and the need for one or two doses of measles, mumps and rubella and of varicella-containing vaccines.*

Method of administration

The vaccine is to be injected by the subcutaneous or intramuscular route in the deltoid region of the upper arm or in the higher anterolateral area of the thigh.

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

For instructions on reconstitution of the medicinal product before administration, see section *6.6 Special precautions for disposal and other handling*.

4.3 Contraindications

As with other vaccines, the administration of *PRIORIX-TETRA* should be postponed in subjects suffering from acute severe febrile illness. However, the presence of a minor infection, such as a cold, should not result in the deferral of vaccination.

Hypersensitivity to the active substances or to any of the excipients listed in section *6.1 List of excipients* or neomycin. A history of contact dermatitis to neomycin is not a contra-indication. For egg allergy, see section *4.4 Special warnings and precautions for use*.

Hypersensitivity after previous administration of measles, mumps, rubella and/or varicella vaccines.

Severe humoral or cellular (primary or acquired) immunodeficiency, e.g. severe combined immunodeficiency, agammaglobulinemia and AIDS or symptomatic HIV infection or an age-specific CD4+ T-lymphocyte percentage in children below 12 months: CD4+ <25%; children

between 12-35 months: CD4+ < 20%; children between 36-59 months: CD4+ < 15% (see section *4.4 Special warnings and precautions for use*).

Pregnancy. Furthermore, pregnancy should be avoided for 1 month following vaccination (see section *4.6 Pregnancy and lactation*).

4.4 Special warnings and 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.

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.

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.

Salicylates should be avoided for 6 weeks after each vaccination with *PRIORIX-TETRA* as Reye's Syndrome has been reported following the use of salicylates during natural varicella infection.

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

Febrile convulsions

There was an increased risk of fever and febrile convulsions 5 to 12 days after the first dose of *PRIORIX-TETRA* observed as compared to concomitant administration of MMR and varicella vaccines (see sections *4.8 Undesirable effects* and *5.1 Pharmacodynamic properties*).

Vaccination of subjects with a personal or family history of convulsions (including febrile convulsions) should be considered with caution. For these subjects, alternative immunisation with separate MMR and varicella vaccines should be considered for the first dose (see section *4.2 Posology and method of administration*). In any case vaccinees should be monitored for fever during the risk period.

Fever rates are usually high after the first dose of measles-containing vaccines. There was no indication of an increased risk of fever after the second dose.

Immunocompromised patients

Vaccination may be considered in patients with selected immune deficiencies where the benefits outweigh the risks (e.g. asymptomatic HIV subjects, IgG subclass deficiencies, congenital neutropenia, chronic granulomatous disease, and complement deficiency diseases).

Immunocompromised patients who have no contraindication for this vaccination (see section *4.3 Contraindications*) may not respond as well as immunocompetent subjects, therefore some of these patients may acquire measles, mumps, rubella or varicella in case of contact, despite appropriate vaccine administration. These patients should be monitored carefully for signs of measles, parotitis, rubella and varicella.

Transmission

Transmission of measles, mumps and rubella viruses from vaccinees to susceptible contacts has never been documented, although pharyngeal excretion of the rubella virus is known to occur about 7 to 28 days after vaccination with peak excretion around the 11th day. Transmission of the Oka vaccine virus has been shown to occur at a very low rate in seronegative contacts of vaccinees with rash. Transmission of the Oka vaccine virus from a vaccinee who does not develop a rash to seronegative contacts cannot be excluded.

Vaccine recipients, even those who do not develop varicella-like rash should attempt to avoid, whenever possible, close association with high risk individuals susceptible to varicella for up to 6 weeks following vaccination. In circumstances where contact with high-risk individuals susceptible to varicella is unavoidable, the potential risk of transmission of the varicella vaccine virus should be weighted against the risk of acquiring and transmitting wild-type varicella virus.

High-risk individuals susceptible to varicella include:

- Immunocompromised individuals (see sections *4.3 Contraindications* and *4.4 Special warnings and precautions for use*)
- Pregnant women without documented positive history of varicella (chickenpox) or laboratory evidence of prior infection.
- Newborns of mothers without documented positive history of chickenpox or laboratory evidence of prior infection.

PRIORIX-TETRA should under no circumstances be administered intravascularly or intradermally.

Thrombocytopenia

Cases of worsening of thrombocytopenia and cases of 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-TETRA* should be carefully evaluated.

Syncope (fainting) can occur following, or even before, any vaccination especially in adolescents as a psychogenic response to the needle injection. This can be accompanied by several neurological signs such as transient visual disturbance, paraesthesia and tonic-clonic limb movements during recovery. It is important that procedures are in place to avoid injury from faints.

As with any vaccine, a protective immune response may not be elicited in all vaccinees. As for other varicella vaccines, cases of varicella disease have been shown to occur in persons who have previously received *PRIORIX-TETRA*. These breakthrough cases are usually mild, with a fewer number of lesions and less fever as compared to cases in unvaccinated individuals.

Very few reports exist on disseminated varicella with internal organ involvement following vaccination with Oka varicella vaccine strain mainly in immunocompromised subjects.

Interference with serological testing (see section *4.5 Interaction with other medicinal products and other forms of interaction*).

4.5 Interaction with other medicinal products and other forms of interaction

Clinical studies have demonstrated that *PRIORIX-TETRA* can be given simultaneously with any of the following monovalent or combination vaccines [including hexavalent vaccines (DTPa-HBV-IPV/Hib)]: diphtheria-tetanus-acellular pertussis vaccine (DTPa), *Haemophilus influenzae* type b vaccine (Hib), inactivated polio vaccine (IPV), hepatitis B vaccine (HBV), meningococcal serogroup B vaccine (MenB), meningococcal serogroup C conjugate vaccine (MenC), meningococcal serogroups A, C, W-135 and Y conjugate vaccine (MenACWY) and 10-valent pneumococcal conjugate vaccine.

Due to an increased risk of fever, tenderness at the injection site, change in eating habits and irritability when *BEXSERO* (MenB) was co-administered with *PRIORIX-TETRA*, separate vaccinations can be considered when possible.

There are currently insufficient data to support the use of *PRIORIX-TETRA* with any other vaccines.

If *PRIORIX-TETRA* is to be given at the same time as another injectable vaccine, the vaccines should always be administered at different injection sites.

Serological testing

If tuberculin testing has to be done it should be carried out before or simultaneously with vaccination since it has been reported that combined measles, mumps and rubella vaccines may cause a temporary depression of tuberculin skin sensitivity. As this anergy may last up to a maximum of 6 weeks, tuberculin testing should not be performed within that period after vaccination to avoid false negative results.

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 antibodies.

Vaccine recipients should avoid use of salicylates for 6 weeks after each vaccination with *PRIORIX-TETRA* (see section *4.4 Special warnings and precautions for use).*

4.6 Pregnancy and lactation

Fertility

PRIORIX-TETRA has not been evaluated in fertility studies.

Pregnancy

Pregnant women should not be vaccinated with *PRIORIX-TETRA.*

However, fetal damage has not been documented when measles, mumps, rubella or varicella vaccines have been given to pregnant women.

Pregnancy should be avoided for 1 month following vaccination. Women who intend to become pregnant should be advised to delay.

Breast-feeding

Adequate human data on the use of *PRIORIX-TETRA* during lactation are not available**.**

4.7 Effects on ability to drive and use machines

Not relevant.

4.8 Undesirable effects

Summary of the safety profile

The safety profile presented below is based on data from clinical trials in which more than 6,700 doses of *PRIORIX-TETRA* were administered to more than 4,000 children from 9 to 27 months of age. Events were recorded for up to 42 days after vaccination.

The most common adverse reactions following *PRIORIX-TETRA* administration were pain and redness at the injection site as well as fever ≥38°C (rectal) or ≥37.5°C (axillary/oral).

Tabulated list of adverse reactions

Adverse reactions reported are listed according to the following frequency:
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)

Clinical trial data

System Organ Class	**Frequency**	**Adverse reactions**
Infections and infestations	Uncommon	upper respiratory tract infection
	Rare	otitis media
Blood and lymphatic system disorders	Uncommon	lymphadenopathy
Metabolism and nutrition disorders	Uncommon	anorexia
Psychiatric disorders	Common	irritability
	Uncommon	crying, nervousness, insomnia
Nervous system disorders	Rare	febrile convulsions*
Respiratory, thoracic and mediastinal disorders	Uncommon	rhinitis
	Rare	cough, bronchitis
Gastrointestinal disorders	Uncommon	parotid gland enlargement, diarrhoea, vomiting

Skin and subcutaneous tissue disorders	Common	rash
General disorders and administration site conditions	Very common	pain and redness at the injection site, fever (rectal ≥38°C - ≤39.5°C; axillary/oral: ≥37.5°C - ≤39°C)**
	Common	swelling at the injection site, fever (rectal >39.5°C; axillary/oral >39°C)**
	Uncommon	lethargy, malaise, fatigue

* The risk of febrile convulsions following the first dose vaccination of children aged 9 to 30 months with *PRIORIX-TETRA* compared with MMR or simultaneous, but separate MMR and varicella vaccination was assessed in a retrospective database analysis.
The study included 82,656 children immunized with MMRV, 149,259 with MMR and 39,203 with separate MMR and varicella vaccines.

Depending on the case definition used to identify febrile convulsions in the main risk period 5 to 12 days following the first dose, incidences of febrile convulsions were 2.18 (95% CI: 1.38; 3.45) or 6.19 (95% CI: 4.71; 8.13) per 10,000 subjects for the MMRV group and 0.49 (95% CI: 0.19; 1.25) or 2.55 (95% CI: 1.67; 3.89) per 10,000 subjects for the matched control cohorts.

These data suggest one additional case of febrile convulsion per 5,882 or 2,747 subjects vaccinated with *PRIORIX-TETRA* compared to matched control cohorts who received MMR or simultaneous, but separate MMR and varicella vaccination (attributable risk of 1.70 (95% CI:-1.86; 3.46) and 3.64 (95% CI: -6.11; 8.30) per 10,000 subjects, respectively) – see section *5.1 Pharmacodynamic properties*.

**Following the administration of the first dose of the combined measles-mumps-rubella-varicella vaccine, higher incidences of fever (approximately 1.5 fold) were observed when compared to the concomitant administration of measles-mumps-rubella and varicella vaccines at separate injection sites.

Post-marketing surveillance data

The following additional adverse reactions have been identified in rare occasions during post-marketing surveillance. Because 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, herpes zoster*, measles-like syndrome, mumps-like syndrome (including orchitis, epididymitis and parotitis)
Blood and lymphatic system disorders	thrombocytopenia, thrombocytopenic purpura
Immune system disorders	allergic reactions (including anaphylactic and anaphylactoid reactions)
Nervous system disorders	encephalitis, cerebellitis, cerebrovascular accident, Guillain Barré syndrome, transverse myelitis, peripheral neuritis, cerebellitis like

	symptoms (including transient gait disturbance and transient ataxia)
Vascular disorders	Vasculitis (including Henoch Schonlein purpura and Kawasaki syndrome).
Skin and subcutaneous tissue disorders	erythema multiforme, varicella-like rash
Musculoskeletal and connective tissue disorders	arthralgia, arthritis

*This adverse drug reaction reported after vaccination is also a consequence of wild-type varicella infection. There is no indication of an increased risk of herpes zoster occurrence following vaccination compared with wild-type disease.

4.9 Overdose

No case of overdose has been reported.

5. PHARMACOLOGICAL PROPERTIES

5.1 Pharmacodynamic properties

Pharmaco-therapeutic group: Viral vaccine, ATC code J07BD54.

Efficacy

The efficacy of GlaxoSmithKline (GSK)'s monovalent Oka (*VARILRIX)* and *PRIORIX-TETRA* vaccines in preventing varicella disease has been evaluated in a large randomised clinical trial, which included GSK combined measles-mumps-rubella vaccine (*PRIORIX*) as active control. The trial has been conducted in Europe where no routine varicella vaccination is implemented. Children aged 12-22 months received two doses of *PRIORIX-TETRA* six weeks apart or one dose of *VARILRIX*. Vaccine efficacy against epidemiologically confirmed or PCR (Polymerase Chain Reaction) confirmed varicella of any severity (defined using a prespecified scale) and against moderate or severe confirmed varicella observed after a primary follow-up period of 2 years (median duration 3.2 years) and after an extended follow-up period of 6 years (median duration 6.4 years) are presented in the Table below (long term 10-year follow-up ongoing).

Group	**Timing**	**Efficacy against confirmed varicella of any severity**	**Efficacy against moderate or severe confirmed varicella**
Priorix-Tetra (2 doses) **N = 2,489**	Year 2	94.9% (97.5% CI: 92.4;96.6)	99.5% (97.5% CI: 97.5;99.9)
	Year 6(1)	95.0% (95% CI: 93.6;96.2)	99.0% (95% CI: 97.7;99.6)
Varilrix (1 dose) **N = 2,487**	Year 2	65.4 % (97.5% CI: 57.2;72.1)	90.7% (97.5% CI: 85.9;93.9)
	Year 6(1)	67.0% (95% CI: 61.8;71.4)	90.3% (95% CI: 86.9;92.8)

N = number of subjects enrolled and vaccinated
(1) descriptive analysis

In a study in Finland specifically designed to evaluate vaccine efficacy of *VARILRIX*, 493 children 10 to 30-month-old were followed up for a period of approximately 2.5 years after vaccination with one dose. The protective efficacy was 100% (95% CI: 80;100) against common or severe clinical cases of varicella ($\geq$ 30 vesicles) and 88% (95% CI: 72;96) against any serological confirmed case of varicella (at least 1 vesicle or papule).

Effectiveness

Effectiveness data suggest a higher level of protection and a decrease in breakthrough varicella following two doses of varicella-containing vaccine than following one dose.

The effectiveness of two doses of *PRIORIX-TETRA* during varicella outbreaks in day care centres in Germany, where routine varicella vaccination is recommended for children as of 11 months of age, was 91% (95% CI: 65;98) against any disease and 94% (95% CI: 54;99) against moderate disease.

The effectiveness of one dose of *VARILRIX* was estimated in different settings (outbreaks, case-control and database studies) and ranged from 20%-92% against any varicella disease and from 86%-100% against moderate or severe disease.

Immune response

Several clinical studies evaluated the immune response elicited by *PRIORIX-TETRA*. Anti-measles, anti-mumps and anti-rubella antibody titres were determined using commercially available enzyme-linked immunosorbent assays (ELISA). In addition, anti-mumps antibodies were titrated using a plaque-reduction neutralisation assay. These serological parameters are widely accepted as surrogate markers for immune protection. A modified commercial indirect immunofluorescence assay (IFA) and a commercial ELISA have been used to compare the immune response against varicella elicited by *PRIORIX-TETRA* to that observed with GSK varicella vaccine.

In three clinical trials conducted in Europe (Austria, Finland, Germany, Greece, Poland) approximately 2,000 previously unvaccinated children from 11 to 23 months of age received 2 doses of *PRIORIX-TETRA* with an interval between doses of 6 weeks. Seroconversion rates (SC) and geometric mean antibody concentrations/titres (GMC/GMT) are summarized in the table below.

Antibody Test (cut-off)	**Post dose 1**		**Post dose 2**	
	SC (95 % CI)	GMC/GMT (95 % CI)	SC (95 % CI)	GMC/GMT (95 % CI)
Measles ELISA (150mIU/ml)	96.4% (CI: 95.5;97.2)	3184.5 (CI: 3046.5;3328.7)	99.1% (CI: 98.6;99.5)	4828.6 (CI: 4644.3;5020.1)
Mumps ELISA (231U/ml)	91.3% (CI: 90.0;92.5)	976.7 (CI: 934.8;1020.5)	98.8% (CI: 98.2;99.2)	1564.4 (CI: 1514.6;1615.8)

Neutralisation (1:28)	95.4% (CI: 94.3;96.3)	147.0 (CI: 138.6;155.8)	99.4% (CI: 98.9;99.7)	478.4 (CI: 455.1;503.0)
Rubella ELISA (4IU/ml)	99.7% (CI: 99.4; 99.9)	62.2 (CI: 60.0;64.5)	99.9% (CI: 99.6;100)	119.7 (CI: 116.4;123.1)
Varicella IFA (1:4)	97.2% (CI: 96.3;97.9)	97.5 (CI: 92.2;103.1)	99.8% (CI: 99.5;100)	2587.8 (CI: 2454.0;2728.9)
ELISA (50mIU/ml)	89.4% (CI: 87.8;90.8)	112.0 (CI: 93.5;134.0)	99.2% (CI: 98.5; 99.6)	2403.9 (CI: 1962.4;2944.6)

Seroconversion rates and geometric mean antibody concentrations/titres were similar to those observed after separate vaccination with *VARILRIX* and *PRIORIX*.

In infants vaccinated at 11 months of age, the proportion of infants with protective measles titers (i.e., $\geq$ 150 mIU/mL) after the first dose is 91-92%, lower than the proportion observed when the first dose is administered since the age of 12 months.

The second dose of *PRIORIX-TETRA* induced an increase in seroconversion rates and/or antibody levels for the measles, mumps and rubella vaccine components. Therefore, to avoid infection during the interval between doses it is preferred that the second dose be administered within three months following the first dose.

Data suggest a higher efficacy and a decrease in breakthrough varicella following two doses of vaccine with respect to one dose. This correlates with an increase in anti-varicella antibodies elicited by the second dose, which suggests that the second dose of varicella antigen acts as a booster.

The immune response of *PRIORIX-TETRA* administered as a second dose of MMR vaccine in children 24 months to 6 years of age was evaluated in 2 clinical studies. Children were previously primed with respectively an MMR vaccine or with an MMR vaccine co-administered with a live attenuated varicella vaccine. Seropositivity rates for anti-varicella antibodies were 98.1% (IFA) in children previously vaccinated with MMR and 100% in children previously vaccinated with an MMR vaccine co-administered with a live attenuated varicella vaccine. Seropositivity rates were 100% for anti-measles, mumps, rubella antibodies in both studies.

Immune response in children aged 9 to 10 months

A clinical trial conducted in Asia (Singapore) enrolled 300 healthy children 9 to 10 months of age at the time of first vaccine dose. Of these, 153 subjects received 2 doses of *PRIORIX-TETRA* with an interval between doses of 3 months and 147 subjects received *PRIORIX* and *VARILRIX*. Seroconversion rates and geometric mean antibody concentrations/titres were similar to those observed after separate vaccination with *VARILRIX* and *PRIORIX*. Seroconversion rates after a first dose of *PRIORIX-TETRA* were comparable for all antigens except measles to those seen in 12-24 months old children in other clinical studies. The

seroconversion rate reported for measles in infants 9 to 10 months of age following 1 dose of *PRIORIX-TETRA* was 93.3% (95% CI: 87.6;96.9). Infants in their first year of life may not respond sufficiently to the components of the vaccine due to the possible interference with maternal antibodies. Therefore a second dose of *PRIORIX-TETRA* should be given three months after the first dose.

The immunogenicity and safety of *PRIORIX-TETRA* administered intramuscularly was evaluated in one comparative study conducted in 328 children who received *PRIORIX-TETRA* either by intramuscular or subcutaneous route. The study demonstrated similar immunogenicity and safety profiles for both administration routes.

Persistence of measles, mumps and rubella immune response

In a clinical trial in which children aged 12-22 months received two doses of *PRIORIX-TETRA* (N = 2,489), the seropositivity rates for anti-measles, mumps and rubella antibodies, in terms of subjects with an antibody concentration equal to or above defined threshold, observed after follow-up periods of 2 years and 6 years are presented in the Table below:

Timing	**Antibody Test (cut-off)**		
	Measles ELISA (150 mIU/ml)	**Mumps ELISA (231 U/ml)**	**Rubella ELISA (4 IU/ml)**
Year 2	99.1%	90.5%	100%
Year 6	99.0%	90.5%	99.8%

ELISA: Enzyme Linked Immuno Sorbent Assay

Post-Marketing Observational Safety Surveillance Study

The risk of febrile convulsions following the first dose of *PRIORIX-TETRA* was assessed in a retrospective database analysis in children aged 9 to 30 months (see section *4.8 Undesirable effects*).

5.2 Pharmacokinetic properties

Not applicable.

5.3 Preclinical safety data

A repeated dose toxicity study in animals did not reveal any local or systemic toxicity of the vaccine.

6. PHARMACEUTICAL PARTICULARS

6.1 List of excipients

Powder:
Amino acids
Lactose anhydrous
Mannitol

Sorbitol
Medium 199

Solvent:
Water for injections

Neomycin sulphate is present as a residual from the manufacturing process.

6.2 Incompatibilities

In the absence of compatibility studies, this medicinal product must not be mixed with other medicinal products.

6.3 Shelf-life

18 months.

After reconstitution, the vaccine should be administered promptly or kept in the refrigerator (2°C – 8°C). If it is not used within 24 hours, it should be discarded.

The expiry date is indicated on the label & packaging.

6.4 Special precautions for storage

Store and transport refrigerated (2°C – 8°C).

Do not freeze.

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

For storage conditions after reconstitution of the medicinal product, see section *6.3 Shelf-life*.

Keep out of reach of children.

6.5 Nature and contents of container

Powder in a vial (type I glass) with a stopper (butyl rubber).

AND

0.5 ml of solvent in a pre-filled syringe (type I glass) with plunger stopper (butyl rubber) with or without separate needles in the following pack sizes:
- with 2 separate needles: pack sizes of 1 or 10.
- without needle: pack sizes of 1, 10, 20 or 50.

OR

0.5 ml of solvent in an ampoule (type I glass).
Pack sizes of 1, 10 or 100.

All presentations or pack sizes may not be marketed in the country.

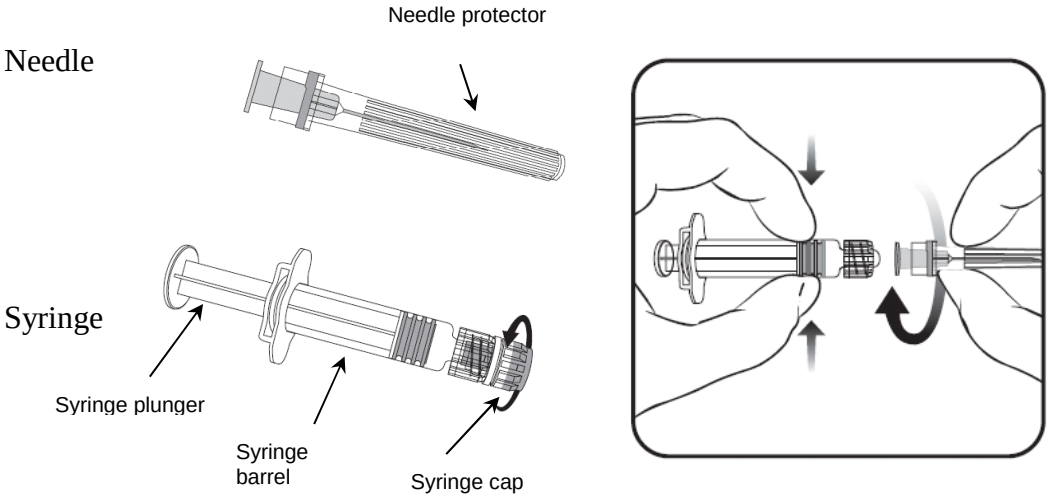
6.6 Special precautions for disposal and other handling

The reconstituted vaccine should be inspected visually for any foreign particulate matter and/or abnormal physical appearance. In the event of either being observed, the vaccine should be discarded.

The vaccine is reconstituted by adding the entire contents of the pre-filled syringe / ampoule of solvent to the vial containing the powder.

To attach the needle to the syringe, refer to the below drawing. However, the syringe provided with *PRIORIX-TETRA* might be slightly different (without screw thread) than the syringe described in the drawing.

In that case, the needle should be attached without screwing.



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 solvent to the powder. After the addition of the solvent to the powder, the mixture should be well shaken until the powder is completely dissolved in the solvent.

The colour of the reconstituted vaccine may vary from clear peach to fuchsia 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.

A new needle should be used to administer the vaccine.

Withdraw the entire contents of the vial.

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

7. MARKETING AUTHORISATION HOLDER

GlaxoSmithKline Pharmaceuticals Limited
Registered Office
Dr Annie Besant Road,
Worli, Mumbai 400030, India.

8. MARKETING AUTHORISATION NUMBER(S)

Import Permission No.: IMP-163/2014.

9. DATE OF FIRST AUTHORISATION/RENEWAL OF THE AUTHORISATION

Date of first authorization (Form 45): 18th July 2014.

For further information, please contact:
GlaxoSmithKline Pharmaceuticals Limited
Registered Office
Dr Annie Besant Road,
Worli, Mumbai 400030, India.

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