PACKAGE LEAFLET: INFORMASI UNTUK PASIEN

Priorix-Tetra

Measles, mumps, rubella and varicella vaccine

Baca leaflet ini dengan saksama sebelum anak Anda mendapatkan vaksin ini.
- Simpan leaflet ini. Anda mungkin butuh untuk membacanya lagi.
- Jika Anda memiliki pertanyaan lebih lanjut, Anda dapat menghubungi dokter Anda.
- Vaksin ini diresepkan untuk anak Anda. Jangan diberikan untuk orang lain.
- Jika ada kejadian ikutan pasca imunisasi (KIPI) yang menjadi serius atau jika Anda mengalami kejadian ikutan pasca imunisasi (KIPI) yang tidak terdapat pada leaflet ini, harap hubungi dokter Anda.

Baca leaflet ini dengan saksama sebelum anak Anda menerima vaksin ini karena berisi informasi penting bagi Anda.

Pada leaflet ini:

1. Apakah *Priorix-Tetra* itu dan digunakan untuk apa

Priorix-Tetra adalah vaksin yang digunakan untuk melindungi anak-anak dari usia 12 bulan sampai dengan 6 tahun terhadap virus campak, gondong, rubella, dan cacar air.

Penggunaan ***Priorix-Tetra*** harus didasarkan pada rekomendasi dokter. Ketika seseorang diberi vaksin ***Priorix-Tetra***, sistem kekebalan tubuh (sistem pertahanan alami tubuh) akan menghasilkan antibodi untuk melindungi dari infeksi virus campak, gondong, rubella, dan cacar air.
- Campak (*measles*): Campak adalah penyakit menular yang disebabkan oleh virus. Penyakit ini menular melalui batuk atau bersin dari orang yang terinfeksi. Gejala utama meliputi ruam, pilek, dan demam. Beberapa orang dapat mengalami gejala seperti infeksi telinga, infeksi saluran pernapasan seperti bronkitis dan pneumonia, dan kejang. Campak dapat berakibat fatal. Efek ini lebih sering terjadi pada anak-anak yang kekurangan nutrisi atau sakit.
- Gondong (*mumps*): Gondong adalah penyakit menular yang juga disebabkan oleh virus. Penyakit ini menular melalui batuk atau bersin dari orang yang terinfeksi. Gejala utama meliputi pembengkakan kelenjar di dekat telinga, pada salah satu atau kedua sisi wajah di daerah pipi. Beberapa orang juga mengalami peradangan pankreas, peradangan indung telur atau testikel yang kadang-kadang menyebabkan masalah kesuburan di kemudian hari, meningitis, dan tuli yang berlanjut setelah sembuh dari penyakit itu sendiri.
- Rubella: Rubella adalah penyakit menular yang juga disebabkan oleh virus. Gejala utama meliputi ruam dan pembengkakan kelenjar. Apabila ibu hamil mengalami infeksi rubella pada 12 minggu pertama kehamilan, dapat menyebabkan kerusakan pada janin pada 9 dari 10 kasus. Kerusakan ini meliputi cacat mental, kebutaan, tuli, dan masalah jantung.
- Cacar air (*varicella*) adalah penyakit menular yang disebabkan oleh virus *varicella zoster*. Ditularkan melalui kontak dekat dengan orang yang terinfeksi dan melalui batuk atau bersin dari orang yang terinfeksi. Penyakit ini paling sering terjadi pada anak-anak di bawah usia 10 tahun yang biasanya ringan. Gejala utama dari penyakit ini adalah ruam dengan bintik-bintik merah di wajah dan kepala yang dapat menyebar ke bagian tubuh yang lain. Cacar air dapat menjadi lebih serius pada orang dewasa, pada wanita hamil dan pasien yang memiliki sistem kekebalan yang buruk.

  Seperti semua vaksin, ***Priorix-Tetra*** mungkin tidak sepenuhnya melindungi setiap orang yang divaksinasi.

2. Apa yang perlu Anda ketahui sebelum anak Anda mendapatkan *Priorix-Tetra*

***Priorix-Tetra* tidak boleh diberikan jika anak Anda:**

- Sebelumnya memiliki reaksi alergi terhadap ***Priorix-Tetra***, neomisin (antibiotik) atau komponen apa pun yang terkandung dalam vaksin ini. Zat aktif dan bahan lain dalam ***Priorix-Tetra*** tercantum dalam daftar pada bagian 5. Namun, jika memiliki ruam kulit (dermatitis) setelah perawatan dengan neomisin, Anda masih dapat divaksinasi dengan ***Priorix-Tetra.***
- Sebelumnya memiliki reaksi alergi terhadap vaksin campak, gondong, rubella dan *varicella* apa pun.
- Memiliki penyakit berat atau mengonsumsi obat apa pun yang melemahkan sistem kekebalan (lihat juga "*Peringatan dan Tindakan Pencegahan*").

Priorix-Tetra tidak boleh diberikan selama kehamilan. Kehamilan harus dihindari selama satu bulan setelah vaksinasi.

Temui dokter Anda segera jika anak Anda mengalami salah satu gejala ini.

Peringatan dan Tindakan Pencegahan
Konsultasikan dengan dokter sebelum anak Anda divaksinasi dengan ***Priorix-Tetra*** jika anak Anda:
- Mengalami infeksi berat dengan panas tinggi. Dalam kasus ini, vaksinasi akan ditunda hingga pemulihan. Infeksi ringan seperti pilek seharusnya tidak menjadi masalah, tetapi konsultasikan dengan dokter Anda terlebih dahulu.
- Memiliki riwayat kejang demam (*febrile convulsions*) atau riwayat kejang pada keluarga. Dalam hal ini anak Anda harus dimonitor secara ketat setelah vaksinasi karena demam dapat terjadi 5 hingga 12 hari setelah vaksinasi.
- Memiliki riwayat alergi pada keluarga
- Pernah mengalami reaksi alergi yang parah terhadap telur atau apa pun yang mengandung telur.
- Memiliki kejadian ikutan pasca imunisasi (KIPI) setelah vaksinasi campak, gondong atau rubella meliputi mudah memar atau pendarahan lebih lama dari biasanya.
- Mendapatkan transfusi darah atau plasma, atau *human immunoglobulin* dalam tiga bulan terakhir. Jika demikian, respon antibodi terhadap ***Priorix-Tetra*** mungkin rendah sehingga biasanya menunggu selama tiga bulan sebelum memberikan ***Priorix-Tetra***.
- Harus menjalani tes kulit untuk pemeriksaan tuberkulosis. Jika tes ini dilakukan dalam 6 minggu setelah menerima ***Priorix-Tetra***, hasilnya mungkin tidak dapat diandalkan.
- Memiliki sistem kekebalan yang lemah. Anak Anda harus dipantau secara ketat karena respon terhadap vaksin mungkin tidak cukup untuk memastikan perlindungan terhadap penyakit.

Pingsan dapat terjadi setelah, atau bahkan sebelum suntikan. Oleh karena itu, beri tahu dokter atau perawat jika anak Anda mempunyai riwayat pingsan pada penyuntikan sebelumnya.

Seperti vaksin lainnya, ***Priorix-Tetra*** tidak dapat sepenuhnya melindungi anak Anda terhadap cacar air. Namun, orang-orang yang telah divaksinasi biasanya mengalami gejala penyakit yang lebih ringan dibandingkan dengan orang yang belum divaksinasi.

Jenis-jenis virus yang terdapat pada ***Priorix-Tetra*** biasanya tidak ditularkan dari orang yang telah mendapatkan vaksin kepada orang lain, dengan pengecualian virus varicella. Ini dapat terjadi ketika orang sehat yang mendapatkan vaksin memiliki tonjolan pada permukaan kulit (*blisters*).

Penggunaan Obat atau Vaksin Lain
Konsultasikan kepada dokter Anda jika anak Anda sedang atau baru saja menggunakan obat lain, termasuk obat-obatan yang diperoleh tanpa resep atau baru saja mendapatkan vaksin lain.

Aspirin atau produk jenis aspirin (juga dikenal sebagai salisilat) tidak boleh dikonsumsi selama 6 minggu setelah vaksinasi, karena ***Reye's Syndrome*** (penyakit langka otak dan hati) dapat terjadi.

Priorix-Tetra dapat diberikan bersamaan dengan vaksin lainnya. Pemberian vaksin harus dilakukan pada tempat penyuntikan yang terpisah.

3. Bagaimana cara pemberian *Priorix-Tetra*

Priorix-Tetra diberikan melalui suntikan di bawah kulit atau otot, baik di lengan atas atau di paha luar.

Priorix-Tetra ditujukan untuk anak-anak mulai dari 12 bulan hingga 6 tahun. Waktu dan jumlah dosis yang tepat yang akan diberikan kepada anak Anda akan ditentukan oleh dokter Anda berdasarkan rekomendasi resmi yang sesuai.

Dokter Anda mungkin akan mengusap kulit dengan alkohol atau bahan desinfektan lainnya dan akan menunggu alkohol menguap sebelum penyuntikan.

4. Kemungkinan kejadian ikutan pasca imunisasi (KIPI)

Seperti semua obat, ***Priorix-Tetra*** dapat menyebabkan kejadian ikutan pasca imunisasi (KIPI), meskipun tidak semua orang mengalaminya.

Seperti halnya semua vaksin, terdapat risiko langka reaksi alergi. Hal ini dapat berupa ruam lokal atau menyebar yang mungkin disertai gatal atau melepuh (*blistering*), pembengkakan pada mata dan wajah, kesulitan bernapas atau menelan, penurunan tekanan darah secara tiba-tiba dan kehilangan kesadaran. Reaksi tersebut dapat terjadi sebelum meninggalkan rumah sakit/ruang praktik dokter. Namun, Anda harus segera mencari pertolongan medis dalam situasi apa pun.

KIPI yang terjadi selama uji klinis dengan ***Priorix-Tetra*** adalah sebagai berikut:
Sangat umum (ini dapat terjadi dengan lebih dari 1 dalam 10 dosis vaksin):

- nyeri pada tempat penyuntikan,
- kemerahan pada tempat penyuntikan,
- demam lebih dari 37,5°C*

Umum (ini dapat terjadi hingga 1 dari 10 dosis vaksin):

- pembengkakan pada tempat penyuntikan,
- demam lebih dari 39°C*,
- iritabilitas,
- ruam (bintik-bintik dan/atau lepuhan)

Tidak umum (ini dapat terjadi hingga 1 dari 100 dosis vaksin):

- infeksi saluran pernapasan bagian atas,
- menangis,
- umumnya merasa tidak enak badan,
- pembengkakan kelenjar di pipi,
- diare,
- muntah,
- kehilangan selera makan,
- ketidakmampuan untuk tidur,
- kelelahan,
- kekurangan energi,
- kegugupan,
- pilek,
- pembengkakan kelenjar di leher, ketiak dan selangkangan

Jarang (ini dapat terjadi hingga 1 dari 1.000 dosis vaksin):

- bronkitis,
- infeksi telinga tengah,
- batuk,
- kejang yang disertai demam

*Tingkat demam yang lebih tinggi diamati setelah pemberian dosis pertama dari ***Priorix-Tetra*** bila dibandingkan dengan vaksin campak-gondong-rubella dan *varicella* yang diberikan secara terpisah pada kunjungan yang sama.

Setelah pemasaran, KIPI tambahan berikut jarang dilaporkan pada orang yang divaksinasi dengan ***Priorix-Tetra***:

- infeksi di otak atau sumsum tulang belakang (meningitis)
- cacar ular (herpes zoster)
- gejala seperti campak
- gejala seperti gondong (termasuk pembengkakan testis dan pembengkakan kelenjar di leher yang bersifat sementara dan terasa nyeri)
- infeksi atau peradangan otak, saraf tulang belakang dan saraf tepi yang mengakibatkan kesulitan sementara ketika berjalan (tidak seimbang dan/atau kehilangan kendali gerakan tubuh sementara), stroke, peradangan pada beberapa saraf (sindrom Guillain-Barré)
- penyempitan atau penyumbatan pembuluh darah. Hal ini mungkin termasuk perdarahan yang tidak biasa atau memar di bawah kulit (*Henoch Schonlein purpura*) atau demam yang

berlangsung selama lebih dari lima hari, terkait dengan ruam pada badan kadang diikuti dengan pengelupasan kulit pada tangan dan jari, mata merah, bibir, tenggorokan dan lidah (penyakit Kawasaki)
- lebih mudah terjadi perdarahan atau memar daripada biasanya karena penurunan trombosit, perdarahan yang tidak biasa atau memar di bawah kulit
- kondisi kulit parah yang dapat mempengaruhi mulut dan bagian lain dari tubuh
- ruam seperti cacar air
- nyeri sendi dan otot

Jika ada KIPI yang serius, atau jika Anda melihat ada KIPI yang tidak tercantum dalam leaflet ini, segera konsultasikan pada dokter atau apoteker Anda.

5. Isi kemasan dan informasi lain

Apa kandungan *Priorix-Tetra*

Zat aktif:

Setelah rekonstitusi, 1 dosis (0.5 mL) mengandung:

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*

[1] *produced in chick embryo cells*

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

[3] *Cell Culture Infective Dose 50%*

Bahan lain: amino acids, lactose, mannitol, sorbitol, *water for injection*.

Residu: neomycin sulphate.

Bagaimana bentuk dari *Priorix-Tetra* dan isi kemasan

Priorix-Tetra tersedia dalam bentuk serbuk dan pelarut injeksi. Serbuk dan pelarut harus dicampur bersama sebelum vaksinasi.

Serbuk injeksi terkandung dalam vial tiap 1 dosis dan pelarut terkandung dalam *pre-filled syringe* (0.5 mL) dalam kemasan berikut:
- vial + *pre-filled syringe* ukuran kemasan 1 dengan 2 jarum terpisah.

Pada proses pembuatannya bersinggungan dengan bahan bersumber babi

HARUS DENGAN RESEP DOKTER

Diproduksi oleh:
GlaxoSmithKline Biologicals s.a
89, rue de l'Institut- 1330
Rixensart, Belgium

Diimpor oleh:
PT Glaxo Wellcome Indonesia, Jakarta, Indonesia.

Dus, 1 vial + 1 *pre-filled syringe* pelarut @ 0,5 mL + 2 jarum Reg. No.XXXXXXXXXXXXXXX

Version 2 – January 2022

Priorix-Tetra

Measles, mumps, rubella and varicella vaccine

Powder and solvent for solution for injection

QUALITATIVE AND QUANTITATIVE COMPOSITION

After reconstitution, 1 dose (0.5 mL) 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]

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

The powder is white to slightly pink.
The solvent is clear and colourless.

Pada proses pembuatannya bersinggungan dengan bahan bersumber babi

CLINICAL INFORMATION

Indications

Priorix-Tetra is indicated for active immunisation in subjects from the age of 12 months up to 6 years of age inclusive against measles, mumps, rubella and varicella (see also "*Warnings and Precautions).*

Dosage and Administration

Posology

Subjects from the age of 12 months up to 6 years of age should receive 2 doses of ***Priorix-Tetra*** to ensure optimal protection against measles, mumps, rubella and varicella (see *Pharmacodynamics*). 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 of measles, mumps and rubella and of varicella-containing vaccines.*

*** A single dose of **Priorix-Tetra** should be administered with an interval of at least 6 months in children who have already received a single dose of another measles vaccine at the age of 9 months up to 12 months.*

Method of administration

The vaccine is to be injected subcutaneously (SC) or intramuscularly (IM) 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).

For instructions on reconstitution of the medicinal product before administration see *Instructions for Use/Handling*.

Contraindications

Priorix-Tetra 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.

Priorix-Tetra is contraindicated in subjects having shown signs of hypersensitivity after previous administration of measles, mumps, rubella and/or varicella vaccines.

Priorix-Tetra is contraindicated in pregnant women. Pregnancy should be avoided for one month after vaccination (see *Pregnancy and Lactation*).

Priorix-Tetra is contraindicated in subjects with severe humoral or cellular (primary or acquired) immunodeficiency (see also *Warnings and Precautions*).

Warnings and Precautions

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.

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.

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.

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

Infants in their first year of life may not respond sufficiently to the measles component of the vaccine, due to the possible persistence of maternal measles antibodies. Additional doses of a measles containing vaccine should be given according to official recommendations.

There is an increased risk of fever and febrile convulsions 5 to 12 days after the first dose of ***Priorix-Tetra*** as compared with 2 separate injections of MMR and varicella vaccines (see *Adverse Reactions and Pharmacodynamics*). There was no indication of an increased risk after the second dose.

Fever rates are usually high after the first dose of measles-containing vaccines.

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

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.

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 varicella vaccine virus has been shown to occur at a very low rate in seronegative contacts of vaccinees with rash. Transmission of the Oka varicella vaccine virus from a vaccinee who does not develop a rash to seronegative contacts cannot be excluded.

Priorix-Tetra must not be administered intravascularly or intradermally.

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.

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-Tetra*** should be carefully evaluated.

There is limited data on the use of ***Priorix-Tetra*** in immunocompromised subjects, therefore vaccination should be considered with caution and only when, in the opinion of the physician, the benefits outweigh the risks.

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, rubella or varicella despite appropriate vaccine administration. Immunocompromised subjects should be monitored carefully for signs of measles, mumps, rubella and varicella.

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

Interactions
Clinical studies have demonstrated that ***Priorix-Tetra*** can be given simultaneously with any of the following monovalent or combination vaccines: 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), 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) and pneumococcal conjugate vaccine (PCV).

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.

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.

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

Pregnancy and Lactation
Fertility
No data available.

Pregnancy
Pregnant women must not be vaccinated with ***Priorix-Tetra***. Pregnancy should be avoided for one month after vaccination. Women who intend to become pregnant should be advised to delay pregnancy.

Adequate human data on the use of ***Priorix-Tetra*** during pregnancy are not available and animal studies on reproductive toxicity have not been conducted.

Lactation
Adequate human data on the use of ***Priorix-Tetra*** during lactation are not available.

Effects on Ability to Drive and Use Machines
No studies on the effects of ***Priorix-Tetra*** on the ability to drive and use machines have been performed.

Adverse Reactions
The safety profile presented below is based on data from more than 6,700 doses administered subcutaneously to children from 9 to 27 months of age. Events were recorded for up to 42 days after vaccination.

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)

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

*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.

During post-marketing surveillance, the following additional reactions have been reported after measles-mumps-rubella and varicella vaccination.

System Organ Class	Frequency	Adverse reactions
Infections and infestations	Rare	meningitis, herpes zoster, measles-like syndrome, mumps-like syndrome (including orchitis, epididymitis and parotitis)

Blood and lymphatic system disorders	Rare	thrombocytopenia, thrombocytopenic purpura
Immune system disorders	Rare	allergic reactions (including anaphylactic and anaphylactoid reactions)
Nervous system disorders	Rare	encephalitis, cerebrovascular accident, cerebellitis, cerebellitis like symptoms (including transient gait disturbance and transient ataxia), Guillain-Barré syndrome, transverse myelitis, peripheral neuritis
Vascular disorders	Rare	vasculitis (including Henoch Schonlein purpura and Kawasaki syndrome)
Skin and subcutaneous tissue disorders	Rare	erythema multiforme, varicella like rash
Musculoskeletal and connective tissue disorders	Rare	arthralgia, arthritis

Overdose
Insufficient data are available.

PHARMACOLOGICAL PROPERTIES
Pharmacodynamics
Efficacy and effectiveness
Clinical trials showed that the vast majority of varicella vaccinees exposed to wild-type virus were either completely protected or developed a milder form of chickenpox (breakthrough varicella).

The efficacy of GlaxoSmithKline's Oka varicella-containing vaccines in preventing confirmed varicella disease (by Polymerase Chain reaction (PCR) or exposure to varicella case) has been evaluated in a large active controlled multicountry clinical trial in which children aged 12-22 months received two doses of ***Priorix-Tetra*** or one dose of monovalent Oka varicella vaccine (***Varilrix***). Vaccine efficacy against confirmed varicella of any severity and against moderate or severe confirmed varicella was demonstrated 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.

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)
Monovalent Oka varicella vaccine (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

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.

In an outbreak situation the effectiveness of two doses of ***Priorix-Tetra*** was 91% (95% CI: 65;98) against any disease and 94% (95% CI: 54;99) against moderate disease.

Immune response
Seroconversion rates after two subcutaneous doses of ***Priorix-Tetra*** given with an interval of 6 weeks in approximately 2,000 previously unvaccinated children from 11 to 23 months of age are summarized in the table below:

Antibody Test (cut-off)	Post dose 1	Post dose 2
Measles, ELISA (150 mIU/mL)	96.4%	99.1%

Mumps, ELISA (231 U/mL) Neutralisations (1:28)	91.3% 95.4%	98.8% 99.4%
Rubella, ELISA (4 IU/mL)	99.7%	99.9%
Varicella, IFA (1:4) ELISA (50 mIU/mL)	97.2% 89.4%	99.8% 99.2%

ELISA: Enzyme Linked Immuno Sorbent Assay
IFA: Immunofluorescence Assay

When ***Priorix-Tetra*** administered as a second dose of MMR vaccine in children 24 months to 6 years of age, previously primed with an MMR vaccine or with MMR co-administered with a live attenuated varicella vaccine, all children were found seropositive for antimeasles, mumps and rubella antibodies. Seropositivity rates for antivaricella antibodies were respectively 98.1% (IFA) and 100% in the children previously vaccinated with MMR or with MMR co-administered with a live attenuated varicella vaccine.

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 antimeasles, 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 vaccination of children aged 9 to 30 months with ***Priorix-Tetra*** compared with a matched cohort who received 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.

The attributable risk of febrile convulsions on cohorts matched for confounding factors in the main risk period of 5 to 12 days following first dose of Priorix-Tetra was 3.64/10,000 (95% CI: -6.11;8.30).

PHARMACEUTICAL PARTICULARS

List of Excipients
Excipients of the vaccine are: amino acids, lactose, mannitol, sorbitol.

Solvent is water for injections.

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

Shelf Life
The expiry date of the vaccine is indicated on the label and packaging.

After reconstitution: immediate use is recommended. However the stability at 2°C-8°C has been demonstrated for 8 hours after reconstitution.

Shelf life: 18 months.

Special Precautions for Storage
Store at 2°C-8°C (in a refrigerator).

Do not freeze.

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

The storage conditions are detailed on the packaging.

Nature and Contents of Container
Powder in a vial (Type I glass) with a stopper.

0.5 mL of solvent in a pre-filled syringe (Type I glass) with rubber stopper, with or without needles.

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

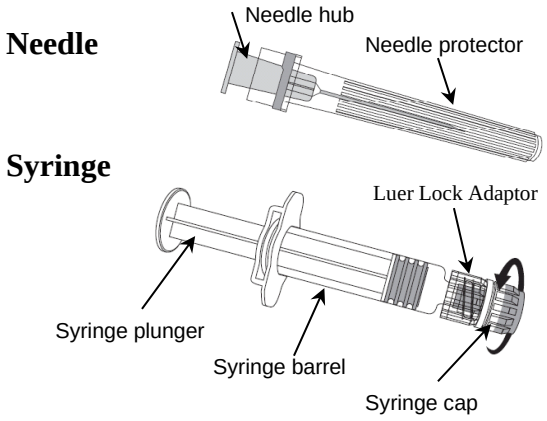
Incompatibilities
In the absence of compatibility studies, this medicinal product must not be mixed with other medicinal products.

Instructions for Use/Handling
The reconstituted vaccine should be inspected visually for any foreign particulate matter and/or abnormal physical appearance prior to administration. In the event of either being observed, do not administer the vaccine.

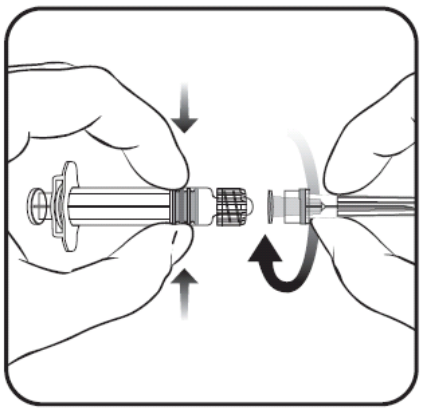
The colour of the reconstituted vaccine may vary from clear peach to fuchsia pink due to minor variations of its pH. This is normal and does not impair the performance of the vaccine. In the event of other variation being observed, do not administer the vaccine.

Instructions for reconstitution of the vaccine with solvent presented in pre-filled syringe
Priorix-Tetra must be reconstituted by adding the entire contents of the pre-filled syringe of solvent 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-Tetra*** might be slightly different than the syringe illustrated.



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 solvent to the powder. The mixture should be well shaken until the powder is completely dissolved in the solvent.

After reconstitution, the vaccine should be used promptly.

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.

Presentations
Box, 1 vial vaccine powder + 1 PFS @ 0.5 mL diluent + 2 needles Reg. No.: XXXXXXXXXXXXXXX

HARUS DENGAN RESEP DOKTER

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