Measles, Mumps, Rubella and Varicella Vaccine Biological Page

Section 7:	**Biological Product Information**		**Standard #: 07.271**
Created by:	Province-wide Immunization Program Standards and Quality		
Approved by:	Province-wide Immunization Program Standards and Quality		
Approval Date:	August 1, 2012	**Revised:**	January 1, 2021

	Priorix-Tetra®	**ProQuad®**
Manufacturer	GlaxoSmithKline Inc.	Merck Canada Inc.
Biological Classification	Live, attenuated	
Indications for Provincially Funded Vaccine	**Solid Organ Transplant (SOT) Candidates (pre-transplant only):** • **9 months up to and including 11 months of age** should receive **Priorix-Tetra®** vaccine. • **12 months of age up to and including 12 years of age** can receive either vaccine. • Combined vaccine is not licensed for individuals 13 years of age and older. Separate MMR and varicella vaccine should be offered to eligible individuals in this age group. • See: *Standard for Immunization of Transplant Candidates and Recipients*.	

	Healthy children 12 months of age up to and including 12 years of age:
	• When both MMR vaccine and varicella vaccine are indicated for children 12 months up to and including 12 years of age, MMR-Varicella combined vaccine should be considered.
	• Verbal history of disease in the varicella vaccine era is not a reliable indicator of immunity.
	  ○ Children born August 1, 2012 or later with a verbal history of chicken pox disease should be offered varicella-containing vaccine**.**
	  ▪ Children with a history of chickenpox disease occurring prior to 12 months of age should be offered varicella vaccine.
	  ▪ For children with lab-confirmed varicella disease after the age of 12 months, varicella vaccine is not required.
	  ○ Children born prior to August 1, 2012 who have a history of chickenpox disease occurring at one year of age and older will not be offered varicella-containing vaccine at this time.
	Notes:
	• A second dose of measles-containing vaccine given as MMR vaccine alone or MMR-Var can be given prior to 18 months of age using the recommended interval between doses for the following individuals:
	  ○ Those travelling to areas where measles is circulating in Canada and all countries outside of Canada.
	  ○ To assist with determining where measles is circulating refer to:
	  ▪ The AHS Measles Immunization webpage - https://www.albertahealthservices.ca/info/Page16365.aspx
	  ▪ The Public Health Agency (PHAC) travel health notices - http://www.phac-aspc.gc.ca/tmp-pmv/notices-avis/index-eng.php
	Scheduling Considerations:
	  ○ If time allows, the second dose should be given on or after 15 months of age.
	  ○ If MMR-Var is given, this dose would be considered adequate and count as the child's second dose of MMR and varicella vaccine.
	  ○ If MMR vaccine is given the child would be offered varicella vaccine at their preschool immunization appointment.
	  ○ The spacing of this dose of vaccine from previous doses of MMR and varicella vaccines must respect the minimum intervals outlined in the schedule section.	

<table>
<tr><th></th><th>Priorix-Tetra®</th><th>ProQuad®</th></tr>
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See MMR Vaccine Biological Page and Varicella Vaccine Biological Page for detailed eligibility information for each vaccine.
Infants with a history of varicella disease prior to 12 months of age should be offered varicella or varicella-containing vaccine.
In Alberta, MMR-Var vaccine is not routinely recommended prior to 12 months of age; therefore doses administered before this age should be repeated at 12 months of age and older using the age appropriate vaccine.
For children with high risk conditions refer to Contraindications/Precautions Section and separate MMR Vaccine Biological Page and Varicella Vaccine Biological Page.
No clinical data are available for MMR-Var vaccines administered after exposure to measles, mumps, rubella, or varicella. However, post-exposure prophylaxis has been demonstrated for measles (within 3 days of exposure) with measles-containing vaccine and for varicella (within 3-5 days of exposure) for varicella virus vaccine, so it is not unreasonable to expect MMR-Var to behave similarly. MMR or univalent varicella vaccines may be used as well.
This vaccine is not indicated for individuals 13 years of age and older. Eligible individuals 13 years of age and older should receive the separate MMR and univalent varicella vaccine. See MMR Vaccine Biological Page and Varicella Vaccine Biological Page.

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<tr><td>Schedule</td><td colspan="2">
Healthy children 12 months of age up to and including 12 years of age:

Dose 1 – 12 months of age (routinely given as MMR-Var).
Dose 2 – 18 months of age (routinely given as MMR-Var) respecting minimum intervals. It is preferable that the second dose be given after 15 months of age but before school entry.

Spacing Considerations:
<table>
<tr><th colspan="4">Recommended Intervals for MMR and Varicella Containing Vaccines</th></tr>
<tr><th rowspan="2">Previous Vaccine Administered</th><th colspan="3">Recommended Interval to Next Dose</th></tr>
<tr><th>MMR-Var</th><th>MMR</th><th>Varicella</th></tr>
<tr><td>MMR-Var</td><td>3 months</td><td>6 weeks</td><td>3 months</td></tr>
<tr><td>MMR</td><td>6 weeks</td><td>4 weeks</td><td>4 weeks</td></tr>
<tr><td>Varicella</td><td>3 months</td><td>4 weeks</td><td>3 months[1]</td></tr>
</table>
[1]This interval can be shortened to 4 weeks if child is off schedule or rapid protection is required.
Notes:

Children who have presented for their 18 month immunization prior to January 1, 2021 will be offered their second dose of measles-containing vaccine when they present for the preschool booster.
Children who receive their first dose of varicella-containing vaccine and at any point subsequently develop laboratory-confirmed vaccine modified varicella disease do not require a second dose of varicella-containing vaccine.
See above for routine recommended intervals between all measles, mumps, rubella and varicella vaccines.
With the exception of Yellow Fever vaccine, MMR-Var can be administered simultaneously with other live vaccines or separated by an interval of at least 4 weeks (See Administration with Other Products section for additional information for MMR-Var and Yellow Fever vaccine spacing).
Live Attenuated Influenza Vaccine (LAIV)/Quadrivalent Live Attenuated Influenza Vaccine (QLAIV) may be administered any time before or after the administration of other live attenuated or inactivated vaccines.

Specialists recommending alternate spacing for specific high risk individuals may be accommodated on a case by case basis.

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	• If live vaccine was inadvertently administered at less than the routine intervals outlined above, the dose can be considered valid and vaccine would not need to be repeated if there is a minimum interval of at least 4 weeks. • Any dose of MMR or MMR-Var vaccine administered before one year of age must be repeated on or after 12 months of age and separated by the appropriate interval. • Parents who refuse the combined MMR-Var vaccine and wish to have the separate MMR and univalent varicella vaccine may be accommodated.	
Preferred Use	There will be no preference indicated for the use of Priorix-Tetra® or ProQuad® in children 12 months of age up to and including 12 years of age. • Both vaccines are safe and immunogenic in individuals 12 months of age up to and including 12 years of age. • Children 9 months of age up to and including 11 months of age requiring MMR-Var prior to SOT are eligible for Priorix-Tetra® only. Persons with medical contraindications to one product should be offered the alternate product if supply is available.	
Dose	0.5 mL **Note:** Withdraw the entire contents of the diluent and inject into the vial containing the powder. Once reconstituted withdraw the entire contents of the vial and inject the entire volume.	
Route	SC	

Contraindications/ Precautions	**Contraindications:**
	• Known severe hypersensitivity to any component of the vaccine.
	• Anaphylactic or other allergic reaction to a previous dose of vaccine containing similar components.
	• Pregnancy.
	• Impaired immune functioning including those with primary or secondary immunodeficiencies. This could include but is not limited to:
	  ○ Congenital immunodeficiency states including defects in antibody production (agammaglobulinaemia or hypogammaglobulinaemia, isotype and IgG subclass deficiencies and common variable immunodeficiency).
	  ○ Persons who are immunocompromised due to blood dyscrasias, leukemia, lymphoma, Hodgkin's disease or generalized malignancy affecting the bone marrow or lymphatic system.
	  ○ Persons receiving immunoablative or immunosuppressive therapy (including high dose corticosteroids) which could include monoclonal antibodies (e.g. rituximab), alkylating agents, tumour necrosis factor (e.g. Enbrel), antimetabolites (e.g. methotrexate) or long-term steroids. For further information refer to:
	  ▪ the Canadian Immunization Guide
	  ▪ PADIS (Poison and Drug Information Service) Drug Information for Health Professionals
	• HIV-infected children (see *MMR Vaccine Biological Page and Varicella Vaccine Biological Page*). The use of Priorix-Tetra® or ProQuad® in asymptomatic individuals with HIV has not been studied (see *MMR Vaccine Biological Page and Varicella Vaccine Biological Page).*
	• Family history of congenital or hereditary immunodeficiency, unless the immune competence of the potential vaccine recipient is demonstrated.
	• Active untreated tuberculosis.
	• Solid Organ Transplant (SOT) recipients: See *Standard for Immunization of Transplant Candidates and Recipients.*
	• Child Hemapoetic Stem Cell Trasplant (HSCT) recipients: *See Standard for Immunization of Transplant Candidates and Recipients.*	

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	• Immune globulins or blood product received within the past 11 months. The interval between the receipt of IG or a blood product and the subsequent MMR-Var administration is dependent upon the IG or blood product received and the dosage administered. Refer to *Standard for Recommended Immunization Schedules* for spacing considerations. • Administration of another live vaccine within the past 1-3 months (see Spacing Considerations above). Refer to *Standard for Recommended Immunization Schedules* for spacing considerations. **Precautions:** • There is an increased risk of fever and febrile seizures 5-12 days after the first dose of MMR-Var vaccine in children 12-47 months of age as compared to MMR and varicella vaccine given separately. However, this risk is highest in children ages 12-23 months. • Research suggests that children with a personal or family (i.e. sibling or parent) history of seizures of any etiology including febrile or epilepsy are at increased risk of febrile seizures. Therefore, the following information should be discussed with parents/caregivers: o The risk for fever and potential for febrile seizures is higher with the first dose (given between 12-47 months) of combined MMR-Var vaccine than MMR and varicella vaccines given separately. o MMR and varicella vaccines can be offered separately. o If the parent/caregiver decides to proceed with combined MMR-Var vaccine they should be counselled to monitor the child for fever. o There is no indication of an increased risk after the second dose of MMR-Var. • Egg allergy, including anaphylaxis, is not a contraindication to immunization with MMR-Var vaccine as the amount of egg protein found in the vaccine is not felt to be enough to cause an allergic reaction. Observation for 30 minutes post immunization is recommended for clients who have experienced anaphylaxis to eggs. • The use of MMR-Var in children who suffered thrombocytopenia after a first dose of live measles, mumps, and rubella vaccines should be carefully evaluated in terms of risk-benefit. Individuals, who develop vaccine-associated thrombocytopenia, should be referred to their physician for serology to assess immunity to measles, mumps and rubella and to determine the need for vaccine. A second dose of vaccine should only be given if non-immune and after consultation with zone MOH/designate. • Avoid the use of salicylates for 6 weeks after vaccination if possible. However, children on long term salicylate therapy are at a higher risk of Reye syndrome following wild varicella and should be considered for immunization with close subsequent monitoring. Medical consultation is recommended before proceeding with immunization in children on salicylate therapy. • Individuals on long term systemic antiviral therapy (e.g., acyclovir, valacyclovir or famciclovir) should discontinue their antivirals at least 24 hours before administration of vaccine and for up to 14 days after administration. Consult with individual's physician before immunizing. • Immunization with a measles-containing vaccine can suppress tuberculin reactivity resulting in false negative results. If tuberculin skin testing is required, it should be done on the same day as immunization with a measles-containing vaccine or delayed for at least four weeks after immunization. See *Tubersol Biological Page.* • Measles-containing vaccines are contraindicated in individuals with active, untreated tuberculosis as a precautionary measure. Tuberculosis may be exacerbated by natural measles infection, but there is no evidence that measles vaccine has the same effect. • If a vaccine recipient develops a varicella-like rash, the rash should be covered and direct contact with susceptible high-risk individuals should be avoided for the duration of the rash.	

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	Note: A history of contact dermatitis to neomycin is not a contraindication.	
Possible Reactions	**Common:** • Pain, redness, swelling, ecchymosis, and rash at injection site • Fever and/or rash appearing between the 6th and 23rd day following immunization **Note:** Following the administration of the first dose of MMR-Var higher incidences of fever (approximately 1.5 fold) were observed when compared to the concomitant administration of MMR and Varicella vaccines at separate injection sites. • Rash (measles-like, rubella-like and varicella-like) – if vaccine recipient develops a varicella-like rash it should be covered when possible and direct contact with susceptible high risk individuals should be avoided for the duration of the rash. High risk individuals include immunocompromised individuals, pregnant woman without a history of disease or negative varicella serology and newborn infants of mothers with no documented history of disease or negative varicella serology. • Diarrhea, vomiting • Irritability **Uncommon:** • Induration, warmth, mass/lump at injection site • Lymphadenopathy • Parotid gland enlargement • Lethargy, malaise, fatigue, insomnia, somnolence • Anorexia, decreased appetite • Crying, nervousness • Gastroenteritis • Ear infection/otitis, nasopharyngitis, pharyngitis, rhinitis • Febrile convulsions • Urticaria **Rare:** • Anaphylaxis • Cough, bronchitis, wheezing • Arthritis, arthralgia 1-3 weeks following immunization • Ataxia • Headache • Conjunctivitis, tearing, visual discomfort • Flushing • As with any immunization, unexpected or unusual side effects can occur. Refer to the product monograph for more detailed information.	
Pregnancy	Live vaccines are contraindicated in pregnant women. **Note:** This vaccine is not licensed for individuals 13 years of age and older and therefore should not be applicable to the majority of women of child-bearing potential. However, MMR-Var vaccine is contraindicated if pregnant and pregnancy should be avoided for at least one month following immunization.	
Lactation	This vaccine is not licensed for individuals 13 years of age and older and therefore should not be applicable to the majority of breastfeeding women. Adequate human data on the use of MMR-Var during breastfeeding is not available.	
Composition	Each 0.5 mL dose of reconstituted vaccine contains: • Not less than $10^{3.0}$ $CCID_{50}$ of Schwarz measles strain • Not less than $10^{4.4}$ $CCID_{50}$ RIT 4385 mumps strain (derived from Jeryl Lynn strain)	Each 0.5 mL dose of reconstituted vaccine contains: • Not less than 3.00 $\log_{10}$ $TCID_{50}$ measles virus (derived from Ender's attenuated Edmonston strain)

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	• Not less than $10^{3.0}$ CCID $_{50}$ of Wistar RA 27/3 rubella virus strain • Not less than $10^{3.3}$ OKA varicella virus strain • Amino acids for injection • Lactose • Mannitol • Neomycin sulphate • Sorbitol • Trace amounts of egg protein (measles and mumps viruses grown in chick embryo cells) • Sterile water for injection (diluent)	• Not less than 4.30 $\log_{10}$ $TCID_{50}$ mumps virus (Jeryl Lynn [B level] strain) • Not less than 3.00 $\log_{10}$ $TCID_{50}$ rubella virus (Wistar RA 27/3 propagated in WI-38 human diploid lung fibroblasts) • Not less than 3.99 $\log_{10}$ PFU varicella virus (Oka/Merck strain propagated in MRC-5 cells) • Sucrose (no more than 20 mg) • Hydrolyzed gelatin (11 mg) • Urea (2.5 mg) • Sodium chloride (2.3 mg) • Sorbitol (16 mg) • Monosodium L-glutamate (0.38 mg) • Sodium phosphate (1.4 mg) • Recombinant human albumin (0.25 mg) • Sodium bicarbonate (0.13 mg) • Potassium phosphate (94 mcg) • Potassium chloride (58 mcg) • Neomycin (5 mcg) • Residual components of MRC-5 cells including DNA and protein • Measles and mumps viruses propagated in chick embryo cell culture • Sterile water for injection (diluent)
Blood/Blood Products	• Does not contain blood/blood products however the rubella and varicella virus is grown in MRC-5 human diploid cell culture.	• Human albumin • Rubella virus propagated in WI-38 human diploid lung fibroblasts. • Varicella virus propagated in human diploid MRC-5 cells
Bovine/Porcine Products	• Contains lactose derived from milk. Bovine serum is used in the early stages of manufacturing. • Porcine products are used in the early stages of manufacturing.	• 0.5 mcg bovine serum albumin.
Latex	Does not contain latex	Does not contain latex
Interchangeability	MMR-Var vaccine may be given to susceptible individuals 12 months up to and including 12 years of age who have previously been immunized with another measles, mumps, rubella or varicella containing vaccine and require a second measles, mumps, rubella and varicella vaccine. See schedule section for spacing considerations.	
Administration with Other Products	• See schedule section for recommended intervals between all measles, mumps, rubella and varicella vaccines. • With the exception of Yellow Fever vaccine, MMR-Var can be administered simultaneously with other live vaccines or separated by an interval of at least 4 weeks. ○ Recent limited data suggest it may be preferable for children aged 12 months up to and including-23 months of age to receive MMR-Var and **Yellow Fever** vaccine **at least 30 days apart** if time permits, because of lower seroconversion rates for mumps, rubella, and yellow fever in those immunized simultaneously than in those immunized 30 days apart. The study did not include infants younger than	

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	12 months of age, but it is reasonable to follow the same guidance for infants under 12 months of age. ○ For individuals 2 years of age and older MMR-Var can be administered simultaneously with Yellow Fever vaccine or separated by an interval of at least 4 weeks. • LAIV/QLAIV may be administered any time before or after the administration of other live attenuated or inactivated vaccines. ○ Specialists recommending alternate spacing for specific high risk individuals may be accommodated on a case by case basis. • May be given at the same time as other inactivated and live vaccines using a separate needle and syringe for each vaccine. • The same limb may be used if necessary, but different sites on the limb must be chosen. • Tuberculin skin tests should be given either before or at the same time as MMR-Var vaccine; otherwise, the tuberculin skin test should be delayed for 4 weeks following MMR-Var vaccine. • Immune globulins (IG) and antibody-containing blood products cannot be given concurrently with live vaccines and need to be separated by specified time frames depending upon the dosage and the biological. MMR-Var vaccine should be given at least 14 days prior to administration of an IG preparation or blood product, or delayed until the antibodies in the IG preparation or blood product have degraded. If the interval between administration of vaccine and subsequent administration of an IG preparation or blood product is less than 14 days, the vaccine dose should be repeated after the recommended interval. See Standard for Recommended Immunization Schedules for spacing considerations.	
Appearance	• Diluent: ○ clear, colourless • Vaccine prior to administration: ○ whitish to slightly pink coloured cake or powder (pellet) • Reconstituted vaccine: ○ clear peach to fuchsia pink (bright pink) coloured solution due to minor variations of its pH. This is normal and does not impair performance of the vaccine.	• Diluent: ○ sterile water, preservative free • Vaccine prior to administration: ○ white to pale yellow compact crystalline plug • Reconstituted vaccine: ○ clear pale yellow to light pink liquid
Storage	• Store at + 2º C to +8º C in its original box • Must be protected from light • Do not freeze • Do not use beyond the labeled expiry date • Diluent may be stored at room temperature or +2º C to +8º C. • Reconstituted vaccine should be used as soon as possible. Discard if not used within 30 minutes (ProQuad®).	
Vaccine Code	MMR-Var	
Antigen Code	Measles - MEA Mumps - MU Rubella - RUB Varicella - VZ	
Licensed for	• Children 9 months of age up to and including 12 years of age. • In Alberta MMR-Var is not used for children less than 12 months of age as they may not respond sufficiently to the measles component of the vaccine due to persistence of maternal antibody.	• Children 12 months of age up to and including 12 years of age.

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Program Notes:

- September 1, 2010: MMR-Var vaccine was introduced into the routine childhood immunization schedule at the 12 month immunization appointment.
- August 1, 2012: Children born on or after August 1, 2005 became eligible to receive 2 doses of varicella vaccine. With 2 doses of MMR vaccine and 2 doses of varicella vaccine recommended in the routine schedule as of August 1, 2012, MMR-Var became the vaccine of choice at the 12 month and 4-6 year immunization appointments.
- January 2015: MMR-Var (Priorix-Tetra®) recommended for SOT candidates beginning at 9 months of age.
- September 1, 2018: Children born August 1, 2012 or later with a verbal history of chicken pox disease became eligible to receive varicella vaccine as they present in child health clinic.
- December 1, 2018: MMR-Var recommended for HSCT recipients.
- August 1, 2020: MMR-Var contraindicated for HSCT recipients.
- January 1, 2021: MMR-Var second dose offered at 18 months instead of 4 years of age.

Related Resources:

- Measles, Mumps, Rubella and Varicella Vaccine Information Sheet (104507).

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