Measles, Mumps, Rubella and Varicella Vaccine

BIOLOGICAL PAGE

Alberta Health Services
Communicable Disease Control

Section 7	Biological Product Information	**Standard # 07.271**	
Created and approved by	Provincial Immunization Program Standards and Quality		
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	Priorix-Tetra	**ProQuad**
Manufacturer	GlaxoSmithKline Inc.	Merck Canada Inc.
Classification	Live, attenuated.	
Areas where measles is circulating in Canada	See the "Travel advice" section at Measles | Alberta.ca.	

Indications for Provincially Funded Vaccine	**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.
	  ▪ Offer varicella-containing vaccine to children with a history of chickenpox disease occurring prior to 12 months of age.
	  ▪ For children with laboratory confirmed varicella disease (positive varicella PCR/NAT swab results) 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 1 year of age and older will not be offered varicella-containing vaccine at this time.
	• Children travelling to or through areas where measles is circulating in Canada and to all countries outside of Canada should have two doses of measles-containing vaccine with the appropriate minimum interval between doses dependent upon the measles-containing vaccine used.
	Note:
	• 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 or through areas where measles is circulating in Canada.
	  ○ Those travelling to any country outside of Canada.
	Scheduling Considerations:
	  ○ If time allows, give the second dose on or after 15 months of age.
	  ○ If MMR-Var is given, this dose is considered adequate and counts as the child's second dose of MMR and varicella vaccine.
	  ○ If MMR vaccine is given, offer the child varicella vaccine at their 18-month 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.	

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	• See MMR Vaccine Biological Page and Varicella Vaccine Biological Page for detailed eligibility information for each vaccine.
	• In Alberta, MMR-Var vaccine is not routinely recommended prior to 12 months of age. Repeat doses administered before this age at 12 months of age and older using the age-appropriate vaccine.
	• For children with high-risk conditions (including SOT and HSCT) refer to the 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.
	  ○ Use MMR or univalent varicella vaccines.
	• This vaccine is not indicated for individuals 13 years of age and older.
	  ○ Use separate MMR and univalent varicella vaccine for eligible individuals 13 years of age and older. See MMR Vaccine Biological Page and Varicella Vaccine Biological Page for detailed eligibility information for each vaccine.	

	Post Exposure:	
	Measles Post-Exposure for children 12 months up to and including 12 years of age • Susceptible contacts of a measles case should receive either MMR, MMR-Var or Immunoglobulin (IG) depending upon the time-lapse from exposure, age and health status. • Susceptible contacts (without contraindications) 12 months of age and older may receive measles-containing vaccine. The vaccine should be administered within 72 hours of exposure and should not be delayed pending serology results. This includes children between 12 and 18 months of age who have received one dose of vaccine and are considered up-to-date, ensuring the minimum interval since the previous dose. • If MMR-Var vaccine is contraindicated or if more than 72 hours since exposure have elapsed, Immunoglobulin (IG) may be indicated. See Immune Globulin Biological Page. • If MMR-Var vaccine is administered more than 72 hours after exposure, it may not provide protection against the current exposure but would offer protection against subsequent exposures. For disease investigation, contact assessment and reporting requirements, refer to Measles Disease-Specific Process.	
Schedule	**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:**	

Recommended Intervals for MMR and Varicella Containing Vaccines

Previous Vaccine Administered	Recommended Interval to Next Dose		
	MMR-Var	MMR	Varicella
MMR-Var	3 months	3 months	3 months
MMR	3 months	4 weeks	3 months
Varicella	3 months	3 months	6 weeks or 3 months[1]

1. An interval of 3 months between doses of varicella-containing vaccines is recommended for individuals under 13 years of age.

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	Note: • Children who receive their first dose of varicella-containing vaccine and at any point subsequently develop laboratory confirmed vaccine modified varicella disease (positive varicella PCR/NAT swab results) 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. • 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. • 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 1 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	None. • Both vaccines are safe and immunogenic in individuals 12 months of age up to and including 12 years of age. • Offer individuals with medical contraindications to one product 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. • Withdraw the entire contents of the vial once reconstituted 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 function 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.
	  ○ Recent treatment with the following categories of immunosuppressive therapies:
	  ▪ anti-B cell therapies (monoclonal antibodies targeting CD19, CD20 and CD22)	

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	▪ high-dose systemic corticosteroids ▪ alkylating agents ▪ antimetabolites ▪ tumor necrosis factor (TNF) inhibitors ▪ other biologic agents that are significantly immunosuppressive. • Children with HIV infection ○ 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 ○ See Precautions section for further details. • Child Solid Organ Transplant (SOT) candidates and recipients. • Child Hematopoietic Stem Cell Transplant (HSCT) recipients. • Administration of immune globulins and/or blood products 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. See Standard For Recommended Immunization Schedules. • Administration of another live vaccine within the past 1-3 months (see Spacing Considerations above). **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. This risk is highest in children ages 12-23 months. • Research suggests that children with a personal or family (such as a sibling or parent) history of seizures of any etiology including febrile or epilepsy are at increased risk of febrile seizures. Discuss the following information with parents/caregivers: ○ 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. ○ MMR and varicella vaccines can be offered separately. ○ Counsel the parent/caregiver to monitor the child for fever if they decide to proceed with combined MMR-Var vaccine. ○ 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. ○ 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. ○ Recommend serology for individuals who develop vaccine-associated thrombocytopenia to assess immunity to measles and rubella. ○ Administer a second dose of vaccine only if non-immune and after consultation with zone MOH/designate. • Avoid the use of salicylates for 6 weeks after immunization. Children on long term salicylate therapy are at a higher risk of Reye syndrome following wild type varicella disease and should be considered for immunization with close subsequent monitoring.	

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	○ Medical consultation is recommended before proceeding with immunization for children on salicylate therapy. • Consult with physician before immunizing individuals on long term systemic antiviral therapy such as acyclovir, valacyclovir or famciclovir. ○ Discontinue antivirals at least 24 hours before administration of vaccine. ○ Do not restart antiviral therapy until 14 days after immunization. • Immunization with a measles-containing vaccine can temporarily suppress tuberculin reactivity resulting in false-negative results. ○ Tuberculin skin testing can be done on the same day as immunization with a measles-containing vaccine or delayed for at least 4 weeks after immunization. • Measles-containing vaccines are contraindicated in individuals with active, untreated tuberculosis as a precautionary measure. ○ Consult with attending physician. ○ Tuberculosis may be exacerbated by natural measles infection, but there is no evidence that measles-containing vaccines have such an effect. ○ Anti-tuberculous therapy for active TB disease is advisable before administering measles-containing vaccines and it may be prudent to avoid vaccine in those with active TB disease until treatment is underway. • Transmission of measles, mumps and rubella vaccine viruses from vaccine recipients to susceptible contacts has not been documented following MMR-Var vaccine. • Transmission of varicella vaccine virus occurs rarely between healthy vaccine recipients who develop a varicella-like rash and their susceptible contacts. If a vaccine recipient develops a varicella-like rash, cover the rash and avoid direct contact with susceptible high-risk individuals for the duration of the rash. **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 measles rash appearing between the fifth and twelfth 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, cover it when possible and avoid direct contact with susceptible high-risk individuals for the duration of the rash. High-risk individuals include immunocompromised individuals, people who are pregnant without a history of disease or negative varicella serology and newborn infants of mothers with no documented history of disease or negative varicella serology. • Exanthema, eczema • Diarrhea, vomiting • Irritability • Upper respiratory infection, nasopharyngitis. **Uncommon:** • Lymphadenopathy • Parotid gland enlargement • Lethargy, malaise, fatigue, insomnia, somnolence	

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	• Anorexia, nausea, decreased appetite • Crying, nervousness • Gastroenteritis • Ear infection/otitis, pharyngitis, rhinitis, cough, respiratory/nasal congestion • Febrile convulsions • Urticaria. **Rare:** • Anaphylaxis, bronchitis, wheezing • Ear pain • Tonsillitis • Varicella • Viral gastroenteritis • 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	Do not use during pregnancy. • Advise people who could become pregnant to delay pregnancy for 4 weeks following immunization.	
Lactation	Do not use for people who are lactating and feeding their milk to infants or children. • It is unknown whether this vaccine is excreted in human milk. • Immunize susceptible individuals with a varicella-containing vaccine according to an age-appropriate schedule.	
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) • Not less than $10^{3.0}$ CCID $_{50}$ of Wistar RA 27/3 rubella** virus strain • Not less than $10^{3.3}$ PFU OKA varicella** virus strain • Amino acids for injection • Lactose • Mannitol • Sorbitol • Residual amounts of neomycin sulphate • Sterile water for injection (diluent). *Produced in chick embryo cells. ** Produced in MRC_5 human diploid cells.	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) • 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 • Hydrolyzed gelatin • Urea • Sodium chloride • Sorbitol • Monosodium L-glutamate • Sodium phosphate • Recombinant human albumin • Sodium bicarbonate • Potassium phosphate

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		• Potassium chloride • Neomycin • Sterile water for injection (diluent). *Produced in chick embryo cell culture. **Produced in human diploid lung fibroblasts.
Blood/Blood Products	Rubella and varicella viruses are grown in MRC_5 human diploid cell culture.	• Manufacturing process residual: human albumin. • Rubella virus propagated in WI-38 human diploid lung fibroblasts. • Varicella virus propagated in human diploid MRC-5 cells.
Bovine/Porcine Products	**Bovine Products:** • Contains lactose and galactose derived from bovine milk. • Fetal bovine serum is used as raw materials during routine manufacturing process. **Porcine Products:** • Trypsin (isolated from porcine pancreas) is used as raw materials during routine manufacturing process.	**Bovine Products:** • Manufacturing process residual: fetal bovine serum. **Porcine Products:** • Gelatin used in manufacturing originates from porcine skin collagen.
Latex	Does not contain latex.	
Interchangeability	MMR-Var vaccines may be used interchangeably. • Use the manufacturer recommended dose and schedule.	

Administration with Other Products	• See schedule section for recommended intervals between all measles, mumps, rubella and varicella vaccines.
	• MMR-Var can be administered simultaneously with other live vaccines or separated by an interval of at least 4 weeks.
	  ○ Exception: Yellow Fever vaccine.
	  ▪ Limited data suggest preferred spacing of 30 days between MMR-containing and Yellow Fever vaccine if time permits. This is because of lower seroconversion rates for mumps, rubella, and yellow fever in those immunized at the same time than in those immunized 30 days apart. However, it is important to ensure that travellers are immunized appropriately before travel, therefore co-administration of Yellow Fever vaccine and MMR-Var vaccine is acceptable.
	• 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.
	  ○ Use a separate needle and syringe for each vaccine.
	  ○ The same limb may be used if necessary, but use different sites on the limb.
	• Give tuberculin skin tests either before or at the same time as MMR-Var vaccine. If not possible, delay the tuberculin skin test for 4 weeks following MMR-Var vaccine.	

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	• Immune globulins (IG) and antibody-containing blood products cannot be given concurrently with live vaccines. They need to be separated by specified time frames depending upon the dosage and the biological. ○ Give MMR-Var vaccine at least 14 days prior to administration of an IG preparation or blood product, or delay until the antibodies in the IG preparation or blood product have degraded. ○ Repeat the vaccine dose if the interval between administration of vaccine and subsequent administration of an IG preparation or blood product is less than 14 days. Ensure adequate spacing between the doses of vaccine. ○ 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 + 2° C to +8° C in its original box • Protect from light • Do not freeze • Do not use beyond the labeled expiry date • Diluent may be stored at room temperature or at +2° C to +8° C • Use reconstituted vaccine as soon as possible ○ ProQuad: discard if not used within 30 minutes.	
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. **Off-license use:** • Second dose of MMR-Var given with less than a 3 month interval from the first dose. • A dose of MMR-Var given for post-exposure prophylaxis.	• Children 12 months of age up to and including 12 years of age. **Off-license use:** • Second dose of MMR-Var given with less than a 3 month interval from the first dose. • A dose of MMR-Var given for post-exposure prophylaxis.
Program Notes	• 2010 September 1: MMR-Var vaccine was introduced into the routine childhood immunization schedule at the 12 month immunization appointment.	

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	• 2012 August 1: 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. • 2015 January: MMR-Var (Priorix-Tetra®) recommended for SOT candidates beginning at 9 months of age. • 2018 September 1: 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. • 2018 December 1: MMR-Var recommended for HSCT recipients. • 2020 August 1: MMR-Var contraindicated for HSCT recipients. • 2021 January 1: MMR-Var second dose offered at 18 months instead of 4 years of age. • 2022 March 15: Updated to align with SOT and HSCT immunization guidelines – MMR-Var is not indicated or recommended for SOT and HSCT as there is limited data on the use of MMR-Var vaccine in these groups. • 2022 December 9: Priorix-Tetra is not currently available in Alberta. • 2024 March 28: Updated to indicate that this vaccine is no longer routinely offered to children between 4 and 6 years of age as a catch-up, because all children in this age group will now have been offered vaccine at 18 months of age. Identified areas where measles is circulating in Canada. • 2024 July 19: Updated the areas where measles is circulating in Canada section. • 2024 November 22: Updated the areas where measles is circulating in Canada section to include New Brunswick. • 2025 January 31: Updated the areas where measles is circulating in Canada section. • 2025 March 3: Updated to indicate that a second dose of MMR-Var given less than 3 months following the first dose is off-license. • 2025 March 14: Updated areas where measles is circulating in Canada section and MMR-Var included as an option for post-exposure prophylxis for individuals 12 months to 12 years of age. • 2025 March 24: Updated areas where measles is circulating in Canada section.	
Related Resources	Measles, Mumps, Rubella and Varicella Vaccine Information Sheet	

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