

MMR-Var

Measles-Mumps-Rubella-Varicella Combined Vaccine

Revision Date: November 20, 2018

Rationale for Update:

- Incorporated recommendations for children with history of febrile seizures.
- Minimum spacing between MMR and/or varicella containing vaccines updated.
- MMR-Var vaccine no longer contraindicated for HSCT recipients as per CIG.

Please consult the Product Monograph ^{1,2} for further information about the vaccine.		
	PRIORIX-TETRA®	ProQuad®
Manufacturer	GlaxoSmithKline Inc.	Merck Canada Inc.
Licensed use	Individuals 9 months of age up to and including 12 years of age. Infants younger than 12 months of age may not respond sufficiently to the measles component of the vaccine in part due to the persistence of maternal antibody: therefore MMR or MMR-varicella combined vaccine doses administered before 12 months of age should be repeated at 12 months of age or older.	Individuals 12 months of age up to and including 12 years of age.
Off-license use	None	
Indications for use of provincially funded vaccine	Healthy children 12 months up to and including 12 years of age. Notes: <ul style="list-style-type: none">• 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.^{3,4}<ul style="list-style-type: none">○ Children born August 1, 2012 or later with a history of chicken pox disease should be offered varicella containing vaccine as they present in child health clinic.○ 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.• Hematopoietic stem cell transplant (HSCT) recipients of See: Immunization for Child Hematopoietic Stem Cell Recipients• Solid Organ Transplant (SOT) candidates (9 months – 12 years of age): See:<ul style="list-style-type: none">○ Immunization for Children Expecting Solid Organ Transplant before 18 Months of Age and○ Immunization for Children Expecting Solid Organ Transplant after 18 Months of Age (Catch-up and Ongoing). <p>Note: Infant SOT candidates younger than 12 months of age should receive Priorix-Tetra® Vaccine.</p>	

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Dose	0.5 mL
Route	Subcutaneous
Schedule	<p>Children 12 months of age up to and including 12 years of age:</p> <ul style="list-style-type: none"> ❖ Dose 1: 12 months of age ❖ Dose 2: 4 – 6 years of age <p>Notes:</p> <ul style="list-style-type: none"> • The recommended interval between two doses of MMR and/or varicella containing vaccines is at least three months, however a four week interval can be used if rapid protection is required.³ • Any dose of MMR or MMR-Var vaccine administered before one year of age must be repeated after 12 months of age. • Parents who refuse the combined vaccine and wish to have the vaccines as separate components (MMR and univalent varicella vaccines) may be accommodated. • Children who received a single dose of varicella-containing vaccine and developed laboratory-confirmed varicella disease do not require the second dose of varicella-containing vaccine.³ • Children traveling to areas where measles is circulating in North America (Canada, USA and Mexico) and all countries outside of North America should have two doses of measles-containing vaccine with the appropriate minimum interval between doses dependent upon the measles-containing vaccine used.^{5,6}
Spacing between MMR-Var and Yellow Fever vaccine	Recent limited data suggest it may be preferable for children aged 12-23 months of age to receive MMR-containing and YF 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 12 months of age, but it is reasonable to follow the same guidance for infants under 12 months of age. ^{7,8}
Contraindications	<ul style="list-style-type: none"> • Known hypersensitivity to any component of the vaccine.^{1,2} • Anaphylactic reaction to a previous dose of vaccine containing measles, mumps, rubella and/or varicella. • Pregnancy. • Impaired immune function including those with primary or secondary immunodeficiencies.^{1,2,3} • HIV-infected children.³ See MMR vaccines and univalent varicella vaccines. • Immunosuppressive therapy (including high dose corticosteroids).^{1,2} • Family history of congenital or hereditary immunodeficiency, unless the immune competence of the potential vaccine recipient is demonstrated.³ • Active untreated tuberculosis³. • Solid organ transplant recipients: See: <ul style="list-style-type: none"> ▪ <u>Immunization for Children Expecting Solid Organ Transplant before 18 Months of Age</u> and ▪ <u>Immunization for Children Expecting Solid Organ Transplant after 18 Months of Age (Catch-up and Ongoing)</u>. • Recent (within the past 11 months) administration of immune globulins and blood products. 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.

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	Refer to Assessment Expected Prior to Vaccine Administration – Guidelines for Interval between Blood Products and Live Vaccines. See also Canadian Immunization Guide ³ – Blood products, human immune globulin and timing of immunization.
Precautions	<ul style="list-style-type: none"> • There is an increased risk of fever and febrile seizures 5 to 12 days after the first dose of MMR-Var vaccine in children 12 to 47 months of age as compared to MMR and varicella given separately.¹⁰ However, this risk is highest in children ages 12-23 months.^{2,3,9} • 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.¹¹ Therefore, the following information should be discussed with parents/caregivers: <ul style="list-style-type: none"> ▪ The risk for fever and potential for febrile seizures is higher with the first dose (given between 12 to 47 months) of combined MMR-Var vaccine than MMR and varicella vaccines given separately.^{3,10} ▪ MMR and varicella vaccines can be offered separately.^{1,10,11} ▪ If the parent/caregiver decides to proceed with combined MMR-Var vaccine they should be counselled to monitor the child for fever.^{10,11} ▪ There is no indication of an increased risk after the second dose of MMR-Var.^{1,12} • Egg allergy is not a contraindication to immunization with MMR-Var vaccine.^{1,2} See Assessment Expected Prior to Vaccine Administration. • Immunization with a measles-containing vaccine can temporarily suppress tuberculin reactivity resulting in false-negative results.³ 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.³ • The use of MMR-Var vaccine 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.^{1,2} Individuals who develop vaccine-associated thrombocytopenia should have serology to assess immunity to measles, mumps and rubella.¹³ A second dose of vaccine should only be administered if non-immune and after careful consideration of the risks and benefits of the vaccine. • Avoid the use of salicylates for six weeks after immunization if possible.^{1,2} Because adverse events have not been reported with the use of salicylates after varicella immunization, children with conditions requiring chronic salicylate therapy should be considered for immunization with close subsequent monitoring.³ Medical consultation is recommended before proceeding with immunization for children on salicylate therapy. • Children taking long-term antiviral therapy should discontinue these drugs (e.g., acyclovir, valacyclovir or famciclovir) if possible from at least 24 hours before administration of varicella-containing vaccine and should not restart antiviral therapy until 14 days after immunization.³ Medical consultation is recommended before proceeding with immunization. • If a vaccine recipient develops a varicella-like rash, the rash should be covered³ and direct contact with susceptible high-risk individuals (e.g., immunocompromised individuals) should be avoided for the duration of the rash.³ • Live attenuated influenza vaccine (LAIV) may be administered any time before or after the administration of live parenteral vaccines (MMR, MMR-Var and VZ).
Possible reactions	<p>Common Reactions:^{1,2}</p> <ul style="list-style-type: none"> • Pain, redness and swelling at the injection site. • Measles-like rash, rubella-like rash, varicella-like rash

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	<ul style="list-style-type: none"> • Irritability • Fever- higher incidence (approximately 1.5 fold) of fever was observed after the first dose when compared to the concomitant administration of MMR and Varicella vaccines at separate sites. • Diarrhea, vomiting <p>Uncommon Reactions:^{1,2}</p> <ul style="list-style-type: none"> • Lymphadenopathy, parotid gland enlargement, lethargy, malaise, fatigue, anorexia, decreased appetite, crying, insomnia, nervousness, rhinitis • Gastroenteritis • Ear infection/otitis, nasopharyngitis, pharyngitis • Febrile convulsions <p>Rare:</p> <ul style="list-style-type: none"> • Otitis media, seizures, cough, bronchitis • Allergic reactions and anaphylaxis <p>Additional adverse events following immunization reported through post-marketing surveillance include:^{1,2}</p> <ul style="list-style-type: none"> • Thrombocytopenia; vasculitis (including Henoch Schonlein purpura and Kawasaki syndrome); meningitis; orchitis; epididymitis; arthralgia/arthritis; encephalitis; cerebrovascular accident; cerebellitis; cerebellitis-like symptoms (including transient gait disturbance and transient ataxia); erythema multiforme, cellulitis, parotitis, aplastic anemia, Bell’s palsy, encephalitis/encephalopathy, acute disseminated encephalomyelitis (ADEM), Guillain-Barré syndrome (GBS), paraesthesia, polyneuritis, transverse myelitis, subacute sclerosing panencephalitis, aseptic meningitis, myalgia,, Stevens-Johnson syndrome, ophthalmologic conditions, bronchial spasm, bronchitis, epistaxis, hematochezia, mouth ulcer, erythema multiforme, purpura, pruritus. <p>Refer to <i>Adverse Events Following Immunization (AEFI), Policy for Alberta Immunization Providers</i>.¹⁴</p>
Pregnancy	Pregnancy should rarely be an issue as MMR-Var vaccine is recommended only for children younger than 13 years of age. However, MMR-Var vaccine is contraindicated if pregnant and pregnancy should be avoided for at least one month following immunization. ³
Lactation	Adequate human data on the use of MMR-Var vaccine during breastfeeding is not available. ^{1,2}
Program Notes	<ul style="list-style-type: none"> • 2010 September - MMR-Var was introduced into the routine childhood immunization schedule for 12 month olds. • 2012 August - MMR-Var second dose introduced for 4 – 6 year olds (i.e. children born August 1, 2005). • 2015 January - MMR-Var (Priorix-Tetra®) for SOT candidates beginning at 9 months of age. • 2018 September - Children with a verbal history of chicken pox disease are eligible to receive varicella containing vaccine as they present in child health clinic. (i.e. children born August 1, 2012 or later) • 2018 December 01 - MMR-Var recommended for HSCT recipients.

References

- ¹ GlaxoSmithKline Inc. (2017, August 11). Priorix-Tetra®: Combined measles, mumps, rubella and varicella vaccine, live, attenuated, Powder and solution for injection, Active immunizing agent. *Product Monograph*.
- ² Merck Canada Inc. (2018, July 4). ProQuad®: Measles, mumps, rubella and varicella vaccine, live. *Product Monograph*.
- ³ National Advisory Committee on Immunization. (2018). *Canadian Immunization Guide*. (Evergreen ed.). Ottawa, ON. Public Health Agency of Canada. <https://www.canada.ca/en/public-health/services/canadian-immunization-guide.html>.
- ⁴ National Advisory Committee on Immunization . (2015 Update). Varicella Proof of Immunity. An Advisory Committee Statement (ACS). <http://www.healthycanadians.gc.ca/publications/healthy-living-vie-saine/varicella-proof-immunity-2015-varicelle-preuve-immunite/alt/varicella-proof-immunity-2015-varicelle-preuve-immunite-eng.pdf>
- ⁵ Measles and Rubella Elimination Working Group – Public Health Agency of Canada. (2013). Guidelines for the prevention and control of measles outbreaks in Canada. *Canadian Communicable Disease Report*; 39 (ACS-3).
- ⁶ Alberta Health, Office of the Chief Medical Officer of Health. (2016, March 8). Updated Recommendations – Measles-containing Vaccine for Residents of Alberta Planning to Travel
- ⁷ Silva, J., Camcho, L., Siqueira, M. et al. (2011). Mutual interference on the immune response to yellow fever vaccine and a combined vaccine against measles, mumps and rubella. *Vaccine* 29 (2011) 6327-6334. www.sciencedirect.com/science/article/pii/S0264410X11007298
- ⁸ Centers for Disease Control and Prevention. (2018). *Yellow Book: Health Information for International Travel*. Oxford University Press. <https://wwwnc.cdc.gov/travel/yellowbook/2018/infectious-diseases-related-to-travel/yellow-fever>.
- ⁹ Schink, T., Holstiege, J., Kowalzik, F., Zepp, F. and Garbe, E. (2014). Risk of febrile convulsions after MMRV vaccination in comparison to MMR or MMR + V vaccination. *Vaccine*: 32 (645–650).
- ¹⁰ National Advisory Committee on Immunization . (2016 Update). Measles-Mumps-Rubella-Varicella Vaccine and Febrile Seizures An Advisory Committee Statement (ACS). <https://www.canada.ca/en/public-health/services/publications/healthy-living/update-measles-mumps-rubella-varicella-vaccine-febrile-seizures.html>
- ¹¹ American Academy of Pediatrics. (2018) *Red book: 2018 Report of the Committee on Infectious Diseases (31st ed.)*. Elk Grove Village, IL.
- ¹² Centers for Disease Control and Prevention. (2015). Varicella. In *Epidemiology and Prevention of Vaccine-preventable Diseases 13th ed.* (chap. 22). Retrieved October 24, 2018 from, <https://www.cdc.gov/vaccines/pubs/pinkbook/varicella.html>
- ¹³ Mantadakis, E., Farmaki, E. and Buchanan, G. R. (2010). Thrombocytopenic purpura after measles-mumps-rubella vaccination: a systematic review of the literature and guidance for management. *Journal of Pediatrics*, 156(4).
- ¹⁴ Alberta Health. (2018, December). *Adverse Events Following Immunization (AEFI), Policy for Alberta Immunization Providers*. <https://open.alberta.ca/dataset/d86b52a9-45f4-4948-8a06-53b2c045135e/resource/f2da2a7a-e350-4bab-b2c2-77677beeb22b/download/aip-adverse-events-following-immunization-policy.pdf>