

Measles, Mumps, Rubella and Varicella (MMRV) Vaccine Questions and Answers for Immunization Providers – December 2013

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1. When was the MMRV vaccine authorized for use?

PRIORIX-TETRA[®], manufactured by GlaxoSmithKline (GSK) Inc., was authorized for use in Canada on July 30th, 2007.¹ ProQuad[®], the comparable MMRV product from Merck, is not yet authorized for use in Canada but has been approved for use in the U.S. since 2005.²

2. What is the intended use of MMRV vaccine in BC?

Beginning July 2014, PRIORIX-TETRA[®] will be routinely offered at school entry (4-6 years of age), as since January 2012 the BC routine immunization schedule for 2nd dose MMR was changed from 18 months of age to school entry. Children who were 18 months of age in January 2012 will be turning 4 beginning July 2014. MMR and varicella vaccines will continue to be available in BC and children who do not require a 2nd dose of both MMR and varicella vaccines at school entry may be immunized with the vaccine they require.

Effective immediately, limited quantities of PRIORIX-TETRA[®] are being made available to BC health authorities to allow for one less injection in school-entry children eligible for both MMR and varicella vaccines. Children of this age may be presenting for school entry doses if they're from provinces where 2nd dose MMR is given at school entry or if they missed receiving their 2nd dose of MMR at 18 months of age. The Provincial CD Nurses requested that the MMRV product be made available earlier for this purpose, and GlaxoSmithKline now has sufficient quantity to meet BC's request.

Schedules in use in Canadian provinces/ territories are posted at this site:

<http://www.phac-aspc.gc.ca/im/ptimprog-progimpt/table-1-eng.php>

3. Who may receive the MMRV vaccine before July 2014?

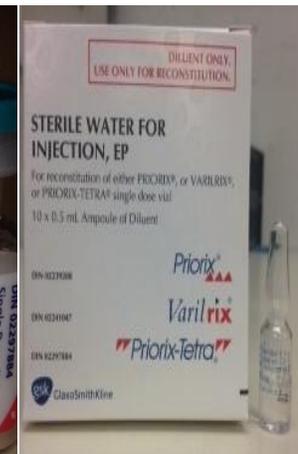
The eligible groups for this vaccine are listed under 'Indications' within the [BC Immunization Manual](#), Section VII page 36a. There are no priority groups within the eligible population.

4. What does the MMRV vaccine packaging look like?

Vaccine:



Diluent:



5. How is the MMRV vaccine supplied?

PRIORIX-TETRA® is supplied in single-dose vials containing lyophilized powder. It should be mixed with the diluent provided by the manufacturer, which is supplied in ampoules or prefilled syringes.¹ The diluent is provided in a separate carton containing 10 single dose ampoules and is labeled for use with PRIORIX-TETRA® as depicted in the picture above.

6. Why are we not using MMRV vaccine at 12 months of age?

The BC Communicable Disease Policy Advisory Committee reviewed the option of using PRIORIX-TETRA® at 12 months of age. This committee concluded that separate MMR and varicella vaccines are preferable in this age group because the vaccine is associated with an excess risk of febrile seizures about two-fold higher than that associated with MMR and varicella vaccines given separately. This risk would translate to about 20 excess febrile seizures each year in 1 year old children in BC. This risk is not seen at older ages such as school entry.

7. Can you tell me more about the risk of febrile seizures?

Febrile seizures are reported in 2% to 5% of children between the ages of 3 months and 5 years.^{1,3} They are frequently associated with underlying viral infections and may follow childhood immunizations.¹ Please direct interested parents to [HealthLinkBC's file #112 - Febrile Seizures](#) for more information.

8. Does the MMRV vaccine cause febrile seizures?

Studies have found that both MMRV vaccine products (the product in use in the U.S. is ProQuad® and product approved for use in Canada is PRIORIX-TETRA®) are associated with higher rates of fever in recipients of the 1st dose than observed among those receiving separately administered MMR and varicella vaccines. Clinical trials had not observed an excess of febrile seizures but consisted of numbers of subjects too small to observe a risk. An excess rate of febrile seizures has been observed in post-marketing U.S. studies using observational data as well as through Vaccine Safety Datalink. These studies of ProQuad® have found a two-fold risk of febrile seizures in 12-23 month old children following the 1st dose of this vaccine compared to separately administered MMR and varicella vaccines; this risk has been seen in the post-vaccine intervals of 7-10 days and 5-12 days and is in the range of 1 excess febrile seizure case per 2,300-2,600 recipients.^{4,5} This risk elevation has not been seen following the 2nd dose; as well, 97% of febrile seizures occur prior to 48 months of age.^{2,5}

The data for PRIORIX-TETRA® is more limited and is based on an unpublished study from Quebec following introduction of PRIORIX-TETRA® in that province. The Canadian Immunization Guide states:

“Experience with the MMRV vaccine available in Canada is more limited; however, one study showed an additional risk of febrile seizures with MMRV vaccine compared to MMR and univalent varicella vaccines given as two separate products administered concomitantly. The risk with the Canadian vaccine was smaller than the risk found with the US product. Close surveillance and further investigation are underway.”⁶

The Canadian product monograph for PRIORIX-TETRA® provides information about the risk of febrile seizures associated with the product. Only the most relevant excerpts are provided below; refer to the full product monograph for additional details:⁷

“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 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). This suggests one additional case of febrile convulsion per 2,747 subjects vaccinated with PRIORIX-TETRA® compared to matched control cohorts who received MMR or simultaneous, but separate MMR and varicella vaccination....”

REFERENCES:

- ¹ National Advisory Committee on Immunization. Statement on measles-mumps-rubella-varicella vaccine. *Canada Communicable Disease Report (CCDR)*. 2010; 36(ACS-9):1-22.
- ² Advisory Committee on Immunization Practices. Centres for Disease Control and Prevention. Use of Combination Measles, Mumps, Rubella, and Varicella Vaccine. *Morbidity and Mortality Weekly Report (MMWR)*. Recommendations and Reports. 2010; 59(RR03):1-12. Available at <http://www.cdc.gov/mmwr/preview/mmwrhtml/rr5903a1.htm>
- ³ Jones T, Jacobsen SJ. Childhood febrile seizures: overview and implications. *International Journal of Medical Science*. 2007;4(2):110–4.
- ⁴ Jacobsen S, Ackerson B, Sy L, Tran T, Jones T, Yao J, Xie F, Cheetham C, Saddier P. Observational safety study of febrile convulsion following first dose MMRV vaccination in a managed care setting. *Vaccine*. 2009; 27: 4656-4661.
- ⁵ Klein N, Fireman B, Yih W, Lewis E, Kulldorff M, Weintraub E, et al. Measles-Mumps-Rubella-Varicella Combination vaccine and the Risk of Febrile Seizures. *Pediatrics*. 2010; 126:e1-e8;originally published online June 29, 2010.
- ⁶ Public Health Agency of Canada. *Canadian Immunization Guide*. December 2012. Active Vaccines: Measles. Available from <http://www.phac-aspc.gc.ca/publicat/cig-gci/p04-meas-roug-eng.php>
- ⁷ GlaxoSmithKline Inc. Product Monograph PRIORIX-TETRA® Combined measles, mumps, rubella and varicella vaccine (live, attenuated). Mississauga (ON): 2013. Available from <http://www.gsk.ca/english/docs-pdf/product-monographs/Priorix-tetra.pdf>