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AT A GLANCE

Bivalent Omicron-Containing COVID-19 mRNA Vaccines

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Background

This document provides an overview of the characteristics of the bivalent Omicron-containing COVID-19 mRNA vaccines that have been authorized for use in Canada and an overview of the real-world evidence of vaccine effectiveness and safety of bivalent vaccines. It is intended for health care providers and public health partners.

Health Canada Authorized Bivalent Vaccine Products

Health Canada has authorized five bivalent Omicron-containing COVID-19 mRNA vaccines for use in Canada:

- Moderna Spikevax Original and Omicron BA.1 bivalent vaccine (50 mcg) and BA.4/5 bivalent vaccine (50 mcg) are authorized for use as a booster dose in individuals ≥18 years of age who have completed a primary series[1,2]
- Pfizer-BioNTech Comirnaty Original and Omicron BA.1 bivalent vaccine (30 mcg) and BA.4/5 bivalent vaccine (30mcg) are authorized for use as a booster dose in individuals ≥12 years of age[3,4]
- Pfizer-BioNTech Comirnaty COVID-19 vaccine Original and Omicron BA.4/5 vaccine (10 mcg) are authorized for use as a booster dose in individuals 5 years to 11 years of age[5]

Authorized Omicron-containing bivalent vaccines are expected to provide broad protection against Omicron variants and subvariants as compared to original mRNA COVID-19 vaccines.[6] The National Advisory Committee on Immunization (NACI) recommends the preferential use of bivalent Omicron-containing COVID-19 mRNA vaccines as a booster for authorized age groups over original formulation booster products.[6] NACI does not provide preferential recommendation for the use of BA.1 versus BA.4/5 bivalent booster vaccines or Moderna (50 mcg) versus Pfizer-BioNTech (30 mcg) products due to the absence of evidence to suggest a difference in protection among the different vaccines products or formulations.[6] Health Canada has not authorized bivalent Omicron-containing mRNA COVID-19 vaccines for use in a primary series at this time. Although authorized, Pfizer-BioNTech Comirnaty BA.1 bivalent COVID-19 vaccine has not been distributed in Canada and is not included in Ontario's 2022 COVID-19 vaccine program.

Moderna Spikevax Omicron-Containing Bivalent Vaccines

On September 1, 2022 and November 3, 2022, Health Canada granted full authorization to the bivalent Omicron-containing COVID-19 vaccines Moderna Spikevax BA.1[1] Bivalent and Moderna Spikevax BA.4/5[2] Bivalent vaccines, respectively. Detailed characteristics of the vaccines are outlined in Table 1.

Table 1: Characteristics of Moderna Spikevax Bivalent Omicron-containing COVID-19 mRNA Vaccines

Characteristic	Moderna Spikevax BA.1 Bivalent Vaccine (50 mcg)	Moderna Spikevax BA.4/5 Bivalent Vaccine (50 mcg)
Generic Name	mRNA-1273.214, elasomeran/imelasomeran[7]	mRNA-1273.222, elasomeran/davesomeran[8]
Antigen Component	Pre-fusion stabilized Spike (S) glycoprotein of original 2019 novel Coronavirus (SARS-CoV-2) AND Pre-fusion stabilized conformation variant of the SARS-CoV-2 Spike (S) glycoprotein Omicron B.1.1.529 [BA.1][7]	Pre-fusion stabilized Spike (S) glycoprotein of SARS-CoV-2 virus (Original) AND Pre-fusion stabilized Spike (S) glycoprotein of SARS-CoV-2 Omicron variant B.1.1.529 [BA.4/5][8]
Dosage and composition	0.5 mL (50 mcg dose): 25 mcg of original SARS-CoV-2 virus and 25 mcg of Omicron BA.1 variant[7]	0.5mL (50 mcg dose): 25 mcg of original SARS-CoV-2 virus and 25 mcg of Omicron B.1.1.529 [BA.4/5] variant[8]
Health Canada authorized indication for use and ages	Booster for ≥ 18 years of age[1] Not authorized or currently recommended for use in Canada as part of the primary series[3]	Booster for ≥ 18 years of age[6] Not authorized or currently recommended for use in Canada as part of the primary series[3]
Booster Dose Interval[a]	**Authorized interval:** 4 months after completing primary series or a previous booster dose[9] **Recommended interval as per NACI:** 6 months after previous COVID-19 vaccine dose or SARS-CoV-2 infection[10]	**Authorized interval:** 4 months after completion of a primary series and/or a previous booster dose[9] **Recommended interval as per NACI:** 6 months after previous COVID-19 vaccine dose or SARS-CoV-2 infection[10]

Characteristic	Moderna Spikevax BA.1 Bivalent Vaccine (50 mcg)	Moderna Spikevax BA.4/5 Bivalent Vaccine (50 mcg)
	Minimum interval as per NACI: 3 months may be considered in the context of heightened epidemiologic risk, evolving SARS-CoV-2 epidemiology, as well as operational considerations for the efficient deployment of the fall vaccine program. [10]	**Minimum interval as per NACI:** 3 months may be considered in the context of heightened epidemiologic risk, evolving SARS-CoV-2 epidemiology, as well as operational considerations for the efficient deployment of the fall vaccine program.[10]

[a] The authorized interval is the dosing schedule approved by Health Canada, based on evidence from clinical trials. The recommended interval is determined by NACI and is included in their recommendations following review of available data and based on expert opinion. The minimum interval is the shortest interval between doses in which an adequate immune response is expected.

Pfizer-BioNTech Comirnaty Omicron-Containing Bivalent Vaccines

On October 21, 2022, October 7, 2022 and December 9, 2022, Health Canada granted full authorization to the bivalent Omicron-containing COVID-19 vaccines Pfizer-BioNTech Comirnaty BA.1[3] Bivalent vaccine (30 mcg), Pfizer-BioNTech Comirnaty BA.4/5[4] Bivalent vaccine (30 mcg) and Pfizer-BioNTech Comirnaty BA.4/5 Bivalent vaccine (10 mcg) for ages 5 to 11 years[5], respectively. Pfizer-BioNTech Comirnaty BA.1 Bivalent vaccine (30 mcg) is not included in Ontario's 2022 COVID-19 vaccine program.

Table 2: Characteristics of Pfizer-BioNTech Bivalent Omicron-containing COVID-19 mRNA vaccines

Characteristic	Pfizer-BioNTech Comirnaty BA.4/5 Bivalent Vaccine (10 mcg)	Pfizer-BioNTech Comirnaty BA.4/5 Bivalent Vaccine (30 mcg)
Generic Name	BNT162b2 BA.1, tozinameran/riltozinameran[11]	BNT162b2 BA.4/5 tozinameran/famtozinameran[11]
Antigen Component	Pre-fusion stabilized Spike (S) glycoprotein of original SARS-CoV-2 AND Pre-fusion stabilized Spike (S) glycoprotein of SARS-CoV-2 Omicron variant lineages BA.4/5[11]	Pre-fusion stabilized Spike (S) glycoprotein of original SARS-CoV-2 AND Pre-fusion stabilized Spike (S) glycoprotein of SARS-CoV-2 Omicron variant lineages BA.4/5[b,11]
Dosage and composition	0.2 mL (10 mcg dose): 5 mcg original + 5 mcg Omicron BA.4/5[11]	0.3 ml (30 mcg dose): 15 mcg original + 15 mcg Omicron BA.4/5[11]

Characteristic	Pfizer-BioNTech Comirnaty BA.4/5 Bivalent Vaccine (10 mcg)	Pfizer-BioNTech Comirnaty BA.4/5 Bivalent Vaccine (30 mcg)
Health Canada authorized ages and indication for use	Booster for 5 years to 11 years of age[5]	Booster for ≥ 12 years of age[4]
Booster Dose Interval[c]	**Authorized interval:** 6 months following a primary series and/or previous booster dose[13] **Recommended interval as per NACI:** 6 months after previous COVID-19 vaccine dose or SARS-CoV-2 infection[10] **Minimum interval as per NACI:** 3 months may be considered in context of heightened epidemiologic risk, evolving SARS-CoV-2 epidemiology, as well as operational considerations for the efficient deployment of the fall vaccine program[10]	**Authorized interval:** 3 to 6 months following a primary series and/or previous booster dose[13] **Recommended interval as per NACI:** 6 months after previous COVID-19 vaccine dose or SARS-CoV-2 infection[10] **Minimum interval as per NACI:** 3 months may be considered in context of heightened epidemiologic risk, evolving SARS-CoV-2 epidemiology, as well as operational considerations for the efficient deployment of the fall vaccine program[10]

[b] The S-proteins of the SARS-CoV-2 Omicron variant lineages BA.4 and BA.5 are identical[13]

[c] The authorized interval is the dosing schedule approved by Health Canada, based on evidence from clinical trials. The recommended interval is determined by NACI and is included in their recommendations following review of available data and based on expert opinion. The minimum interval is the shortest interval between doses in which an adequate immune response is expected.

Real-World Evidence of Bivalent Vaccine Effectiveness and Safety

Bivalent Omicron-containing COVID-19 mRNA vaccines authorized by Health Canada underwent an independent drug review process which showed the vaccines to be safe and effective. Since the time of regulatory approval, real-world evidence of the safety and effectiveness of bivalent COVID-19 vaccines has emerged.

Vaccine Effectiveness

Three recent studies from the United States have examined the effectiveness of a bivalent vaccine booster dose in preventing SARS-CoV-2 associated outcomes. In the United States, only BA.4/5 Omicron-containing vaccines have been used and monovalent vaccines are no longer authorized as booster doses. As a result, studies from the United States cannot compare BA.1 with BA.4/5 containing bivalent vaccines and cannot compare monovalent with bivalent vaccines when used as booster doses during the fall of 2022.

- **Symptomatic COVID-19:** In this study, adults who had previously received 2, 3 or 4 monovalent vaccine doses were found to have a reduction in symptomatic SARS-CoV-2 infection after a booster dose of BA.4/5 bivalent mRNA vaccine as compared to those who did not receive a bivalent booster dose. For those who had received their last monovalent vaccine dose 4-5 months prior to their bivalent booster, symptomatic infection was reduced by 43%, 36% and 33% for those aged 18-49 years, 50-64 years and 65 years and older, respectively.[14]

- **COVID-19 associated emergency department (ED)/urgent care (UC) visits and hospitalizations:** In this study of immunocompetent adults aged ≥18 years, individuals who received a BA.4/5 bivalent booster dose experienced an additional 31% protection against ED/UC encounters when compared to those with monovalent vaccination only (2, 3, or 4 doses with last dose 2 to 4 months earlier). Similarly, individuals who received a BA.4/5 bivalent booster dose experienced an additional 38% protection against hospitalizations when compared to those with monovalent vaccination only (2, 3, or 4 doses with last dose 5 to 7 months earlier).[15]

- **COVID-19 hospitalization among older adults:** In this study of immunocompetent adults 65 years of age and older, individuals who received a booster dose using a BA.4/5 bivalent Omicron-containing mRNA vaccine experienced an additional 73% protection against COVID-19 hospitalization as compared to those who had been previously vaccinated with monovalent mRNA COVID-19 vaccines only (at least two monovalent vaccine doses, with the last vaccine dose given at least 2 months prior to illness onset).[16]

Vaccine Safety

According to data from the United States, early safety findings from v-safe and the Vaccine Adverse Events Reporting System (VAERS) following the administration of more than 22 million bivalent booster doses to individuals during the first 7 weeks of its availability are similar to the safety data previously reported for booster doses of the monovalent vaccine.[17]

- The frequency of health impacts and injection site and systemic reactions reported by individuals ≥ 12 years who received an age-appropriate bivalent booster vaccination are similar to those reported by adults ≥ 50 years after receiving their first and second monovalent booster doses
    - Similar to those reported after first and second monovalent boosters among individuals ≥50 years, most reports of adverse reactions among individuals ≥ 12 years after receiving a bivalent booster dose were non-serious
    - There were 5 reports of myocarditis and pericarditis in the first 7 weeks of bivalent booster availability
    - Continual safety monitoring is occurring during the course of the bivalent booster vaccination program
- In Ontario, over one million doses of Pfizer BioNtech Comirnaty bivalent BA.4/5 vaccine and over one million doses of Moderna Spikevax bivalent BA.1 vaccine have been administered. At the time of writing, AEFI reporting rates temporally related with receipt of COVID-19 bivalent vaccines are observed to be lower than the reporting rates for AEFIs temporally related with receipt of COVID-19 monovalent vaccines.[18] Ontario continues to monitor all AEFIs reported following receipt of COVID-19 immunizations.

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