## COVID-19 Vaccine – mRNA Pfizer BioNTech Bivalent (Original and Omicron BA.4/BA.5) Frozen Vaccine (Comirnaty) Biological Page

<table>
<thead>
<tr>
<th>Section 7: Biological Product Information</th>
<th>Standard #: 07.218</th>
</tr>
</thead>
<tbody>
<tr>
<td>Created by: Provincial Immunization Program</td>
<td></td>
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<tr>
<td>Approved by: Provincial Immunization Program</td>
<td></td>
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<tr>
<td>Approval Date: October 24, 2022</td>
<td>Revised: June 30, 2023</td>
</tr>
</tbody>
</table>

### COVID-19 Vaccine – mRNA Pfizer BioNTech Bivalent (Original and Omicron BA.4/BA.5) Frozen Vaccine (Comirnaty) Adult Formulation 12 Years of Age and Older

#### Gray Cap – Dilution NOT Required

**Manufacturer** Pfizer-BioNTech

**Biological Classification**
- mRNA (new technology) – nucleoside-modified messenger RNA (modRNA) encoding the viral spike glycoprotein (S)
- Formulated in lipid nanoparticles (LNPs)

**Indications for Provincially Funded Vaccine**
- Booster dose for individuals 12 years of age and older after completion of a primary series and/or a previous mRNA original (non-bivalent) or non-mRNA booster dose of COVID-19 vaccine (regardless of vaccine type).
- Additional booster dose for individuals 18 years of age and older who have received one dose of an Omicron-containing bivalent booster vaccine and who are at an increased risk of severe outcomes from COVID-19 (see below for eligibility).

**Preferred Use** N/A

**Dose** Booster 0.3 mL (30 mcg)

**Route** IM in the deltoid or vastus lateralis muscle

**Schedule** Booster dose

All individuals 12 years of age and older are eligible for a single bivalent booster dose:
- At least 6 calendar months after completion of a primary series (regardless of vaccine type), or an mRNA original (non-bivalent) or non-mRNA booster dose, or infection.
  - If an individual received an mRNA original (non-bivalent) or non-mRNA booster on or after September 21, 2022 and an Omicron-containing bivalent booster dose is refused, no additional original (non-bivalent) or non-mRNA booster doses are to be offered.

Additional booster dose

The following individuals are eligible for an additional Omicron-containing bivalent COVID-19 booster dose:
- Individuals 65 years of age and older
- Individuals 18 years of age and older who are residents of a long term care facility or other congregate care living setting.
- Individuals 18 years of age and older who are moderately to severely immunocompromised (due to underlying condition or treatment).
- At least 6 calendar months after previous Omicron-containing bivalent booster dose or infection.
## Immunization Program Standards Manual

**Provincial Population & Public Health**

<table>
<thead>
<tr>
<th>COVID-19 Vaccine – mRNA Pfizer BioNTech Bivalent (Original and Omicron BA.4/BA.5 – Frozen Vaccine (Comirnaty)) Adult Formulation 12 Years of Age and Older</th>
</tr>
</thead>
<tbody>
<tr>
<td>○ A shortened interval of at least 3 calendar months between the previous COVID-19 vaccine dose (or infection) and the Omicron-containing bivalent booster may be considered for individuals who are living in a long-term care facility or in other congregate care living settings. However, a longer interval of at least 6 calendar months leads to a better immune response against COVID-19 that is also expected to last longer, because it allows time for the immune response to mature in breadth and strength. Notes:</td>
</tr>
<tr>
<td>- Applicable congregate care settings include, but are not limited to, all private and public long-term care facilities, licensed supportive living facilities and seniors’ lodges including First Nations elder care lodges.</td>
</tr>
<tr>
<td>- Documentation of immunocompromising conditions is not required. Individuals who identify themselves as meeting at least one of the criteria below could be offered the additional Omicron-containing bivalent booster dose.</td>
</tr>
<tr>
<td>- Immunization for immunocompromised individuals should occur at a time when the individual is most likely to mount an immune response. Clients are recommended to consult with their physician regarding the timing of immunization based on their individual treatment and unique circumstances, respecting the NACI recommended minimum spacing of at least 6 months since last COVID-19 dose (or infection). See exception below for HSCT / CAR T-cell therapy recipients.</td>
</tr>
<tr>
<td>- Hematopoietic stem cell transplant (HSCT) recipients who received COVID-19 vaccine pre-transplant are eligible to restart their COVID-19 vaccine series beginning at least 3 months post-transplant. Consultation with their HSCT physician is not necessary as long as the initial clearance letter has been received to proceed with inactivated vaccines.</td>
</tr>
<tr>
<td>- CAR T-cell therapy recipients without a prior history of HSCT who received COVID-19 vaccine pre-CAR T-cell therapy are eligible to restart their COVID-19 vaccine series, beginning at least 3 months post-CAR T-cell therapy. Consultation with their physician is not necessary as long as a clearance letter has been received to proceed with inactivated vaccines.</td>
</tr>
<tr>
<td>- If requested by their specialist, a shortened interval of at least 3 calendar months between the previous COVID-19 vaccine dose (or infection) and the Omicron-containing bivalent booster doses may be provided for HSCT and/or CAR T-cell therapy recipients. A written request from the specialist is not required if the client provides verbal confirmation. For HSCT recipients whose post-HSCT vaccine series were interrupted by CAR T-cell therapy, see the following HSCT guidance:</td>
</tr>
<tr>
<td>- Principles of Immunization in Hematopoietic Stem Cell Transplant Recipients and Solid Organ Transplant Recipients</td>
</tr>
<tr>
<td>- Immunization for Adult HSCT Recipients</td>
</tr>
<tr>
<td>- Immunization for Child HSCT Recipients</td>
</tr>
</tbody>
</table>

### Immunocompromising conditions that place individuals at high risk of severe outcomes due to COVID-19

- Specific immunocompromising conditions that make an individual eligible for an additional Omicron-containing bivalent booster dose include:
  - Solid organ transplant recipients — pre-transplant and post-transplant
  - Hematopoietic stem cell transplants recipients — pre-transplant and post-transplant while in immunosuppressed state (post-HSCT individuals are generally considered to be immunocompetent after 3 years as long as they are not on immunosuppressive drugs)
  - Individuals with malignant hematologic disorders and non-hematologic malignant solid tumors prior to receiving or receiving active treatment which includes chemotherapy, targeted therapies, and immunotherapy or having received previous COVID-19 vaccines while on active treatment (does not include
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- Individuals receiving solely hormonal therapy, radiation therapy or a surgical intervention).
  - Individuals with chronic kidney disease on peritoneal dialysis or hemodialysis.
  - Individuals receiving chimeric antigen receptor (CAR) T-cell therapy.
  - Individuals on:
    - long term high-dose systemic steroid treatment (prednisone equivalent of ≥ 2 mg/kg/day or 20 mg/day if weight > 10 kg, for ≥ 14 days), or
    - alkylating agents, or
    - Individuals on anti-B-cell therapies – including anti-CD19, anti-CD20, anti-CD22 and anti-CD52 monoclonal antibodies (such as rituximab, ocrelizumab, and ofatumumab), or
    - antimetabolites (e.g., methotrexate, azathioprine, mycophenolate), or
    - tumor-necrosis factor (TNF) inhibitors (e.g., adalimumab, certolizumab, etanercept, golimumab, infliximab), or
    - other agents that are significantly immunosuppressive at clinicians’ discretion
  - HIV-infected individuals without viral suppression or those with acquired immunodeficiency syndrome (AIDS).
  - Individuals with moderate to severe primary immunodeficiency (e.g., DiGeorge syndrome, Wiskott-Aldrich syndrome).

Contraindications/Precautions

Contraindications:
- Known severe hypersensitivity to any component of the vaccine.
- Two non-medicinal ingredients in the vaccine that have been associated with allergic reactions in other products:
  - Polyethylene glycol (PEG). The potential allergen may be found in bowel preparation products for colonoscopy, laxatives, cough syrup, cosmetics, contact lens care solutions, skin products and some food and drinks.
  - Tromethamine (trometamol or Tris) – component found in contrast media, oral and parenteral medications.
- Anaphylaxis to a previous dose of COVID-19 mRNA vaccine may not be an absolute contraindication. See COVID-19 Immunization for Individuals with Allergies and Other Health Conditions for recommendations.

Precautions:
- Individuals who have had a serious allergic reaction to another vaccine, drug or food should talk to their health care provider before receiving the vaccine.
- Individuals receiving anticoagulant therapy or those with a bleeding disorder that would contraindicate intramuscular injection should not be given the vaccine unless the potential benefit clearly outweighs the risk of administration.
- Administration should be postponed in individuals suffering from acute severe febrile illness.
- There are no clinical data currently available for the use of Pfizer bivalent (Original & Omicron BA.4/5) vaccine. However, indirect data (clinical and post-market safety data from Pfizer-BioNTech Comirnaty BA.1 Bivalent and Comirnaty original (non-bivalent) mRNA vaccine, respectively) suggest that Pfizer-BioNTech Comirnaty BA.4/5 Bivalent (30 mcg) will likely be well tolerated with a similar safety profile to Comirnaty original (non-bivalent) (30 mcg) and Comirnaty BA.1 Bivalent (30 mcg), when used as a booster dose.

Myocarditis/Pericarditis
- There were no vaccine-related cases of myocarditis or pericarditis in the Pfizer bivalent BA.1 vaccine clinical trial. However, given the number of participants enrolled in the bivalent clinical trial it is unlikely that rare adverse events would be detected.
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- Very rare cases of myocarditis and/or pericarditis following immunization with original (non-bivalent) mRNA COVID-19 vaccines have been reported during post-authorization use. However, the risk of myocarditis and/or pericarditis following a first and second booster dose of an original (non-bivalent) mRNA COVID-19 vaccine appears to be lower than the risk following the second dose of the primary series.
- Anyone receiving an mRNA COVID-19 vaccine should be informed of the risk of myocarditis and pericarditis and advised to seek medical attention if they develop related symptoms including shortness of breath, chest pain, or the feeling of a rapid or abnormal heart rhythm.
- Healthcare professionals are advised to consider the possibility of myocarditis and/or pericarditis in their differential diagnosis if individuals present with chest pain, shortness of breath, palpitations or other signs and symptoms of myocarditis and/or pericarditis following immunization with an mRNA COVID-19 vaccine.
- Generally, deferral of COVID-19 immunization is not required for those with a prior history of myocarditis or pericarditis that is unrelated to COVID-19 mRNA vaccines.
  - If these individuals have questions or concerns about their prior history of myocarditis or pericarditis and immunization, it is recommended that individuals consult with their clinician. However, consultation with a clinician is not required to receive COVID-19 vaccines.
- Individuals with a history compatible with pericarditis within 6 weeks of receiving a dose of an mRNA COVID-19 vaccine, who either had no cardiac workup or who had normal cardiac investigations, can be re-immunized when they are symptom free and at least 90 days have passed since previous immunization.
- In most circumstances, further doses of mRNA COVID-19 vaccines should be deferred among people who experienced myocarditis (with or without pericarditis) within 6 weeks of receiving a previous dose of an mRNA COVID-19 vaccine.
  - However, further doses may be offered if individuals with confirmed myocarditis or pericarditis with abnormal cardiac investigation choose to receive another dose of vaccine after discussing the risks and benefits with their clinician. Informed consent should discuss the unknown risk of recurrence of myocarditis and/or pericarditis following additional doses of COVID-19 vaccine in individuals with a history of confirmed myocarditis and/or pericarditis after a previous dose of mRNA COVID-19 vaccine.

### Pregnancy

- A COVID-19 vaccine booster should be offered at any stage of pregnancy, regardless of the number of previous doses received.
- The safety and efficacy of this bivalent COVID-19 mRNA vaccine in pregnant women have not yet been established in the clinical trial. However, data available so far on original (non-bivalent) mRNA vaccines administered in pregnancy did not detect safety signals from post-marketing surveillance. The Omicron-containing bivalent COVID-19 mRNA vaccine can be offered to pregnant individuals as they are more at risk for severe illness from COVID-19 compared with non-pregnant individuals.
  - Evidence to date shows that COVID-19 immunization during pregnancy is safe and does not increase risk for miscarriage, stillbirth, low birth weight, preterm birth, NICU admission, or other adverse pregnancy/birth outcomes.
  - It is recommended that individuals consult with their primary health care provider or obstetrician for any vaccine related questions or concerns.
  - However, consultation with a primary health care provider or obstetrician is not required to receive COVID-19 vaccine.

**Additional resources:**

[Society of Obstetricians and Gynecologists of Canada Statement on COVID-19 Immunization in Pregnancy](#)
### Lactation
- It is unknown whether this vaccine is excreted in human milk as breastfeeding individuals were excluded from the initial trials. A risk to the newborns/infants cannot be excluded.
- However, based on how this vaccine works, the Omicron-containing bivalent COVID-19 mRNA vaccine is not expected to be a risk to lactating individuals or their breastfed newborns/infants.
- COVID-19 vaccine should be offered to individuals in the eligible group who are breastfeeding.
  - It is recommended that individuals consult with their primary health care provider or medical specialist for any vaccine related questions or concerns.
  - However, consultation with a primary health care provider or medical specialist is not required to receive COVID-19 vaccine.

### Other Considerations
- Individuals presenting for immunization do not need to be tested for previous COVID-19 infection.
- It is not recommended that serology testing be completed to determine if an immune response to the COVID-19 vaccine has been mounted in individuals and serology testing should not be used as evidence to inform whether vaccine doses have been effective.
- Immunization of individuals who may be currently infected with SARS-CoV-2 is not known to have a detrimental effect on the illness.
- Individuals with COVID-19-like symptoms, should not go to an immunization venue in order to minimize the risk of COVID-19 transmission and their immunization should be deferred.

### Possible Reactions
**Common:**
- Pain, redness, and swelling at the injection site
- Fever, chills
- Fatigue
- Headache, myalgia, arthralgia
- Pain in extremity*
- Nausea*, vomiting, diarrhea
- Lymphadenopathy*

**Uncommon:**
- Malaise*
- Asthenia*
- Decreased appetite*
- Hyperhidrosis*
- Lethargy*
- Night sweats*

**Rare:**
- Anaphylaxis
- Allergic reaction
- Facial swelling/Bell’s Palsy*
- Myocarditis/pericarditis*
- Erythema multiforme*
- Hypoesthesia* (decreased sense of touch or sensation, numbness) or paraesthesia* (tingling, itching or prickling sensation)
- Skin rash*
- As with any immunization, unexpected or unusual side effects can occur
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*No reported cases following Pfizer-BioNTech Omicron-containing bivalent during the study period; however these were reported following Pfizer-BioNTech (original). Refer to product monograph for more detailed information*

<table>
<thead>
<tr>
<th>Composition</th>
<th>Each 0.3 mL dose contains:</th>
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<tbody>
<tr>
<td></td>
<td>Tozinameran encodes for the viral spike protein of SARS-CoV-2 Original strain and famtozinameran encodes for the viral spike(s) protein of SARS-CoV-2 Omicron BA.4/BA.5 strain.</td>
</tr>
<tr>
<td></td>
<td>Non-medicinal ingredients:</td>
</tr>
<tr>
<td></td>
<td>Lipid nanoparticles (these help the mRNA enter the cell):</td>
</tr>
<tr>
<td></td>
<td>• ALC-0315 = (4-hydroxybutyl) azanediyl)bis(hexane-6,1-diyl)bis(2-hexyldecanoate)</td>
</tr>
<tr>
<td></td>
<td>• ALC-0159 = 2-[(polyethylene glycol)-2000]-N,N-ditetradecylacetamide (PEG)</td>
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<tr>
<td></td>
<td>Other Lipids: (provide structural integrity of the nanoparticles)</td>
</tr>
<tr>
<td></td>
<td>• 1,2-distearoyl-sn-glycero-3-phosphocholine</td>
</tr>
<tr>
<td></td>
<td>• cholesterol</td>
</tr>
<tr>
<td></td>
<td>pH Stabilizers:</td>
</tr>
<tr>
<td></td>
<td>• tromethamine</td>
</tr>
<tr>
<td></td>
<td>• tromethamine hydrochloride</td>
</tr>
<tr>
<td></td>
<td>Other:</td>
</tr>
<tr>
<td></td>
<td>• sodium chloride</td>
</tr>
<tr>
<td></td>
<td>• sucrose (protects the nanoparticles when frozen)</td>
</tr>
<tr>
<td></td>
<td>• water for injection</td>
</tr>
<tr>
<td></td>
<td>No adjuvants or preservatives</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Blood/Blood Products</th>
<th>Contains no human blood/blood products</th>
</tr>
</thead>
<tbody>
<tr>
<td>Bovine/Porcine Products</td>
<td>Contains no bovine/porcine products</td>
</tr>
<tr>
<td>Latex</td>
<td>Does not contain latex</td>
</tr>
</tbody>
</table>

**Interchangeability**

<table>
<thead>
<tr>
<th>Administration with Other Products</th>
</tr>
</thead>
<tbody>
<tr>
<td>Can be used as a booster dose following any previously received COVID-19 vaccines.</td>
</tr>
</tbody>
</table>

- No participants in the Omicron-containing bivalent COVID-19 vaccine clinical trials were concurrently administered other vaccines. Data with regard to the safety and immunogenicity of other authorized COVID-19 vaccines (including original (non-bivalent) mRNA vaccines) when given concurrently with other vaccines, are currently limited. However, no specific safety concerns have been identified to date.

- COVID-19 vaccines may be co-administered with, or at any time before or after other vaccines (including, live, inactivated, adjuvanted, or unadjuvanted vaccines) to individuals 6 months of age and older.

- Currently there is no data on the impact of the COVID-19 mRNA vaccines on tuberculin skin testing or IGRA (QFT) test results. There is a theoretical risk that COVID-19 vaccines may temporarily affect cell-mediated immunity, resulting in false-negative tuberculin skin testing or IGRA (QFT) test results.
  - In the absence of data, and acknowledging the importance of both timely tuberculosis testing and immunization, immunization with COVID-19 vaccines can take place at any time before, after or at the same visit as the TST or IGRA test.
  - However, repeat tuberculin skin testing or IGRA (at least 28 days after a dose of COVID-19 vaccine) of individuals with negative results for whom there is high suspicion of latent tuberculosis may be considered in order to avoid missing cases with TB infection due to potentially false-negative results.
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- Deferral of COVID-19 immunization is not recommended for individuals who have received anti-SARS-CoV-2 monoclonal antibodies or convalescent plasma provided for treatment or prophylaxis of COVID-19 just because they received these pharmacological interventions. This applies to people who received these before receiving any COVID-19 vaccine dose or between doses.
  - A study among nursing home residents and staff demonstrated that recipients of a SARS-CoV-2 monoclonal antibody (bamlanivimab), mounted a robust immune response to mRNA immunization, regardless of age, risk category or vaccine type.
  - Although antibody response was numerically lower in people who received monoclonal antibodies, they were still considered to be high and the clinical significance of the reduction is unknown.
  - There was no correlation between interval to COVID-19 immunization and neutralizing titres in recent monoclonal antibody recipients.
  - Intervals between previous COVID-19 infection and COVID-19 immunization outlined in this document would still apply to individuals who received the monoclonal antibodies or convalescent plasma for their infection.
- Individuals who are to receive Evusheld (tixagevimab and cilgavimab) as pre-exposure prophylaxis should wait at least 2 weeks following COVID-19 immunization to minimize interference.

**Note:** Anti-SARS-CoV-2 monoclonal antibodies or convalescent plasma should not be administered concomitantly with COVID-19 vaccines (i.e. administer on different days).

- Timing of administration and potential interference between COVID-19 vaccine and monoclonal products not used for treatment or prophylaxis of COVID-19 infection are currently unknown and the primary health care provider or medical specialist should be consulted on a case-by-case basis.
- mRNA COVID-19 vaccines may be given at any time before or after an immunoglobulin preparation (including RhIg) or blood product has been administered. There is no recommended minimum interval between these products and COVID-19 vaccine.

### Appearance

- Thawed (prior to mixing) – may contain white to off-white opaque particles.
- Thawed (after mixing) – white to off-white with no visible particles.

### Storage

- Before being thawed, can be stored in a freezer between -90°C to -60°C storage for up to 18 months.
- Do not store at -25°C to -15°C.
- Thawed vials can be stored:
  - in the refrigerator at +2°C to +8°C for up to 10 weeks, or
  - at room temperature (up to +25°C) for no more than 12 hours.
- Do not refreeze.
- After first puncture, the vaccine can be stored at +2°C to +25°C for up to 12 hours.
- During storage, minimize exposure to room light, and avoid exposure to direct sunlight and ultraviolet light.
- Thawed vials can be handled in room light conditions.

### Packaging

- **Vaccine:**
  - 6 doses per vial
  - 10 multiple dose vials per carton

### Preparation/Reconstitution

- **Thaw vaccine before use:**
  - Vials may be thawed in the refrigerator (+2°C to +8°C) or at room temperature (up to +25°C).
  - Thaw for 30 minutes at room temperature.
**COVID-19 Vaccine – mRNA Pfizer BioNTech Bivalent (Original and Omicron BA.4/BA.5 – Frozen Vaccine (Comirnaty))**  
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<table>
<thead>
<tr>
<th>Vaccine Code</th>
<th>COVPBmRNABA45</th>
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<tbody>
<tr>
<td>Antigen Code</td>
<td>COVID-19-20</td>
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<tr>
<td>Licensed for</td>
<td>Booster dose for individuals 12 years of age and older at least 3 to 6 calendar months after completion of the primary series and/or a previous booster of COVID-19 vaccine. Off-license use: Second Omicron-containing bivalent booster dose for eligible individuals.</td>
</tr>
</tbody>
</table>

**Program Notes:**
- 2022 October 7: Licensed for use in Canada.
- 2022 October 24: Implemented in Alberta.
- 2022 October 31: Updated booster dose, pregnancy and breastfeeding recommendations.
- 2023 March 1: Updated booster dose recommendations.
- 2023 March 21: Updated to include additional Omicron-containing bivalent booster dose indications for eligible individuals and updated booster spacing considerations to 6 months between last dose or infection.
- 2023 June 30: Storage updated to indicate product can be stored for up to 18 months prior to being thawed.

**Related Resources:**
- Alberta Health Services Website (2022). COVID-19 Vaccine Information
- See [www.CVDvaccine.ca](http://www.CVDvaccine.ca) for additional information

**References:**

**Mix Before Use**
- Thaw for 6 hours in the refrigerator; and allow the vial to come to room temperature before use.
- Before use, mix by inverting vial gently 10 times. Do not shake.
- After mixing, the vaccine should appear as a white to off-white suspension with no visible particles.
- Do not use if liquid is discoloured or if particles are observed after mixing.
- Discard any unused vaccine 12 hours after first puncture.

- Thaw for 6 hours in the refrigerator; and allow the vial to come to room temperature before use.
- Before use, mix by inverting vial gently 10 times. Do not shake.
- After mixing, the vaccine should appear as a white to off-white suspension with no visible particles.
- Do not use if liquid is discoloured or if particles are observed after mixing.
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