Manitoba COVID-19 Vaccine: Clinical Practice Guidelines for Immunizers and Health Care Providers

This Clinical Practice Guideline is current as of April 7, 2021 and is intended for use by immunizers and health care providers who are participating in the Manitoba COVID-19 Immunization Program.

Manitoba

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Summary of Changes

April 6, 2021

- Updates to the eligibility criteria for AstraZeneca/COVISHIELD (page 15).
- Clarification that low-dose methotrexate is not a contraindication/precaution to vaccination (page 11).

Purpose of this Clinical Practice Guideline

The goal of Canada's pandemic response is to minimize serious illness and death while minimizing societal disruption as a result of the COVID-19 pandemic. Safe and effective COVID-19 vaccines could help achieve this goal. Clinical trials of numerous candidate COVID-19 vaccines are currently underway.

Manitoba's Vaccine Implementation Task Force, compromised of vaccine experts from Manitoba Health and Seniors Care makes COVID-19 vaccine recommendations by critically conducting a review of:

- provincial epidemiology, to guide determination of priority populations.
- clinical trial data on safety and effectiveness.
- post-marketing studies, including reports of adverse events following immunization.
- plans and practices of other jurisdictions in Canada and around the globe.
- summary statements and recommendations from national and international expert committees, including NACI.

Consultation with experts form the medical community across the province is also undertaken in various stage of the review and development process.

The COVID-19 landscape is constantly changing as we learn more about the disease and the vaccines that protect against it. Vaccine recommendations are subject to change as the evidence continues to evolve.

This Clinical Practice Guidance for Immunizers and Health Care Providers in Manitoba is intended to accompany the National Advisory Committee on Immunization (NACI) recommendations and statements, which can be accessed at: https://www.canada.ca/en/public-health/services/immunization/national-advisory-committee-on-immunization-naci.html; Manitoba-specific recommendations and policies are contained herein.

Resources for health care providers including the most up-to-date version of these Clinical Practice Guidelines as well as questions & answers and provincial memos can be found online at: https://www.gov.mb.ca/covid19/vaccine/healthcare-professionals.html. Information and resources specifically for pharmacists and physicians can be found here: https://www.gov.mb.ca/covid19/vaccine/partners/index.html.

Product monographs, factsheets for general public use and the **COVID-19 Vaccine Consent Form** can be found here: https://www.gov.mb.ca/covid19/vaccine/resources.html.

Guidance for use in Special Populations for all Authorized COVID-19 Vaccines used in Manitoba

The National Advisory Committee on Immunization (NACI) recommends that the COVID-19 vaccine may be offered to people who are immunosuppressed due to disease or treatment, to people who have an autoimmune condition, or to those who are pregnant and/or breastfeeding, provided certain conditions are met. Specifically, people in these special populations *may* be immunized if a risk assessment deems that the benefits outweigh the potential risks for the individual *and* if informed consent includes a discussion about the lack of or limited evidence pertaining to the use of COVID-19 vaccine in these special populations.

This section of the Clinical Practice Guidelines includes information on currently known risks and benefits related to immunizing special populations, for conducting a risk-benefit analysis and for obtaining informed consent. As evidence continues to evolve, these guidelines will be updated accordingly. The most up-to-date version will be available online at: www.manitoba.ca/covid19/vaccine/healthcare-professionals.html.

Clients/patients are to review and complete the **COVID-19 Vaccine Consent Form** (www.manitoba.ca/covid19/vaccine/resources.html) before immunization. Clients/patients who fall into the special populations (i.e., are immunosuppressed due to disease or treatment, have an autoimmune condition, are pregnant and/or breastfeeding) will indicate so by answering yes to questions 8, 9 &/or 10 of section B on the **COVID-19 Vaccine Consent Form.** This is the signal to the immunizer that they must ensure the client reviews at least two of the following factsheets (available online at: www.manitoba.ca/covid19/vaccine/resources.html):

1. **COVID-19 mRNA Vaccines Factsheet**
2. **COVID-19 Viral Vector Vaccine Factsheet**
3. **COVID-19 Vaccine Information for Individuals who are Immunosuppressed &/or have an Autoimmune Condition**
4. **COVID-19 Vaccine Information for Pregnant and Breastfeeding Individuals**

The immunizer or health care provider must also reference to the client/patient, the pertinent information contained in these guidelines. After the client/patient independently reviews the factsheets and listens to the information provided by the immunizer or health care provider, the immunizer or health care provider should address any remaining questions the client/patient has about the risks and benefits of vaccination, and sign and date the appropriate section of the **COVID-19 Vaccine Consent Form**.

There are limited situations (as written on page 10, “People who Require Further Consultation before Immunization”) where a client/patient in one or more special populations is unlikely to mount an acceptable immune response to the COVID-19 vaccine and therefore, require further consultation with a relevant specialist before proceeding with immunization.

Clients/patients in these special populations that sign section C of the **COVID-19 Vaccine Consent Form** are acknowledging that they have read and understood the information in the factsheets. They are also acknowledging that their immunizer or health care provider has

satisfactorily answered their questions through an information exchange aided by these guidelines.

There may be situations where a client/patient and health care provider discuss the information in these guidelines (in-person or virtually) before the immunization appointment (i.e., information is **not** provided by the immunizer at the point of immunization). In this situation, the health care provider can document that this information exchange has occurred by fully completing and signing the **COVID-19 Vaccine Consent Form**, signaling to the immunizer that the client/patient has been given the necessary information to provide informed consent. In this case, the health care provider can do one of the following things to ensure the signed, fully completed **COVID-19 Vaccine Consent Form** is available at the point of immunization:

1. Securely fax the signed and completed **COVID-19 Vaccine Consent Form** to 204-948-3044 on the same day as the client/patient's (in-person or virtual) appointment. Designated staff at Manitoba Health and Seniors Care will retrieve and securely upload the signed and completed **COVID-19 Vaccine Consent Form** to the Public Health Information Management System (PHIMS) within 24 hours of receipt of the consent form.
    - Health care providers are to instruct their client/patient to **(re)schedule their immunization appointment 48 hours following their health care provider** appointment to allow enough time for the signed and completed **COVID-19 Vaccine Consent Form** to be uploaded into PHIMS.
    - If the health care provider is submitting the **COVID-19 Vaccine Consent Form** by fax, they are also asked to provide the client/patient with a hardcopy through one of the means listed below (as feasible):
2. Provide the completed and signed hardcopy of the **COVID-19 Vaccine Consent Form** to the client/patient and instruct them to bring it with them to their scheduled immunization appointment. (It will be accepted at the point of immunization as documented evidence that the risk-benefit discussion took place prior to the appointment).
3. Mail (via Canada Post) the completed and signed hardcopy of the **COVID-19 Vaccine Consent Form** to the client/patient (or have them pick up the signed and completed **COVID-19 Vaccine Consent Form** from the health care provider's clinic location). The health care provider must instruct the client/patient to bring the signed/completed form with them to their scheduled immunization appointment. They must also ask the client/patient not to (re)schedule their immunization appointment until they have the signed and completed hardcopy **COVID-19 Vaccine Consent Form.**

There are two pathways for clients/patients in one or more of the special populations to sign and complete the **COVID-19 Vaccine Consent Form**:

1. At the point of immunization, after reviewing the factsheets and following the information exchange with the immunizer
2. At a virtual or in-person appointment with a health care provider. In this situation, a signed and completed **COVID-19 Vaccine Consent Form** is either:
    a. Electronically uploaded into PHIMS and/or

b. Directly provided to the client/patient (at their scheduled appointment, via mail or picked up from the clinic location) to bring with them to their appointment

The immunizer must ensure the entire consent form is completed. If the risk-benefit information exchange occurred in advance of the immunization appointment with another health care provider, the immunizer must review the completed and signed **COVID-19 Vaccine Consent Form**, either as a hardcopy or on the client/patient's PHIMS file, to provide COVID-19 immunization services.

The sections below contain pertinent information that the immunizer or health care provider is to verbally paraphrase or summarize for the client/patient for the sole purposes of knowledge transfer to obtain informed consent.

Vaccination Risks and Benefits for Pregnant &/or Breastfeeding Clients/Patients

The Society of Obstetricians and Gynecologists of Canada (SOGC) states that vaccination should be offered to pregnant and/or breastfeeding individuals who are at high-risk of infection and/or morbidity from COVID-19 because the documented risk of not getting the vaccine outweighs the theorized and undescribed risk of being vaccinated during pregnancy or while breastfeeding.

Most people who become infected with SARS-CoV-2 during pregnancy will have mild to moderate symptoms and many can be asymptomatic. However, both Canadian and international data from large studies spanning multiple jurisdictions demonstrate that approximately eight to 11 per cent of pregnant individuals will require hospitalization for COVID-related morbidity and between two to four per cent will require admission to an intensive care unit (ICU). Compared to non-pregnant individuals with COVID-19, pregnant individuals are at increased risk of invasive ventilation with an equivalent mortality to age-matched peers. The risk of severe morbidity from COVID-19 in pregnancy appears to be associated with risk factors including:

- an age of 35 or older
- obesity
- pre-existing or gestational diabetes
- pre-existing hypertension
- heart disease
- severe and/or uncontrolled asthma

Some respiratory infections (e.g. influenza and COVID-19) during pregnancy may also lead to other adverse outcomes, such as premature labor and delivery.

While there have been no red flags or hypothesized mechanisms for potential harm associated with administering a COVID-19 mRNA vaccine during pregnancy, currently there is limited data on the safety and efficacy of COVID-19 vaccines in pregnancy or during breastfeeding.[1] The potential risks of vaccination to a pregnant individual and fetus remain unknown. What *is* known, however, is that an unvaccinated pregnant individual remains at risk of COVID-19 infection and remains at heightened risk of severe morbidity if infected compared to non-pregnant counterparts. Severe infection with COVID-19 carries risks to both maternal and fetal health. While pregnancy itself does not appear to increase the risk of becoming infected with SARS-CoV-2, pregnant individuals may be in work-related (e.g., health care worker, front line workers etc.) or community situations (e.g., caregiver, indigenous communities, outbreak setting, etc.) where the risk of exposure is considerable. Owing to maternal age or underlying comorbidities, some pregnant individuals are at high risk of severe COVID-related morbidity.

With respect to breastfeeding specifically, there is no data on the safety of COVID-19 vaccines in lactating women or the effects of COVID-19 vaccines on the breastfed infant or on milk

[1] Due to rare instances of vaccine-induced pro-thrombotic immune thrombocytopenia (VIPIT) following AstraZeneca (AZ) vaccination reported in Europe, provincial and national guidance is to pause AstraZeneca/COVISHIELD in people aged < 55 years.

production. Because COVID-19 vaccines are not live virus vaccines, they are not hypothesized to be a risk to the breastfeeding infant.

The National Advisory Committee on Immunization (NACI) recommends that the COVID-19 vaccine may be offered to pregnant and/or breastfeeding individuals if a risk assessment deems that the benefits outweigh the potential risk for the individual and the fetus/infant and if informed consent includes discussion about the absence of evidence on the use of COVID-19 vaccine in this population.

Pregnant and/or breastfeeding individuals will likely seek counsel from their prenatal care provider to assist in weighing the risks and benefits, so that they might arrive at an informed and autonomous decision that is right for them as an individual. Such a discussion should prioritize patient autonomy and may include the following:

- Currently, there is evidence that pregnancy complicated by advanced maternal age, obesity, pre-existing or gestational diabetes, hypertension or cardio/respiratory comorbidity is an independent risk factor for severe COVID-19.
- Some individuals who are pregnant, breastfeeding or of reproductive age may be at increased risk of exposure to SARS-CoV-2 (e.g., healthcare or essential workers) and/or at increased risk of severe COVID-19 disease (e.g., due to a pre-existing medical condition or a body mass index of 35 kg/m2 or more).
- Currently, there is no data to describe outcomes of inadvertent administration of COVID-19 vaccine to pregnant individuals or their developing fetuses in clinical trials. It is unknown whether the vaccines are excreted in human milk, but there is no data on outcomes in breastfeeding individuals or their breastfed infants.
- There is currently no evidence to guide the time interval between the completion of the COVID-19 vaccine series and conception. In the face of scientific uncertainty, it may be prudent to delay pregnancy by 28 days or more after administering the complete two-dose series of COVID-19 vaccine to permit turnover of the vaccine's target cells (a half-life of two to five days). Individuals who become pregnant during their vaccine series or shortly thereafter should not be counselled to terminate pregnancy because they received the COVID-19 vaccine. NOTE: for the general population, COVID-19 vaccine doses are administered up to four months apart.
- If pregnancy is determined after initiation of the vaccination series, completion of the series should be delayed until after pregnancy, unless risk factors for increased exposure or severe COVID-19 are present.
- Relevant epidemiology and risk of community acquisition of COVID-19.
- Workplace situation and risk of work-related acquisition of COVID-19.
- Individual risk for COVID-related morbidity including consideration for comorbidities including advanced maternal age, immunosuppressive conditions, pre-existing or gestational diabetes, pre-existing hypertension, obesity or chronic respiratory conditions.

Vaccination Risks and Benefits for Clients/Patients who are Immunosuppressed &/or have an Autoimmune Condition

The National Advisory Committee on Immunization (NACI) recommends that the COVID-19 vaccine may be offered to individuals who are immunosuppressed and/or those who have an autoimmune condition if:

- a risk assessment deems that the benefits outweigh the potential risk for the individual and,
- informed consent includes discussion about the absence of evidence on the use of COVID-19 vaccine in this population.

Immunosuppressed people or those with autoimmune conditions will likely seek counsel from a health care provider to assist in weighing the risks and benefits, so they can make informed and autonomous decisions that are right for them as individuals. Such a discussion should prioritize patient autonomy and may include the following information:

- Although there is limited evidence to indicate that immunosuppression or having an autoimmune condition is an independent risk factor for severe COVID-19, these conditions have been identified as independent risk factors for severe outcomes from other infectious disease, such as influenza.
- Immunocompromising conditions vary in their impact on the immune system and may alter the response to immunization depending on the underlying condition, the progression of disease and use of medications that suppress immune function.
- No safety signals of concern have been noted to date in non-immunosuppressed individuals with an immunocompromising condition (e.g., stable HIV infection) including in clinical trials. People living with HIV that are considered immunocompetent may be vaccinated.
- Autoimmune conditions vary in their impact on the immune system and may alter the response to immunization depending on the underlying condition, the severity and progression of disease and use of medications that impact immune function.
- There is still very limited data on COVID-19 vaccinations in people who are immunosuppressed, or who have an autoimmune condition, or both. Furthermore, there is limited evidence to demonstrate that people who are immunosuppressed due to disease or treatment or who have an autoimmune condition will benefit from vaccination, or the duration of benefit.
- People who are immunosuppressed or those with autoimmune conditions are known to benefit from other vaccinations, such as the annual seasonal influenza vaccine.
- There is no evidence to suggest that people who are immunosuppressed have increased adverse events associated with COVID-19 vaccines (unlike live vaccines).
- Fever is a possible side effect of vaccination and this could make symptoms of an autoimmune disease temporarily worse.

People who Require Further Consultation before Immunization

People who fall into one or more of the below categories are unlikely to mount an acceptable immune response to the COVID-19 vaccine at this time and therefore, require further consultation with a relevant specialist before immunizing:

- People receiving CAR-T therapy within the last three months.*
- People receiving an allogenic or autologous stem cell transplant within the last three months.*
- Solid organ transplant recipients: pre-transplant within two weeks of transplant and post-transplant within the last month regardless of induction therapy.*
- People receiving active chemotherapy including cyclical chemotherapy:¥ administer vaccine after consultation with prescribing physician. In some cases, it may be possible to administer vaccine one week before the next cycle. If this is not possible, administer vaccine when neutrophil recovery has occurred.* For more detailed clinical guidance on the timing of vaccination, please see Appendix A.
- People who are taking, or have taken, one or more of the following medications¥ within the last six months:*
    - Alemtuzumab
    - Anti-Thymocyte Globulin (ATG) / Thymoglobulin
    - Basiliximab
    - Blinatumomab
    - Obinatuzumab
    - Ocrelizumab
    - Ofatumumab
    - Rituximab
- People with an immediate allergic reaction of any severity to:
    - Polyethylene glycol (PEG) which may be found in a multitude of products including bowel preparation products for colonoscopies, laxatives, cough syrup, cosmetics, contact lens care solutions, skin care products, and as an additive in some food and drinks
    - Polysorbate 80 (due to potential cross-reactive hypersensitivity with the vaccine ingredient PEG)
    - Tromethamine (trometamol or Tris), which is a component in contrast media, oral and parenteral medications **contained in the <u>Moderna vaccine only</u>**

The COVID-19 vaccine should not be given to people who are allergic to an active substance or any of the ingredients of the COVID-19 vaccine being administered, or if they have had a severe allergic reaction after the first dose. For information about a COVID-19 vaccine's ingredients, review the vaccine manufacturer's product monograph at: www.manitoba.ca/vaccine.

**The attending physician or specialist may recommend a different time interval based on client/patient assessment.*

¥Low dose methotrexate (5mg to 25mg), once weekly, given orally or injected, is not a contraindication/ precaution to vaccination.

This information is current as of April 7, 2021.

Resources

- the National Advisory Committee on Immunization (NACI) Statement on the Recommendations on the use of the COVID-19 vaccines at: www.canada.ca/en/public-health/services/immunization/national-advisory-committee-on-immunization-naci/recommendations-use-covid-19-vaccines.html#a7
- the Canadian Rheumatology Association Position Statement on COVID-19 Vaccination at: https://rheum.ca/wp-content/uploads/2020/12/CRA-Position-Statement-on-COVID-19-Vaccination-v2-FINAL.pdf
- National Transplant Consensus Guidance on COVID-19 Vaccine at: www.cst-transplant.ca/_Library/Reference_Documents/National_Transplant_Guidance_on_COVID_vaccine_-_Dec_18_2020_Final_1_.pdf
- the Society of Obstetricians and Gynecologists of Canada Statement on COVID-19 Vaccination in Pregnancy at: www.sogc.org/en/-COVID-19/COVID-19/en/content/COVID-19/COVID-19.aspx?hkey=dd7d7494-49fa-4966-ab4d-4dca362a9655
- the Multiple Sclerosis Society of Canada COVID-19 Vaccine Guidance for People Living with MS at: https://mssociety.ca/resources/news/article/covid-19-vaccine-guidance-for-people-living-with-ms
- the Canadian Stem Cell Transplant and Cellular Therapy Director Consensus Statement at: https://www.cttcanada.org/page/covid19
- the International Society of Heart & Lung Transplantation Recommendations from the COVID-19 Task Force (released March 15, 2021) at: https://ishlt.org/ishlt/media/Documents/COVID19_Vaccine-Recommendations_3-15-2021.pdf

Guidance for use of the Viral Vector Vaccine

Health Canada authorized the use of a non-replicating viral vector vaccine ChAdOx1 Oxford-AstraZeneca (AstraZeneca/COVISHIELD[2]) in individuals 18 years of age and older on February 26, 2021. Originally, the National Advisory Committee on Immunization (NACI) recommended against the use of AstraZeneca/COVISHIELD in individuals 65 years of age and older due to limited information on vaccine efficacy in this age group. Since then, however, the upper age limit has been removed based on real-world effectiveness data in persons aged ≥ 65 years.

In clinical trials, AstraZeneca/ COVISHIELD demonstrated an average efficacy of 62% in participants aged 18 to ≤ 64 years of age (all intervals from 4 to 12 weeks between doses) and 81.6% with a 12 week or longer interval. Emerging estimates of real-world effectiveness from Public Health England demonstrate that vaccination with a single dose of AstraZeneca/COVISHIELD produced a significant reduction in symptomatic SARS-CoV-2 positive cases in older adults with even greater protection against severe disease (80% reduction in hospitalizations).[3] The effectiveness of the first dose of AstraZeneca/*COVISHIELD in Scotland demonstrated a 94% reduction in hospitalizations due to COVID-19.[4] See question 20 of the Clinical Practice Questions and Answers for updated information on vaccine effectiveness of AstraZeneca/COVISHIELD.*

Results from four clinical trials (two Phase 1/2, one Phase 2/3, and one Phase 3) were available at the time of Health Canada authorization. Results from an ongoing Phase 3 trial in the US were not available at the time of authorization. Evidence on efficacy, immunogenicity and safety is available for adults ≥ 18 years of age. The Phase 2/3 trial (COV002), which was based in the United Kingdom and Phase 3 trial (COV003) was based in Brazil, assessed the efficacy, safety and immunogenicity of AstraZeneca/COVISHIELD. These two studies underwent a series of protocol amendments and logistical challenges during the conduct of the trials that resulted in significant changes to the trials' methodology. There were changes from a single to a two-dose vaccine regimen, the use of both a low dose/standard dose (LD/SD) (in COV002 only, due to dosing error) and standard dose/standard dose (SD/SD) vaccine regimen, and the recruitment of progressively older study participants (56 to 69 and then ≥ 70 years of age) after the initial focus on adults 18 to 55 years of age.

[2] COVISHIELD (manufactured by Serum Institute of India) and AstraZeneca COVID-19 vaccine (manufactured by AstraZeneca) are ChAdOx1-S recombinant vaccines developed by AstraZeneca and the University of Oxford. Health Canada has reviewed the manufacturing information for these vaccines and found them to be comparable.
[3] https://www.medrxiv.org/content/10.1101/2021.03.01.21252652v1
[4] https://www.ed.ac.uk/files/atoms/files/scotland_firstvaccinedata_preprint.pdf

Estimates of vaccine efficacy against the first occurrence of confirmed COVID-19 beginning ≥ 15 days after dose 2 in <u>all</u> participants, by dosing interval (SD/SD seronegative baseline efficacy set[a])

Dosing interval	Event in vaccine group (AZD1222) n/N (%)	Events in control group (MenACWY) n/N (%)	Vaccine efficacy (95% CI)
4–12 weeks	67/5,473 (1.2)	162/5,422 (3.0)	59.6% (46.4 to 69.6%)
4 – 8 weeks	52/4,188 (1.2)	113/4,098 (2.8)	55.7% (38.5 to 68.1%)
9–12 weeks	15/1,285 (1.2)	49/1,324 (3.7)	69.0% (44.8 to 82.6%)
>12 weeks	4/571 (0.7)	22/599 (3.7)	81.6% (47.0 to 93.6%)

[a]Participants without prior evidence of SARS-CoV-2 infection at baseline; all SD/SD vaccine recipients (or respective controls)

Serious adverse events were reported by less than 1% of study participants and was similar between the vaccine and control groups. Two serious adverse events (pyrexia, transverse myelitis) in the vaccine recipients were considered related to the vaccine by the study investigators. The case of pyrexia (40.5°) occurred 2 days after dose 1 and resolved the same day following the administration of acetaminophen. The event of transverse myelitis occurred in a 37-year-old female who developed sensory symptoms about 10 days after first (and only) vaccination. The clinical episode had a duration of 3 weeks. Further follow up with MRI of spine and brain showed an acute spinal lesion and older cerebral lesions, revealing pre-existing, but previously unrecognized, multiple sclerosis. A third SAE was originally identified (C-reactive protein increase) however after the cut-off date, causality for the SAE of C-reactive protein increase was updated by the investigator to be not treatment related.

NACI recommends that in the context of limited vaccine supply and published clinical trial data, initial doses of mRNA COVID-19 vaccine is preferentially recommended for individuals in the authorized age group without contraindications, especially among those at highest risk of severe illness and death and highest risk of exposure to COVID-19.

- AstraZeneca/COVISHIELD vaccine may be offered to individuals aged ≥ 55 years without contraindications if:
    i. The advantages of earlier vaccination outweigh the limitations of vaccinating with a less efficacious vaccine, depending on:
        - local COVID-19 epidemic conditions,
        - local vaccine supply,
        - risk of severe illness or death,
        - risk of exposure, and
        - logistical consideration.
    ii. Ease of transport, storage and handling of this vaccine facilitates access to vaccination which may otherwise be challenging.
    iii. Informed consent includes discussion about current vaccine options and the timing of future vaccine options.

Eligibility Criteria for AstraZeneca/COVISHIELD

Please be advised that the AstraZeneca/COVISHIELD vaccine eligibility has been updated following provincial and national guidance to pause use of AstraZeneca/COVISHIELD in people aged < 55 years due to rare instances of vaccine-induced pro-thrombotic immune thrombocytopenia (VIPIT) following AstraZeneca vaccination reported in Europe.

In the context of limited COVID-19 vaccine supply, AstraZeneca/COVISHIELD vaccine doses are to be administered to:

- People aged 55 to ≤ 64 years in the general population and among First Nation people,[5] prioritized using health conditions that increase individual risk of severe outcomes[6] from COVID-19. Providers are expected to work through priority 1 conditions in their patient population before moving to priority 2 individuals; however, this does not replace clinical judgement concerning the practitioner's assessment of the patient's risk.
- People aged ≥ 65 years in the general population and among First Nation people (regardless of priority 1 or 2 conditions), with priority given to those who are unable to visit a Super-site or Pop-up Clinic.

Eligibility criteria is subject to frequent change; check the website for up-to-date eligibility criteria: https://www.gov.mb.ca/covid19/vaccine/eligibility-criteria.html.

Priority 1:[7]

- Individuals with the following chronic health conditions:
    - end stage renal disease undergoing hemodialysis **OR** peritoneal dialysis
    - cirrhosis due to any cause **OR** portal hypertension
    - heart failure (class III/IV), ventricular assist device **OR** adult congenital heart disease stage C and D
    - severe COPD, pulmonary hypertension, pulmonary fibrosis, interstitial lung disease **OR** cystic fibrosis
    - history of cerebral vascular accident with residual deficits
    - malignant hematologic disorders including leukemia and lymphoma **OR** clonal blood disorder
    - malignant neoplasms (solid tissue) who will receive or are currently receiving immunosuppressive therapy including chemotherapy
    - severe obesity (BMI ≥ 40)
    - receiving one or more of the following immunosuppressive therapies: B cell therapies (e.g., rituximab, ocrelizumab), cyclophosphamide, alemtuzumab, calcineurin inhibitors, chronic dose prednisone >=20mg/day, mycophenolate, sulfasalazine and JAK inhibitors (e.g., tofacitinib)[8]
    - solid organ or hematopoietic stem cell transplant (candidate or recipient)

[5] Previously, persons aged 50 to ≤ 64 years in the general population, and 30 to ≤ 64 year old First Nation people, were eligible for the AstraZeneca/COVISHIELD vaccine; this has since changed due to rare instances of VIPIT in those aged < 55 years.
[6] Serious outcomes includes death or hospitalization including ICU admission.
[7] Pregnant individuals (18 to ≤ 64 years of age) with one of: aged ≥ 35 years, BMI ≥ 30, pre-existing diabetes, pre-existing hypertensions, cardiac or pulmonary disease, were originally eligible under priority 1 but have since been removed (on March 29, 2021) due to rare incidents of VIPIT following vaccination in those aged < 55 years.
[8] The attending physician or specialist may recommend a different time interval based on client/patient assessment.

    - trisomy 21 (Down's syndrome)
    - asplenia or hyposplenism (including sickle cell disease)
- Individuals receiving home care ≥ 4 times/week **OR** receive 24/7 support from Community Living Disability Services.

Priority 2:

- Individuals with the following chronic health conditions:
    - Chronic cardiovascular disease including heart failure (class I/II), coronary artery disease, malignant tachyarrythmia **OR** cardiomyopathies
    - chronic liver disease
    - chronic neurologic **OR** neurodevelopmental conditions including cerebral palsy, Parkinson's disease, multiple sclerosis, ALS **OR** dementia (including Alzheimer's disease)
    - chronic pulmonary disease including COPD **OR** severe and/or uncontrolled asthma
    - chronic renal disease
    - HIV (CD4 cell count ≥ 200 x 106/L and CD4 percentage ≥ 15%)
    - severe systemic autoimmune disorders (e.g., systemic lupus erythematosus, scleroderma, myocarditis, rheumatoid arthritis)
    - type 1 or 2 diabetes mellitus (poorly controlled and/or with complications)
    - active tuberculosis (current or previous) **OR** current latent tuberculosis (LTBI)
    - receiving immunosuppressing therapy*
- Individuals receiving homecare ≤ 3 times/week **OR** any level of Community Living Disability Services supports (or as per family physician determination of equivalent levels of family support).
- Household contacts of individuals with Priority 1 chronic health conditions **OR** designated family caregiver(s) for personal care home residents.

** See the Canadian Immunization Guide: https://www.canada.ca/en/public-health/services/publications/healthy-living/canadian-immunization-guide-part-3-vaccination-specific-populations/page-8-immunization-immunocompromised-persons.html#a25*

Information on Vaccine-Induced Pro-thrombotic Immune Thrombocytopenia

On March 24, 2021**,** Health Canada issued a label change and guidance on the AstraZeneca COVID-19 vaccine, following European reports of rare but very serious cases of blood clots associated with low levels of blood platelets (i.e., thrombocytopenia) following immunization with the AstraZeneca vaccine. While these reported adverse events have occurred primarily in women, investigations are ongoing as it is possible that more women received the AstraZeneca vaccine making it difficult to assess risk based on sex. Health Canada has also issued terms and conditions requiring AstraZeneca manufacturers to conduct a detailed assessment of the benefits and risks of the vaccine by age and gender in the Canadian context. This information, along with further international evidence, will be used to determine if additional regulatory actions are necessary.

In the interim, the National Advisory Committee on Immunization (NACI) is recommending that AstraZeneca COVID-19 vaccine should not be used in adults < 55 years of age at this time while the safety signal of Vaccine-Induced Pro-thrombotic Immune Thrombocytopenia (VIPIT) following vaccination with AstraZeneca COVID-19 vaccine is investigated further.[9] VIPIT is associated with high mortality and other serious outcomes, occurring in anywhere from one in every 125,000 to 1 in 1 million people following vaccination with AstraZeneca vaccine. This is a precautionary approach while Health Canada completes its full risk assessment and, while more information and analysis are gathered from international partners. To date, such adverse events have not been reported in Canada and AstraZeneca/COVISHIELD vaccine has not yet been used in large numbers in Canada.

The outcome of VIPIT can be serious, including death. If diagnosed early, VIPIT can be treated and the risk of serious outcomes reduced. Based on current evidence, for those individuals who have already been vaccinated with AstraZeneca more than 20 days ago, there is no cause for concern. For those who have been vaccinated with AstraZeneca less than 20 days ago, be alert to the signs and symptoms of thromboembolism and thrombocytopenia. Symptoms to be vigilant for include: shortness of breath, chest pain, leg swelling, persistent abdominal pain, neurological symptoms including sudden onset of severe or persistent worsening headaches or blurred vision, skin bruising (other than at the site of vaccination) or petechiae. A decision tree to assist clinicians in the diagnosis of VIPIT is included below however, specialist consultation may be required. For more information, refer to https://doi.org/10.47326/ocsat.2021.02 and https://covid-vaccine.canada.ca/info/pdf/astrazeneca-covid-19-vaccine-letter.pdf.

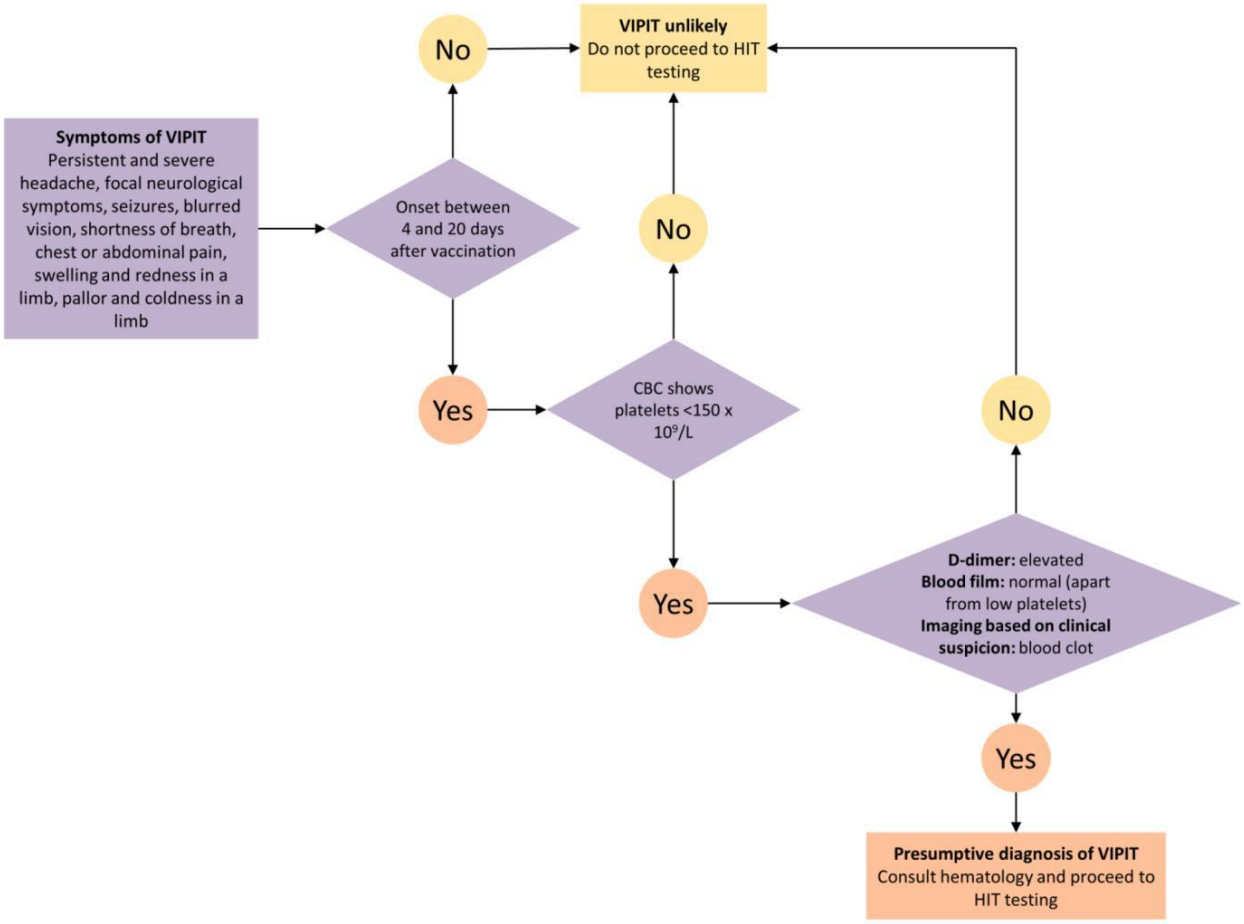
Note that active monitoring of asymptomatic immunized clients/patients aged < 55 years is not required at this time. To date, VIPIT has not been identified following receipt of mRNA COVID-19 vaccines.

Decisions on the type of second dose that will be offered to individuals < 55 years of age who have been vaccinated with AstraZeneca/COVISHIELD will be determined based on the latest

[9] *NACI rapid response: Recommended use of AstraZeneca COVID-19 vaccine younger adults* released March 29, 2021 and available at: https://www.canada.ca/en/public-health/services/immunization/national-advisory-committeeon-immunization-naci/rapid-response-recommended-use-astrazeneca-covid-19-vaccine-younger-adults.html.

evidence and research. Manitoba public health officials will continue to review the evidence as it emerges, including evidence on mixed COVID-19 vaccine schedules, and update health care providers accordingly.

The below diagram is a decision tree for diagnosing and ruling out VIPIT.[10]



[10] Pai M, Grill A, Ivers N, et al. Vaccine-induced prothrombotic immune thrombocytopenia VIPIT following AstraZeneca COVID-19 vaccination. *Science Briefs of the Ontario COVID-19 Science Advisory Table*. 2021;1(17). https://doi.org/10.47326/ocsat.2021.02

This information is current as of April 7, 2021.

Clinical Practice Questions and Answers

The COVID-19 vaccine landscape is rapidly evolving. Clinical trials are ongoing and emerging data from post-marketing studies, often in pre-print, are released daily. The following is a list of evidence-based sources of information that immunizers and health care providers can refer to for the most current information and evidence about the COVID-19 vaccines authorized in Canada.

- the National Advisory Committee on Immunization (NACI) releases statements with guidelines and recommendations around the use of the COVID-19 vaccines authorized in Canada as well as priority population sequencing: https://www.canada.ca/en/public-health/services/immunization/national-advisory-committee-on-immunization-naci.html.
    - To subscribe for notification of updates, go to: https://health.canada.ca/en/health-canada/services/healthy-living/immunization-and-vaccines/canadian-immunization-guide/subscribe.html.
- the manufacturer's product monograph is available online:
    - Pfizer-BioNTech: https://www.gov.mb.ca/asset_library/en/covidvaccine/pfizer-biontech-covid19vaccine.pdf
    - Moderna: https://covid-vaccine.canada.ca/info/pdf/covid-19-vaccine-moderna-pm-en.pdf
    - AstraZeneca: https://www.gov.mb.ca/asset_library/en/covidvaccine/astrazeneca-covid-19-vaccine.pdf
    - COVISHIELD: https://www.gov.mb.ca/asset_library/en/covidvaccine/covishield-pm.pdf
- information about Health Canada's regulatory approval processes and other regulator-role specific information is available at: https://www.canada.ca/en/health-canada/services/drugs-health-products/covid19-industry/drugs-vaccines-treatments/vaccines.html.
- the Public Health Agency of Canada (https://www.canada.ca/en/public-health/services/diseases/coronavirus-disease-covid-19/vaccines.html) develops resources as well as prepares national summary statistics on population coverage and summary reports of adverse events following immunization (AEFI).
- provincial resources, guidelines and information for immunizers and health care providers can be found online at: https://www.gov.mb.ca/covid19/vaccine/index.html. Questions and answers specifically for community pharmacists and physicians that are participating in the COVID-19 Immunization Program can be found at: https://manitoba.ca/covid19/vaccine/partners/faq.html.

The following questions and answers are intended to supplement information from NACI, the product monographs, Health Canada, the Public Health Agency of Canada and the Government of Manitoba. Where available, links to new studies will be provided in the footnotes. Please note that this is not intended to be an exhaustive list of questions and answers but rather, is a central repository of emerging evidence and information that is being highlighted for your attention and action. Should you have a clinical question that is not addressed below or in one of the aforementioned resources linked above, please email your question to COVID@gov.mb.ca.

This information is current as of April 7, 2021.

General Vaccine Information

1. Health Canada approved the Janssen COVID-19 vaccine on March 5, 2021. When is Canada receiving supply?

Janssen is a one-dose viral vector vaccine (Ad26.COV2.S) that is approved for people who are 18 years of age and older. The Government of Canada secured access to up to 38 million doses, with 10 million doses expected by the end of September. The federal government is working with the manufacturer to determine allocations and shipping timelines.

2. What should I do if I receive a fraudulent offering of COVID-19 vaccine?

Please be advised that Health Canada and other Canadian jurisdictions are reporting fraudulent offers to procure COVID-19 vaccines direct from manufacture. Please be advised that all COVID-19 vaccines are procured federally; any direct offering is fraudulent and should be reported to the police or RCMP, whichever has jurisdiction in your area.

3. How should I communicate with vaccine hesitant clients/patients?

As per the Canadian Immunization Guide, vaccine hesitancy is a term used to describe a refusal of vaccination or a delay in an immunization schedule due to concerns about immunization. Vaccines evoke concerns different from other health interventions because vaccines are generally offered to individuals who are healthy, as opposed to other health interventions that are predominantly intended for individuals with a disease. Vaccine hesitancy is a complex issue with multiple determinants, the most important being:

- lack of understanding about the vaccine being given and about immunizations in general
- conflicting information from a variety of sources (for example, alternative medicine practitioners, anti-vaccination websites);
- mistrust of the source of information (for example, perceptions of business and financial motives of the vaccine industry)
- perceived risk of serious adverse events and concerns regarding injections (for example, pain and anxiety associated with immunization; coincidental rather than causal adverse events that are perceived as vaccine-related)
- lack of appreciation of the severity and incidence of vaccine preventable diseases;
- sociocultural beliefs (for example, religious beliefs)

With respect to COVID-19 vaccines, the hesitancy could focus specifically around:

- the speed in which the vaccines are being developed
- perceived perception that regulators and manufacturers are cutting corners (i.e. lack of transparency of the process in which a vaccine is approved and what is required from manufacturers)

This information is current as of April 7, 2021.

- new technology of vaccine manufacturing
- reports of adverse events following immunization
- perceived perception that one vaccine is better than another vaccine

It is therefore vital that immunizers and health care providers endeavor to address these concerns at an individual level, to ensure completion of the COVID-19 vaccine series as well as eliminate the spread of misinformation that can impact decision-making of other people. Health care providers can use different techniques of addressing vaccine hesitancy with their clients/patients, by:

- using presumptive and motivational interviewing techniques to identify and address specific vaccine concerns
- using effective and clear language to present evidence for disease risks and vaccine benefits fairly and accurately
- respecting differences of opinion about immunization in a non-judgemental, open dialogue approach
- managing pain from immunization[11]

Health care providers should have a multitude of evidence-based resources available that are tailored to a range of socio-cultural groups, including:

- factsheets
- product monographs
- information on Health Canada's independent drug authorization process[12]

4. What is the process for obtaining and documenting informed consent?

A provincial COVID-19 Vaccine Consent Form is available for immunizers and health care providers to use for the purposes of obtaining and documenting informed consent from clients/patients. Informed consent can be given verbally or in writing, and must be documented. A consent form or client/patients medical chart or electronic health record may be used to document informed consent. For more information, review the provincial Informed Consent Guidelines for Immunization (https://www.gov.mb.ca/health/publichealth/cdc/protocol/consentguidelines.pdf).

As per NACI, the COVID-19 vaccine may be offered to people who fall into one or more of the following categories, provided that the risks and benefits of immunization are adequately conveyed to the client/patient:

a. Immunosuppressed due to disease or treatment
b. Autoimmune disorder
c. Pregnant and/or breastfeeding

[11] Clinician focused immunization pain management resources are available through Immunize Canada at: https://immunize.ca/immunization-pain-management-clinician.
[12] For more information on vaccine hesitancy and communicating effectively about immunization, go to: https://www.canada.ca/en/public-health/services/publications/healthy-living/canadian-immunization-guide-part-1-key-immunization-information/page-5-communicating-effectively-immunization.html.

The process of obtaining informed consent from persons who fall into one or more of the above categories requires the immunizer or health care provider to review the pertinent information contained in the factsheets and have a risk-benefit discussion with the client/patient that is guided by the information in the Clinical Practice Guidelines.

Only in situations where the client/patient is getting immunized at a Super-Site or Pop-up Clinic is a health care provider required to provide a hard copy of the completed form to the client/patient and/or fax the form to Manitoba Health and Seniors Care (MHSC) for upload into the Public Health Information Management System (PHIMS).

5. What is the process for approving COVID-19 vaccines in Canada?

As per Health Canada, to market a vaccine in Canada, manufacturers must file an application to Health Canada via one of the following regulatory processes:

a. the interim order for COVID-19 drug authorization
b. the Food and Drug Regulations

The interim order regulatory process is a fast-tracked review process that allows Health Canada to start the review process as evidence becomes available instead of waiting until all studies are complete. Health Canada authorizes a vaccine under the interim order if the evidence demonstrates that the vaccine is:

- safe, effective and of good quality **AND**
- the intended benefits outweigh the material risks (March 15, 2021).

6. What is the interval between COVID-19 vaccine doses that I should follow?

As per NACI, there is no data on a maximum interval between doses or on medium or long-term efficacy of COVID-19 vaccines. In general, interruption of a vaccine series resulting in a greater than recommended interval between doses does not require restarting the series as delays between doses do not result in a reduction in final antibody concentrations for most multi-dose (prime-boost) products.

Morbidity and mortality from COVID-19 is ongoing. Based on emerging evidence of the protection provided by the first dose of a two-dose series for COVID-19 vaccines authorized in Canada, in the context of limited COVID-19 vaccine supply and ongoing pandemic disease, Manitoba is maximizing the number of individuals benefiting from the first dose by extending the interval between doses to four months (16 weeks).

Some specific patient populations including people scheduled to start immunosuppressing therapy and transplant candidates may require an alternative schedule that follows the authorized intervals.

The recommended schedule is as follows:

Vaccine	Schedule	Minimum interval	Authorized interval	Extended interval
Pfizer-BioNTech	2 doses	19 days [a]	21 days	16 weeks
Moderna	2 doses	21 days [b]	28 days	16 weeks
AZ/COVISHIELD	2 doses	28 days	4 to 12 weeks [c]	16 weeks

NOTES:

[a] pre-protocol design for the Pfizer-BioNTech vaccine clinical trial was 19-23 days.

[b] majority of participants in the Moderna clinical trial received the second dose 21 to 42 days after the first dose.

[c] AZ/COVISHIELD clinical trial demonstrated optimal efficacy when the interval between doses was ≥ 12 weeks.

7. NACI updated its recommendations for the use of AstraZeneca/COVISHIELD by removing the upper age limit; why did provincial eligibility criteria remain unchanged when NACI updated its recommendation?

NACI updated its recommendation based on real world effectiveness data from the United Kingdom showing single-dose effectiveness of AZ/COVISHIELD in persons aged 70 years of age and older of at least 70%.

The timing of NACI's updated recommendation came shortly after Manitoba communicated its provincial AZ/COVISHIELD vaccine eligibility criteria to community pharmacies and medical clinics that were being allocated the AZ/COVISHIELD vaccine. Community pharmacies and medical clinics had already reached out and scheduled their eligible patient populations to for their first doses of AZ/COVISHIELD based on the original age cut-off recommended by NACI of people ≤ 64 years of age.

Furthermore, mRNA vaccine eligibility criteria continues to expand to include more cohorts of the general population as supply and population coverage of those already eligible cohorts continues to increase. In the coming weeks, it is anticipated that the minimum age eligibility for the mRNA vaccine will converge with the maximum age eligibility for the AZ/COVISHIELD vaccine.

8. Some of my clients/patients are health care workers but are younger than 18 years of age; can I offer them the COVID-19 vaccine?

No. At this time, Health Canada has authorized both Moderna and AstraZeneca/COVISHIELD for use in persons 18 years of age and older, while Pfizer-BioNTech is authorized for use in persons aged 16 years and older. Currently, there is no data on COVID-19 vaccinations in children less than 12 years of age, and only limited data on the Pfizer-BioNTech vaccine in those 12 to 15 years of age.

According to the National Advisory Committee on Immunization (NACI), the Pfizer-BioNTech vaccine should not be routinely offered to children 12 to 15 years of age. NACI recommends that Pfizer-BioNTech may be offered to children 12 to 15 years of

age after they have reviewed the risks and benefits with their immunizer or health care provider, and informed consent is obtained. Clinical trials and post-marketing studies are ongoing and NACI is monitoring the evidence as it evolves.

As per provincial eligibility criteria (https://manitoba.ca/covid19/vaccine/eligibility-criteria.html) and recommendation for use, all clients/patients, regardless for the reason for immunization (i.e., eligibility criterion), must be 18 years of age or older to receive an mRNA vaccine. *Note that at this time, AstraZeneca/COVISHIELD is not recommended for use in persons aged < 55 years.*

9. Will clients/patients receiving a viral vector vaccine need a booster dose with an mRNA vaccine, given the suggested higher efficacy of the mRNA vaccines?

There is currently no evidence on the need for booster doses of COVID-19 vaccine after the vaccine series is complete. Given the emergence of variants of concern against which vaccine effectiveness may be decreased, additional vaccine doses may be necessary.

Furthermore, there is currently no data on the interchangeability of COVID-19 vaccines although clinical trials are underway to assess the efficacy and safety of a mixed schedule.

10. Do Health Canada-approved COVID-19 vaccines protect against variants of concern?

Yes, although the level of protection (i.e., efficacy) varies by vaccine and variant of concern.

COVID-19 variants of concern, such as those first identified in the United Kingdom, South Africa and Brazil, continue to spread globally. The first variant of concern detected in Canada was in December 2020. This variant was originally identified in the United Kingdom. Since then, cases of COVID-19 due to variants of concern have been identified in Manitoba.

11. Explain the discrepancy between the priority 1 list of immunosuppressing conditions for the AstraZeneca/COVISHIELD vaccine and the list of patients on immunosuppressive therapy that require further consult before immunization.

The important distinction between the two lists is the timing of the vaccine in relationship to the dose of immunosuppressing medication. The attending physician or specialist may recommend a different time interval (than what is suggested on page 10) based on client/patient assessment. NOTE: earlier iterations of the Clinical Practice Guidelines referred to the list of patients on immunosuppressive therapy (page 10) as “people who should not be immunized and require further consultation.” This has since been updated to say, “People who require further consultation before immunization.”

12. Is there an increased risk of thromboembolic events with the AstraZeneca/COVISHIELD vaccine?

On March 8, 2021, Health Canada was informed by the European Medicines Agency (EMA) that Austria stopped using a batch of AstraZeneca (AZ) following three reports of thromboembolic events following vaccination. As a result, several countries in Europe including Denmark, temporarily paused the use of specific batches of AZ in their campaigns as a precautionary measure, pending investigation.

On March 18, 2021, following their investigation, the EMA and the United Kingdom Medicines and Healthcare products Regulatory Agency (MHRA) issued a statement that the benefits of the use of AZ continue to outweigh the risks. EMA's safety committee reports that overall the number of thromboembolic events reported after vaccination, both in studies before licensing and in reports after rollout of vaccination campaigns, was lower than that expected in the general population. This allows EMA's safety committee to confirm that there is no increase in overall risk of blood clots. However, in younger patients there remain some concerns, related in particular to these rare cases. The reported cases were almost all in women under 55 years of age.[13]

On March 18, Health Canada issued a statement that it had assessed the available data on the reported events and determined that the AZ vaccine has not been associated with an increase in the overall risk of blood clots. On March 24, Health Canada updated the AstraZeneca and COVISHIELD Product Monographs, as well as issued a Health Product Risk Communication to health care professionals. These updates highlight a combination of thrombosis and thrombocytopenia, in some cases accompanied by bleeding, has been observed very rarely following vaccination with the AstraZeneca COVID-19 vaccine, and provides further guidance for health care professionals and vaccine recipients.

- AstraZeneca Product Monograph: https://covid-vaccine.canada.ca/info/pdf/astrazeneca-covid-19-vaccine-pm-en.pdf
- COVISHIELD Product Monograph: https://covid-vaccine.canada.ca/info/pdf/covishield-pm-en.pdf
- Health Product Risk Communication: https://covid-vaccine.canada.ca/info/pdf/astrazeneca-covid-19-vaccine-letter.pdf

On March 29, 2021, the National Advisory Committee on Immunization (NACI) recommended that AstraZeneca COVID-19 vaccine should not be used in adults < 55 years of age at this time while the safety signal of Vaccine-Induced Pro-thrombotic Immune Thrombocytopenia (VIPIT) following vaccination with AstraZeneca COVID-19

[13] https://www.ema.europa.eu/en/news/covid-19-vaccine-astrazeneca-benefits-still-outweigh-risks-despite-possible-link-rare-blood-clots

vaccine is investigated further. For more information, go to pages 16 - 17.

13. I have a client/patient who experienced an AEFI; what do I do?

An adverse event following immunization (AEFI) is any untoward medical occurrence in a vaccinee that follows immunization. It may be any unfavorable and/or unintended sign, abnormal laboratory finding, symptom or disease.

Report AEFIs as per www.gov.mb.ca/health/publichealth/cdc/div/aefi.html#rrp. In accordance with Section 59 of The Public Health Act, health care providers are to report a reportable AEFI within seven days of becoming aware of the AEFI. Furthermore, health care providers should report a serious AEFI within one business day, which can be by telephone, followed by the complete written report within 72 hours.

A reportable AEFI is an event that:

1. is temporally associated with a vaccine AND
2. has no other clear cause at the time of reporting

Of particular interest are AEFIs that are serious, unexpected and/or of special interest. But all AEFIs that meet (1) or (2) above should be reported, unless they are only mild local reactions that are not overly concerning to the vaccine recipient.

An AEFI is considered “unexpected” if either of the following criteria is met:

- it is not listed in the most current Health Canada-approved product monograph for vaccines marketed in Canada
- listed in the product monograph but is different in nature, severity, frequency, specificity or outcome

Provide clients/patients with the following factsheet before immunization: What to do if you experience an adverse reaction after receiving the COVID-19 vaccine (https://www.gov.mb.ca/asset_library/en/covid/covid19_vaccine_reaction_factsheet.pdf).

Recommendations around future COVID-19 vaccine doses will depend on the type and severity of reaction. If there is any ambiguity, consult a relevant specialist.

14. Can a client/patient who had a previous anaphylactic reaction to a vaccine and underwent allergy testing thereafter, receive a COVID-19 vaccine?

Yes. History of a prior anaphylactic reaction to vaccine is a precaution but not a contraindication to receiving a COVID-19 vaccine, provided the client does not have any known allergies to any of the ingredients found in the vaccine (or other known contraindications). If no component of the vaccine was identified by an allergist as a cause for the previous reported anaphylactic reaction, it is deemed safe to proceed. However, it is recommended that the client/patient be observed for 30 minutes post-vaccination (as opposed to the routine recommendation of 15 minutes post-vaccination).

If the client/patient did not undergo allergy testing following the previous anaphylactic reaction to a vaccine which has shared ingredients to the COVID-19 vaccine to be given, it would be prudent to consult allergy/immunology.

15. I have a client/patient who experienced a mild, non-anaphylactic, allergic reaction following the first dose of COVID-19 vaccine; should I proceed to offer the second dose?

Generally speaking, subsequent doses can be offered provided that the client/patient is not allergic to an active substance or allergic to any of the ingredients of the vaccine. The client/patient should be counselled prior to vaccination on the possibility of experiencing another allergic reaction, and may need to stay in the clinic for at least 30 minutes post-vaccination to monitor for signs of a more severe allergic reaction. If there is any ambiguity, consult a relevant specialist.

16. I have a client/patient who experienced an anaphylactic reaction following their first dose of COVID-19 vaccine; what does this mean for future doses?

Consult allergist before administering further doses of COVID-19 vaccine.

17. Should I counsel patients to take acetaminophen or ibuprofen before getting immunized to mitigate or minimize potential side-effects or pain from immunization?

No. NACI recommends that acetaminophen or ibuprofen should not be routinely used before or at the time of vaccination, but their use is not a contraindication to vaccination. There is currently no evidence on the benefit from administration of oral analgesics for the prevention of immunization injection pain or systemic reactions.

Acetaminophen or ibuprofen after vaccination may be used for the management of pain and/or fever after vaccination.

18. If a client/patient experiences side effect(s) after vaccination that mimic COVID-19, should they isolate and get tested for COVID-19?

Public health officials strongly urge anyone who has cold or flu-like symptoms, such as a cough, fever, runny nose, sore throat, headache, or any of the symptoms listed in the screening tool to isolate and get tested for COVID-19. The Manitoba COVID-19 Screening Tool is available at: https://sharedhealthmb.ca/covid19/screening-tool/.

Vaccine Efficacy

19. Due to suggested higher efficacy, NACI preferentially recommends mRNA vaccines for those at highest risk of severe illness and death, and highest risk of exposure to COVID-19. Should I therefore advise my patients who are eligible for a non-mRNA vaccine now, to wait until they are eligible for an mRNA vaccine?

No. Persons who are eligible now for a non-mRNA vaccine should be counselled to receive the non-mRNA vaccine.

20. What is the difference between vaccine efficacy and effectiveness, and what does the data tell us about the efficacy and effectiveness of the COVID-19 vaccines authorized for use in Canada?

Vaccine efficacy provides an estimate of how well a vaccine works under optimal conditions (e.g., clinical trial). **Vaccine effectiveness** provides an estimate of how well a vaccine works in the real world, under "normal" conditions. Estimates of efficacy or effectiveness can be expressed in differing ways, such as the vaccines affect on lab-confirmed (a)symptomatic disease or in reducing hospitalizations or death.

mRNA Vaccines

Clinical trail data for both Pfizer-BioNTech and Moderna demonstrated approx. 95 per cent **efficacy** in preventing lab-confirmed COVID-19 after two doses among adult participants. Emerging **effectiveness** data from the UK, Scotland and Israel suggests that one dose of mRNA vaccine is 70 to 80 per cent effective in preventing lab-confirmed COVID-19 infection and significantly reduces hospitalizations and death.

Viral Vector Vaccine

Early clinical trial data for AstraZeneca/COVISHIELD demonstrated an average **vaccine efficacy** of 81.6% in participants aged 18 to ≤ 64 years with ≥ 12 week interval. **Effectiveness** data from Public Health England demonstrated that vaccination with a single dose of AstraZeneca/COVISHIELD produced a significant reduction in symptomatic SARS-CoV-2 positive cases in adults aged ≥ 70 years of at least a 70 per cent, with even greater protection against severe disease (80% reduction in hospitalizations).[14] The **effectiveness** of the first dose of AstraZeneca/COVISHIELD in Scotland demonstrated a 94% reduction in hospitalizations due to COVID-19.[15]

On March 22, 2021, AstraZeneca released interim safety and efficacy analysis from the AZD1222 US Phase III trial[16], suggesting:

- 79% efficacy at preventing symptomatic COVID-19
- 100% efficacy against severe or critical disease and hospitalization
- Comparable efficacy result across ethnicity and age, with 80% efficacy in participants aged 65 years and older
- Favorable reactogenicity and overall safety profile

Since releasing the (above) interim data, AstraZeneca has since responded to the controversy around claims that the manufacturer used outdated information in its trial results. AZ now says its COVID-19 vaccine was 76% effective at preventing symptomatic illness (based on the latest data of 190 infections versus earlier interim data based on 141 infections). A peer reviewed publication is expected in the future.[17]

[14] https://www.medrxiv.org/content/10.1101/2021.03.01.21252652v1
[15] https://www.ed.ac.uk/files/atoms/files/scotland_firstvaccinedata_preprint.pdf
[16] https://www.astrazeneca.com/content/astraz/media-centre/press-releases/2021/astrazeneca-us-vaccine-trial-met-primary-endpoint.html
[17] https://globalnews.ca/news/7718106/astrazeneca-vaccine-new-us-data/

21. How long does protection after vaccination last (i.e., duration of protection)?

The duration of protection of mRNA or viral vector COVID-19 vaccine is currently unknown. This information will start emerging as clinical trials reach a certain level of maturity.

Vaccine Storage, Handling and Transport

22. In some situations, I am able to draw more vaccine from a multi-dose vial than what is listed on the label. Is this okay?

Yes, provided doses administered and inventory is updated accordingly, and all administration-related infection, prevention and control guidelines are followed. The Province recommends that only additional doses from a multi-dose vial should be drawn if the full dose can be drawn from one vial (i.e., it is recommended that health care providers do not pool vaccine and draw from multiple vials to make additional doses).

23. What are some general storage and handling guidelines?

- Ensure empty vaccine vials are properly disposed of in sharps containers (i.e., do not discard empty vials in garbage cans or bins) and the box that doses are shipped in that comes from a manufacturer should be shredded (this is to avoid fraudulent claims).
- The storage requirements of all COVID-19 authorized vaccines in Canada is as follows:

	Primary storage requirements pre-puncture	**Storage requirements pre-puncture**	**Usage limit post-puncture**
Pfizer-BioNTech	-80˚C to -60˚C **OR** -25vC to -15˚C for up to 2 weeks	120 hours (5 days) at +2˚C to +8˚C **and/or** 2 hours up to +25˚C	6 hours at +2˚C to +25˚C
Moderna	-25˚C to -15˚C	30 days at +2˚C to +8˚C **and/or** 12 hours at +8˚C to +25˚C	6 hours at +2˚C to +25˚C
AZ/COVISHIELD	+2˚C to +8˚C	+2˚C to +8˚C	6 hours at room temperature (up to +30˚C) **OR** 48 hours at +2˚C to +8˚C[a]
NOTES: [a] punctured vial can be re-refrigerated however, note that cumulative storage time at room temperature cannot exceed 6 hours, and total cumulative storage time cannot exceed 48 hours. After this time, discard vial.			

This information is current as of April 7, 2021.

24. What do I do if I experience a cold chain break?

Please refer to Manitoba Health and Seniors Care's (MHSC) Adverse Storage Condition (ASC) Form and Procedure (https://www.gov.mb.ca/health/publichealth/cdc/docs/ccf.pdf) for detailed information on what constitutes a cold chain break and protocols for reporting the excursion to MHSC and handling the affected product.

Appendix A

Advisability and timing of COVID-19 vaccination in cancer/serious blood disorder patients with Pfizer-BioNTech, Moderna or AstraZeneca/COVISHIELD vaccine

The current strategy is to provide a first dose of vaccine as soon as possible. The second dose may be delayed for up to 4 months. The recommendations below reflect this strategy. These recommendations are subject to change, particularly if the strategy for second dose delivery changes again.

Specific recommendations for cancer patients is as follows:

- When a patient's age group becomes eligible, they should get vaccinated as soon as possible.
- The patients CCMB clinical team should be made aware that the patient will be getting vaccinated, when, and with what product.
- As a general principle, the first dose of vaccine should be administered at least 5-6 weeks before commencing anti-cancer drug treatment or radiation treatment. Given current eligibility guidelines, this is likely not feasible, and vaccination should take place when possible, using the following guidelines:

Type of Treatment	Suggested Timing of Vaccination
Cyclical chemotherapy	During active chemotherapy treatment, vaccine should be administered within a few days prior to next chemotherapy cycle (away from the neutrophil and platelet nadir), if possible. Vaccine should not be administered on the same day as chemotherapy If neutrophil count is not anticipated to recover, vaccination can occur at any time during the cycle, avoiding the day of chemotherapy administration.
Tyrosine kinase inhibitors Endocrine therapy (including PARP inhibitors) Continuous oral chemotherapy	No specific timing required
Immune checkpoint inhibitors Proteasome inhibitors Immunomodulatory agents	Avoid vaccinating on day of treatment
Monoclonal antibodies (including those targeting CD19 , CD 20 and CD 22)	No specific timing; avoid vaccinating on day of treatment.
Corticosteroids	If administered cyclically, aim to vaccinate when not receiving the steroids.

This information is current as of April 7, 2021.

	If continuous, no specific timing
Auto and allo HSCT and CAR-T	Delay vaccination until > 3 months post HSCT
IVIG	No specific timing
Patients due to commence radiotherapy	If delaying radiotherapy will not compromise outcomes, consider delaying radiotherapy until immunity is likely to have occurred post immunization. If outcomes could be compromised by delay, immunization should proceed, preferably as early in the course of radiotherapy as possible.

Important points:

1. Although many cancer treatments may impair vaccine effectiveness, there is currently no evidence that vaccines will harm patients on such treatments. As such, the default should be to proceed with vaccination if there is no other contraindication.
2. Vaccination should generally be avoided on the day a cyclical therapy is administered to minimize the chance of ascribing a treatment-related adverse event to the wrong agent.