Ontario

Ministry of Health

AstraZeneca/COVISHIELD COVID-19 Vaccine Second Dose Q&A for Health Care Providers

Version 1.0 – June 4, 2021

This document provides basic information only and is not intended to provide or take the place of medical advice, diagnosis or treatment, or legal advice.

What has changed?

The National Advisory Committee on Immunization (NACI) released their recommendation on the use of an mRNA vaccine to complete a COVID-19 vaccine series that was started with the AstraZeneca/COVISHIELD COVID-19 vaccine on June 1st 2021. Based on the available evidence NACI has provided the following recommendation:

- Persons who received a first dose of the AstraZeneca/COVISHIELD COVID-19 vaccine may be offered either AstraZeneca/COVISHIELD COVID-19 vaccine or an mRNA COVID-19 vaccine (Pfizer-BioNTech or Moderna) for their second dose, unless contraindicated. The previous dose should be counted, and the series need not be restarted.

In the case of COVID-19 vaccines, NACI considered the risk of Vaccine-Induced Immune Thrombotic Thrombocytopenia (VITT) associated with the use of viral vector vaccines, the availability of alternative mRNA COVID-19 vaccines without this risk, general principles of vaccinology, as well as evidence on the safety and immunogenicity of a mixed COVID-19 vaccine schedule.

Read the full statement with rationale and evidence base here: NACI Rapid Response: Interchangeability of Authorized COVID-19 Vaccines

All second dose appointments have been accelerated in Ontario in response to improved vaccine supply. Aligned with the province's accelerated second dose plan, all individuals who received AstraZeneca/COVISHIELD COVID-19 vaccine as a first dose will be eligible to receive their second dose at a 12-week interval, regardless of which vaccine product they choose. The timeline eligibility for 2nd doses may change as more is understood about vaccine supply in Ontario over the summer.

Individuals who received a first dose of the AstraZeneca/COVISHIELD COVID-19 vaccine may want to complete their series with this product, while others may prefer to receive an mRNA vaccine for their second dose. Individual decision-making should assess the risks and benefits based on individual circumstances and preferences. The information in this document intended to help support this decision-making process and providers in having conversations with their patients.

What is the evidence to support each option for my patient/client?

Option 1: Receive an AstraZeneca COVID-19 vaccine for the second dose

A. What do we know about how well the AstraZeneca/COVISHIELD COVID-19 vaccine protects against COVID-19?
    - Clinical trial data and real-world evidence have demonstrated that a complete 2 dose series of the AstraZeneca/COVISHILED COVID-19 vaccines provide good protection against symptomatic COVID-19 and severe outcomes. Clinical trials demonstrated that when two doses of the AstraZeneca are spread out by 12 weeks, it provided an estimated 82% protection against symptomatic disease. When the two doses were given closer together (9-12 weeks), protection was estimated at 69%.

B. What do we know about the risk of VITT associated with this series?

- Rare cases of a specific syndrome that involves serious blood clots (at unusual sites such as cerebral venous sinus thrombosis) associated with thrombocytopenia have recently been reported after vaccination with viral vector vaccines. These cases often occur between 4 and 28 days after receipt of the vaccine.
    - Early identification and appropriate treatment are critical.
    - Investigations to better understand this syndrome, often referred to as Vaccine-Induced Immune Thrombotic Thrombocytopenia (VITT), are ongoing.
    - Clots related to VITT can be very aggressive and challenging to treat with potential associated long-term morbidity.
    - The case fatality rate of VITT also varies between countries, and ranges between 20 and 50%.
- Currently the reported risk of VITT after the second dose of AstraZeneca / COVISHIELD COVID-19 vaccine is lower than after the first dose. With increased observation times, VITT rates have generally increased, including the risk estimate following the second dose. Risk estimates are continually updated as new data become available.
    - The rate of VIIT in Canada after a first dose has been estimated to be approximately 1 in 55,000 doses administered (Ontario Science Advisory Table).
    - At this time data from the United Kingdom (UK) suggests that the rate of VITT following the second dose is approximately 1 in 600,000 doses administered. (18 events following 13.4 million second doses administered in the UK as of May 26, 2021). Information from the UK is regularly reviewed and reported because many millions of second doses have been administered in this country. This report is updated weekly and can be found here: Coronavirus vaccine - weekly summary of Yellow Card reporting - GOV.UK (www.gov.uk)

C. If an individual received a first dose of the AstraZeneca/COVISHIELD COVID-19 vaccine, when are they eligible to receive their second dose of the AstraZeneca vaccine and how will they book?
    - Aligned with the province's accelerated second dose plan, all individuals who received AstraZeneca/COVISHIELD COVID-19 vaccine as a first dose will be eligible to receive their second dose at a 12 week interval, regardless of which vaccine product they choose.
    - Individuals with exceptions to the extended dose interval as per the provincial vaccine rollout plan, may continue to receive the vaccine at the product monograph interval (between 4 to 12 weeks).
    - Beginning June 4, 2021, individuals who received their first dose of the AstraZeneca vaccine 12 weeks prior and who would like their second dose of the AstraZeneca vaccine, can contact the pharmacy or primary care provider where they received their first dose to book an appointment.

Option 2: Receive an mRNA vaccine for a second dose

A. What do we know about how well an AstraZeneca/COVISHIELD COVID-19 vaccine followed by an mRNA vaccine protects against COVID-19?

- There is evidence that providing an mRNA vaccine after AstraZeneca vaccine will boost the immune response, which is what we expect from a second dose.
    - A recent study from Spain (CombiVacS trial) has demonstrated that that a mixed vaccine schedule of AstraZeneca COVID-19 vaccine followed by a dose of the Pfizer BioNTech COVID-19 vaccine produces a strong immune response, as measured by antibodies following the second dose, when compared to study participants with only a single dose of the AstraZeneca vaccine .
    - Studies involving mixed schedules with vaccines using different platforms are ongoing. The CoM-Cov randomised clinical trial from the United Kingdom (UK), compared four permutations of the AstraZeneca and Pfizer-BioNTech vaccines at 28-day intervals and data on

immunogenicity is forthcoming. For more information, see the study website: https://comcovstudy.org.uk/home

- This is not a new concept. Similar vaccines from different manufacturers are used when vaccine supply or public health programs change. For example, different vaccine products have been safely and effectively used to complete vaccine series for influenza, hepatitis A, and many others. General vaccine principles suggest that vaccines from different manufacturers can be used interchangeably when vaccines are authorized for the same purpose, for the same populations, have similar schedules, have similar contain or produce similar type(s) antigens and are similar in terms of vaccine safety, immune responses and protection provided.
- The National Advisory Committee on Immunization (NACI) has indicated an mRNA COVID-19 vaccine (Pfizer BioNTech or Moderna) may be offered as the second dose in a vaccine series for those that received a first dose of AstraZeneca/COVISHIELD COVID-19 vaccine

B. What do we know about the risks associated with an AstraZeneca/COVISHIELD COVID-19 vaccine followed by an mRNA vaccine?

- Emerging evidence indicates that mixed COVID-19 schedules have an acceptable safety profile. There is direct evidence on the safety of mixed COVID-19 immunization schedules (AstraZeneca and Pfizer-BioNTech) from three studies at dosing intervals between 4 and 12 weeks.
- There is a possibility of increased short-term side effects when using mixed COVID-19 vaccine schedules, including headache, fatigue and feeling generally ill. This was particularly noted with a short interval of 4 weeks between the first and second dose. These side effects are temporary and resolve without complications.

C. If an individual received a first dose of the AstraZeneca/COVISHIELD COVID-19 vaccine, when are they eligible to receive their second dose of an mRNA vaccine and how will they book?

- Aligned with the province's accelerated second dose plan, all individuals who received AstraZeneca/COVISHIELD COVID-19 as a first dose will be eligible to receive their second dose at a 12-week interval, regardless of which vaccine product they choose.
- Individuals with exceptions to the extended dose interval as per the provincial vaccine rollout plan, may continue to receive the vaccine at the product monograph interval (between 4 to 12 weeks).
- Beginning June 4, 2021, individuals who received their first dose of the AstraZeneca vaccine and are opting to receive an mRNA vaccine have the option to schedule their second dose appointment at a participating pharmacy where the Pfizer or Moderna vaccines are administered. Primary care settings and pharmacies may also be reaching out to eligible Ontarians.
- In addition, expected the week of June 7, 2021, individuals who received their first dose of the AstraZeneca vaccine and who choose to receive an mRNA vaccine for their second dose can register for a "second dose only" at a 12-week interval through the provincial booking system. Eligible individuals will also be able to schedule their second dose appointment directly through public health units that use their own booking system

Will the guidance about second dose for those who received a first dose of AstraZeneca change again?

Studies involving mixed schedules with vaccines using different vaccine platforms are ongoing and real-world evidence will also be forthcoming. Immunogenicity data from the UK Com-COV clinical trial is expected later in June 2021 and recommendations may be updated upon review of the findings. Investigations

Intervals for 2nd doses may change as more is known about vaccine supply levels over the summer months.

Additional Information

National Advisory Committee on Immunization's (NACI) Recommendations on the use of COVID-19 vaccines - Canada.ca

NACI Rapid Response: Interchangeability of Authorized COVID-19 Vaccines

Public Health Agency of Canada: Interchangeability of Authorized COVID-19 vaccines

Vaccine Safety | Public Health Ontario

Comparing COVID-19 Vaccine Schedule Combinations | Com-CoV (comcovstudy.org.uk)

Lancet Correspondence: Heterologous prime-boost COVID-19 vaccination: initial reactogenicity data

Lancet PrePrint: Reactogenicity and immunogenicity of BNT162b2 in subjects having received 1 a first dose of 2 ChAdOx1S: initial results of a randomised, adaptive, phase 2 trial (CombiVacS)

The Canadian MOSAIC Study (Mix and match of the second COVID-19 vaccine dose for SAfety and ImmunogeniCity)

Weekly summary of Yellow Card reporting from the UK: https://www.gov.uk/government/publications/coronavirus-covid-19-vaccine-adverse-reactions/coronavirus-vaccine-summary-of-yellow-card-reporting (under the section: Blood clots with concurrent low platelets)

Risk of Vaccine-Induced Thrombotic Thrombocytopenia (VITT) following the AstraZeneca/COVISHIELD Adenovirus Vector COVID-19 Vaccines - Ontario COVID-19 Science Advisory Table (covid19-sciencetable.ca)

Vaccine-Induced Immune Thrombotic Thrombocytopenia (VITT) Following Adenovirus Vector COVID-19 Vaccination: Interim Guidance for Healthcare

Professionals in the Outpatient Setting - Ontario COVID-19 Science Advisory Table (covid19-sciencetable.ca)

Vaccine-Induced Immune Thrombotic Thrombocytopenia (VITT) Following Adenovirus Vector COVID-19 Vaccination: Interim Guidance for Healthcare Professionals in Emergency Department and Inpatient Settings - Ontario COVID-19 Science Advisory Table (covid19-sciencetable.ca)

Vaccine-Induced Immune Thrombotic Thrombocytopenia (VITT) Following Adenovirus Vector COVID-19 Vaccination: Lay Summary - Ontario COVID-19 Science Advisory Table (covid19-sciencetable.ca)