BC Centre for Disease Control
Provincial Health Services Authority

Second dose considerations for those who received AstraZeneca or COVISHIELD for first dose COVID-19 immunization

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The following Q&A is intended for health care professionals.

This document is adapted from the Public Health Agency of Canada.

1. Why did BC update its recommendations on the interchangeability of COVID-19 vaccines and what is the scientific basis for these updated recommendations?

The updated recommendations are based on current evidence and NACI's expert opinion. Recent studies on the safety of and immune responses produced by mixed COVID-19 vaccine schedules provide the evidence for vaccine interchangeability. An observational study of healthcare workers in Germany[i] and the Com-COV randomized clinical trial from the United Kingdom[ii] report on the safety of mixed schedules, and the Spanish CombiVacS trial reports[iii] [iv], on both the safety and immune responses produced from mixed COVID-19 vaccine schedules. Current evidence suggests a first dose of the AstraZeneca vaccine followed by a second dose of an mRNA vaccine (Pfizer-BioNTech was used in studies) has a good safety profile at shorter (4 week) and longer (8 to 12 week) intervals. There is a possibility of increased short-term side effects with mixed COVID-19 vaccine schedules, especially with shorter intervals. These side effects are temporary and resolve without complications. Current evidence suggests a first dose of the AstraZeneca vaccine followed by a second dose of an mRNA vaccine (Pfizer-BioNTech was used in studies) is safe at shorter (4-week) and longer (8- to 12-week) intervals.

NACI also considered the risk of Thrombosis with Thrombocytopenia Syndrome (TTS) associated with the AstraZeneca vaccine, Canada's current and projected mRNA vaccine supply and principles of ethical decision-making.

The rate of TTS after the second dose of AstraZeneca vaccine appears to be lower than with the first dose but has increased over time, with current estimates of approximately 1 per 600,000 people vaccinated.

More results from ongoing studies on mixed COVID-19 vaccine schedules, including results from the UK Com-COV trial, are expected in the coming weeks and months. NACI continues to closely monitor evolving evidence on mixed COVID-19 vaccine schedules and will update recommendations as needed.

2. What is the recommendation in B.C. for people who received the AstraZeneca/COVISHIELD vaccine to offer as their second dose?

People who received AstraZeneca or COVISHIELD vaccine for their first dose may be offered the option of receiving either AstraZeneca or an mRNA vaccine (Pfizer-BioNTech or Moderna) for their second dose.

Some individuals who received the AstraZeneca/COVISHIELD vaccine for their first dose may want to complete their series with the same vaccine product, while others may want to receive an mRNA vaccine for their second dose. A resource for the public will be available on the BCCDC's Vaccine

registration and eligibility page that can support individuals to make an informed decision based on the information available at this time. This resource is translated into several different languages. Individuals are recommended to confer with their primary care provider, pharmacist or call 8-1-1 (HealthLink BC) if they have questions prior to booking an appointment for one or the other vaccine.

In making an informed decision, individuals should know:

- mRNA and AstraZeneca vaccines are both available in Canada and there will be sufficient supply of both types of vaccine to provide second doses;
- There is a risk of TTS associated with the AstraZeneca/COVISHIELD viral vector vaccine but not the mRNA (Pfizer-BioNTech, Moderna) vaccines; and
- There is a possibility of increased short-term side effects when mixed COVID-19 vaccine schedules are used. These side effects are temporary and resolve without complications.

People who experienced TTS following vaccination with the AstraZeneca/COVISHIELD viral vector COVID-19 vaccine should not receive a second dose of the AstraZeneca/COVISHIELD viral vector vaccine.

It is important to inform clients that AstraZeneca vaccine will only be available through pharmacies and not through mass immunization clinics, whereas mRNA vaccines will only be available through mass clinics. For further information regarding booking a second dose, go to the Get Your Second Vaccine Dose webpage on the BC Government website.

3. Is immune response data from the Com-COV randomised clinical trial from the UK publically available? Why is Com-COV immune response data not included in this NACI decision?

Initial safety results from the Oxford Vaccine Group's Com-COV vaccine trial were published on May 12, 2021, and show no serious safety concerns. The data to date show higher rates of mild or moderate short-term side effects, including fever, redness, and local reactions, if the AstraZeneca viral vector vaccine is received first and is followed by the Pfizer-BioNTech mRNA vaccine 4 weeks later.

Data on immune responses from the Com-COV vaccine trial have not been published at this time. However, immune response data from the CombiVacS trial in Spain is now available and was presented in detail to NACI. This evidence and NACI's expert opinion on the current scientific data formed the foundation of NACI's current position on the immune response of mixed schedules for COVID-19 vaccines.

More results from ongoing studies on mixed COVID-19 vaccine schedules, including results of the UK Com-COV trial, are expected in the coming weeks and months. NACI continues to closely monitor evolving evidence and will update recommendations as needed.

4. Does NACI also recommend Janssen as a second dose to AstraZeneca if the AstraZeneca vaccine is not available?

Janssen is authorized as a one-dose vaccine. If someone receives one dose of the Janssen vaccine they are considered fully immunized regardless of any previous COVID-19 vaccine doses they may have received. Therefore, Janssen should not be used to complete a series started with AstraZeneca. Please note that Janssen vaccine is not currently available in B.C.

5. If people are allowed to use mixed COVID-19 vaccine schedules, what interval should they use? The mRNA vaccines have different intervals from AstraZeneca and COVISHIELD. Will the interval of a mixed dose schedule impact the side effects?

The current interval between doses in B.C. is based on vaccine supply and operational recommendations as outlined on the government of B.C. website. As of May 27, 2021, the recommended interval between dose 1 and 2 is 8 weeks for all COVID-19 vaccines requiring a 2-dose series. Therefore, individuals who received AstraZeneca/COVISHIELD for dose 1 can receive either AstraZeneca or an mRNA vaccine on the same interval as those who received an mRNA vaccine for dose 1 (i.e., 8 weeks).

While the approved minimum interval between dose 1 and 2 of AstraZeneca is 4 weeks, the preferred interval is 8 to 12 weeks. The National Advisory Committee on Immunization (NACI) recommends a minimum of 12 weeks between doses because of a trend toward improved vaccine performance following this longer interval in an exploratory analysis[v]. However, clear superiority of the 12-week interval has not been demonstrated, with 95% confidence intervals overlapping with the 2 week interval. In the UK program, an 8-week interval between AstraZeneca doses is recommended, with 4 weeks used when early protection is required such as in immunocompromised individuals.

6. Are other countries offering mixed dose schedules for COVID-19 vaccines?

Following the emergence of TTS, several European countries, including Denmark, Finland, France, Germany, Sweden, Norway and Spain began offering a second dose of an mRNA vaccine (Pfizer-BioNTech or Moderna) to those who received a first dose of the AstraZeneca/COVISHIELD vaccine. Other countries are also considering the option to implement mixed vaccine schedules.

7. While mixed vaccine schedules are permitted under NACI guidance, why is B.C. not preferentially recommending mRNA vaccines for all second doses as does NACI ?

All COVID-19 vaccines approved by Health Canada, including the AstraZeneca/COVISHIELD COVID-19 vaccine, meet strict efficacy and quality standards. All authorized vaccines have demonstrated efficacy in preventing severe outcomes from COVID-19, including severe illness and death.

For individuals who received a first dose of the AstraZeneca/COVISHIELD vaccine, NACI indicates that either AstraZeneca vaccine or an mRNA vaccine (Pfizer-BioNTech or Moderna) may be offered for the next dose, however preferentially recommends an mRNA vaccine for the second dose. In making this recommendation, NACI considered:

- The risk of TTS associated with the AstraZeneca viral vector vaccine but not the mRNA (Pfizer-BioNTech, Moderna) vaccines;
- The possibility of increased short-term side effects of mixed COVID-19 vaccine schedules; and
- Available data on the immune responses produced by a first dose of the AstraZeneca vaccine followed by a second dose of the Pfizer-BioNTech vaccine.

However, the data available on the effectiveness of first dose AstraZeneca vaccine followed by a second dose of an mRNA vaccine is limited and based on small study populations. Although the results of these studies found a strong immune response to a mixed series, there is currently no immunological correlate of protection (i.e., antibody level) that has been determined for SARS-CoV-2, and therefore it is unknown if a stronger immune response directly relates to improved protection. Additionally, clinical trial data and real world effectiveness data, particularly from the United Kingdom where AstraZeneca has been used for the majority of its COVID-19 immunization program, show that a complete series of AstraZeneca vaccine is comparable to a complete series of an mRNA vaccine in protecting against severe COVID-19 outcomes (e.g., hospitalization and death). Therefore, BC continues to offer either mRNA vaccine or AstraZeneca vaccine for AstraZeneca/COVISHIELD first dose recipients, as either vaccine is a safe and effective option.

While some individuals who started their series with the AstraZeneca/COVISHIELD vaccine may want to complete their series with the same vaccine product, others will want an mRNA vaccine for their second dose. Individuals should consider talking to a healthcare professional to help assess their unique situation in order to make an informed decision.

People who experienced TTS following vaccination with the AstraZeneca/COVISHIELD viral vector COVID-19 vaccine, or who have other contraindications, should not receive a second dose of the AstraZeneca/COVISHIELD viral vector vaccine.

8. What is the current rate and risk of Thrombosis with Thrombocytopenia Syndrome with viral vector COVID-19 vaccines? Why is it changing?

Canada is continuing to monitor and assess reports of rare but serious medical events involving blood clots (thrombosis) with low blood platelets (thrombocytopenia) following COVID-19 immunization, referred to as Thrombosis with Thrombocytopenia Syndrome (TTS).

The rate of TTS is about 1 per 50,000 cases in persons vaccinated with a first dose of AstraZeneca/COVISHIELD vaccine. The rate of TTS after the second dose of the AstraZeneca/COVISHIELD vaccine appears to be lower than with the first dose but has increased over time, with current estimates of approximately 1 per 600,000 (17 cases out of 10.7 million second doses administered). Rates of TTS continue to evolve as cases continue to be reported and investigated, and varies between countries.

9. Is the risk and rate of TTS the same for the first and second dose for the AstraZeneca COVID-19 vaccine?

The rate of TTS after the second dose of the AstraZeneca vaccine appears to be lower than with the first dose but has increased over time as more people globally get a second dose, with current estimates of approximately 1 per 600,000 persons vaccinated.

The rate of TTS after the second and first dose may continue to change. This is being monitored closely.

10. If an individual received an mRNA vaccine for dose 1, do they have the option to receive AstraZeneca for dose 2?

No, a vaccine series initiated with either Pfizer-BioNTech or Moderna should be completed with the same product, or if it is not possible to determine what product was used for the first dose, or if the same product is unavailable, the second dose may be given with an available mRNA product. However, if a second dose of an mRNA vaccine is contraindicated (e.g., due to a serious allergic event following the first dose) or the Medical Health Officer and/or allergist has recommended that they not receive a subsequent dose of an mRNA vaccine, AstraZeneca vaccine may be offered as a second dose with a prolonged period of observation for at least 30 minutes after immunization.

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