March 29, 2021

Key messages for the Council of Chief Medical Officers of Health
Use of AstraZeneca COVID-19 vaccine in younger adults

- As Chief Medical Officers of Health, the health and safety of everyone in Canada is our top priority and we take vaccine safety very seriously.

- In Canada, there are mechanisms to investigate and share reports of serious adverse events following COVID-19 vaccination to determine if they are causally linked to COVID-19 vaccines.

- On March 24, Health Canada issued a label change and guidance on the AstraZeneca COVID-19 vaccine, following European reports of rare but serious cases of blood clots associated with low levels of blood platelets following immunization with the AstraZeneca vaccine.

- Health Canada has issued additional 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, Canada's National Advisory Committee on Immunization (NACI) is recommending an immediate pause in the use of the AstraZeneca vaccine in all individuals less than 55 years of age in Canada.

- In line with this recommendation, and as a precautionary measure, Chief Medical Officers of Health and our respective province are collectively taking action to pause the use of AstraZeneca vaccine in Canada in those under age 55 at this time.

- To-date, there have been no vaccine-induced pro-thrombotic immune thrombocytopenia (VIPIT) adverse events reported in Canada and AstraZeneca vaccine has not yet been used in large numbers in Canada.

- It is important to note that the outcome of VIPIT can be serious but it can be treated if diagnosed early.

- Individuals who have been vaccinated with AstraZeneca in the last 20 days, and anyone vaccinated with the AstraZeneca vaccine going forward, should monitor for symptoms and seek immediate medical attention in the unlikely event that they develop: shortness of breath, chest pain, leg swelling, persistent abdominal pain, sudden onset of severe or persistent worsening headaches or blurred vision, and skin bruising (other than at the site of vaccination).

- We are responding to this safety signal with the information we have at this time and we will be reviewing new information to inform any changes in our position in the days ahead. We will keep you informed as new information becomes available, and will not hesitate to take action as necessary.

Questions and Answers

March 29, 2021

Q1. How many doses were given in Canada?

As of March 20, 2021, 309,462 doses of COVISHIELD (a version of the AstraZeneca vaccine manufactured by Verity Pharmaceuticals and the Serum Institute of India) have been administered in Canada.

Q2. Are there safety signals for AstraZeneca in Canada? Have there been safety signals for other vaccines?

There have been no reports of these very rare blood clotting events with low platelets in Canada. However, there have been reports in Europe of blood clots associated with low levels of blood platelets (thrombocytopenia) following vaccination with the AstraZeneca COVID-19 vaccine.

Once a vaccine is in use, Canada has a comprehensive vaccine safety monitoring system to alert public health authorities to changing trends or unusual adverse events not previously reported. These alerts trigger expert medical reviews, which are conducted on all serious adverse events to identify any safety concerns and respond to these quickly and appropriately. Together, this system, referred to as "post-market surveillance", is an essential part of the Government of Canada's ongoing monitoring to ensure the continued quality, safety and effectiveness of all vaccines and other health products that are in use in Canada.

In Canada, there are also mechanisms to investigate and share reports of serious adverse events following COVID-19 vaccination to determine if they are causally linked to COVID-19 vaccines. NACI's recommendation and the decision by the Council of Chief Medical Officers of Health to pause the use of the AstraZeneca vaccine in all individuals less than 55 years of age in Canada, following recently reported events out of Europe, is an example of this in action.

Q3. If I received my first dose of the AstraZeneca vaccine, should I follow through with my second dose, or should the vaccine series be completed with an mRNA vaccine?

Decisions on the type of second dose that will be offered to those who have been vaccinated with AstraZeneca will be determined based on the latest evidence and research.

NACI will continue to review evidence as it emerges, including evidence on mixed COVID-19 vaccine schedules, to provide advice to public health programs on the potential for completing the vaccine series with other vaccine products. For now, you do not need a second dose for up to 16 weeks from your first dose.

Q4. What is Vaccine-Induced Prothrombotic Immune Thrombocytopenia (VIPIT)? Is there a test, treatment? Any risk factors?

The United Kingdom, European Union, and Scandinavian countries have reported rare cases of serious blood clots, including blood clots in the brain following the AstraZeneca COVID-19 vaccine. The cases of these blood clots reported to date have two important features: the majority have occurred between 7-14 days after vaccination, and they are associated with low platelets (tiny blood cells that help form blood clots to stop bleeding). This rare adverse event is being referred to as "Vaccine-Induced

Prothrombotic Immune Thrombocytopenia" (VIPIT). VIPIT seems to be rare, occurring in anywhere from 1 in every 100,000 to 1 in 1 million people.

Based on what we know to date, 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, you should seek immediate medical attention in the unlikely event that you develop symptoms starting a few days or more after vaccination, such as: shortness of breath, chest pain, leg swelling, persistent abdominal pain, sudden onset of severe or persistent worsening headaches or blurred vision, and skin bruising (other than at the site of vaccination). Decisions on the type of second dose that will be offered to those who have been vaccinated with AstraZeneca will be determined by provincial and territorial health systems, based on the latest evidence and research.

At this time, no risk factors have consistently been identified in patients who develop VIPIT. This adverse event has not been identified following receipt of mRNA COVID-19 vaccines.

Q5. What if I just got the vaccine, should I be worrying? What are the symptoms?
The expected rate of VIPIT following receipt of AstraZeneca vaccine is not yet known, due to ongoing investigations and monitoring. However, based on cases identified to date in Europe, VIPIT seems to be very rare, and has been reported to occur in anywhere from 1 in 100,000 to 1 in 1,000,000 cases per persons vaccinated.

People who have been vaccinated with AstraZeneca less than 20 days ago should seek immediate medical attention in the rare event that they develop symptoms starting a few days or more after vaccination, such as:

- shortness of breath;
- chest pain;
- leg swelling;
- persistent abdominal pain;
- sudden onset of severe or persistent worsening headaches or blurred vision, and
- skin bruising (other than at the site of vaccination).

Q6. How quickly were provinces and territories informed? When will this change come into effect in jurisdictions?
The Council of Chief Medical Officers of Health (CCMOH) includes the Chief Medical Officer of Health from each provincial and territorial jurisdiction, Canada's Chief Public Health Officer, the Chief Medical Advisor of Health Canada, the Chief Medical Officer of Public Health of Indigenous Services Canada, the Chief Medical Officer from the First Nations Health Authority, and ex-officio members from other federal government departments.

Given new scientific evidence from haematology/thrombosis experts and further cases of blood clotting and low platelets being reported in Europe, CCMOH members met over March 27 and 28 to discuss population-based analyses of VIPIT in comparison to the risk of COVID-19 by age in the context of what is known at this time. CCMOH came to consensus in support of the NACI recommendation and the need for a precautionary measure to pause use of AZ vaccine in those under age 55 years pending further information gathering and risk/benefit analysis.

Chief Medical Officers of Health are aligned and working closely together to review and act on the latest evidence on safety and effectiveness of COVID-19 vaccines.

Q7. What data prompted NACI's Rapid Response recommendation?
Rare cases of serious blood clots associated with thrombocytopenia and thrombosis, including cerebral venous sinus thrombosis (blood clots in the brain), have been recently reported in Europe use of AstraZeneca COVID-19 vaccine. Cases identified so far have been primarily in women under the age of 55 years.

The rate was originally estimated at approximately 1 per 1,000,000 on March 19, 2021 by the European Medicines Agency (EMA). However, additional cases have been identified in Europe and the United Kingdom since that time, making it difficult to precisely identify the rate. Based on cases identified to date in Europe, the rate of VIPIT could be in the magnitude of 1 case in 100,000 to 1 in 1,000,000 persons vaccinated.

A number of factors and evidence were considered by the Council of Chief Medical Officers of Health regarding use of AZ vaccine including: population-based analyses of VIPIT and risk assessment of COVID-19 disease by age based on what is known at this time, and considering that alternate products are available (i.e., mRNA vaccines). There is substantial uncertainty about the benefit of providing AstraZeneca COVID-19 vaccine to adults under 55 years of age given the potential risks associated with VIPIT, particularly at the lower estimated rates. As a precautionary measure, while Health Canada carries out an updated benefit/risk analysis based on emerging data, NACI recommends that the AstraZeneca vaccine not be offered to adults under the age of 55.

Q8. Why is NACI recommending that older adults over the age of 55 may still be offered the AstraZeneca vaccine?
Adults 55 years of age and older may still be offered the AstraZeneca vaccine, given the increased risk of hospitalization and death due to COVID-19 disease in this population and since VIPIT appears to be a rarer event in this age group based on reported cases to date.

Anyone receiving the AstraZeneca COVID-19 vaccine should be informed of this potential adverse event and advised to seek immediate medical attention if they develop symptoms of thromboembolism, and especially signs of thrombocytopenia and cerebral blood clots, such as easy bruising or bleeding, and persistent or severe headache between days 4 to 20 after receipt of vaccine.

Q9. NACI originally recommended that the AstraZeneca vaccine should not be used in older adults over the age of 65. Why is NACI now recommending that the vaccine may be used in older adults over 55, but should not be used in younger adults under the age of 55?

NACI made its original recommendation based on available evidence of the vaccine efficacy in those 65 years of age and over at the time. At that time Phase 3 clinical trials of the AstraZeneca vaccine had an insufficient number of participants over 65 years of age that contracted COVID-19 to determine the efficacy of the vaccine in this age group. However, since NACI's original recommendation further studies were published showing safety and effectiveness in the older adult population and there are no concerns about safety of the AstraZeneca vaccine among this population at this time.

NACI's update that the AstraZeneca vaccine should be paused for younger adults at this time is based on rare cases of serious blood clots associated with thrombocytopenia, including cerebral venous sinus thrombosis, having been recently reported in Europe following post-licensure use of AstraZeneca COVID-19 vaccine. Cases identified so far have been primarily in women under the age of 55 years.

However, while vaccine supply is limited, NACI continues to recommend that initial doses of mRNA vaccines (Pfizer-BioNTech and Moderna) should be prioritized for key populations listed in NACI's guidance on the prioritization of key populations for COVID-19 immunization, especially those at highest risk of severe illness and death and highest risk of exposure to COVID-19.

Q10. Will this update delay Canada's vaccine timelines?
Canada is on track to receive sufficient COVID-19 vaccine doses for every eligible person in Canada who wants one by September 2021. Given that the AstraZeneca vaccine doses make up a small portion of the total cumulative doses expected in Canada by the end of Q3, COVID-19 vaccinations will not be significantly delayed without using AstraZeneca COVID-19 vaccine in adults under 55.