

# Summary Safety Review - AstraZeneca and COVISHIELD COVID-19 Vaccines - Assessing the Potential Risk of Thrombosis in combination with Thrombocytopenia

**Product:** AstraZeneca COVID-19 Vaccine and COVISHIELD

**Potential Safety Issue:** Reports of very rare Thrombosis (blood clots) in combination with thrombocytopenia (low blood platelets)

## Key Messages

- AstraZeneca COVID-19 Vaccine and COVISHIELD are authorized in Canada for active immunization of individuals 18 years of age and over for the prevention of coronavirus disease 2019 (COVID-19).
- Health Canada reviewed the risk of blood clots in combination with low platelets with the use of AstraZeneca COVID-19 Vaccine and COVISHIELD after cases were reported in Europe following immunization with AstraZeneca COVID-19 Vaccine.
- Health Canada's review of the available information concluded that a link between the use of AstraZeneca COVID-19 Vaccine and COVISHIELD and the risk of these blood clots with low platelets is possible. The risk of these events is very rare, and the overall benefits of the vaccine in protecting Canadians from COVID-19 continue to outweigh its potential risks.
- Health Canada did not identify risk factors, such as age or gender, for these very rare events, and is not restricting the use of the vaccine at this time.
- A potential mechanism for the combination of blood clots with low platelets is the triggering of an immune response by the vaccine, leading to a condition similar to that seen sometimes in patients treated with the blood thinner medication heparin.
- Health Canada worked with the manufacturers of AstraZeneca COVID-19 Vaccine and COVISHIELD to update the Canadian Product Monographs (CPM) for these products to include new safety information about these events. Health Canada also communicated<sup>1</sup> to Canadians and healthcare professionals about this risk.
- Health Canada will continue to monitor the safety of AstraZeneca COVID-19 Vaccine and COVISHIELD. Health Canada will also continue to work closely with international regulators to review information as it becomes available on these very rare events, and will make further updates to the CPM or take other actions as needed.

## Overview

Health Canada reviewed the risk of blood clots in combination with low blood platelets following immunization with AstraZeneca COVID-19 Vaccine and COVISHIELD to evaluate emerging information and determine if further measures are needed to mitigate the risk in Canada. This safety review was initiated after cases of blood clots following immunization with AstraZeneca COVID-19 Vaccine were reported in Europe.

As of April 12, 2021, no regulatory authorities have restricted use of the vaccine, although public health authorities in Canada and several other countries, including France, Germany and Australia, have recently restricted use of the vaccine to older age groups.

## Use in Canada

- AstraZeneca COVID-19 Vaccine and COVISHIELD are authorized for sale in Canada for active immunization of individuals 18 years of age and over for the prevention of COVID-19. This authorization includes conditions requiring the manufacturer to provide additional information to Health Canada on the vaccine's effectiveness, along with active safety monitoring.
- AstraZeneca COVID-19 Vaccine is manufactured by AstraZeneca and COVISHIELD is manufactured by Serum Institute of India. Health Canada reviewed the manufacturing information for these vaccines and found them to be comparable, which means individuals could complete the vaccination course with either AstraZeneca COVID-19 Vaccine or COVISHIELD.
- AstraZeneca COVID-19 Vaccine and COVISHIELD have been authorized in Canada since February 2021. Currently, AstraZeneca COVID-19 Vaccine and COVISHIELD are available as solutions for injection into the muscle, in multiple dose vials.
- As of April 3, 2021, 6,158 doses of AstraZeneca COVID-19 Vaccine and 478,535 doses of COVISHIELD have been administered in Canada.

## Safety Review Findings

- Health Canada reviewed the available information from searches of the Canada Vigilance database, international databases, and information received from the manufacturers and international regulators.
- At the time of the review, Health Canada was aware of one report of a Canadian vaccine recipient who experienced blood clots with low platelets following immunization with COVISHIELD.
- Health Canada's review considered all currently available information. This included information submitted by the manufacturers in response to terms and conditions that were put in place by Health Canada. Health Canada also reviewed information shared by international regulators, including their assessment of the reports received in their jurisdictions.
- A link between these events and AstraZeneca COVID-19 Vaccine and COVISHIELD was considered possible. Health Canada's findings are in line with the conclusions of international regulators.
- The potential risk of blood clots with low platelets is very rare. Based on their vaccination rate as of March 31, 2021, the United Kingdom Medicines and Healthcare Products Regulatory Agency estimated the overall risk of these blood clots to be approximately 4 people in a million who receive the vaccine. Reported cases of these adverse events have been seen after the first dose, usually within the first 14 days after immunization.
- Health Canada's review of available information from Europe, the United Kingdom and the manufacturers did not identify any specific risk factors, such as age or gender for these events. It is recognized that the benefit versus risk of receiving the vaccine may vary by age due to differences in the risk of severe disease associated with COVID-19 illness, which continues to change as the nature of the pandemic changes.
- A potential mechanism for the combination of blood clots with low platelets is the triggering of an immune response by the vaccine, leading to a condition similar to heparin-induced thrombocytopenia seen sometimes in patients treated with the blood thinner medication heparin.

## Conclusions and Actions

- Health Canada's review of the available information concluded that a link between the use of AstraZeneca COVID-19 Vaccine and COVISHIELD and the risk of blood clots with low platelets is possible. The risk of these events is very rare.
- The benefits of AstraZeneca COVID-19 Vaccine and COVISHIELD in preventing COVID-19 continue to outweigh the risk of very rare events of blood clots in combination with low platelets. At this time, information provided by the manufacturers demonstrate the potential benefits of the vaccine across all age groups.
- Health Canada's review of available information from Europe, the United Kingdom and the manufacturers did not identify specific risk factors, such as age or gender, for these very rare events. Therefore, Health Canada is not restricting the use of the vaccine at this time for certain populations or age groups. The risk of severe disease associated with COVID-19 illness varies with age and continues to change as the nature of the pandemic changes.
- Health Canada has published information for vaccine recipients on signs and symptoms of these events and when to seek medical attention. Health Canada has also provided healthcare professionals with information to identify and promptly treat these conditions according to available evidence and clinical guidelines.
- Health Canada worked with the manufacturers of AstraZeneca COVID-19 Vaccine and COVISHIELD to update the CPMs for these products with this safety information. Health Canada also requested that the manufacturers update the risk management plans for the AstraZeneca COVID-19 Vaccine and COVISHIELD to reflect the latest information about this safety issue, and to include plans for studies that will address remaining knowledge gaps.
- Health Canada will continue to monitor the safety of AstraZeneca COVID-19 Vaccine and COVISHIELD, as it does for all health products on the Canadian market. Health Canada will also continue to work closely with international regulators, the manufacturers, the Public Health Agency of Canada, and Provincial and Territorial public health authorities to review information as it becomes available on these very rare events, and will make further updates to the CPMs or take other actions as needed.

## Additional Information

The analysis that contributed to this safety review included information provided by the manufacturer, consultations with scientific experts, Canadian and international information, and what is known about the use of AstraZeneca COVID-19 Vaccine and COVISHIELD both in Canada and internationally.

As of April 10, 2021, 221,484 doses of AstraZeneca COVID-19 Vaccine and 488,038 doses of COVISHIELD have been administered in Canada.

The [COVID-19 vaccines and treatments portal](#) provides information for consumers, healthcare professionals and researchers on vaccines and treatments authorized for COVID-19, as well as those currently under review.

For additional information, contact the [Marketed Health Products Directorate](#).

## Reference

- 1) [Health Canada provides update on the AstraZeneca and COVISHIELD COVID-19 vaccines](#)