

**Important Safety Information on  
AstraZeneca COVID-19 Vaccine and COVISHIELD:  
Risk of Capillary Leak Syndrome**



2021/06/29

**Audience**

Healthcare professionals including infectious disease physicians, family physicians, emergency room physicians, hematologists, neurologists, pharmacists, public health officials, nurses and nurse practitioners, and healthcare professionals at identified points of use.

**Key messages**

- **Very rare cases of capillary leak syndrome (CLS) have been reported following vaccination with AstraZeneca COVID-19 Vaccine. A history of CLS was noted in some of the cases. A fatal outcome has been reported.**
- **AstraZeneca COVID-19 Vaccine and COVISHIELD (the version of the AstraZeneca COVID-19 Vaccine manufactured by the Serum Institute of India) are now contraindicated in individuals who have previously experienced episodes of CLS.**
- **CLS is characterised by acute episodes of limb edema, hemoconcentration, hypoalbuminemia and hypotension leading to organ damage. Patients with an acute episode of CLS following vaccination require an urgent medical assessment. Intensive supportive therapy is usually warranted for this life-threatening condition.**
- **Health Canada worked with the manufacturers of [AstraZeneca COVID-19 Vaccine](#) and [COVISHIELD](#) to update the Product Monographs for these products to include this new safety information, as well as other updates including additional guidance for healthcare professionals regarding thrombosis with thrombocytopenia syndrome.**
- **The benefits of the AstraZeneca COVID-19 Vaccine and COVISHIELD in protecting Canadians from COVID-19 continue to outweigh the risks. Canadians are encouraged to get immunized with any of the COVID-19 vaccines that are authorized and available in Canada.**

**What is the issue?**

The AstraZeneca COVID-19 Vaccine and COVISHIELD were authorized for use in Canada on February 26, 2021, in accordance with the [Interim Order Respecting the Importation, Sale and Advertising of Drugs for Use in Relation to COVID-19](#). Since the time of authorization, there have been very rare reports of capillary leak

syndrome (CLS) following administration of the AstraZeneca COVID-19 Vaccine. Health Canada is working with international regulators and public health authorities to review data and evidence as it becomes available on these very rare events.

### **Products affected**

AstraZeneca COVID-19 Vaccine, COVID-19 Vaccine (ChAdOx1-S [recombinant])

5 mL solution for intramuscular injection, multiple dose vials.

Each vial contains 10 doses (each dose is 0.5 mL).

DIN: 02510847

4 mL solution for intramuscular injection, multiple dose vials.

Each vial contains 8 doses (each dose is 0.5 mL).

DIN: 02511444

Manufacturer: AstraZeneca Canada Inc.

Canadian Importer and Distributor: AstraZeneca Canada Inc.

COVISHIELD, COVID-19 Vaccine (ChAdOx1-S [recombinant])

5 mL solution for intramuscular injection, multiple dose vials.

Each vial contains 10 doses (each dose is 0.5 mL).

DIN: 02512947

Manufacturer: Serum Institute of India Pvt. Ltd.

Canadian Importer and Distributor: Verity Pharmaceuticals Inc.

### **Background information**

The AstraZeneca COVID-19 Vaccine and COVISHIELD are indicated for active immunization of individuals 18 years of age and older for the prevention of coronavirus disease 2019 (COVID-19).

Very rare cases of CLS, a life-threatening condition characterized by acute episodes of limb edema, hemoconcentration, hypoalbuminemia and hypotension leading to organ damage, have been reported following vaccination with AstraZeneca COVID-19 Vaccine. The European Medicines Agency reviewed 6 cases in depth, and a history of CLS was noted in 3 of these cases. One of these cases had a fatal outcome.

As of June 18, 2021, one case of CLS following vaccination with the AstraZeneca COVID-19 Vaccine has been reported in Canada.

AstraZeneca COVID-19 Vaccine and COVISHIELD are now contraindicated in individuals who have previously experienced episodes of CLS.

Health Canada continues to work with international regulators to review data and evidence as it becomes available on these very rare events.

AstraZeneca Canada Inc. and Verity Pharmaceuticals Inc. will continue to work closely with Health Canada and other regulators to monitor and ensure that the appropriate analysis and reporting of adverse events are shared with regulatory authorities around the world.

**Information for consumers**

Very rare cases of CLS have been reported following vaccination with AstraZeneca COVID-19 Vaccine. Some affected patients had a previous diagnosis of CLS.

Individuals who have previously experienced episodes of CLS should not be vaccinated with AstraZeneca COVID-19 Vaccine or COVISHIELD and should discuss options for COVID-19 vaccines with their healthcare professional.

CLS is a serious, potentially fatal condition causing fluid leakage from small blood vessels (capillaries) resulting in rapid swelling of the arms and legs, sudden weight gain and feeling faint (due to low blood pressure) leading to organ damage. Individuals should seek medical attention immediately if they develop these symptoms following vaccination.

The benefits of the AstraZeneca COVID-19 Vaccine and COVISHIELD in protecting Canadians from COVID-19 continue to outweigh the risks. Canadians are encouraged to get immunized with any of the COVID-19 vaccines that are authorized and available in Canada.

**Information for healthcare professionals**

The [AstraZeneca COVID-19 Vaccine](#) and [COVISHIELD](#) Product Monographs have been updated to include the risk of CLS, as well as other updates including additional guidance for healthcare professionals regarding thrombosis with thrombocytopenia syndrome.

Patients who have previously experienced episodes of CLS should not be vaccinated with AstraZeneca COVID-19 Vaccine or COVISHIELD.

Healthcare professionals should be alert to the signs and symptoms of CLS. CLS is a very rare disorder, which is frequently life threatening, characterised by a dysfunctional inflammatory response, endothelial dysfunction, extravasation of fluid from the vascular space to the interstitial space leading to shock, hemoconcentration, hypoalbuminemia and consequent organ failure. Patients may present with a rapid swelling of the arms and legs, sudden weight gain and have symptoms associated with low blood pressure/shock.

Patients with an acute episode of CLS following vaccination require urgent medical attention and treatment. Intensive supportive therapy is usually warranted.

Individuals vaccinated with AstraZeneca COVID-19 Vaccine or COVISHIELD should be instructed to seek immediate medical attention if they develop symptoms such as rapid swelling of the arms and legs, sudden weight gain and feel faint due to low blood pressure.

Healthcare professionals should report cases of CLS through their respective

jurisdiction's Adverse Events Following Immunization (AEFI) surveillance system.

### Action taken by Health Canada

Health Canada has worked closely with international regulators and reviewed the available data. Health Canada continues to gather Canadian and international information from manufacturers, international regulators and other experts, and will communicate any new information as needed.

Health Canada worked with the manufacturers to update the respective Product Monographs of AstraZeneca COVID-19 Vaccine and COVISHIELD to reflect current knowledge of this safety issue in a timely manner. Further updates will be made or other actions will be taken, if required, based on emerging evidence.

Health Canada is communicating this important safety information to healthcare professionals and Canadians via the [Recalls and Safety Alerts Database](#) on the Healthy Canadians Web Site. This communication will be further distributed through the MedEffect™ e-Notice email notification system, as well as through social media channels, including LinkedIn and Twitter.

### Report health or safety concerns

Managing marketed health product-related side effects depends on healthcare professionals and consumers reporting them. Any serious or unexpected side effects in patients receiving the AstraZeneca COVID-19 Vaccine or COVISHIELD should be reported to your local Health Unit or the manufacturers (see "Products affected").

<p><b>AstraZeneca Canada Inc.</b> 1004 Middlegate Road, Suite 5000 Mississauga Ontario, Canada, L4Y 1M4 <i>For any medical questions related to AstraZeneca COVID-19 Vaccine, contact Medical Information at 1-800-668-6000) or submit a form online at <a href="http://www.azcovid-19.com">www.azcovid-19.com</a>.</i></p>	<p><b>Verity Pharmaceuticals Inc.</b> 2560 Matheson Blvd. East, Suite 220 Mississauga Ontario, Canada, L4W 4Y9 <i>For any medical questions related to COVISHIELD, contact Medical Information at 1-800-977-9778) or submit a form online at <a href="http://www.covishield-canada.ca">www.covishield-canada.ca</a>.</i></p>
<p>If a patient experiences a side effect following immunization, please complete the Adverse Events Following Immunization (AEFI) Form appropriate for your province/territory (<a href="https://www.canada.ca/en/public-health/services/immunization/reporting-adverse-events-following-immunization/form.html">https://www.canada.ca/en/public-health/services/immunization/reporting-adverse-events-following-immunization/form.html</a>) and send it to your local Health Unit. Alternatively, you can report adverse events to AstraZeneca online at <a href="https://contactazmedical.astrazeneca.com">https://contactazmedical.astrazeneca.com</a>.</p> <p>For other health product inquiries related to this communication, contact Health Canada at:</p> <p>Biologic and Radiopharmaceutical Drugs Directorate E-mail: <a href="mailto:hc.brdd.dgo.enquiries.sc@canada.ca">hc.brdd.dgo.enquiries.sc@canada.ca</a></p>	

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