VAXZEVRIA™

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

INFORMATION FOR CANADIAN HEALTHCARE PROFESSIONALS

REVIEWED BY PAAB

MEMBER OF INNOVATIVE MEDICINES CANADA

VAX2101E

About this guide

- This guide is for Canadian healthcare professionals and covers information about VAXZEVRIA, known as ChAdOx1-S (recombinant) COVID-19 Vaccine, that may be important.
- It does not cover other non-ChAdOx1-S (recombinant) COVID-19 vaccines, COVID-19 treatments or the disease.
- This should be used in conjunction with the Health Canada Product Monograph.[1]
- It does not include national or local guidelines for immunization of COVID-19.

There is a separate guide written for the general public here www.azcovid-19.com, suitable for discussion with your patients. The public guide should be used in conjunction with the Health Canada Patient Medication Information section of the Product Monograph.[1]

Contents

How to use this guide

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Checklist

Before vaccination

- ☐ Indicated for active immunization of individuals **18 years of age and older** for the prevention of COVID-19.
- ☐ **Consult local guidelines** on who is included in local vaccination programs.
- ☐ **Consider the benefits and potential risks** of vaccination for each individual, including:
  - ☐ review of ***Contraindications*** and ***Precautions***
  - ☐ review of ***Benefits and risks***

Hypersensitivity reactions, including anaphylaxis and angioedema, have occurred following administration of VAXZEVRIA. Appropriate medical treatment and supervision should always be readily available in case of an anaphylactic event following administration.

At the time of vaccination

- ☐ **Educate the recipient on key points** relevant to vaccination including:
  - ☐ benefits and risks
  - ☐ possible side effects after vaccination
  - ☐ that the vaccine cannot cause COVID-19
  - ☐ use of acetaminophen or ibuprofen
- ☐ Inspect the vaccine for particulate matter or discolouration prior to administration. The vaccine is colourless to slightly brown, clear to slightly opaque. Discard if the solution is discoloured or visible particles are observed.
- ☐ Administer 0.5 mL (1 dose) injection **intramuscularly**, preferably in the deltoid muscle. See ***Administering the vaccine***.
- ☐ Each vial contains at least the number of doses stated. It is normal for liquid to remain in the vial after withdrawing the final dose. When low dead volume syringes and/or needles are used, the amount remaining in the vial may be sufficient for an additional dose. Care should be taken to ensure a full 0.5 mL dose is administered. Where a full 0.5 mL dose cannot be extracted, the remaining volume should be discarded. Do not pool excess vaccine from multiple vials.

After vaccination

- ☐ Advise the recipient:
  - ☐ to return for their next vaccination in 4 to 12 weeks or as recommended by the clinic
  - ☐ that information is available in the public guide and Patient Medication Information is available at www.azcovid-19.com
  - ☐ to contact a healthcare professional if they have any concerns about side effects
  - ☐ to retain record of vaccine name, batch/lot number and date they receive the vaccine
  - ☐ to report any adverse effects after vaccination
- ☐ Observe the vaccine recipient for at least 15 minutes for possible anaphylaxis.[4]
- ☐ Retain appropriate vaccination records, including vaccine name and batch/lot number.

What the vaccine is

About this vaccine

VAXZEVRIA is a replication-defective chimpanzee adenovirus-vectored vaccine (ChAdOx1 - Chimpanzee Adenovirus Oxford 1) which expresses the gene for the unmodified Severe Acute Respiratory Syndrome Coronavirus 2 (SARS-CoV-2) spike protein.

This vaccine stimulates neutralizing antibody and cellular immune responses, to help protect against COVID-19.[1,13]

Is it a live vaccine?

This vaccine is not a conventional live vaccine and it does not contain live coronavirus. The replication-defective adenovirus is live but it cannot multiply or spread throughout the body.[7,11]

How the vaccine works

After administration, the modified adenovirus (viral vector) binds to the surface of human cells and delivers the genetic code for the coronavirus spike protein to the cell, where it is processed to form the spike protein itself.

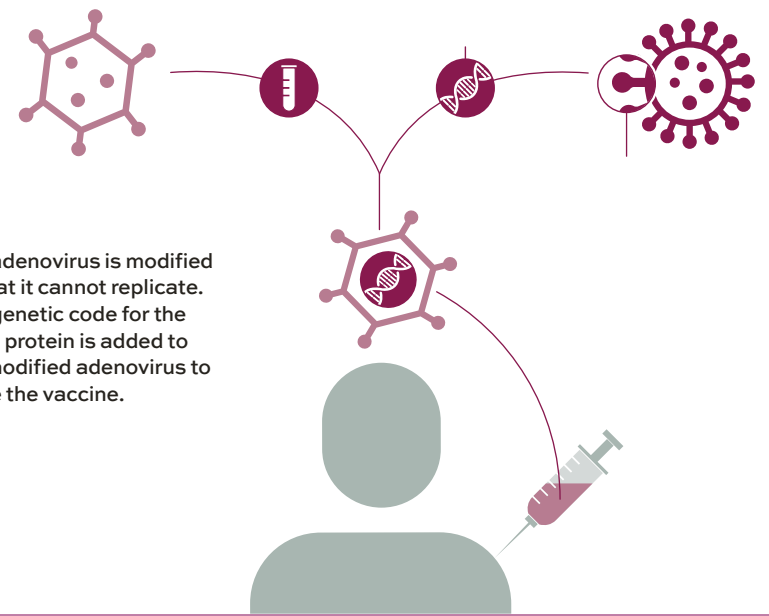
Antibodies and immune cells (T-cells) in the circulation recognize the spike protein which instigates the neutralising antibody and cellular immune responses.

The immune system subsequently forms an immune memory of the coronavirus spike protein, which facilitates quick recognition and rapid immune response in the case of future SARS-CoV-2 coronavirus exposure.[13,14,17]

Click to see more details on:

▶ *Vaccine ingredients*

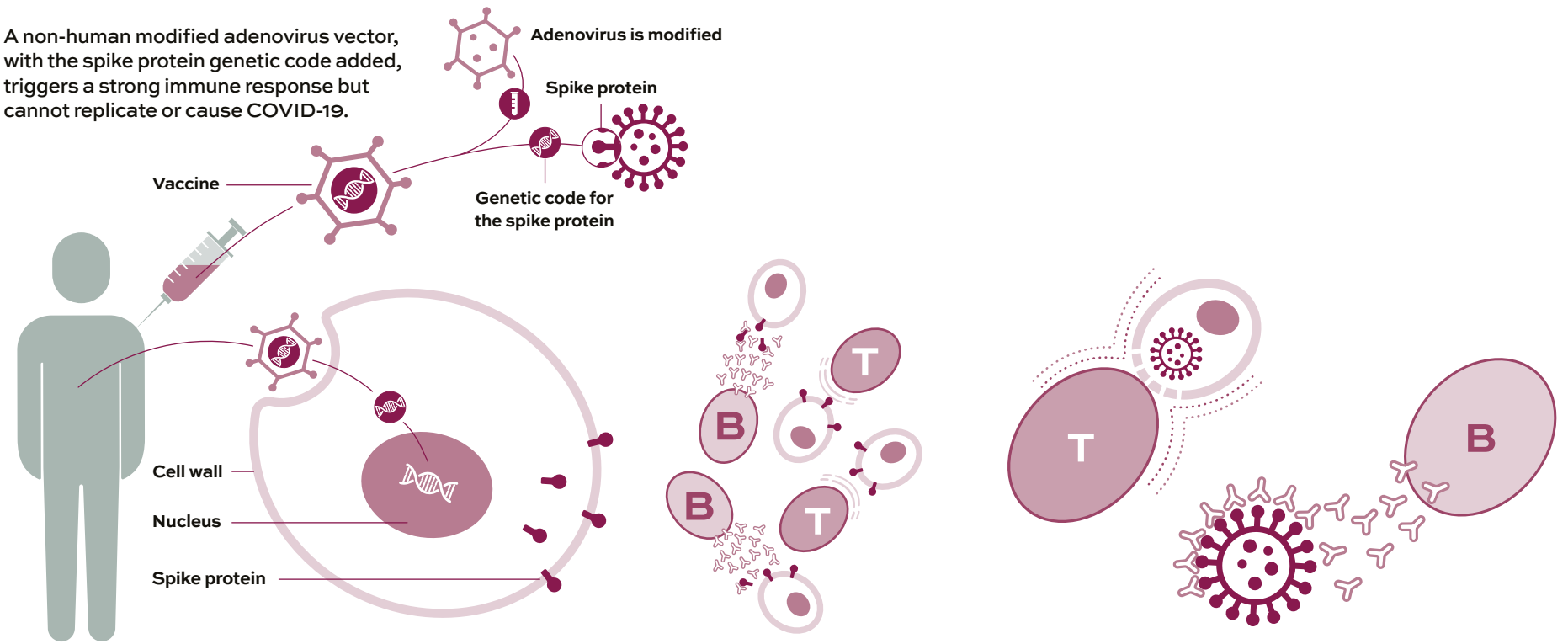
How the vaccine is made



The adenovirus is modified so that it cannot replicate. The genetic code for the spike protein is added to the modified adenovirus to make the vaccine.

How this vaccine works

A non-human modified adenovirus vector, with the spike protein genetic code added, triggers a strong immune response but cannot replicate or cause COVID-19.



The viral vector enters the body's cells and delivers the genetic code for the spike protein. The human cells then produce the spike protein but there are no changes to the human DNA.

T-cells and B-cells recognize the spike protein and multiply. B-cells start releasing antibodies.

The immune system also produces memory cells. If they spot SARS-CoV-2 in the future, antibodies and T-cells are rapidly produced in response.

T-cells destroy cells infected with the virus. Antibodies bind to the spike proteins, blocking the ability for viruses to enter cells. Together they can help prevent disease.

More details on what the vaccine is

Vaccine ingredients

As in all vaccines, VAXZEVRIA consists of an active ingredient as well as inactive ingredients which facilitate administration by injection. These inactive ingredients also stabilize the product. The vaccine does not contain any preservatives.[1,13]

The **active ingredient** is a genetically modified adenovirus (ChAdOx1) containing spike protein genetic code.[1,13]

The **inactive ingredients** are L-Histidine (an amino acid); L-Histidine hydrochloride monohydrate (an amino acid); magnesium chloride hexahydrate (supports many activities inside cells); polysorbate 80 (a stabiliser); ethanol (alcohol); sucrose (sugar); sodium chloride (salt); disodium edetate dihydrate (EDTA, a binding agent); water for injection.[1]

Latex: There is no latex in the vial or stopper.[9]

Origin of ingredients

- It does not contain milk, lactose, soya, egg, maize/corn starch, peanuts, gluten.[9]
- None of the ingredients are of human or animal origin. However, the active ingredient, a genetically modified adenovirus, is grown using cells that are of human origin called human embryonic kidney cells (HEK293). None of these cells remain at the time the vaccine is administered.[a,3,9]

Two genetic alterations have been made to the adenovirus in order to make the vaccine:[3]

- Genes essential for adenovirus replication have been deleted.
- The coronavirus (SARS-CoV-2) spike protein gene has been added.

These changes allow the vaccine to deliver the spike protein genetic code to the cells without causing COVID-19.

Click to see more details on:

▶ *Disposal*

Religious beliefs

Information on the ingredients is included in the public guide. Individuals should decide themselves whether their treatment is compliant with their own religious belief systems.

Before vaccination

Indication

VAXZEVRIA is indicated for active immunization of individuals 18 years of age and older for the prevention of coronavirus disease 2019 (COVID-19).[1]

Consult provincial/territorial guidelines on who is included in local vaccination programs.

Contraindications

Do not give the vaccine to anyone with a history of **hypersensitivity** to any of the vaccine ingredients.[1]

See ***What the vaccine is-vaccine ingredients and excipients***.

As with all injectable vaccines, always be prepared in case of anaphylaxis following the administration of the vaccine.

Do not give the vaccine to anyone who has experienced thrombosis with thrombocytopenia syndrome (TTS) following vaccination with VAXZEVRIA.

Do not give the vaccine to anyone who has previously experienced episodes of capillary leak syndrome.

Serious warnings and precautions

A combination of thrombosis and thrombocytopenia, in some cases accompanied by bleeding, has been observed very rarely following vaccination with VAXZEVRIA.

Children

The safety and efficacy of VAXZEVRIA in children and adolescents (aged <18 years old) have not yet been established. No data are available.[1]

Pregnancy

The safety and efficacy of VAXZEVRIA in pregnant women have not yet been established.[1]

Animal studies do not indicate direct or indirect harmful effects with respect to pregnancy, embryo/fetal development, parturition, or post-natal development.

Use of VAXZEVRIA in pregnant women should be based on an assessment of whether the benefits of vaccination outweigh the potential risks.

There is a pregnancy exposure registry that monitors pregnancy outcomes in women exposed to VAXZEVRIA during pregnancy. Women who are vaccinated with VAXZEVRIA during pregnancy are encouraged to enrol in the registry by visiting https://c-viper.pregistry.com or calling 1-800-616-3791.

Breast-feeding

In animal studies, lactational transfer of anti-SARS-CoV-2 S antibodies from maternal female mice to pups was observed. It is unknown whether the vaccine itself is excreted in human milk. The developmental and health benefits of breast-feeding should be considered along with the mother's clinical need for immunization against COVID-19.[1]

Fertility

It is unknown whether VAXZEVRIA may impact fertility in humans. No data are available in humans.[1]

Elderly

Clinical studies of VAXZEVRIA include participants 65 years of age and older and their data contributes to the overall assessment of its safety profile and efficacy. No dose adjustment is required in elderly individuals (65 years or older).[1]

Before vaccination

Precautions (continued)

Medical history

- Use caution when vaccinating anyone with **thrombocytopenia**, any **coagulation disorders** and/or receiving **anticoagulation therapy**. This is because, as with other intramuscular injections, **bleeding or bruising** may occur following administration.[1] For more information about optimizing vaccinations for bleeding disorders, refer to the Canadian Immunization Guide at https://www.canada.ca/en/public-health/services/publications/healthy-living/canadian-immunization-guide-part-3-vaccination-specific-populations/page-7-immunization-persons-with-chronic-diseases.html.
- **Immunocompromised persons**, including individuals receiving immunosuppressant therapy, may have a diminished immune response to the vaccine.
- **Fainting** can occur following, or even before, any vaccination as a psychogenic response to a needle injection. Procedures should be in place to prevent injury from syncopal reactions.

Coagulation disorders

Thromboembolism in combination with thrombocytopenia syndrome

- Thrombosis with thrombocytopenia syndrome (TTS), in some cases accompanied by bleeding, has been observed very rarely following vaccination with VAXZEVRIA during post-authorization use. This includes severe cases in unusual sites such as cerebral venous sinus thrombosis (CVST) and splanchnic vein thrombosis, as well as arterial thrombosis, concomitant with thrombocytopenia. The majority of these cases occurred within the first 3 weeks following vaccination. Some cases had a fatal outcome. The reporting rates after the second dose are lower compared to after the first dose. Healthcare professionals should consult applicable guidance and, if available, seek advice from specialists (e.g., hematologists, specialists in coagulation) to diagnose and treat this condition.
- While specific risk factors for thrombosis in combination with thrombocytopenia have not been identified, cases have occurred in patients with a previous history of thrombosis, as well as in patients with autoimmune disorders, including idiopathic thrombocytopenia purpura. The benefits and risks of vaccination should be considered in these patients.
- Individuals who have experienced a previous CVST with thrombocytopenia or heparin-induced thrombocytopenia (HIT) should only receive VAXZEVRIA if the potential benefits outweigh the potential risks. Patients who have experienced major venous or arterial thrombosis with thrombocytopenia following vaccination with VAXZEVRIA should not receive a second dose of VAXZEVRIA.

Cerebrovascular venous and sinus thrombosis without thrombocytopenia

- Events of cerebrovascular venous and sinus thrombosis without thrombocytopenia have been reported very rarely following vaccination with VAXZEVRIA. The majority of these cases occurred within the first four weeks following vaccination. Although a causal relationship has not been established, these events can be fatal and may require different treatment approaches than TTS. Healthcare professionals should consult applicable guidance.

Thrombocytopenia

- Cases of thrombocytopenia, including immune thrombocytopenia (ITP), have been reported after receiving VAXZEVRIA, typically within the first four weeks after vaccination. Very rarely, these presented with very low platelet levels (<20,000 per µL) and/or were associated with bleeding. Some of these cases occurred in individuals with a history of immune thrombocytopenia. Cases with fatal outcome have been reported. If an individual has a history of ITP, the risks of developing low platelet levels should be considered before vaccination, and platelet monitoring is recommended after vaccination.

Before vaccination

Precautions (continued)

- Healthcare professionals should be alert to the signs and symptoms of thrombosis, thromboembolism, and/or thrombocytopenia. Vaccinated individuals should be instructed to seek immediate medical attention if they develop symptoms such as shortness of breath, chest pain, leg swelling or pain, or persistent abdominal pain following vaccination. Additionally, anyone with neurological symptoms after vaccination including sudden onset of severe headaches, persistent or worsening headaches, blurred vision, confusion or seizures, or who experiences spontaneous bleeding, unusual skin bruising or petechiae beyond the site of vaccination after a few days, should seek prompt medical attention.
- Since medical management of a post-vaccine thrombosis, thromboembolism and/or thrombocytopenia may be different than medical management of other thromboses, if patients present with thrombosis, thromboembolism and/or thrombocytopenia, healthcare professionals should consult with current guidance and hematologic specialists to diagnose and treat this post-vaccine event.
- Individuals diagnosed with thrombocytopenia following vaccination with VAXZEVRIA should be evaluated for signs of thrombosis, and similarly individuals who present with thrombosis following vaccination should be evaluated for thrombocytopenia.

Capillary leak syndrome

- Cases of capillary leak syndrome (CLS) have been observed very rarely following vaccination with VAXZEVRIA during post-authorization use. Some of the reported cases had a history of CLS. Some cases had a fatal outcome. CLS is a rare disease characterized by acute episodes of limb edema, hypotension, hemoconcentration and hypoalbuminemia. Patients with an acute episode of CLS following vaccination require prompt medical attention and treatment. Intensive supportive therapy is usually warranted. Individuals with a known history of CLS should not be vaccinated with this vaccine.

Neurological events

- Very rare events of demyelinating disorders, such as Guillain-Barré Syndrome (GBS) and transverse myelitis, have been reported following vaccination with VAXZEVRIA during post-authorization use. Healthcare professionals should be alert to GBS and transverse myelitis signs and symptoms to ensure correct diagnosis in order to initiate adequate supportive care and treatment and to rule out other causes.

Concurrent illness

- Screen for COVID-19 symptoms prior to vaccination.[1] Vaccination should be deferred in symptomatic individuals with confirmed or suspected SARS-CoV-2 infection, or those with respiratory symptoms, in order to avoid attributing any complications resulting from infection with SARS-CoV-2 to vaccine-related AEFI and to minimize the risk of COVID-19 transmission at an immunization clinic/venue (National Advisory Committee on Immunization, NACI).
- Postpone vaccination in individuals suffering from an acute severe febrile illness or acute infection. However, the presence of a minor infection and/or low-grade fever should not delay vaccination.
- Clients with symptoms that could be COVID-19 should be advised to contact their health care provider before going out for a vaccination.

Important! Consider the potential ***benefits and risks*** of vaccination with VAXZEVRIA for each individual.

More details on before vaccination

Administration with other vaccines

- The safety, efficacy and immunogenicity (strength of immune response) of co-administration of VAXZEVRIA with other vaccines have not been evaluated.[1]
- In the clinical trials, other vaccines were not permitted during the 30 days before or after administration of VAXZEVRIA.[14,15]
- Further studies are planned to evaluate use with other vaccines.

Administration with other medicines

- Drug interaction studies have not yet been conducted.[1]
- Refer to ***Precautions*** for guidance on medical history.[1]

Vaccine interchangeability

- There are no safety, immunogenicity or efficacy data to support interchangeability of VAXZEVRIA with other non-ChAdOx1-S (recombinant) COVID-19 vaccines.[1]

Duration and level of protection

The duration of protection has not yet been established.[1]

As with any vaccine, vaccination with VAXZEVRIA may not protect all vaccine recipients. Individuals may not be optimally protected until after receiving the second dose of the vaccine.[1]

Vaccination of individuals with previous COVID-19 infection

Subjects with previous COVID-19 infection can be vaccinated with VAXZEVRIA.

Administering the vaccine

Before administration

- Consider the benefits and potential risks of vaccination with VAXZEVRIA for each individual.[1]
  – see ***Before vaccination***
- When a recipient is due for the second dose, ensure the first dose was with VAXZEVRIA and that there were no adverse events with the first dose that would preclude re-vaccination.[1]
- Individuals should complete the vaccination course with VAXZEVRIA.[1]

Do not give the vaccine to anyone with **hypersensitivity** to any of the vaccine ingredients or a previous dose of the vaccine
– see ***Vaccine ingredients and excipients***.

At administration

- Ensure appropriate medical supervision and treatment is available and observe the vaccine recipient for at least 15 minutes in case of anaphylaxis following the administration of the vaccine. An additional dose of the vaccine should not be given to those who have experienced a hypersensitivity reaction to a previous dose of VAXZEVRIA.[1]
- Educate the vaccine recipient on key points in the Health Canada Patient Medication Information section of the Product Monograph and Public Guide related to vaccination with VAXZEVRIA, including:[1]
  - ☐ benefits of vaccination
  - ☐ risks, including injection site reactions and other vaccine related adverse reactions (including signs, symptoms and duration of effects)
  - ☐ possible side effects after vaccination
  - ☐ the vaccine cannot cause COVID-19
  - ☐ when to call a doctor or seek medical attention immediately
  - ☐ when they need to come back for their next vaccination
- Inspect the vaccine for particulate matter or discolouration. It is a colourless to slightly brown, clear to slightly opaque solution. Discard if the solution is discoloured or visible particles are observed.[1]
- Withdraw 0.5 mL into a syringe. Choice of needle length/gauge must be made by each healthcare professional based on individual patient needs.[1]

- Use a separate sterile needle and syringe for each recipient.[1]
  – Multidose vials contain 10 vaccine doses. See ***Multidose vials***.[1]
  – It is presumed that some liquid may remain in the vial after withdrawing the final dose. This will not be enough for a full dose and should be discarded.[1]
- Administer the vaccine by **intramuscular** (IM) injection, preferably into the deltoid muscle.[1]

Administering the vaccine

Administer two injections, between 4 and 12 weeks apart or as recommended by the local clinic

2 doses administered **4-12 weeks apart**

Advise the recipient to:[1]

- return between 4 and 12 weeks or as recommended by the clinic after the first dose
- complete the full 2-dose treatment with VAXZEVRIA

Click to see more details on:

- ▶ *Vaccine ingredients*
- ▶ *Multidose vials*
- ▶ *Storage and stability details*
- ▶ *Shelf life*
- ▶ *What to do if a vial has been shaken*
- ▶ *Disposal*
- ▶ *Vaccine interchangeability*

After administration

Monitor vaccine recipients for anaphylactic reaction for **at least 15 min** or as directed by local guidelines.

- Manage any unused vaccine as per storage guidance (see ***Storage and stability details***).[1]
- Advise vaccine recipients:[1]
  - ☐ to retain records of vaccine name, vaccination dates and batch/lot number. These will be needed if they report an adverse event
  - ☐ to contact you or another healthcare provider if they have any health concerns they think may be related to the vaccine
  - ☐ to seek medical attention as soon as possible if symptoms or signs of an allergic reaction develop
  - ☐ to return for their next vaccination in 4 to 12 weeks' time or as recommended by the local clinic
  - ☐ that there is further information available to them (Public Guide and Health Canada Patient Medication Information section of the Product Monograph)
- Retain appropriate vaccination records, including vaccine name, date of vaccination and batch/lot number.[1]

Click to see more details on:

- ▶ *COVID-19 restrictions following vaccination*
- ▶ *COVID-19 tests following vaccination*
- ▶ *Reporting side effects*

More details on administering the vaccine

COVID-19 restrictions following vaccination

Advise vaccine recipients to continue to follow local public health/government guidance to reduce transmission of COVID-19, such as mask wearing, handwashing and social distancing. Vaccines do not protect everyone vaccinated and may not prevent transmission.

COVID-19 tests after vaccination

Polymerase Chain Reaction (PCR) tests

The vaccine will not lead to a positive PCR test for COVID-19. The vaccine does not contain live coronavirus or the part of the virus the PCR test looks for.[6]

Antibody tests

The antibodies produced following vaccination may affect the result of a COVID-19 antibody test, but only if the test looks for antibodies against the spike protein of the coronavirus.

Reporting side effects

Reporting suspected side effects is important. It allows continued monitoring of the benefit and risk balance of the medicine.

- Side effects can be reported at:

Reporting Suspected Side Effects for Vaccines

For the general public: Should you experience a side effect following immunization, please report it to your healthcare professional.

Should you require information related to the management of the side effect, please contact your healthcare professional. The Public Health Agency of Canada, Health Canada and AstraZeneca Canada Inc. cannot provide medical advice.

For healthcare professionals: If a patient experiences a side effect following immunization, please complete the Adverse Events Following Immunization (AEFI) Form appropriate for your province/territory (https://www.canada.ca/en/public-health/services/immunization/reporting-adverse-events-following-immunization/form.html) and send it to your local Health Unit.

- When reporting side effects, provide as much information as possible about the event including vaccine administration and timing of onset of symptoms including:
  - ☐ recipient's medical history
  - ☐ any other medicines they are taking
  - ☐ date and batch/lot number of vaccination(s)

Multidose vials

- VAXZEVRIA multidose vials come in packages of 5 mL of solution in a 10-dose vial (clear type I glass) with stopper (elastomeric with aluminium overseal).

More details on administering the vaccine

Storage and stability details[1]

- The vaccine does not contain any preservative.
- Unopened (unpunctured) multidose vial
  - Store in a refrigerator (2 to 8°C) until expiration date.
  - Do not freeze.
  - Store in outer carton in order to protect from light.
- Opened multidose vial
  After first opening, chemical and physical in-use stability has been demonstrated from the time of vial puncture to administration for no more than:
  - 6 hours at room temperature (up to 30°C)
  - 48 hours in a refrigerator (2 to 8°C)

  The vial can be re-refrigerated, but the cumulative storage time at room temperature must not exceed 6 hours, and the total cumulative storage time must not exceed 48 hours after first puncture.

VAXZEVRIA is not provided in pre-filled syringes. There are no available data on storing VAXZEVRIA in syringes filled in advance.

Shelf life

- Unopened multidose vials of VAXZEVRIA should be stored until the expiration date.[1]

What to do if a vial has been shaken

- The vial does not need to be shaken but can still be used if it has been shaken.

Disposal[1]

- VAXZEVRIA contains genetically modified organisms. Any unused vaccine or waste material should be disposed of in accordance with local requirements.
- Spills should be disinfected with an appropriate antiviral disinfectant.

Benefits and risks

Background to benefit analysis[1]

- The overall efficacy of VAXZEVRIA is based on an interim analysis of pooled data from two randomized blinded clinical trials in the UK and Brazil, and based on analysis from a randomized, double-blinded, placebo-controlled Phase III trial conducted in the United States, Peru and Chile.

Overall benefits[1]

Refer to the Health Canada Product Monograph for a detailed description of clinical trial results.

Duration and level of protection[1]

The duration of protection has not yet been established. Further studies are planned to evaluate the duration of protection.

As with any vaccine, vaccination with VAXZEVRIA may not protect all vaccine recipients. Individuals may not be optimally protected until after receiving the second dose of the vaccine.

Click to see more details on:

- ▶ *Vaccine development and authorization*
- ▶ *Scientific publications for VAXZEVRIA*
- ▶ *Reporting side effects*

Benefits and risks

Refer to the Health Canada Product Monograph for a detailed description of the benefits and risks.

Background to safety analysis[1]

- The safety profile of VAXZEVRIA is based on primary analysis of pooled data from four clinical trials conducted in the United Kingdom, Brazil and South Africa as well as data from a Phase III trial conducted in the United States, Peru and Chile.

United Kingdom, Brazil, and South Africa Clinical Trials

- At the time of analysis, 24,244 participants ≥18 years of age had been randomized and received either one or two doses of VAXZEVRIA or control.
- The majority of participants were white (75.5%), black (9.8%) or Asian (3.7%).

Gender and age of study participants[1]

		%
Gender	Male	44.2
	Female	55.8
Age	18 to 64 years	89.8
	65 years of age and older	10.2

United States, Peru and Chile Clinical Trials

- At the time of analysis, 32,379 participants ≥18 years of age had been randomized and received either one or two doses of VAXZEVRIA or placebo.
- The majority of participants were white (79%), black (8.3%) or Asian (4.4%).

Gender and age of study participants[1]

		%
Gender	Male	55.6
	Female	44.4
Age	18 to 64 years	77.6
	65 years of age and older	22.4

Side effects[1]

- The most frequently reported clinical trial adverse reactions in subjects ≥18 years old who received VAXZEVRIA (percentage of subjects) were injection site tenderness (63.8%), injection site pain (54.3%), fatigue (53.0%), headache (52.7%), myalgia (muscle pain; 43.9%), malaise (44.4%), pyrexia (feverishness: defined as a self-reported feeling of having a fever; 33.5%), chills (32.2%), arthralgia (joint pain; 26.6%), and nausea (22.2%). Refer to the Health Canada Product Monograph for a detailed description on side effects.
- Following vaccination, recipients may experience multiple adverse reactions occurring at the same time (e.g., myalgia/arthralgia, headache, chills, pyrexia and malaise).
- Most side effects were mild to moderate and usually resolved within a few days.
- When compared with the first dose, side effects were generally milder and reported less often after the second dose.
- Side effects were generally milder and reported less frequently in older adults (≥65 years old).

Vaccine development and authorization

Clinical trials

Adenovirus-vectored vaccines, similar to VAXZEVRIA but targeted for other diseases, have been developed and tested in thousands of people.[13]

Extensive clinical trials to test VAXZEVRIA have been conducted. The vaccine has undergone the phase I, II and III clinical trials that are expected of all new vaccines. So far, over 55,000 people have taken part in clinical trials, in countries including the USA, UK, Brazil, South Africa, India, Kenya and Japan. Trials include a broad range of ages and co-morbidities, and diverse racial, ethnic and geographic groups.[2,14-16]

Clinical trials are continuing to evaluate long term effects and additional studies are planned.[a,15,16] See ***Planned and ongoing clinical trials*** for more detail.

Accelerated product development

Patient safety is of paramount importance. Although the development of this vaccine has been accelerated, it has not been rushed.

Timelines have been accelerated by:

- running clinical trials to overlap each other, instead of one after another
- increasing personnel resources to start trials as quickly as possible
- including more investigators and trial sites so that participants can be recruited more quickly than usual
- manufacturing the vaccine before having final evidence that it works

Vaccine development and authorization

How the development of VAXZEVRIA has been accelerated

Regulatory review and authorization

Health Canada has completed a 'rolling review' of VAXZEVRIA.

Health Canada has clear and stringent efficacy and safety standards for the authorization of any new medicine.

During a public health emergency, Health Canada can allow the use of medicines and new vaccines more quickly than usual, when there is no alternative available. In this way, VAXZEVRIA has been granted Health Canada authorization with terms and conditions. Read more on how the authorization mechanism process works below.

Summary of authorization mechanism in Canada

VAXZEVRIA was authorized for use in relation to the COVID-19 pandemic. Terms and conditions were imposed upon the authorization. For more information, refer to the Authorization Terms and Conditions for VAXZEVRIA.

Click to see more details on:

- ▶ *Planned and ongoing clinical trials*
- ▶ *Scientific publications for VAXZEVRIA*

Planned and ongoing clinical trials

Further clinical studies are planned to evaluate long-term effectiveness and safety, as well as effectiveness in the wider population, including use in groups such as pregnant women, children and people who are immunocompromised.

References and further information

Scientific publications for VAXZEVRIA

Phase I, II and III studies are published:

a) Folegatti PM, Ewer KJ, Aley PK, *et al*. Safety and immunogenicity of the ChAdOx1 nCoV-19 vaccine against SARS-CoV-2: a preliminary report of a phase 1/2, single-blind, randomised controlled trial. *Lancet* 2020;396:467–78.

b) Ramasamy MN, Minassian AM, Ewer KJ. Safety and immunogenicity of ChAdOx1 nCoV-19 vaccine administered in a prime-boost regimen in young and old adults (COV002): a single-blind, randomised, controlled, phase 2/3 trial. *Lancet* 2020;396:1979–93.

c) Voysey M, Costa Clemens SA, Madhi SA, *et al*. Safety and efficacy of the ChAdOx1 nCoV-19 vaccine (AZD1222) against SARS-CoV-2: an interim analysis of four randomised controlled trials in Brazil, South Africa, and the UK. *Lancet* 2020;Dec 8. Online ahead of print.

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For more information, see

- Product Monograph[1]
- Patient Medication Information section of the Product Monograph[1]
- Public guide available at www.azcovid-19.com[18]

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