PRODUCT MONOGRAPH

INCLUDING PATIENT MEDICATION INFORMATION

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

Solution for Intramuscular Injection

Multiple Dose Vial
(10 dose vial presentation, 5 x 10^{10} viral particles per dose)

Active Immunizing Agent

AstraZeneca Canada Inc.
1004 Middlegate Road
Mississauga, Ontario
L4Y 1M4
www.astrazeneca.ca

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RECENT MAJOR LABEL CHANGES

CONTRAINDICATIONS (2)	04-2021
CONTRAINDICATIONS (2)	06-2021
SERIOUS WARNINGS AND PRECAUTIONS (3)	04-2021
DOSAGE AND ADMINISTRATION (4.4)	03-2021
WARNINGS AND PRECAUTIONS (7)	03-2021
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Sections or subsections that are not applicable at the time of authorization are not listed.

PART I: HEALTH PROFESSIONAL INFORMATION

1 INDICATIONS

VAXZEVRIA (COVID-19 Vaccine (ChAdOx1-S [recombinant])) is indicated for active immunization of individuals 18 years of age and older for the prevention of coronavirus disease 2019 (COVID-19).

1.1 Pediatrics

The safety and efficacy of VAXZEVRIA in children under 18 years of age have not yet been established. No data are available.

1.2 Geriatrics

Clinical studies of VAXZEVRIA include participants 65 years of age and older and their data contributes to the overall assessment of safety and efficacy (see 8 ADVERSE REACTIONS and 14 CLINICAL TRIALS).

2 CONTRAINDICATIONS

VAXZEVRIA is contraindicated in individuals who are hypersensitive to the active substance or to any ingredient in the formulation. For a complete listing, see **DOSAGE FORMS, STRENGTHS, COMPOSITION AND PACKAGING** section.

VAXZEVRIA is contraindicated in individuals who have experienced major venous and/or arterial thrombosis with thrombocytopenia following vaccination with VAXZEVRIA.

VAXZEVRIA is contraindicated in individuals who have previously experienced episodes of capillary leak syndrome.

3 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 (see **WARNINGS AND PRECAUTIONS, Hematologic** section).

4 DOSAGE AND ADMINISTRATION

4.1 Dosing Considerations

VAXZEVRIA is a solution for intramuscular injection that should be administered by a trained healthcare worker.

4.2 Recommended Dose and Dosage Adjustment

The VAXZEVRIA vaccination course consists of two separate doses of 0.5 mL each. The second dose should be administered between 4 and 12 weeks after the first dose.

Individuals should complete the vaccination course with VAXZEVRIA (see WARNINGS AND PRECAUTIONS).

There are no data available on the interchangeability of VAXZEVRIA with other non ChAdOx1-S (recombinant) COVID-19 vaccines.

4.3 Reconstitution

VAXZEVRIA **must not** be reconstituted, mixed with other medicinal products, or diluted.

4.4 Administration

VAXZEVRIA is a colourless to slightly brown, clear to slightly opaque solution. The vaccine should be inspected visually for particulate matter and discolouration prior to administration. Discard the vial if the solution is discoloured or visible particles are observed.

Each vaccine dose of 0.5 mL is withdrawn into a syringe for injection to be administered intramuscularly, preferably in the deltoid muscle. Use a separate sterile needle and syringe for each individual.

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.

The vaccine does not contain any preservative. After first opening, use the vial within:

- 6 hours when stored at room temperature (up to 30ºC), or
- 48 hours when stored in a refrigerator (2 to 8ºC).

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 this time, the vial must be discarded.

5 OVERDOSAGE

In the case of a suspected vaccine overdose, monitoring of vital functions and symptomatic treatment are recommended. Contact your regional poison control centre.

6 DOSAGE FORMS, STRENGTHS, COMPOSITION AND PACKAGING

Table – Dosage Forms, Strengths, Composition and Packaging

Route of Administration	Dosage Form / Strength/Composition	Non-medicinal Ingredients
Intramuscular injection	Solution Multidose vial (10 dose vial presentation)	• Disodium edetate dihydrate (EDTA) • Ethanol • L-Histidine • L-Histidine hydrochloride monohydrate • Magnesium chloride hexahydrate • Polysorbate 80 • Sodium chloride • Sucrose • Water for injection

VAXZEVRIA is a clear to slightly opaque, colourless to slightly brown, sterile, particle free, preservative-free, solution for intramuscular injection.

One dose (0.5 ml) of VAXZEVRIA contains:

COVID-19 Vaccine (ChAdOx1-S* recombinant) 5 x 10^{10} viral particles (not less than 2.5 x 10^{8} infectious units)

*Recombinant, replication-deficient chimpanzee adenovirus vector encoding the unmodified SARS-CoV-2 Spike (S) glycoprotein (GP) produced in genetically modified human embryonic kidney (HEK) 293 cells by recombinant DNA technology.

VAXZEVRIA is packaged in 5 mL of solution in a 10-dose vial (clear type I glass) with stopper (elastomeric with aluminium overseal).

To help ensure the traceability of vaccines for patient immunization record-keeping as well as safety monitoring, health professionals should record the time and date of administration, quantity of administered dose (if applicable), anatomical site and route of administration, brand name and generic name of the vaccine, the product lot number and expiry date.

7 WARNINGS AND PRECAUTIONS

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.

General

Hypersensitivity and anaphylaxis

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 the administration of the vaccine.

Vaccine recipients should be kept under observation for at least 15 minutes after immunization.

A second dose of the vaccine should not be given to those who have experienced a hypersensitivity reaction to the first dose of VAXZEVRIA.

Concurrent illness

Vaccination should be postponed 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.

Interchangeability

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

Driving and Operating Machinery

VAXZEVRIA has no or negligible influence on the ability to drive and use machines. However, some of the adverse reactions mentioned under **ADVERSE REACTIONS** may temporarily affect the ability to drive or use machines.

Hematologic

Coagulation disorders

- Thrombosis and thrombocytopenia

A combination of thrombosis and thrombocytopenia including 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.

Whilst 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 thrombocytopenic 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 the 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.

- 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.

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 the VAXZEVRIA should be evaluated for signs of thrombosis, and similarly individuals who present with thrombosis following vaccination should be evaluated for thrombocytopenia.

Risk of bleeding with intramuscular administration

As with other intramuscular injections, VAXZEVRIA should be given with caution to individuals with thrombocytopenia, any coagulation disorder or to persons on anticoagulation therapy, because bleeding or bruising may occur following an intramuscular administration in these individuals.

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.

Immune

Immunocompromised individuals

Immunocompromised persons, including individuals receiving immunosuppressant therapy, may have a diminished immune response to the vaccine.

Neurologic

Neurological events

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

Syncope

Syncope (fainting) can occur following, or even before, any vaccination as a psychogenic response to the needle injection. Procedures should be in place to prevent injury from syncopal reactions.

Fertility

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

7.1 Special Populations

7.1.1 Pregnant Women

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

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 enroll in the registry by visiting https://c-viper.pregistry.com or calling 1-800-616-3791.

7.1.2 Breast-feeding

It is unknown if VAXZEVRIA is excreted in human milk. A risk to the newborns/ infants cannot be excluded. The developmental and health benefits of breast feeding should be considered along with the mother's clinical need for immunization against COVID-19.

7.1.3 Pediatrics

The safety and efficacy of VAXZEVRIA in children and adolescents (under 18 years of age) have not yet been established. No data are available.

7.1.4 Geriatrics

Clinical studies of VAXZEVRIA include participants 65 years of age and older and their data contributes to the overall assessment of safety and efficacy (see 8 ADVERSE REACTIONS and 14 CLINICAL TRIALS).

8 ADVERSE REACTIONS

8.1 Adverse Reaction Overview

Studies COV001, COV002, COV003 and COV005

The overall safety of VAXZEVRIA is based on a primary analysis (data cut-off December 7, 2020) of pooled data from four ongoing clinical trials conducted in the United Kingdom (COV001 and COV002), Brazil (COV003), and South Africa (COV005) (see section 14 Clinical Trials). At the time of analysis, 24,244 participants ≥18 years of age had been randomised and received either one or two doses of VAXZEVRIA (n=12,282) or a control treatment (n=11,962). The median duration of follow-up in the VAXZEVRIA group was 137 days post-dose 1, and 81 days post-dose 2.

Control treatments consisted of a licensed meningococcal vaccine (MenACWY), a saline placebo, or a combination of the two.

Demographic characteristics were generally similar among participants who received VAXZEVRIA and those who received control. Overall, among the participants who received VAXZEVRIA, 89.8% were aged 18 to 64 years and 10.2% were 65 years of age or older. The majority of recipients were White (75.5%), 9.8% were Black and 3.7% were Asian; 55.8% were female and 44.2% male.

Following vaccination, recipients may experience multiple adverse reactions occurring at the same time (for example, myalgia/arthralgia, headache, chills, pyrexia and malaise).

When compared with the first dose, adverse reactions reported after the second dose were generally milder and reported less frequently.

Adverse reactions were generally milder and reported less frequently in older adults (≥65 years old).

Study D8110C00001

Safety of VAXZEVRIA was evaluated in a randomized Phase III clinical trial conducted in the United States, Peru and Chile. At the time of analysis, 32,379 participants ≥18 years of age had been randomised and received at least one dose of VAXZEVRIA

(n=21,587) or a placebo treatment (n=10,792) (see Section 14 Clinical Trials). Of these participants, 30,720 participants received two doses of VAXZEVRIA (n=20,773) or placebo (n=9,947). The median duration of follow-up in the VAXZEVRIA group was 92 days post-dose 1, and 61 days post-dose 2.

Demographic characteristics were generally similar among participants who received VAXZEVRIA and those who received placebo. Overall, among the participants who received VAXZEVRIA 77.6% were 18 to 64 years and 22.4% were ≥65 years of age. Seventy-nine percent of the participants were White, 8.3% were Black, 4.4% were Asian, 3.9% were American Indian or Alaska Native, 0.3% were Native Hawaiian or Other Pacific Islander, 2.4% were of multiple races and 1.7% were not reported or unknown; 44.4% were female and 55.6% male.

8.2 Clinical Trial Adverse Reactions

Studies COV001, COV002, COV003 and COV005

Clinical trials are conducted under very specific conditions. The adverse reaction rates observed in the clinical trials; therefore, may not reflect the rates observed in practice and should not be compared to the rates in the clinical trials of another drug. Adverse reaction information from clinical trials may be useful in identifying and approximating rates of adverse drug reactions in real-world use.

Solicited Adverse Reactions

Solicited adverse reaction data were collected from Day 1 to Day 7 and reported by participants in a symptom diary card after each dose and on electronic case report forms.

The most frequently reported adverse reactions in subjects 18 years of age and older 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%). Other less frequently reported adverse reactions include injection site warmth (17.9%), injection site itch (injection site pruritus) (13.1%), fever (≥38°C/100.4°F) (7.6%), injection site swelling (3.4%), injection site redness (injection site erythema) (3.1%), and vomiting (1.8%).

Unsolicited Adverse Events

In the pooled analysis of subjects aged ≥18 years of age who received any dose of study intervention (data cut-off December 7, 2020; VAXZEVRIA = 12,282 of whom 1,256 were aged ≥65 years and control = 11,962 of whom 1,018 were aged ≥65 years), unsolicited adverse events occurring within 28 days following any vaccination were reported by 41.8% of participants who received VAXZEVRIA and 31.6% of participants who received the control. Most of these events occurred within 7 days after receipt of any dose of the vaccine, with 11.4% of participants in the VAXZEVRIA group and

10.9% of participants in the control group reporting adverse events between 8 and 28 days after any dose. The adverse events occurring in ≥ 2% participants who received VAXZEVRIA were predominantly reactogenicity events (vaccination site pain, headache, fever, myalgia, fatigue, chills, asthenia, malaise, and nausea). Other less frequently reported adverse reactions include lymphadenopathy (0.3%), dizziness (0.7%), somnolence (0.5%), diarrhea (1.6%), abdominal pain (0.6%), hyperhidrosis (0.4%), pruritus (0.3%), rash (0.2%), urticaria (0.1%), pain in extremity (1.3%), and influenza-like illness (1.1%).

Unsolicited AEs affecting the nervous system occurred in 13.6 % of participants in the VAXZEVRIA group and 9.5% of participants in the control group. Most of these events were due to reactogenicity, were self-limited and occurred in the first 7 days following vaccination. The events that occurred at higher rates in the VAXZEVRIA group than the control group included headache (12.4% vs 8.6% respectively), lethargy (0.3% vs 0.2%) and somnolence (0.5% vs 0.3%). Facial paralysis occurred in 4 subjects in the VAXZEVRIA group and 3 subjects in the control group, all of whom had received meningococcal vaccine.

No deaths related to the vaccine were reported in the pooled safety analysis.

Other unsolicited events where there was an imbalance of AEs between VAXZEVRIA and control group and that occurred at rates >0.1% in the vaccine group included: hyperhydrosis (0.3% in the vaccine and 0.1% in the control group) and decreased appetite (0.2% in the vaccine and 0.1% in the control group).

Serious Adverse Events

One hundred and eight (0.9%) of subjects in the VAXZEVRIA group and 127 (1.1%) of subjects in the control group experienced a serious adverse event (SAE) between the first vaccination and the analysis (data cut-off December 7, 2020).

Two SAEs were possibly related to the VAXZEVRIA: one case of pyrexia (40.5°C) occurring 2 days after dose 1, and one case of transverse myelitis occurring 14 days after dose 2. Two possibly related SAEs occurred in the control group: a case of autoimmune haemolytic anemia occurring 9 days after a single dose of the MenACWY vaccine and one case of myelitis occurring 54 days after a single dose of MenACWY.

Study D8110C00001

Solicited Adverse Reactions

Solicited adverse reaction data were collected from Day 1 to Day 7 and reported by participants in a symptom diary card after each dose and on electronic case report forms. Reported solicited local and systemic adverse reactions are presented in Table 1 and 2, respectively.

Table 1 – Solicited Local Adverse Reactions Collected Within 7 Days After Each Vaccination (Safety Analysis Set, Study D8110C00001)

Solicited Local AEs	Dose 1		Dose 2	
	Vaccine Group n(%) N=2,037	Placebo n(%) N=1,013	Vaccine Group n(%) N=1,962	Placebo n(%) N=968
Pain				
Any Grade	945 (51.7)	95 (10.3)	639 (34.9)	83 (9.1)
Grade 3 or 4[a]	6 (0.3)	0	0	0
Tenderness				
Any Grade	1128 (62.3)	135 (14.7)	891 (48.8)	91 (10.0)
Grade 3 or 4[b]	9 (0.5)	0	0	0
Erythema/redness[c]				
Any Grade	44 (2.4)	5 (0.5)	23 (1.3)	1 (0.1)
>6 cm	9 (0.5)	1 (0.1)	3 (0.2)	0
Induration/swelling[c]				
Any Grade	49 (2.7)	1 (0.1)	26 (1.4)	0
>6 cm	12 (0.7)	0	2 (0.1)	0

Safety analysis set is defined as all participants who received at least one dose of study intervention.
[a]Grade 3 defined as any use of narcotic pain reliever or prevents daily activity; Grade 4 defined as emergency room visit or hospitalization.
[b] Grade 3 defined as significant discomfort at rest; Grade 4 defined as emergency room visit or hospitalization.
[c] Intensity categories for erythema and swelling were defined as follows: Mild: 2.5 to 5 cm, Moderate: 5.1 to 10 cm, Severe: >10 cm, Any: ≥2.5 cm, None: <2.5 cm. Due to limitations in the e-participant e-diary, the maximum measurement possible to be recorded was ">6 cm".

Table 2 – Solicited Systemic Adverse Reactions Collected Within 7 Days After Each Vaccination (Safety Analysis Set, Study D8110C00001)

Solicited Systemic AEs	Dose 1		Dose 2	
	Vaccine Group n(%) N=2,037	Placebo n(%) N=1,013	Vaccine Group n(%) N=1,962	Placebo n(%) N=968
Fever				
Any Grade (>37.8°C)	126 (6.9)	6 (0.7)	13 (0.7)	1 (0.1)
Grade 3 or 4[a]	8 (0.4)	2 (0.2)	2 (0.1)	0
Chills				
Any Grade	454 (25.0)	54 (5.9)	164 (9.0)	56 (6.2)
Grade 3 or 4[b]	47 (2.6)	2 (0.2)	3 (0.2)	0
Muscle pains				
Any Grade	672 (36.9)	132 (14.4)	338 (18.6)	99 (11.0)
Grade 3 or 4[b]	37 (2.0)	3 (0.3)	3 (0.2)	1 (0.1)
Fatigue				
Any Grade	797 (43.9)	221 (24.0)	490 (26.9)	164 (18.2)
Grade 3 or 4[b]	65 (3.6)	4 (0.4)	12 (0.7)	6 (0.7)
Headache				
Any Grade	774 (42.3)	265 (28.8)	521 (28.6)	173 (19.2)
Grade 3 or 4[c]	24 (1.3)	5 (0.5)	8 (0.4)	3 (0.3)
Malaise				
Any Grade	543 (30.0)	112 (12.2)	291 (16.0)	84 (9.3)
Grade 3 or 4[b]	38 (2.1)	2 (0.2)	10 (0.5)	0
Nausea				
Any Grade	207 (11.4)	71 (7.7)	139 (7.6)	63 (7.0)
Grade 3 or 4[d]	0	1 (0.1)	0	0
Vomiting				
Any Grade	22 (1.2)	11 (1.2)	14 (0.8)	7 (0.8)
Grade 3 or 4[d]	0	0	0	0

Safety analysis set is defined as all participants who received at least one dose of study intervention.
[a] Defined as ≥39.0°C.
[b] Grade 3 defined as significant; prevents daily activity. Grade 4 defined as emergency room visit or hospitalization.
[c] Grade 3 defined as significant; prevents daily activity or any use of narcotic pain reliever. Grade 4 defined as emergency room visit or hospitalization.
[d] Grade 3 defined as prevents daily activity, required outpatient intravenous hydration. Grade 4 defined as emergency room visit or hospitalization for hypotensive shock.

Unsolicited Adverse Events

In Study D8110C00001 of subjects aged ≥18 who received any dose of study intervention (VAXZEVRIA = 21,587 and placebo = 10,792), unsolicited adverse events occurring within 28 days were reported by 40.6% of participants who received VAXZEVRIA and 29.7% of participants who received placebo. The majority of the unsolicited events were mild to moderate in severity. The adverse events occurring in ≥ 2% participants who received VAXZEVRIA were pain, injection site pain, headache, fatigue, body temperature increased, diarrhea, rhinorrhea, myalgia, chills and oropharyngeal pain. Other less frequently reported adverse reactions include pain in extremity (1.4%), dizziness (0.8%), hyperhidrosis (0.3%), rash (0.3%), lymphadenopathy (0.2%), abdominal pain (0.2%), influenza-like illness (0.2%), urticaria (0.1%), pruritus (0.1%) and somnolence (<0.1%).

Unsolicited AEs affecting the nervous system occurred in 8.4% of participants in the VAXZEVRIA group and 6.5% of participants in the placebo group. Most of these events were due to reactogenicity, were self-limited and occurred in the first 7 days following vaccination. The events that occurred at higher rates in the VAXZEVRIA group than the placebo group included headache (6.2% vs 4.6% respectively) and dizziness (0.8 % vs 0.7%). In addition, episodes of tinnitus were more common in the VAXZEVRIA group than in the placebo group (0.1% [26 participants] vs <0.1% [3 participants]).

No deaths related to the vaccine were reported in Study D8110C00001.

Serious Adverse Events

One hundred and forty (0.6%) of subjects in the VAXZEVRIA group and 78 (0.7%) of subjects in the placebo group experienced a SAE in Study D8110C00001.

Two serious adverse events reported by 1 participant were considered related to VAXZEVRIA by the investigator: hypoaesthesia and chronic inflammatory demyelinating polyradiculoneuropathy. The participant experienced hypoesthesia 7 days after the first dose of VAXZEVRIA, and the event worsened and the participant was hospitalized (SAE) 7 days later. 51 days after the first dose of VAXZEVRIA, the participant was diagnosed with Guillain-Barre syndrome (GBS); 105 days after the first dose of VAXZEVRIA, the diagnosis was updated from GBS to chronic inflammatory demyelinating polyneuropathy which was considered as serious. The event of hypoaesthesia resolved, and the event of chronic inflammatory demyelinating polyneuropathy was not resolved at the time of data cut-off. In addition, 1 participant experienced paraesthesia on the same day of the second dose and 28 days after the first dose of VAXZEVRIA. The event worsened and the participant was hospitalized (SAE) 27 days after the second dose and 55 days after the first dose of VAXZEVRIA; the SAE resolved within one day and grade 2 paraesthesia was reported as an ongoing event. The paraesthesia was considered related to VAXZEVRIA by the investigator.

Adverse Events of Special Interest

Adverse Events of Special Interest (AESI), including neurologic, vascular, haematologic, and immunologic events, were analysed. During the double-blind period, the incidence of AESI was 2.4% of participants (525 participants) in the VAXZEVRIA group and 3.9% of participants (416 participants) in the placebo group.

The proportion of participants that reported neurological AESIs was 0.5% (114 participants) in the VAXZEVRIA group and 0.4% (48 participants) in the placebo group. The most frequently reported neurologic events were paraesthesia (0.3% [61 participants] in the VAXZEVRIA group and 0.3% [27 participants] in the placebo group), hypoaesthesia (0.1% [31 participants] in the VAXZEVRIA group and < 0.1% [10 participants] in the placebo group), and muscular weakness (< 0.1% [10 participants] in the VAXZEVRIA group and < 0.1% [1 participant] in the placebo group).

Facial paralysis occurred in 5 subjects in the VAXZEVRIA group and 0 subjects in the placebo group. These events were nonserious and a causal relationship with the vaccine could not be determined, due to the presence of underlying medical conditions that may have predisposed individuals to these events.

8.3 Post-Market Adverse Reactions

The following adverse reactions have been spontaneously reported during worldwide post-authorization use of VAXZEVRIA. Because these reactions are reported voluntarily from a population of uncertain size, it is not always possible to reliably estimate their frequency or establish a causal relationship to product exposure. They are included because: a) they represent reactions that are known to occur following immunizations generally; or b) they are potentially serious; or c) on the basis of their frequency of reporting.

Blood and lymphatic system disorders: Thrombocytopenia.

Immune system disorders: Anaphylactic reaction.

Nervous system disorders: Guillain-Barré Syndrome.

Skin and subcutaneous tissue disorders: Angioedema.

Vascular disorders: A combination of thrombosis and thrombocytopenia including thrombosis with thrombocytopenia syndrome (TTS), in some cases accompanied by bleeding, has been observed very rarely following vaccination with VAXZEVRIA. This includes severe cases in unusual sites such as cerebral venous sinus thrombosis and splanchnic vein thrombosis, as well as arterial thrombosis, concomitant with thrombocytopenia. See **WARNINGS AND PRECAUTIONS**.

In addition, cases of capillary leak syndrome (CLS) have been observed following vaccination with VAXZEVRIA. See **WARNINGS AND PRECAUTIONS**.

9 DRUG INTERACTIONS

No interaction studies have been performed.

Do not mix VAXZEVRIA with other vaccines/products in the same syringe.

10 CLINICAL PHARMACOLOGY

10.1 Mechanism of Action

VAXZEVRIA is a monovalent vaccine composed of a single recombinant, replication-deficient chimpanzee adenovirus (ChAdOx1) vector encoding the S glycoprotein of SARS-CoV-2. The SARS-CoV-2 S immunogen in the vaccine is expressed in the trimeric pre-fusion conformation; the coding sequence has not been modified in order to stabilise the expressed S-protein in the pre-fusion conformation. Following administration, the S glycoprotein of SARS-CoV-2 is expressed locally stimulating neutralising antibody and cellular immune responses, which may contribute to protection against COVID-19.

11 STORAGE, STABILITY AND DISPOSAL

Unopened multidose vial

Store in a refrigerator (2 to 8ºC).

Do not freeze.

Store in outer carton in order to protect from light.

Use the product before the expiration date on the vial label.

Opened multidose vial

For storage conditions after first opening of the medicinal product, see below.

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 30ºC, or
- 48 hours in a refrigerator (2 to 8ºC).

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.

12 SPECIAL HANDLING INSTRUCTIONS

Disposal

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

PART II: SCIENTIFIC INFORMATION

13 PHARMACEUTICAL INFORMATION

Drug Substance

Proper name: COVID-19 Vaccine (ChAdOx1-S [recombinant])

Product Characteristics:

VAXZEVRIA is a clear to slightly opaque, colourless to slightly brown, sterile, particle free, pH 6.6, preservative-free, solution for intramuscular injection.

One dose (0.5 ml) of VAXZEVRIA contains:

COVID-19 Vaccine (ChAdOx1-S* recombinant) 5×10^{10} viral particles

*Recombinant, replication-deficient chimpanzee adenovirus vector encoding the unmodified SARS-CoV-2 Spike (S) glycoprotein (GP) produced in genetically modified human embryonic kidney (HEK) 293 cells by recombinant DNA technology.

14 CLINICAL TRIALS

14.1 Trial Design and Study Demographics

Interim analysis of pooled data from COV001, COV002, COV003, and COV005

VAXZEVRIA has been evaluated based on an interim analysis of pooled data from four on-going randomised, blinded, controlled trials: a Phase I/II Study in healthy adults 18 to 55 years of age in the UK (COV001; NCT04324606), a Phase II/III Study in adults ≥18 years of age in the UK (COV002; NCT04400838), a Phase III Study in adults ≥18 years of age in Brazil (COV003; ISRCTN89951424), and a Phase I/II study in adults aged 18 to 65 years of age in South Africa (COV005; NCT04444674). The studies excluded participants with a history of anaphylaxis or angioedema; participants with severe and/or uncontrolled cardiovascular, gastrointestinal, liver, renal, endocrine/metabolic disease, or neurological illnesses; pregnant or breastfeeding women; participants with known history of SARS-CoV-2 infection as well as those with severe immunosuppression.

The primary efficacy endpoint was virologically-confirmed symptomatic cases of COVID-19* confirmed by a clinical adjudication committee.

**PCR confirmed SARS-CoV-2 and at least one of the following symptoms: objective fever (defined as ≥37.8 °C), cough, shortness of breath, anosmia, or ageusia.*

Based on the pre-defined criteria for the interim efficacy analysis (data cut-off November 4, 2020), COV002 and COV003 exceeded the threshold of ≥5 adjudication committee confirmed COVID-19 cases per study and therefore contributed to the efficacy analysis; COV001 and COV005 did not exceed such threshold and were excluded from this interim analysis. In the pooled analysis for efficacy (COV002 and

COV003), participants ≥18 years of age that received two doses of VAXZEVRIA or control (meningococcal vaccine or saline placebo) were included. The planned dose was 5×10^{10} viral particles (vp) per dose administered via IM injection. The population used for the interim analysis of the primary efficacy endpoint included participants who received two doses of the VAXZEVRIA or control and did not have evidence of prior infection with SARS-CoV-2 through 15 days after the second dose. Study COV002 contributed a total of 7548 participants (3744 receiving the VAXZEVRIA, 3804 receiving two doses of a meningococcal vaccine control) and Study COV003 contributed a total of 4088 participants (2063 receiving the VAXZEVRIA, 2025 receiving meningococcal vaccine followed by saline placebo control) to this analysis.

Participants are planned to be followed for up to 12 months, for assessments of safety and efficacy against COVID-19 disease.

Table 3 – Demographic Characteristics – Subjects Without Evidence of Infection Prior to 15 Days After Dose 2 – Evaluable Efficacy Population (COV002 and COV003)

Characteristic	Study COV002 (United Kingdom)		Study COV003 (Brazil)	
	VAXZEVRIA (N=3744)	Meningococcal Vaccine (N=3804)	VAXZEVRIA (N=2063)	Meningococcal Vaccine/ Placebo (N=2025)
Sex				
Female	2264 (60.5)	2365 (62.2)	1261 (61.1)	1156 (57.1)
Male	1480 (39.5)	1438 (37.8)	802 (38.9)	869 (42.9)
Age (years)				
Mean (SD)	43.0 (13.1)	43.2 (13.0)	38.9 (11.5)	38.6 (11.2)
Median	42	42	37	36
Min, max	18, 86	18, 88	19, 84	18, 77
Age group				
18 to 64 years	3467 (92.6)	3525 (92.7)	1999 (96.9)	1985 (98.0)
≥65 years	277 (7.4)	279 (7.3)	64 (3.1)	40 (2.0)
Race				
White	3450 (92.1)	3534 (92.9)	1357 (65.8)	1366 (67.5)
Asian	213 (5.7)	197 (5.2)	54 (2.6)	53 (2.6)
Black	23 (0.6)	16 (0.4)	230 (11.1)	210 (10.4)
Other	22 (0.6)	19 (0.5)	260 (12.6)	260 (12.8)
Mixed	34 (0.9)	37 (1.0)	159 (7.7)	133 (6.6)
Not reported	2 (0.1)	1 (<0.1)	3 (0.1)	3 (0.1)
Comorbidity at baseline[a]				
Yes	1311 (35.0)	1398 (36.8)	759 (36.8)	735 (36.3)
No	2432 (65.0)	2401 (63.1)	1301 (63.1)	1282 (63.3)

Table 3 – Demographic Characteristics – Subjects Without Evidence of Infection Prior to 15 Days After Dose 2 – Evaluable Efficacy Population (COV002 and COV003)

Characteristic	Study COV002 (United Kingdom)		Study COV003 (Brazil)	
	VAXZEVRIA (N=3744)	Meningococcal Vaccine (N=3804)	VAXZEVRIA (N=2063)	Meningococcal Vaccine/ Placebo (N=2025)
Missing	1 (<0.1)	5 (0.1)	3 (0.1)	8 (0.4)

[a] Number (%) of subjects who have 1 or more of that following comorbidities at baseline that increase the risk of sever COVID19 disease: BMI $\geq$30 kg/m^2, cardiovascular disorder, respiratory disease, or diabetes.

Analysis of data from D8110C00001

VAXZEVRIA has been evaluated based on an analysis from a randomised, double-blinded, placebo-controlled Phase III trial conducted in the United States, Peru and Chile (data cut-off March 05, 2021). The trial randomised 32,451 healthy adults or those with medically-stable chronic diseases ≥18 years of age. The study excluded participants with severe and/or uncontrolled cardiovascular, gastrointestinal, liver, renal, endocrine/metabolic disease, and neurological illnesses; as well as those with severe immunosuppression. The study permitted enrolment of individuals with pre-existing medically-stable comorbidities defined as chronic kidney disease, chronic obstructive pulmonary disease (COPD), lower immune health because of a solid organ transplant, history of obesity (BMI>30), serious heart conditions, sickle cell disease, type 1 and 2 diabetes, asthma, dementia, cerebrovascular diseases, cystic fibrosis, high blood pressure, liver disease, scarring in the lungs (pulmonary fibrosis), thalassemia, history of smoking. All participants are planned to be followed for up to 1 year for assessments of efficacy against COVID-19 disease.

Determination of COVID-19 cases was made by an adjudication committee. The case for the primary endpoint was defined as having SARS-CoV-2 virologically confirmed COVID-19 occurring ≥15 days post second dose and met either the Category A or Category B criteria, and had no prior evidence of a previous SARS-CoV-2 infection:

Category A: One or more of the following:

- Pneumonia diagnosed by chest x-ray, or computed tomography scan
- Oxygen saturation of ≤94% on room air or requiring either new initiation or escalation in supplemental oxygen
- New or worsening dyspnoea/shortness of breath

Category B: Two or more of the following:

- Fever >100°F (>37.8°C) or feverishness
- New or worsening cough
- Myalgia/muscle pain
- Fatigue that interferes with activities of daily living
- Vomiting and/or diarrhoea (only one finding to be counted toward endpoint definition)

- Anosmia and/or ageusia (only one finding to be counted toward endpoint definition)

In the fully vaccinated analysis set, 26,212 participants received two doses of VAXZEVRIA (N=17,662) or placebo (N=8,550), were seronegative at baseline and remained on-study ≥15 days post second dose without having a prior SARS-CoV-2 infection. Participants randomised to VAXZEVRIA received (5×10^{10} vp per dose) administered via IM injection on Day 1 and Day 29 (-3 to +7 days). The median dose interval was 29 days for both VAXZEVRIA and placebo groups and the majority of participants in the VAXZEVRIA and placebo groups received the second dose ≥26 to ≤36 days (95.7% and 95.3% respectively) after dose 1.

Baseline demographics were balanced across the VAXZEVRIA and the placebo groups. Of the participants who received VAXZEVRIA, 79.1% were aged 18 to 64 years and 20.9% were ≥65 years of age; 43.8% of subjects were female. 79.3% were White, 7.9% were Black, 4.2% were Asian, 4.2% were American Indian or Alaska Native, 0.3% were Native Hawaiian or Other Pacific Islander, and 2.4% were of multiple races (1.7% were unknown or not reported). A total of 10,376 (58.8%) participants who received VAXZEVRIA versus 5,105 (59.7%) who received placebo had at least one pre-existing comorbidity. In the fully vaccinated analysis set, the median duration of follow-up ≥15 days post dose 2 was 64 days regardless of unblinding.

14.2 Study Results

Interim analysis of pooled data from COV001, COV002, COV003, and COV005

The interim analysis of the primary efficacy endpoint (data cut-off November 4, 2020) included 11,636 participants 18 years of age and older (5,807 in the VAXZEVRIA group and 5,829 in the control group). At the time of the interim analysis, participants had been followed for symptomatic COVID 19 disease for a median of 63 days (range: 16-94 days) after the second dose, corresponding to exposure of 921 person-years in the VAXZEVRIA and 925 person-years in the control group.

Participants randomised to VAXZEVRIA received either two standard doses [SD] (5×10^{10} vp per dose) (SD/SD) or, due to a difference in concentration determination between two analytical methods, one low dose [LD] (2.2×10^{10} vp) followed by one SD (5×10^{10} vp) (LD/SD).

The interval between dose 1 and dose 2 ranged from 3 to 26 weeks for these data. In these 11,636 seronegative participants, 86 (0.7%) had a dose interval of less than 4 weeks, 8,786 (75.5%) had a dose interval of 4-12 weeks and 2,764 (23.8%) had a dose interval of more than 12 weeks.

A total of 131 participants had SARS-CoV-2 virologically confirmed COVID-19 occurring ≥15 days post second dose. There were 30 confirmed COVID-19 cases identified in the VAXZEVRIA group and 101 in the control group, respectively, for the primary interim efficacy analysis. Compared to control, efficacy of VAXZEVRIA in participants with first COVID-19 occurrence from 15 days after Dose 2 was 70.42% (two-sided 95.84% confidence interval of 58.84% to 80.63%, p<0.001). There were no cases of COVID-19 hospitalisation (WHO severity score ≥4) in the participants that received VAXZEVRIA as compared to 5 cases in control participants.

The vaccine efficacy was based on pre-specified analysis; however the results should be interpreted with caution given that it excludes 51% of randomized and vaccinated subjects, the majority of which had only received a single dose. In addition, a significant difference was observed in vaccine efficacy between the LD/SD cohort and the SD/SD cohort. The findings may also be confounded by the variability in dosing interval.

In participants who received two standard doses of the vaccine (SD/SD) or the corresponding control (4,440 in the VAXZEVRIA group and 4,455 in the control group), a total of 98 participants had SARS-CoV-2 virologically confirmed COVID-19 occurring ≥15 days post second dose (27 cases in the VAXZEVRIA group and 71 cases in the control group). In this population, vaccine efficacy from 15 days post second dose was 62.10% (two-sided 95% confidence interval of 39.96% to 76.08%).

Evidence shows protection starts from approximately 3 weeks after first dose of vaccine. A second dose should be given at a 4-to-12-week interval after the first dose.

Updated analysis of pooled data from COV001, COV002, COV003, and COV005

Based on an updated analysis (data cut-off December 7, 2020, from COV001, COV002, COV003, and COV005), vaccine efficacy was 63.1% (two-sided 95% confidence interval of 51.8% to 71.3%) in participants who received two standard doses with any interval (N=7201 in the VAXZEVRIA group, and N=7191 in the control group); there were 74 COVID-19 cases in participants receiving VAXZEVRIA and 197 COVID-19 cases in participants receiving control. Regarding COVID-19 hospitalisation (WHO severity score ≥4) in these data, there were 0 cases of COVID-19 hospitalisation in participants who received two doses of VAXZEVRIA (≥15 days post dose 2) as compared to 8 for control, including one severe case (WHO severity score ≥6), reported for control and 0 severe cases reported for VAXZEVRIA.

At the time of interim and updated analyses, there were limited number of COVID-19 cases in participants ≥65 years old.

Analysis of data from D8110C00001

In the primary efficacy analysis, based on 203 adjudicated cases, there were 73 (0.4%) COVID-19 cases in participants receiving VAXZEVRIA (N=17,662) and 130 (1.5%) COVID-19 cases in participants receiving placebo (N=8,550), with a vaccine efficacy of 74.0%, (95% CI: 65.3, 80.5) (see Table 4).

Table 4 – VAXZEVRIA efficacy against COVID-19[a]

	VAXZEVRIA		Placebo		Vaccine efficacy % (95% CI)
	N	Number of COVID-19 cases[b], n (%)	N	Number of COVID-19 cases[b], n (%)	
Primary Efficacy Analysis					
Symptomatic Illness	17,662	73 (0.4)	8,550	130 (1.5)	73.98 (65.34, 80.47)
Key Secondary Efficacy Analyses					
Symptomatic Illness Regardless of Evidence of Prior COVID-19 Infection	18,563	76 (0.4)	9,031	135 (1.5)	73.68 (65.13, 80.13)
Severe or Critical Symptomatic COVID-19[c]	17,662	0 (0.0)	8,550	8 (<0.1)	100.0 (71.62, NE)

N = Number of subjects included in each group; n = Number of subjects having a confirmed event; CI = Confidence Interval;

[a] Based on confirmed COVID-19 cases in subjects aged 18 years and over who were seronegative at baseline, who had received two doses and were on-study ≥15 days post second dose.

[b] Virologically confirmed SARS-CoV-2 using the Category A and B criteria.

[c] Based on laboratory-confirmed COVID-19, plus any of the following: clinical signs at rest indicative of severe systemic illness (respiratory rate ≥30 breaths per minute, heart rate ≥125 beats per minute, oxygen saturation ≤93% on room air at sea level, or partial pressure of oxygen to fraction of inspired oxygen ratio <300 mmHg); or respiratory failure (defined as needing high-flow oxygen, non-invasive ventilation, mechanical ventilation, or extracorporeal membrane oxygenation), evidence of shock (systolic blood pressure <90 mmHg, diastolic blood pressure <60 mmHg or requiring vasopressors); or significant acute renal, hepatic, or neurological dysfunction; or admission to an intensive care unit, or death.

For COVID-19 Emergency Department Visits, there was 1 case in participants receiving VAXZEVRIA and 9 cases in participants receiving placebo, with a vaccine efficacy of 94.80% (95% CI: 58.98, 99.34). For Post-treatment response for SARS-CoV-2 Nucleocapsid antibodies (negative at baseline to positive post treatment with study intervention), there were 156 cases in participants receiving VAXZEVRIA and 202 cases in participants receiving placebo, with a vaccine efficacy of 64.32% (95% CI: 56.05, 71.03).

Efficacy in subgroups

In the fully vaccinated analysis set (n=26,212) participants with one or more comorbidities who received VAXZEVRIA ≥15 days post dose-2 had an efficacy of 75.24% (95% CI: 64.18, 82.88) and participants without comorbidities had a vaccine efficacy of 71.81% (95% CI: 55.5, 82.14).

In participants ≥65 years old who had received VAXZEVRIA (≥15 days post dose 2 N=3,696), there were 5 (0.1%) cases of COVID-19 compared to 14 (0.8%) cases for placebo (N=1,812), corresponding to a vaccine efficacy of 83.5% (95% CI: 54.17, 94.06). In participants <65 years old, the vaccine efficacy was 72.83% (95% CI: 63.35, 79.87).

15 MICROBIOLOGY

No microbiological information is required for this drug product.

16 NON-CLINICAL TOXICOLOGY

General Toxicology

In a repeat-dose toxicity study in mice, Intramuscular (IM) administration of VAXZEVRIA was well tolerated.

IM administration of VAXZEVRIA at a dose of $3.7x10^{10}$ vp/animal once every 3 weeks for 6 weeks (total of 3 doses) resulted in transient inflammation at the site of injection and underlying fascia and connective tissue, slightly increased body temperature, increased spleen weights, mildly decreased monocyte counts, and minimal to mild clinical chemistry changes indicative of an active phase response.

Non-adverse, mixed and/or mononuclear cell inflammation was observed in the subcutaneous tissues and skeletal muscle of the administration sites and adjacent sciatic nerve consistent with the anticipated findings after IM injection of vaccines. There were no findings in the administration sites or sciatic nerves at the end of a 4-week recovery period, indicating complete recovery of the VAXZEVRIA-related inflammation.

Full recovery from all findings was observed following the 4 week recovery period. These changes are consistent with an expected immunostimulatory response following intramuscular administration of a vaccine.

Carcinogenicity

VAXZEVRIA has not been evaluated for carcinogenicity in animals, as carcinogenicity studies were not considered relevant to this vaccine.

Genotoxicity

VAXZEVRIA has not been evaluated for genotoxicity, as genotoxicity studies were not considered relevant to this vaccine.

Reproductive and Developmental Toxicology

In a pre- and post-natal development toxicity study in mice, VAXZEVRIA was well tolerated. In this study, F0 female mice were administrated two doses of $3.71x10^{10}$ vp/animal of VAXZEVRIA by IM injection 13 days prior to mating and on gestational day (GD) 6 or on GD 6 and GD 15. IM administration of VAXZEVRIA elicited detectable anti-SARS-CoV-2 S-glycoprotein maternal antibodies in dams that were detected in foetuses and pups, indicating placental and lactational transfer, respectively. There were no VAXZEVRIA-related adverse effects on female fertility, fetal or pup survival, or pup physical development. There were also no VAXZEVRIA-related fetal external, visceral, or skeletal findings or abnormal gross pathology findings in pups prior to or post weaning or in dams.

A biodistribution study conducted in mice did not show measurable distribution of VAXZEVRIA to the gonads (testes, ovaries) following a single IM injection at a dose of $3.7x10^{10}$ vp/animal.

PATIENT MEDICATION INFORMATION

READ THIS FOR SAFE AND EFFECTIVE USE OF YOUR MEDICINE

VAXZEVRIA™
COVID-19 Vaccine (ChAdOx1-S [recombinant]), Solution for Intramuscular Injection

Health Canada has authorized the sale of this COVID-19 vaccine under an Interim Order. This leaflet is a summary and will not tell you everything about this vaccine. Talk to your healthcare professional about your medical condition and treatment and ask if there is any new information about VAXZEVRIA.

What is VAXZEVRIA used for?

VAXZEVRIA is a vaccine used to prevent the coronavirus disease 2019 (COVID-19) caused by the SARS-CoV-2 virus. It can be given to adults 18 years of age and older.

How does VAXZEVRIA work?

COVID-19 is caused by a virus called coronavirus (SARS-CoV-2).

VAXZEVRIA stimulates the body's natural defences (immune system), by causing the body to produce its own protection (antibodies) against the SARS-CoV-2 virus that causes the COVID-19 infection. You cannot get COVID-19 from this vaccine.

The vaccine is given by injection with a needle, usually in the upper arm, and will require two doses given between 4 and 12 weeks apart. Individuals may not be optimally protected until after receiving the second dose of the vaccine. As with any vaccine, VAXZEVRIA may not fully protect all those who receive it. It is not yet known how long people who receive the vaccine will be protected.

Even after you have had both doses of the vaccine, continue to follow the recommendations of local public health officials to prevent spread of COVID-19.

What are the ingredients in VAXZEVRIA?

Medicinal ingredients: ChAdOx1-S [recombinant]

Non-medicinal ingredients:

- Ethanol,
- Disodium edetate dihydrate (EDTA),
- L-Histidine,
  L-Histidine hydrochloride monohydrate,
- Magnesium chloride hexahydrate,
- Polysorbate 80,
- Sodium chloride,
- Sucrose,
- Water for injection

VAXZEVRIA comes in the following dosage forms:

Clear to opalescent, colourless to slightly brown, particle-free, preservative-free, solution for injection. It is provided in a multiple dose vial of 10 doses, one dose is 0.5 mL.

You should not receive VAXZEVRIA if you:

- Have had a severe allergic reaction to any of the medicinal ingredients or any of the other ingredients in this vaccine (see ***What are the ingredients in VAXZEVRIA***). If you are not sure, talk to your healthcare professional;
- Had an allergic reaction to a previous dose of VAXZEVRIA;
- Had had a major blood clot occurring at the same time as having low levels of platelets (thrombocytopenia) after receiving VAXZEVRIA;
- Have previously experienced episodes of capillary leak syndrome (see ***What are possible side effects from using VAXZEVRIA***);
- Have any symptoms that could be due to COVID-19. Talk with your healthcare professional about your symptoms and getting a COVID-19 test. Your healthcare professional will advise you when you are able to receive the vaccine.

To help avoid side effects and ensure proper use, talk to your healthcare professional before you take VAXZEVRIA. Talk about any health conditions or problems you may have, including if you:

- Had any allergies or previous problems following administration of VAXZEVRIA Vaccine such as an allergic reaction or breathing problems, or major venous or arterial thrombosis with thrombocytopenia;
- Have ever had a blood clot or low blood platelets (thrombocytopenia) in the past or if you have an autoimmune disorder (illness where the body's immune system attacks its own cells) including very low levels of blood platelets;
- Have ever had venous sinus thrombosis in the brain (CVST) with low platelets (thrombocytopenia) or heparin-induced thrombocytopenia (HIT);
- Have previously experienced episodes of capillary leak syndrome (see ***What are possible side effects from using VAXZEVRIA***);
- Have had a severe allergic reaction after any other vaccine injection;
- Have a weakened immune system due to a medical condition (immunodeficiency) or are on a medicine that affects your immune system (such as high-dose corticosteroids, immunosuppressants or cancer medicines);
- Currently have a severe infection with a high temperature (over 38°C);
- Have a problem with bleeding or bruising, or if you are taking a blood thinning medicine (anticoagulant);
- Are pregnant, think you may be pregnant or plan to become pregnant;
- Are breastfeeding or plan to breastfeed.

If you are not sure if any of the above applies to you, talk to your healthcare professional before you are given the vaccine.

Neurological events

Guillain-Barré syndrome (GBS) is a neurological disorder where inflammation of peripheral nerves causes rapid muscle weakness and can sometimes lead to paralysis. This has been reported very rarely after vaccination with VAXZEVRIA. Seek immediate medical attention if you develop weakness and paralysis in the extremities that can progress to the chest and face.

Driving and using machines

VAXZEVRIA has no known effect on the ability to drive and use machines. However, side effects listed in ***What are possible side effects from using VAXZEVRIA*** may impact your ability to drive and use machines. If you feel unwell, do not drive or use machines.

Tell your healthcare professional about all the medicines you take, including any drugs, vitamins, minerals, natural supplements or alternative medicines.

Tell your healthcare professional if you are taking, have recently taken or might take, any other medicines or vaccines.

How VAXZEVRIA is given:

- A healthcare provider will inject the vaccine into a muscle (intramuscular injection), usually in your upper arm.
- During and after each injection of the vaccine, your doctor, pharmacist or nurse will watch over you for around 15 minutes to monitor for signs of an allergic reaction.

Usual dose:

You will receive 2 injections. You will be told when you need to return for your second injection of VAXZEVRIA.

The second injection can be given between 4 and 12 weeks after the first injection.

It is very important that you return for the second injection, or the vaccine may not work as well.

Individuals should complete the vaccination course with VAXZEVRIA.

Overdose:

In the event of suspected overdose with VAXZEVRIA, contact your regional poison control centre.

Missed Dose:

If you forget to go back to your healthcare professional at the scheduled time for your next dose, ask your healthcare professional for advice. It is important that you return for your second injection of VAXZEVRIA.

What are possible side effects from using VAXZEVRIA?

Like all medicines, VAXZEVRIA can cause side effects, although not everybody gets them. Most side effects are mild to moderate in nature and resolve within a few days. Fewer side effects were reported after the second dose.

Severe allergic reaction (anaphylaxis), severe swelling of the lips, mouth, throat (which may cause difficulty in swallowing or breathing) have been reported following VAXZEVRIA. Should you develop any serious symptoms or symptoms that could be an allergic reaction, seek medical attention right away. Symptoms of an allergic reaction include:

- hives (bumps on the skin that are often very itchy)
- feeling faint or light-headed
- changes in your heartbeat
- swelling of your face, lips, tongue or throat

- difficulty breathing, shortness of breath or wheezing

A combination of major blood clots and low level of platelets, in some cases together with bleeding, has been observed very rarely following vaccination with VAXZEVRIA in post-authorization use. The majority of the cases occurred within the first 3 weeks following vaccination and some cases had a fatal outcome. Very low levels of blood platelets (immune thrombocytopenia), that can be associated with bleeding, have also been reported very rarely, usually within the first four weeks following vaccination with VAXZEVRIA. Seek medical attention right away if any of the following symptoms occur within the first month following vaccination:

- new severe headaches, worsening or persistent headaches, blurred vision, confusion or seizures
- shortness of breath, chest pain, leg swelling, leg pain or persistent abdominal pain
- unusual skin bruising or pinpoint round spots beyond the site of vaccination
- unexplained bleeding

After vaccination, you may have more than one side effect at the same time (for example, muscle/joint aches, headaches, chills and generally feeling unwell). If any of your symptoms are persistent, please seek advice from your healthcare professional.

Very rare cases of capillary leak syndrome (CLS) have been reported following vaccination with VAXZEVRIA. Some affected patients had a previous diagnosis of CLS. 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 (low blood pressure). Seek medical attention right away if you develop these symptoms in the days following vaccination.

Side effects that have been reported with VAXZEVRIA were as follows:

Very Common (may affect more than 1 in 10 people)

- tenderness, pain, warmth, or itching where the injection is given
- generally feeling unwell
- feeling tired (fatigue)
- chills or feeling feverish
- headache
- feeling sick (nausea)
- joint pain or muscle ache

Common (may affect up to 1 in 10 people)

- swelling or redness where the injection is given
- fever
- being sick (vomiting) or diarrhea
- pain in legs or arms
- flu-like symptoms, such as high temperature, sore throat, runny nose, cough and chills

Uncommon (may affect up to 1 in 100 people)

- sleepiness or feeling dizzy
- decreased appetite
- abdominal pain
- enlarged lymph nodes

- excessive sweating, itchy skin, rash or hives

These are not all the possible side effects you may have when taking VAXZEVRIA. If you experience any side effects not listed here, tell your healthcare professional.

If you experience a severe allergic reaction, call 9-1-1, or go to the nearest hospital.

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.

Storage:

Your healthcare professional is responsible for storing this vaccine and disposing of any unused product correctly.

Keep out of reach and sight of children.

If you want more information about VAXZEVRIA:

- Talk to your healthcare professional
- Find the full product monograph that is prepared for healthcare professionals and includes this Patient Medication Information by visiting the Health Canada website: (https://www.canada.ca/en/health-canada/services/drugs-health-products/drug-products/drug-product-database.html; the manufacturer's website www.astrazeneca.ca, or www.azcovid-19.com, or by calling 1-800-668-6000.

This leaflet was prepared by AstraZeneca Canada Inc., Mississauga, Ontario L4Y 1M4

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