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VAXZEVRIA
(COVID-19 Vaccine AstraZeneca)

Solution for injection

USE UPON PRESCRIPTION ONLY.

KEEP OUT OF REACH OF CHILDREN. READ THE PACKAGE INSERT CAREFULLY BEFORE USING.

INTRAMUSCULAR INJECTION (IM)

COMPOSITION AND STRENGTH

Active ingredients:

One dose (0.5 ml) contains:

COVID-19 Vaccine (ChAdOx1-S* recombinant) 5×10^{10} viral particles (vp) (corresponding to not less than 2.5×10^8 ifu)

*Recombinant, replication-deficient chimpanzee adenovirus vector encoding the SARS-CoV-2 Spike (S) glycoprotein. Produced in genetically modified human embryonic kidney (HEK) 293 cells.

This product contains genetically modified organisms (GMOs).

List of Excipients:

L-Histidine

L-Histidine hydrochloride monohydrate

Magnesium chloride hexahydrate

Polysorbate 80

Ethanol

Sucrose

Sodium chloride

Disodium edetate dihydrate (EDTA)

Water for injection

PHARMACEUTICAL DOSAGE FORM

Solution for injection

The solution is colourless to slightly brown, clear to slightly opaque with a pH of 6.6.

THERAPEUTIC INDICATIONS

Vaxzevria is indicated for active immunisation to prevent COVID-19 caused by SARS-CoV-2 in individuals ≥ 18 years old.

The use of Vaxzevria should be in accordance with official recommendations.

POSODOLOGY AND METHOD OF ADMINISTRATION

Posology

Individuals 18 years of age and older

The Vaxzevria primary 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 (see section *Pharmacodynamic properties*).

There are no data available on the interchangeability of Vaxzevria with other COVID-19 vaccines to complete the vaccination course. Individuals who have received the first dose of Vaxzevria should receive the second dose of Vaxzevria to complete the vaccination course.

A booster dose (third dose) of 0.5 ml may be given to individuals who previously received a 2-dose primary vaccination course with Vaxzevria. The third dose should be administered at least 6 months after completing the primary vaccination course.

Elderly population

No dosage adjustment is required. See sections *Special warnings and precautions for use* and *Pharmacodynamic properties*.

Paediatric population

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

Method of administration

Vaxzevria is for intramuscular (IM) injection only, preferably in the deltoid muscle.

The vaccine should not be mixed in the same syringe with any other vaccines or medicinal products.

For precautions to be taken before administering the vaccine, see section *Special warnings and precautions for use*.

For instructions on administration, see section *Instructions for use and handling, and disposal*.

CONTRAINDICATIONS

Hypersensitivity to the active substance or to any of the excipients listed in section *List of Excipients*.

Individuals who have experienced thrombosis with thrombocytopenia syndrome (TTS) following vaccination with Vaxzevria.

SPECIAL WARNINGS AND PRECAUTIONS FOR USE

Traceability

In order to improve the traceability of biological medicinal products, the name and the batch number of the administered product should be clearly recorded.

Hypersensitivity including 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.

An additional dose of the vaccine should not be given to those who have experienced a severe hypersensitivity reaction to a previous dose of Vaxzevria.

Anxiety-related reactions

Anxiety-related reactions, including vasovagal reactions (syncope), hyperventilation or stress-related reactions may occur in association with vaccination as a psychogenic response to the needle injection. It is important that precautions are in place to avoid injury from fainting.

Concurrent illness

As with other vaccines, administration of Vaxzevria should be postponed in individuals suffering from an acute severe febrile illness or acute infection. However, the presence of a minor infection, such as cold, and/or low-grade fever should not delay vaccination.

Thrombosis with thrombocytopenia and coagulation disorders

Thrombosis with thrombocytopenia syndrome (TTS), in some cases accompanied by bleeding, has been observed very rarely following vaccination with Vaxzevria. This includes severe cases presenting as venous thrombosis, including unusual sites such as cerebral venous sinus thrombosis, splanchnic vein thrombosis, as well as arterial thrombosis, concomitant with thrombocytopenia. Some cases had a fatal outcome. The majority of these cases occurred within the first three weeks following vaccination but have also been reported after this period. Risk factors have not been identified. Some cases had increased D-dimer levels >4000ng/ml, positive platelet factor 4

antibodies and/or laboratory evidence of platelet activation. The reporting rates after the second dose are lower compared to after the first dose. See section *Contraindications*.

As a precautionary measure, administration of the Vaxzevria in patients with a history of heparin-induced thrombocytopenia and thrombosis (HITT or HIT type 2) or cerebral venous sinus thrombosis should only be considered when the benefit outweighs any potential risks.

Healthcare professionals should be alert to the signs and symptoms of thromboembolism and/or thrombocytopenia. Vaccinated individuals should be instructed to seek immediate medical attention if four or more days after vaccination they develop new onset or worsening severe or persistent headaches with blurred vision, which do not respond to simple painkillers, or if they develop new symptoms such as shortness of breath, chest pain, leg swelling, leg pain, persistent abdominal pain, any neurological symptoms or signs such as confusion or seizures, or unusual skin bruising and/or petechiae beyond the site of vaccination.

Individuals diagnosed with thrombocytopenia within three weeks after vaccination with Vaxzevria should be actively investigated for signs of thrombosis. Similarly, individuals who present with thrombosis within three weeks of vaccination should be evaluated for thrombocytopenia.

Patients with TTS require specialised clinical management and should be urgently referred to a secondary healthcare centre and to a specialist in haematology for advice on further management.

Events of cerebrovascular venous and sinus thrombosis without thrombocytopenia have been reported very rarely following vaccination with Vaxzevria, 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.

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.

Immunocompromised individuals

The efficacy, safety and immunogenicity of the vaccine have not been assessed in immunocompromised individuals including those receiving immunosuppressant therapy. The efficacy of Vaxzevria may be lower in immunosuppressed individuals.

Duration of protection

The duration of protection afforded by the vaccine is unknown as it is still being determined by ongoing clinical trials.

Limitations of vaccine effectiveness

Protection starts from approximately 3 weeks after the first dose of Vaxzevria. Individuals may not be fully protected until 15 days after the second dose is administered. As with any vaccine, vaccination with Vaxzevria may not protect all vaccine recipients. (see section *Pharmacodynamic Properties*).

Excipients

Sodium

This medicinal product contains less than 1 mmol sodium (23 mg) per dose, and is considered to be essentially sodium-free.

Ethanol

This medicinal product contains 2 mg of alcohol (ethanol) per 0.5 ml dose. The small amount of alcohol in this medicinal product will not have any noticeable effects.

PREGNANCY AND LACTATION

Pregnancy

There is a limited experience with the use of Vaxzevria in pregnant women.

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

Administration of Vaxzevria during pregnancy should only be considered when the potential benefits outweigh any potential risks (including those described in sections *Special warnings and precautions for use* and *Undesirable effects*) for the mother and fetus.

Breastfeeding

It is unknown whether Vaxzevria is excreted in human milk.

Fertility

Animal studies do not indicate direct or indirect harmful effects with respect to fertility.

EFFECTS ON ABILITY TO DRIVE AND USE MACHINES

Vaxzevria has no or negligible influence on the ability to drive and use machines. However, some of the adverse reactions mentioned under section *Undesirable effects* may temporarily affect the ability to drive or use machines.

INTERACTION WITH OTHER MEDICINAL PRODUCTS AND OTHER FORMS OF INTERACTION

No interaction studies have been performed.

Concomitant administration of Vaxzevria with other vaccines has not been studied (see section *Pharmacodynamic properties*).

UNDESIRABLE EFFECTS

Summary of the safety profile

The overall safety of Vaxzevria is based on an analysis of pooled data from four clinical trials conducted in the United Kingdom, Brazil, and South Africa. At the time of analysis, 24,244 participants ≥ 18 years old had been randomised and received either Vaxzevria or control. Out of these, 12,282 participants received at least one dose of Vaxzevria and 10,448 received 2 doses. The median duration of follow-up in the Vaxzevria group was 137 days post-dose 1, and 81 days post-dose 2.

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.

The most frequently reported adverse reactions were injection site tenderness (63.8%); injection site pain (54.3%), headache (52.7%), fatigue (53.0%); myalgia (43.9%), malaise (44.4%); pyrexia (includes feverishness (33.5%) and fever $\geq 38^{\circ}\text{C}$ (7.6%)), chills (32.2%), arthralgia (26.6%) and nausea (22.2%). The majority of adverse reactions were mild to moderate in severity and usually resolved within a few days of vaccination. By day 7 the incidence of subjects with at least one local or systemic reaction was 4% and 14% respectively. When compared with the first dose, adverse reactions reported after the second dose were milder and reported less frequently.

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

In the COV001 study, the observed reactogenicity in participants who received a booster dose (third dose) following a 2-dose primary vaccination course was consistent with the known reactogenicity profile of Vaxzevria, and was lower after the third dose compared with after the first dose.

If required, analgesic and/or anti-pyretic medicinal products (e.g. paracetamol-containing products) may be used to provide symptomatic relief from post-vaccination adverse reactions.

The safety profile was consistent across participants with or without prior evidence of SARS-CoV-2 infection at baseline; the number of seropositive participants at baseline was 753 (3.1%).

Tabulated list of adverse reactions

Adverse drug reactions (ADRs) are organised by MedDRA System Organ Class (SOC). Within each SOC, preferred terms are arranged by decreasing frequency and then by decreasing seriousness. Frequencies of occurrence of adverse reactions are defined as: very common ($\geq 1/10$); common ($\geq 1/100$ to $< 1/10$); uncommon ($\geq 1/1,000$ to $< 1/100$); rare ($\geq 1/10,000$ to $< 1/1000$); very rare ($< 1/10,000$) and not known (cannot be estimated from available data).

Table 1 **Adverse drug reactions**

MedDRA SOC	Frequency	Adverse Reactions
Blood and lymphatic system disorders	Uncommon	Lymphadenopathy
	Not known	Thrombocytopenia
Immune system disorders	Not known	Anaphylaxis Hypersensitivity
Metabolism and nutrition disorders	Uncommon	Decreased appetite
Nervous system disorders	Very common	Headache
	Uncommon	Dizziness, somnolence
Vascular disorders	Very rare	Thrombosis with thrombocytopenia syndrome*
Gastrointestinal disorders	Very common	Nausea
	Common	Vomiting, diarrhoea
	Uncommon	Abdominal pain
Skin and subcutaneous tissue disorders	Uncommon	Hyperhidrosis, pruritus, rash, urticaria
	Not known	Angioedema
Musculoskeletal and connective tissue disorders	Very common	Myalgia, arthralgia
	Common	Pain in extremity

MedDRA SOC	Frequency	Adverse Reactions
General disorders and administration site conditions	Very common	Injection site tenderness, injection site pain, injection site warmth, injection site pruritus, , injection site bruising ^a , fatigue, malaise, feverishness, chills
	Common	Injection site swelling, injection site erythema, injection site induration, pyrexia ^b , influenza-like illness

^a Injection site bruising includes injection site haematoma (uncommon, unsolicited adverse reaction)

^b Measured fever $\geq 38^{\circ}\text{C}$ (common)

* Severe and very rare cases of thrombosis with thrombocytopenia syndrome have been reported post marketing. These included venous thrombosis such as cerebral venous sinus thrombosis, splanchnic vein thrombosis, as well as arterial thrombosis (see section *Special warnings and precautions for use*).

Very rare events of neuroinflammatory disorders have been reported following vaccination with Vaxzevria. A causal relationship has not been established.

Post-authorisation reports of influenza-like illness

Some recipients have reported chills, shivering (in some cases rigors), and increased body temperature possibly with sweating, headache (including migraine-like headaches), nausea, myalgia and malaise, starting within a day of vaccination. These effects usually lasted for a day or two.

If a patient reports unusually high or prolonged fever, or other symptoms, alternative causes should be considered and appropriate advice should be provided for diagnostic investigation and medical management as required.

OVERDOSE AND TREATMENT

There is no specific treatment for an overdose with Vaxzevria. In the event of an overdose, the individual should be monitored and provided with symptomatic treatment as appropriate.

PHARMACODYNAMIC PROPERTIES

Pharmacotherapeutic group: Vaccine, other viral vaccines, ATC code: J07BX03

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.

Following administration, the S glycoprotein of SARS-CoV-2 is expressed locally stimulating neutralizing antibody and cellular immune responses.

Clinical efficacy

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, COV001, in healthy adults 18 to 55 years of age in the UK; a Phase II/III Study, COV002, in adults ≥ 18 years of age (including the elderly) in the UK; a Phase III Study, COV003, in adults ≥ 18 years of age (including the elderly) in Brazil; and a Phase I/II study, COV005, in adults aged 18 to 65 years of age in South Africa. The studies excluded participants with history of anaphylaxis or angioedema; participants with severe and/or uncontrolled cardiovascular, gastrointestinal, liver, renal, endocrine/metabolic disease, and neurological illnesses; as well as those with immunosuppression. In studies COV001 and COV002, licensed seasonal influenza and pneumococcal vaccinations were permitted (at least 7 days before or after their study vaccine). All participants are planned to be followed for up to 12 months, for assessments of safety and efficacy against COVID-19 disease.

Based on the pre-defined criteria for interim efficacy analysis, COV002 and COV003 exceeded the threshold of ≥ 5 virologically confirmed COVID-19 cases per study and therefore contributed to the efficacy analysis; COV001 and COV005 were excluded.

In the pooled analysis for efficacy (COV002 and COV003), participants ≥ 18 years of age and seronegative at baseline received two doses of Vaxzevria (N=5,807) or control (meningococcal vaccine or saline) (N=5,829). Because of logistical constraints, the interval between dose 1 and dose 2 ranged from 4 to 26 weeks.

Baseline demographics were well balanced across Vaxzevria and control treatment groups. Overall, among the participants who received Vaxzevria, 94.1% of participants were 18 to 64 years old (with 5.9% aged 65 or older); 60.7% of subjects were female; 82.8% were White, 4.6% were Asian, and 4.4% were Black. A total of 2,070 (35.6%) participants had at least one pre-existing comorbidity (defined as a BMI ≥ 30 kg/m², cardiovascular disorder, respiratory disease or diabetes). The median follow up time post-dose 1 and post-dose 2 was 132 days and 63 days, respectively.

Final determination of COVID-19 cases were made by an adjudication committee, who also assigned disease severity according to the WHO clinical progression scale. A total of 131 participants had SARS-CoV-2 virologically confirmed (by nucleic acid amplification tests) COVID-19 occurring ≥ 15 days post-dose 2 with at least one COVID-19 symptom (objective fever (defined as $\geq 37.8^\circ\text{C}$), cough, shortness of breath, anosmia, or ageusia) and were without evidence of previous SARS-CoV-2 infection. Vaxzevria significantly decreased the incidence of COVID-19 compared to control.

An updated efficacy analysis included 17,178 participants from all four studies. Among the participants who received Vaxzevria, 83.8% were 18 to 55 years old, 10.5% were 56 to 69 years old and 5.6% were aged 70 or older. The median follow-up time post-dose 1 and post-dose 2 was 143 days and 83 days, respectively. The results of these analyses, interim and updated efficacy analyses, are presented in Table 2.

Table 2 – Vaxzevria efficacy against COVID-19

Population	Vaxzevria		Control		Vaccine efficacy % (CI)
	N	Number of COVID-19 cases, n (%)	N	Number of COVID-19 cases, n (%)	
Interim analysis (cut-off date: 04 Nov 2020)					
Primary (see above)	5,807		5,829		
COVID-19 cases		30 (0.5)		101 (1.7)	70.4 (54.8, 80.6) ^a
Hospitalisations ^b		0		5 (0.1)	-
Severe disease ^c		0		1 (<0.1)	-
Updated analysis (cut-off date: 07 Dec 2020)					
Primary (see above)	8,597		8,581		
COVID-19 cases		84 (1.0)		248 (2.9)	66.7 (57.4, 74.0) ^d
Hospitalisations ^b		0		9 (0.1)	100 (50.2, NE) ^d
Severe disease ^c		0		2 (<0.1)	-

N = Number of subjects included in each group; n = Number of subjects having a confirmed event; CI = Confidence Interval; NE = Not Evaluable; ^a95.84% CI; ^b WHO severity grading ≥ 4 ; ^c WHO severity grading ≥ 6 ; ^d 95% CI

In the interim analysis, participants who had one or more comorbidities had a vaccine efficacy (VE) of 73.4% [95% CI: 48.5; 86.3]; 11 (0.5%) vs 43 (2.0%) cases of COVID-19 for Vaxzevria (N=2,070) and control (N=2,113), respectively; which was similar to the VE observed in the overall population. In the updated analysis, the VE in this subgroup of participants with one or more comorbidities was 62.7% (95% CI: 44.8; 74.8 [Vaxzevria 34/3,056 vs control 93/3,102]).

The number of COVID-19 cases in participants ≥ 65 years old were too few to draw conclusions on efficacy. However, in this subpopulation, immunogenicity data are available, see below. In the interim analysis there were 2 cases of COVID-19 in 660 participants. In the updated analysis, there were 12 cases in 1,383 participants (4 for Vaxzevria vs 8 for control; VE = 51.9% [95% CI: -60.0, 85.5]). The majority of participants ≥ 65 years old received their doses with an interval shorter than 6 weeks.

The level of protection gained from a single dose of Vaxzevria was assessed in an exploratory analysis that included participants who had received one dose. Participants were censored from the analysis at the earliest time point of when they received a second dose or at 12 weeks post-dose 1. In this population, vaccine efficacy from 22 days post-dose 1 was 73.0% (95% CI: 48.8; 85.8 [Vaxzevria 12/7,998 vs control 44/7,982]). In the updated analysis, this was 69.2% (95% CI: 48.5; 82.4 [Vaxzevria 20/11,044 vs control 65/11,015]).

Exploratory analyses showed that increased immunogenicity was associated with a longer dose interval (see *Immunogenicity* Table 4). Efficacy results from subgroup analyses using the updated dataset were consistent with the immunogenicity data (Table 3).

Table 3 Vaxzevria efficacy by dosing interval^a

Dosing interval	Vaxzevria		Control		Vaccine efficacy % (95% CI)
	N	Number of COVID-19 cases, n (%)	N	Number of COVID-19 cases, n (%)	
<6 weeks	3,905	35 (0.9)	3,871	76 (2.0)	55.1 (33.0, 69.9)
6-8 weeks	1,124	20 (1.8)	1,023	44 (4.3)	59.7 (31.7, 76.3)
9-11 weeks	1,530	14 (0.9)	1,594	52 (3.3)	72.3 (50.0, 84.6)
≥12 weeks	2,038	15 (0.7)	2,093	76 (3.6)	80.0 (65.2, 88.5)

N = Number of subjects included in each group; n = Number of subjects having a confirmed event; CI = Confidence Interval; ^a Data from the updated analyses (07 December 2020 data cut off).

Immunogenicity

Following vaccination with Vaxzevria, in participants who were seronegative at baseline, seroconversion (as measured by a ≥4 fold increase from baseline in S-binding antibodies) was demonstrated in ≥98% of participants at 28 days after the first dose and >99% at 28 days after the second. Higher S-binding antibodies were observed with increasing dose interval (Table 4).

Generally similar trends were observed between analyses of neutralising antibodies and S-binding antibodies. An immunological correlate of protection has not been established; therefore the level of immune response that provides protection against COVID-19 is unknown. Table 4 – SARS CoV-2 S-binding antibody response to Vaxzevria ^{a, b}

Population	Baseline	28 days after dose 1	28 days after dose 2
	GMT (95% CI)	GMT (95% CI)	GMT (95% CI)
Overall	(N=1,538) 57.1	(N=1,466) 8,358.0	(N=1,511) 30,599.8

Population	Baseline	28 days after dose 1	28 days after dose 2
	GMT (95% CI)	GMT (95% CI)	GMT (95% CI)
	(53.8; 60.6)	(7,879.2; 8,866.0)	(29,137.1; 32,135.9)
<i>Dose Interval</i>			
<6 weeks	(N=578) 61.4 (55.3; 68.0)	(N=578) 8,184.5 (7,423.9; 9023.1)	(N=564) 21,384.2 (19,750.7; 23,152.8)
6-8 weeks	(N=339) 56.1 (49.6; 63.3)	(N=290) 9,103.9 (8,063.1; 10,279.1)	(N=331) 28,764.8 (25,990.8; 31,834.9)
9-11 weeks	(N=331) 53.6 (47.5; 60.4)	(N=309) 8,120.9 (7,100.2; 9,288.4)	(N=327) 37,596.1 (34,494.2; 40,976.8)
≥12 weeks	(N=290) 54.3 (47.6; 61.9)	(N=289) 8,249.7 (7,254.5; 9,381.4)	(N=289) 52,360.9 (47,135.2; 58,165.9)

N = Number of subjects included in each group; GMT = Geometric mean titre; CI = Confidence interval; S = Spike

^a Immune response evaluated using a multiplex immunoassay; ^b in seronegative individuals who received two recommended doses of vaccine.

The immune response observed in participants with one or more comorbidities was consistent with the overall population.

High seroconversion rates were observed in older adults (≥65 years) after the first (97.3%; N=149) and second dose (100.0%; N=156). The increase in S binding antibodies 28 days after second dose was lower for participants ≥65 years old (GMT=19,258.5 [N=161, 95% CI: 16,650.4; 22,275.1]) when compared to participants aged 18-64 years (GMT=32,337.1 [N=1,350, 95% CI: 30,720.8; 34,038.4]). The majority of participants ≥65 years old had a dose interval of <6 weeks, which may have contributed to the lower titres observed.

In participants with serological evidence of prior SARS-CoV-2 infection at baseline (GMT=10,979.1 [N=36; 95% CI: 6,452.7; 18,680.5]), S-antibody titres peaked 28 days after dose 1 (GMT=139,010.4 [N=35; 95% CI: 95,429.0; 202,495.1]) but did not increase further after the second dose.

Spike-specific T cell responses as measured by IFN- γ enzyme-linked immunospot (ELISpot) assay were induced after a first dose of Vaxzevria. These did not rise further after a second dose.

Immunogenicity data in individuals receiving a booster dose (third dose)

COV001 included 90 participants aged 18-55 years who received a booster dose with Vaxzevria. Antibody responses were assessed in 75 participants who had received their two doses of the primary vaccination course within an 8-16 week interval, followed by a booster dose administered

between 28-38 weeks after the second dose. Spike IgG antibody titres after the booster dose were significantly higher than after the second dose (median total IgG titre was 1792 EUs [IQR 899–4634] at 28 days after the second dose vs 3746 EUs [2047–6420] 28 days after the booster dose; pairwise comparison in 73 participants for whom samples were available using Wilcoxon signed rank test; $p=0.0043$).

PHARMACOKINETIC PROPERTIES

Not applicable

INSTRUCTIONS FOR USE AND HANDLING, AND DISPOSAL

Administration

Vaxzevria is a colourless to slightly brown, clear to slightly opaque solution. The vaccine should be inspected visually prior to administration and discarded if particulate matter or differences in the described appearance are observed. Do not shake the vial. Do not dilute the solution.

The vaccine should not be mixed in the same syringe with any other vaccines or medicinal products.

The 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 who have received the first dose of Vaxzevria should receive the second dose of the same vaccine to complete the vaccination course.

Each vaccine dose of 0.5 ml is withdrawn into a syringe for injection to be administered intramuscularly, preferably in the deltoid muscle of the upper arm. 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. Aseptic technique should be used for withdrawing the dose for administration.

To facilitate the traceability of the vaccine, the name and the batch number of the administered product should be clearly recorded for each recipient.

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 activity against adenovirus.

PACK SIZE:

Multidose vial

- 5 ml of solution in a 10-dose vial (clear type I glass) with a halobutyl rubber stopper and an aluminium overseal with a plastic flip-off cap. Packs of 10 vials.
- 4 ml of solution in an 8-dose vial (clear type I glass) with a halobutyl rubber stopper and an aluminium overseal with a plastic flip-off cap. Packs of 10 vials.

STORAGE CONDITION:

Unopened vial

Store in a refrigerator (2 to 8°C). Do not freeze.

Keep vials in outer carton to protect from light.

After first use

For storage conditions after first opening of the medicinal product, see section SHELF-LIFE

SHELF-LIFE:

Unopened vial

6 months when stored in a refrigerator (2°C – 8°C).

The following information is intended to guide healthcare professionals only in case of an unforeseen temporary temperature excursion. It is not a recommended storage or shipping condition.

The shelf-life of unopened vials includes the following unforeseen excursions from refrigerated storage (2°C – 8°C) for a single period of:

- 12 hours up to 30°C
- 72 hours down to -3°C

Unopened vials must always be returned to refrigerated storage (2°C – 8°C) following a temperature excursion.

The occurrence of a temperature excursion for unopened vials does not impact how the vials should be stored after first opening (first vial puncture).

Opened vial

Chemical and physical in-use stability have been demonstrated for 6 hours when stored at temperatures up to 30°C and for 48 hours when stored in a refrigerator (2°C – 8°C). After this time, the vial must be discarded. Do not return it to the refrigerator after storage outside the refrigerator.

Alternatively, an opened vial may be stored in a refrigerator (2°C – 8°C) for a maximum of 48 hours if it is immediately returned to the refrigerator following each puncture.

From a microbiological point of view, after first opening the vaccine should be used immediately. If the vaccine is not used immediately, in-use storage times and conditions are the responsibility of the user.

SPECIFICATION: Manufacturer's

MANUFACTURER:

Siam Bioscience Co. Ltd.,

99 Moo 4, Banmai, Bangyai, Nonthaburi 11140 - **Thailand.**

IMPORTER:

AstraZeneca Vietnam Company Limited

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