ANNEX I

SUMMARY OF PRODUCT CHARACTERISTICS

▼This medicinal product is subject to additional monitoring. This will allow quick identification of new safety information. Healthcare professionals are asked to report any suspected adverse reactions. See section 4.8 for how to report adverse reactions.

1. NAME OF THE MEDICINAL PRODUCT

Vaxzevria suspension for injection
COVID-19 Vaccine (ChAdOx1-S [recombinant])

2. QUALITATIVE AND QUANTITATIVE COMPOSITION

These are multidose vials which contain 8 doses or 10 doses of 0.5 ml per vial (see section 6.5).

One dose (0.5 ml) contains:
Chimpanzee Adenovirus encoding the SARS-CoV-2 Spike glycoprotein (ChAdOx1-S)[*], not less than 2.5×10^8 infectious units (Inf.U)
[*]Produced in genetically modified human embryonic kidney (HEK) 293 cells and by recombinant DNA technology.

This product contains genetically modified organisms (GMOs).

Excipient with known effect
Each dose (0.5 ml) contains approximately 2 mg of ethanol.

For the full list of excipients, see section 6.1.

3. PHARMACEUTICAL FORM

Suspension for injection (injection).

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

4. CLINICAL PARTICULARS

4.1 Therapeutic indications

Vaxzevria is indicated for active immunisation to prevent COVID-19 caused by SARS-CoV-2, in individuals 18 years of age and older.

The use of this vaccine should be in accordance with official recommendations.

4.2 Posology and method of administration

Posology

Individuals 18 years of age and older
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 (28 to 84 days) after the first dose (see section 5.1).

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.

Paediatric population
The safety and efficacy of Vaxzevria in children and adolescents (less than 18 years of age) have not yet been established. No data are available.

Elderly population
No dose adjustment is required. See also sections 4.4 and 5.1.

Method of administration

Vaxzevria is for intramuscular injection only, preferably in the deltoid muscle of the upper arm.

Do not inject the vaccine intravascularly, subcutaneously or intradermally.

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 4.4.

For instructions on handling and disposal, see section 6.6.

4.3 Contraindications

Hypersensitivity to the active substance or to any of the excipients listed in section 6.1.

4.4 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 and anaphylaxis

Events of anaphylaxis have been reported. Appropriate medical treatment and supervision should always be readily available in case of an anaphylactic event following the administration of the vaccine. Close observation for at least 15 minutes is recommended following vaccination. A second dose of the vaccine should not be given to those who have experienced anaphylaxis to the first 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

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.

Thrombocytopenia and coagulation disorders

A combination of thrombosis and thrombocytopenia, 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 fourteen days following vaccination and occurred mostly in women under 60 years of age.

Healthcare professionals should be alert to the signs and symptoms of thromboembolism and/or thrombocytopenia. Those vaccinated should be instructed to seek immediate medical attention if they develop symptoms such as shortness of breath, chest pain, leg swelling, persistent abdominal pain following vaccination. Additionally, anyone with neurological symptoms including severe or persistent headaches or blurred vision after vaccination, or who experiences skin bruising (petechia) beyond the site of vaccination after a few days, should seek prompt medical attention.

Risk of bleeding with intramuscular administration

As with other intramuscular injections, the vaccine should be given with caution in individuals receiving anticoagulant therapy or those with thrombocytopenia or any coagulation disorder (such as haemophilia) 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 all vaccines, vaccination with Vaxzevria may not protect all vaccine recipients (see section 5.1).

Currently available clinical trial data do not allow an estimate of vaccine efficacy in subjects over 55 years of age.

Excipients

Sodium
This medicinal product contains less than 1 mmol sodium (23 mg) per 0.5 ml dose, that is to say 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.

4.5 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.

4.6 Fertility, pregnancy and lactation

Pregnancy

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

Animal reproductive toxicity studies have not been completed. Based upon results from the preliminary study, no effects are expected on development of the fetus (see section 5.3).

Administration of Vaxzevria during pregnancy should only be considered when the potential benefits outweigh any potential risks 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 reproductive toxicity (see section 5.3).

4.7 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 4.8 may temporarily affect the ability to drive or use machines.

4.8 Undesirable effects

Summary of the safety profile

The overall safety of Vaxzevria is based on an interim analysis of pooled data from four clinical trials conducted in the United Kingdom, Brazil, and South Africa. At the time of analysis, 23,745 participants ≥18 years old had been randomised and received either Vaxzevria or control. Out of these, 12,021 received at least one dose of Vaxzevria and 8,266 received two doses. The median duration of follow-up was 62 days post-dose 2.

The most frequently reported adverse reactions were injection site tenderness (63.7%), injection site pain (54.2%), headache (52.6%), fatigue (53.1%), myalgia (44.0%), malaise (44.2%), pyrexia (includes feverishness (33.6%) and fever >38°C (7.9%)), chills (31.9%), arthralgia (26.4%) and nausea (21.9%). The majority of adverse reactions were mild to moderate in severity and usually resolved within a few days of vaccination. When compared with the first dose, adverse reactions reported after the second dose were milder and reported less frequently.

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

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 718 (3.0%).

Tabulated list of adverse reactions

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

Table 1 Adverse drug reactions

MedDRA SOC	Frequency	Adverse Reactions
Blood and lymphatic system disorders	Common	Thrombocytopenia
	Uncommon	Lymphadenopathy
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 in combination with thrombocytopenia*
Gastrointestinal disorders	Very common	Nausea
	Common	Vomiting Diarrhoea
Skin and subcutaneous tissue disorders	Uncommon	Hyperhidrosis Pruritus Rash
Musculoskeletal and connective tissue disorders	Very common	Myalgia Arthralgia
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 Fever[b]

[a] Injection site bruising includes injection site haematoma (uncommon)
[b] Measured fever ≥38°C
*Severe and very rare cases of thrombosis in combination with thrombocytopenia 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 4.4).

Reporting of suspected adverse reactions

Reporting suspected adverse reactions after authorisation of the medicinal product is important. It allows continued monitoring of the benefit/risk balance of the medicinal product. Healthcare professionals are asked to report any suspected adverse reactions via the national reporting system listed in Appendix V and include batch/Lot number if available.

4.9 Overdose

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.

5. PHARMACOLOGICAL PROPERTIES

5.1 Pharmacodynamic properties

Pharmacotherapeutic group: Vaccines, 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. 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 to COVID-19.

Clinical efficacy

Analysis of pooled data from COV002 and COV003

The clinical efficacy of Vaxzevria has been evaluated based on an analysis of pooled data from two on-going randomised, blinded, controlled trials: a phase II/III study, COV002, in adults ≥18 years of age (including the elderly) in the UK; and a phase III study, COV003, in adults ≥18 years of age (including the elderly) in Brazil. The studies excluded participants with severe and/or uncontrolled cardiovascular, gastrointestinal, liver, renal, endocrine/metabolic disease, and neurological illnesses; as well as those with severe immunosuppression, pregnant women and participants with a known history of SARS-CoV-2 infection. Influenza vaccines could be administered 7 days before or after any dose of Vaxzevria. All participants are planned to be followed for up to 12 months, for assessments of safety and efficacy against COVID-19 disease.

In the pooled analysis for efficacy, participants ≥18 years of age received two doses (5×10^{10} viral particles per dose corresponding to not less than 2.5×10^{8} infectious units) of Vaxzevria (N=6,106) or control (meningococcal vaccine or saline) (N=6,090), administered via IM injection.

Because of logistical constraints, the interval between dose 1 and dose 2 ranged from 3 to 23 weeks (21 to 159 days), with 86.1% of participants receiving their two doses within the interval of 4 to 12 weeks (28 to 84 days).

Baseline demographics were well balanced across Vaxzevria and control treatment groups. In the pooled analysis, among the participants who received Vaxzevria with a dose interval of between 4 and 12 weeks, 87.0% of participants were 18 to 64 years old (with 13.0% aged 65 or older and 2.8% aged 75 or older); 55.1% of subjects were female; 76.2% were White, 6.4% were Black and 3.4% were Asian. A total of 2,068 (39.3%) participants had at least one pre-existing comorbidity (defined as a BMI ≥30 kg/m^2, cardiovascular disorder, respiratory disease or diabetes). At the time of analysis the median follow up time post-dose 2 was 78 days.

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 218 participants had SARS-CoV-2 virologically confirmed COVID-19 occurring ≥15 days post second dose with at least one COVID-19 symptom (objective fever (defined as ≥37.8°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 (see Table 2).

Table 2 Vaxzevria efficacy against COVID-19[a]

Population	Vaxzevria		Control		Vaccine efficacy % (95% CI)[b]
	N	Number of COVID-19 cases, n (%)	N	Number of COVID-19 cases, n (%)	
Licensing regimen					
4 – 12 weeks (28 to 84 days)	5,258	64 (1.2)	5,210	154 (3.0)	59.5 (45.8, 69.7)

N = Number of subjects included in each group; n = Number of subjects having a confirmed event; CI = Confidence Interval;
[a] Efficacy endpoint was 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] CI not adjusted for multiplicity.

Vaccine efficacy was 62.6% (95% CI: 50.9; 71.5) in participants receiving two recommended doses with any dose interval (ranging from 3 to 23 weeks), in a pre-specified analysis.

Regarding COVID-19 hospitalisation (WHO Severity grading ≥4) there were 0 (0.0%; N=5,258) cases of COVID-19 hospitalisation in participants who received two doses of Vaxzevria (≥15 days post dose 2) as compared to 8 (0.2%; N=5,210) for control, including one severe case (WHO Severity grading ≥6), reported for control. In all participants who received at least one dose, as from 22 days post dose 1, there were 0 (0.0%, N=8,032) cases of COVID-19 hospitalisation in participants who received Vaxzevria, as compared to 14 (0.2%, N=8,026), including one fatality, reported for control.

Participants who had one or more comorbidities had a vaccine efficacy of 58.3% [95% CI: 33.6; 73.9]; 25 (1.2%) vs 60 (2.9%) for Vaxzevria (N=2,068) and control (N=2,040), respectively; which was similar to the vaccine efficacy observed in the overall population.

Evidence shows protection starts from approximately 3 weeks after first dose of vaccine and persists up to 12 weeks. A second dose should be given at a 4 to 12 week interval after the first dose (see section 4.4).

Elderly population

Among participants aged between 56 and 65 years old, 8 cases of COVID-19 were reported in those receiving Vaxzevria (≥15 days post dose 2) compared with 9 cases for control; 2 and 6 cases of COVID-19 were reported in participants older than 65 years of age, for Vaxzevria (≥15 days post dose 2) and control, respectively.

Paediatric population

The European Medicines Agency has deferred the obligation to submit the results of studies with Vaxzevria in one or more subsets of the paediatric population in prevention of COVID-19 (see section 4.2 for information on paediatric use).

Conditional approval

This medicinal product has been authorised under a so-called 'conditional approval' scheme. This means that further evidence on this medicinal product is awaited.
The European Medicines Agency will review new information on this medicinal product at least every year and this SmPC will be updated as necessary.

5.2 Pharmacokinetic properties

Not applicable.

5.3 Preclinical safety data

Non-clinical data reveal no special hazard for humans based on a conventional study of repeat dose toxicity.

Genotoxicity/Carcinogenicity

Neither genotoxicity nor carcinogenicity studies were performed. The components of the vaccine are not expected to have genotoxic potential.

Reproductive toxicity

Animal studies of potential toxicity to reproduction and development have not yet been completed. A preliminary reproductive toxicity study in mice does not show toxicity in dams or foetuses.

6. PHARMACEUTICAL PARTICULARS

6.1 List of excipients

L-Histidine
L-Histidine hydrochloride monohydrate
Magnesium chloride hexahydrate
Polysorbate 80 (E 433)
Ethanol
Sucrose
Sodium chloride
Disodium edetate (dihydrate)
Water for injections

6.2 Incompatibilities

This medicinal product must not be mixed with other medicinal products or diluted.

6.3 Shelf life

Unopened vial

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

Opened vial

Chemical and physical in-use stability have been demonstrated from the time of vial opening (first needle puncture) to administration for no more than 48 hours in a refrigerator (2°C – 8°C). Within this time period the product may be kept and used at temperatures up to 30°C for a single period of up to 6 hours. After this time period, the product must be discarded. Do not return it to the refrigerator.

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.

6.4 Special precautions for storage

Store in a refrigerator (2°C – 8°C).
Do not freeze.
Keep vials in outer carton in order to protect from light.

For storage conditions after first opening of the medicinal product, see section 6.3.

6.5 Nature and contents of container

Multidose vial

8-dose vial
4 ml of suspension in an 8-dose vial (clear type I glass) with stopper (elastomeric with aluminium overseal). Each vial contains 8 doses of 0.5 ml. Pack sizes of 10 multidose vials.

10-dose vial
5 ml of suspension in a 10-dose vial (clear type I glass) with stopper (elastomeric with aluminium overseal). Each vial contains 10 doses of 0.5 ml. Pack sizes of 10 multidose vials.

Not all pack sizes may be marketed.

6.6 Special precautions for disposal and other handling

Handling instructions and administration

This vaccine should be handled by a healthcare professional using aseptic technique to ensure the sterility of each dose.

Do not use this vaccine after the expiry date which is stated on the label after EXP. The expiry date refers to the last day of that month.

Unopened multidose vial should be stored in a refrigerator (2°C – 8°C). Do not freeze.

Keep the vials in outer carton in order to protect from light.

The vaccine should be inspected visually for particulate matter and discolouration prior to administration. Vaxzevria is a colourless to slightly brown, clear to slightly opaque suspension. Discard the vial if the suspension is discoloured or visible particles are observed. Do not shake. Do not dilute the suspension.

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

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 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 new needle for administration, when possible.

It is normal for liquid to remain in the vial after withdrawing the final dose. An additional overfill is included in each vial to ensure that 8 doses (vial of 4 ml) or 10 doses (vial of 5 ml) of 0.5 ml can be delivered. Do not pool excess vaccine from multiple vials. Discard any unused vaccine.

Chemical and physical in-use stability have been demonstrated from the time of vial opening (first needle puncture) to administration for no more than 48 hours in a refrigerator (2°C – 8°C). Within this time period the product may be kept and used at temperatures up to 30°C for a single period of up to 6 hours. After this time period, the product must be discarded. Do not return it to the refrigerator.

Disposal

Vaxzevria contains genetically modified organisms (GMOs). Any unused vaccine or waste material should be disposed of in compliance with the local guidance for genetically modified organisms or biohazardous waste. Spills should be disinfected using agents with activity against adenovirus.

7. MARKETING AUTHORISATION HOLDER

AstraZeneca AB
SE-151 85 Södertälje
Sweden

8. MARKETING AUTHORISATION NUMBER(S)

EU/1/21/1529/001 10 multidose vials (8 doses per vial)
EU/1/21/1529/002 10 multidose vials (10 doses per vial)

9. DATE OF FIRST AUTHORISATION/RENEWAL OF THE AUTHORISATION

Date of first authorisation: 29 January 2021

10. DATE OF REVISION OF THE TEXT

Detailed information on this medicinal product is available on the website of the European Medicines Agency http://www.ema.europa.eu

ANNEX II

A. MANUFACTURER(S) OF THE BIOLOGICAL ACTIVE SUBSTANCE(S) AND MANUFACTURER(S) RESPONSIBLE FOR BATCH RELEASE

B. CONDITIONS OR RESTRICTIONS REGARDING SUPPLY AND USE

C. OTHER CONDITIONS AND REQUIREMENTS OF THE MARKETING AUTHORISATION

D. CONDITIONS OR RESTRICTIONS WITH REGARD TO THE SAFE AND EFFECTIVE USE OF THE MEDICINAL PRODUCT

E. SPECIFIC OBLIGATION TO COMPLETE POST-AUTHORISATION MEASURES FOR THE CONDITIONAL MARKETING AUTHORISATION

A. MANUFACTURER(S) OF THE BIOLOGICAL ACTIVE SUBSTANCE(S) AND MANUFACTURER(S) RESPONSIBLE FOR BATCH RELEASE

Name and address of the manufacturer(s) of the biological active substance

Henogen S.A.
Rue de la Marlette 14
7180 Seneffe
Belgium

Catalent Maryland, Inc
7555 Harmans Road
Harmans, MD 21077
United States

Oxford Biomedica (UK) Limited
Unit A
Plot 7000
Alec Issigonis Way
Oxford OX4 2ZY
United Kingdom

Halix B.V.
Tinbergenweg 1
2333 BB Leiden
Netherlands

SK Bioscience Co Limited (No. 97)
150, Saneopdanji-gil, Pungsan-eup
Andong-si, Gyeongsangbuk-do
Republic of Korea

WuXi Biologics Co., Ltd
108 Meiliang Road
Mashan
Binhu District
WuXi
Jiangsu 214092
China

Name and address of the manufacturer(s) responsible for batch release

AstraZeneca Nijmegen B.V.
Lagelandseweg 78
Nijmegen, 6545CG
Netherlands

B. CONDITIONS OR RESTRICTIONS REGARDING SUPPLY AND USE

Medicinal product subject to medical prescription.

- **Official batch release**

In accordance with Article 114 of Directive 2001/83/EC, the official batch release will be undertaken by a state laboratory or a laboratory designated for that purpose.

C. OTHER CONDITIONS AND REQUIREMENTS OF THE MARKETING AUTHORISATION

- **Periodic safety update reports (PSURs)**

The requirements for submission of PSURs for this medicinal product are set out in the list of Union reference dates (EURD list) provided for under Article 107c(7) of Directive 2001/83/EC and any subsequent updates published on the European medicines web-portal.

The marketing authorisation holder (MAH) shall submit the first PSUR for this product within 6 months following authorisation.

D. CONDITIONS OR RESTRICTIONS WITH REGARD TO THE SAFE AND EFFECTIVE USE OF THE MEDICINAL PRODUCT

- **Risk management plan (RMP)**

The marketing authorisation holder (MAH) shall perform the required pharmacovigilance activities and interventions detailed in the agreed RMP presented in Module 1.8.2 of the marketing authorisation and any agreed subsequent updates of the RMP.

An updated RMP should be submitted:

- At the request of the European Medicines Agency;
- Whenever the risk management system is modified, especially as the result of new information being received that may lead to a significant change to the benefit/risk profile or as the result of an important (pharmacovigilance or risk minimisation) milestone being reached.

- **Obligation to conduct post-authorisation measures**

The MAH shall complete, within the stated timeframe, the below measures:

Description	Due date
In order to elucidate the possible mechanisms of platelet activation after vaccination and to identify the possible triggers, the MAH should submit the final report for the biodistribution study for Vaxzevria.	30 April 2021
In order to elucidate the possible mechanisms of platelet activation after vaccination and to identify the possible triggers, the MAH should conduct and submit the final report for a non-clinical study to test in-vitro expression of the S protein of Vaxzevria.	7 July 2021
In order to ensure that all reported thrombotic events with thrombocytopenia and/or bleeding events are investigated by performing an in-depth exploration of platelet function in the interventional study in immunocompromised subjects, the MAH should submit the clinical study report, in accordance with a revised and agreed study protocol.	30 November 2023

E. SPECIFIC OBLIGATION TO COMPLETE POST-AUTHORISATION MEASURES FOR THE CONDITIONAL MARKETING AUTHORISATION

This being a conditional marketing authorisation and pursuant to Article 14-a of Regulation (EC) No 726/2004, the MAH shall complete, within the stated timeframe, the following measures:

Description	Due date
In order to confirm the consistency of the active substance and finished product manufacturing process, the applicant should provide additional validation and comparability data and, introduce enhanced testing.	December 2021 with interim monthly updates beginning February 2021
In order to ensure consistent product quality, the applicant should provide additional information on stability of the active substance and finished product and review the finished product specifications following further manufacturing experience.	June 2022 with interim monthly updates beginning February 2021
In order to confirm the efficacy and safety of Vaxzevria, the MAH should submit the final Clinical Study Reports for the randomised, controlled, COV001, COV002, COV003 and COV005.	31 May 2022
In order to confirm the efficacy and safety of Vaxzevria, the MAH should provide the primary analysis (based on the 7th December data cut-off (post data-base lock) and final analysis from the pooled pivotal studies.	Primary analysis: 5 March 2021 Final pooled analysis: 31 May 2022
In order to confirm the efficacy and safety of Vaxzevria in the elderly and subjects with underlying disease, the MAH should submit the overview and summaries of the primary analysis and final clinical study report for study D8110C00001.	Primary analysis: 30 April 2021 Final CSR: 31 March 2024

ANNEX III

LABELLING AND PACKAGE LEAFLET

A. LABELLING

PARTICULARS TO APPEAR ON THE OUTER PACKAGING

CARTON - EIGHT-DOSE VIAL, PACK OF 10 VIALS

1. NAME OF THE MEDICINAL PRODUCT

Vaxzevria suspension for injection
COVID-19 Vaccine (ChAdOx1-S [recombinant])

2. STATEMENT OF ACTIVE SUBSTANCE(S)

One dose (0.5 ml) contains not less than 2.5×10^8 infectious units

Chimpanzee Adenovirus encoding the SARS-CoV-2 Spike glycoprotein ChAdOx1-S

3. LIST OF EXCIPIENTS

Excipients: L-histidine, L-histidine hydrochloride monohydrate, magnesium chloride hexahydrate, polysorbate 80 (E 433), ethanol, sucrose, sodium chloride, disodium edetate (dihydrate), water for injections.
See leaflet for further information.

4. PHARMACEUTICAL FORM AND CONTENTS

Suspension for injection
10 multidose vials
(8 doses per vial - 0.5ml per dose)
4 ml

5. METHOD AND ROUTE(S) OF ADMINISTRATION

Intramuscular use
Read the package leaflet before use.
For more information, scan here or visit www.azcovid-19.com
QR code to be included

6. SPECIAL WARNING THAT THE MEDICINAL PRODUCT MUST BE STORED OUT OF THE SIGHT AND REACH OF CHILDREN

Keep out of the sight and reach of children.

7. OTHER SPECIAL WARNING(S), IF NECESSARY

8. EXPIRY DATE

EXP

9. SPECIAL STORAGE CONDITIONS

Store in a refrigerator.
Keep vials in outer carton in order to protect from light.
Do not freeze. Do not shake.
For information on the shelf life after first opening and additonal storage information, see the package leaflet.

10. SPECIAL PRECAUTIONS FOR DISPOSAL OF UNUSED MEDICINAL PRODUCTS OR WASTE MATERIALS DERIVED FROM SUCH MEDICINAL PRODUCTS, IF APPROPRIATE

This medicine contains genetically modified organisms (GMOs). Dispose of in compliance with the local guidance for GMOs or biohazardous waste.

11. NAME AND ADDRESS OF THE MARKETING AUTHORISATION HOLDER

AstraZeneca AB
SE-151 85 Södertälje
Sweden

12. MARKETING AUTHORISATION NUMBER(S)

EU/1/21/1529/001 10 multidose vials (8 doses per vial)

13. BATCH NUMBER

Lot

14. GENERAL CLASSIFICATION FOR SUPPLY

15. INSTRUCTIONS ON USE

16. INFORMATION IN BRAILLE

Justification for not including Braille accepted.

17. UNIQUE IDENTIFIER – 2D BARCODE

2D barcode carrying the unique identifier included.

18. UNIQUE IDENTIFIER - HUMAN READABLE DATA

PC
SN

NN

MINIMUM PARTICULARS TO APPEAR ON SMALL IMMEDIATE PACKAGING UNITS

VIAL LABEL - EIGHT-DOSE VIAL

1. NAME OF THE MEDICINAL PRODUCT AND ROUTE(S) OF ADMINISTRATION

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

Intramuscular use

2. METHOD OF ADMINISTRATION

3. EXPIRY DATE

EXP

4. BATCH NUMBER

Lot

5. CONTENTS BY WEIGHT, BY VOLUME OR BY UNIT

Multidose vial (8 × 0.5 ml doses)
4 ml

6. OTHER

AstraZeneca

PARTICULARS TO APPEAR ON THE OUTER PACKAGING

CARTON - TEN-DOSE VIAL, PACK OF 10 VIALS

1. NAME OF THE MEDICINAL PRODUCT

Vaxzevria suspension for injection
COVID-19 Vaccine (ChAdOx1-S [recombinant])

2. STATEMENT OF ACTIVE SUBSTANCE(S)

One dose (0.5 ml) contains not less than 2.5×10^8 infectious units

Chimpanzee Adenovirus encoding the SARS-CoV-2 Spike glycoprotein ChAdOx1-S

3. LIST OF EXCIPIENTS

Excipients: L-histidine, L-histidine hydrochloride monohydrate, magnesium chloride hexahydrate, Polysorbate 80 (E 433), ethanol, sucrose, sodium chloride, disodium edetate (dihydrate), water for injections.
See leaflet for further information.

4. PHARMACEUTICAL FORM AND CONTENTS

Suspension for injection
10 multidose vials
(10 doses per vial - 0.5 ml per dose)
5 ml

5. METHOD AND ROUTE(S) OF ADMINISTRATION

Intramuscular use
Read the package leaflet before use.
For more information, scan here or visit www.azcovid-19.com
QR code to be included

6. SPECIAL WARNING THAT THE MEDICINAL PRODUCT MUST BE STORED OUT OF THE SIGHT AND REACH OF CHILDREN

Keep out of the sight and reach of children.

7. OTHER SPECIAL WARNING(S), IF NECESSARY

8. EXPIRY DATE

EXP

9. SPECIAL STORAGE CONDITIONS

Store in a refrigerator.
Keep vials in outer carton in order to protect from light.
Do not freeze. Do not shake.
For information on the shelf life after first opening and additonal storage information, see the package leaflet.

10. SPECIAL PRECAUTIONS FOR DISPOSAL OF UNUSED MEDICINAL PRODUCTS OR WASTE MATERIALS DERIVED FROM SUCH MEDICINAL PRODUCTS, IF APPROPRIATE

This medicine contains genetically modified organisms (GMOs). Dispose of in compliance with the local guidance for GMOs or biohazardous waste.

11. NAME AND ADDRESS OF THE MARKETING AUTHORISATION HOLDER

AstraZeneca AB
SE-151 85 Södertälje
Sweden

12. MARKETING AUTHORISATION NUMBER(S)

EU/1/21/1529/002 10 multidose vials (10 doses per vial)

13. BATCH NUMBER

Lot

14. GENERAL CLASSIFICATION FOR SUPPLY

15. INSTRUCTIONS ON USE

16. INFORMATION IN BRAILLE

Justification for not including Braille accepted.

17. UNIQUE IDENTIFIER – 2D BARCODE

2D barcode carrying the unique identifier included.

18. UNIQUE IDENTIFIER - HUMAN READABLE DATA

PC
SN
NN

MINIMUM PARTICULARS TO APPEAR ON SMALL IMMEDIATE PACKAGING UNITS

VIAL LABEL - TEN-DOSE VIAL

1. NAME OF THE MEDICINAL PRODUCT AND ROUTE(S) OF ADMINISTRATION

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

Intramuscular use

2. METHOD OF ADMINISTRATION

3. EXPIRY DATE

EXP

4. BATCH NUMBER

Lot

5. CONTENTS BY WEIGHT, BY VOLUME OR BY UNIT

Multidose vial (10 × 0.5 ml doses)
5 ml

6. OTHER

AstraZeneca

B. PACKAGE LEAFLET

Package leaflet: Information for the user

Vaxzevria suspension for injection
COVID-19 Vaccine (ChAdOx1-S [recombinant])

▼This medicine is subject to additional monitoring. This will allow quick identification of new safety information. You can help by reporting any side effects you may get. See the end of section 4 for how to report side effects.

Read all of this leaflet carefully before the vaccine is given because it contains important information for you.
- Keep this leaflet. You may need to read it again.
- If you have any further questions, ask your doctor, pharmacist or nurse.
- If you get any side effects, talk to your doctor, pharmacist or nurse. This includes any possible side effects not listed in this leaflet. See section 4.

What is in this leaflet

1. What Vaxzevria is and what it is used for
2. What you need to know before you are given Vaxzevria
3. How Vaxzevria is given
4. Possible side effects
5. How to store Vaxzevria
6. Contents of the pack and other information

1. What Vaxzevria is and what it is used for

Vaxzevria is used for preventing COVID-19 caused by the SARS-CoV-2 virus.

Vaxzevria is given to adults aged 18 years and older.

The vaccine causes the immune system (the body's natural defences) to produce antibodies and specialised white blood cells that work against the virus, so giving protection against COVID-19. None of the ingredients in this vaccine can cause COVID-19.

2. What you need to know before you are given Vaxzevria

The vaccine must not be given:
- If you are allergic to the active substance or any of the other ingredients of this vaccine (listed in section 6).

Warnings and precautions
Talk to your doctor, pharmacist or nurse before you are given Vaxzevria:
- If you have ever had a severe allergic reaction after any other vaccine injection or after you were given Vaxzevria in the past;
- If you have ever fainted following any needle injection;
- If you have a severe infection with a high temperature (over 38°C). However, you can have your vaccination if you have a mild fever or upper airway infection like a cold;
- If you have a problem with bleeding or bruising, or if you are taking an anticoagulant medicine (to prevent blood clots);
- If your immune system does not work properly (immunodeficiency) or you are taking medicines that weaken the immune system (such as high-dose corticosteroids, immunosuppressants or cancer medicines).

If you are not sure if any of the above applies to you, talk to your doctor, pharmacist or nurse before you are given the vaccine.

As with any vaccine, the 2-dose vaccination course of Vaxzevria may not fully protect all those who receive it. It is not known how long you will be protected for. Currently there are limited data on the efficacy of Vaxzevria in individuals aged 55 and older.

Blood disorders
Very rare blood clots, often in unusual locations (e.g. brain, bowel, liver, spleen), in combination with low level of blood platelets, in some cases together with bleeding, has been observed following vaccination with Vaxzevria. This included some severe cases with blood clots in different or unusual locations and excessive clotting or bleeding throughout the body. The majority of these cases occurred within the first fourteen days following vaccination and occurred mostly in women under 60 years of age. Some cases had a fatal outcome.

Seek immediate medical attention if you develop shortness of breath, chest pain, leg swelling, or persistent abdominal pain following vaccination.

Also, seek immediate medical attention if you experience after a few days severe or persistent headaches or blurred vision after vaccination, or experience skin bruising or pinpoint round spots beyond the site of vaccination which appears after a few days.

Children and adolescents
Vaxzevria is not recommended for children aged below 18 years. Currently there is not enough information available on the use of Vaxzevria in children and adolescents younger than 18 years of age.

Other medicines and Vaxzevria
Tell your doctor, pharmacist or nurse if you are taking, have recently taken or might take, any other medicines or vaccines.

Pregnancy and breastfeeding
If you are pregnant or breastfeeding, think you may be pregnant, or are planning to have a baby, ask your doctor, pharmacist or nurse for advice before you receive this vaccine.

Driving and using machines
Some of the side effects of Vaxzevria listed in section 4 (Possible side effects) may temporarily reduce your ability to drive and use machines. If you feel unwell after vaccination, do not drive or use machines. Wait until any effects of the vaccine have worn off before you drive or use machines.

Vaxzevria contains sodium and alcohol (ethanol)
This medicine contains less than 1 mmol sodium (23 mg) per 0.5 ml dose, that is to say essentially 'sodium-free'.
This medicine contains 2 mg of alcohol (ethanol) per 0.5 ml dose. The small amount of alcohol in this medicine will not have any noticeable effects.

3. How Vaxzevria is given

Vaxzevria is given as an injection of 0.5 ml into a muscle (usually in the 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.

You will receive 2 injections of Vaxzevria. The second injection can be given between 4 and 12 weeks after the first injection**.** You will be told when you need to return for your second injection.

When Vaxzevria is given for the first injection, the second injection to complete the vaccination course should also be with Vaxzevria.

If you miss an appointment for your second injection of Vaxzevria
If you forget to go back at the scheduled time, ask your doctor, pharmacist or nurse for advice. It is important that you return for your second injection of Vaxzevria. If you miss a scheduled injection, you may not be fully protected against COVID-19.

4. Possible side effects

Like all medicines, this vaccine can cause side effects, although not everybody gets them. If you notice any side effects not mentioned in this package leaflet, please tell your doctor, pharmacist or nurse.

Get urgent medical attention if you get symptoms of a severe allergic reaction. Such reactions may include a combination of any of the following symptoms:
- feeling faint or light-headed
- changes in your heartbeat
- shortness of breath
- wheezing
- swelling of your lips, face, or throat
- hives or rash
- nausea or vomiting
- stomach pain.

The following side effects may occur with Vaxzevria:

Very Common (may affect more than 1 in 10 people)
- tenderness, pain, warmth, itching, or bruising where the injection is given
- feeling tired (fatigue) or generally feeling unwell
- 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 (>38°C)
- being sick (vomiting) or diarrhoea
- low level of blood platelets

Uncommon (may affect up to 1 in 100 people)
- sleepiness or feeling dizzy
- decreased appetite
- enlarged lymph nodes
- excessive sweating, itchy skin or rash

Very Rare (may affect up to 1 in 10,000 people)
- blood clots often in unusual locations (e.g. brain, bowel, liver, spleen) in combination with low level of blood platelets

Not known (cannot be estimated from the available data)
- severe allergic reaction (anaphylaxis)
- hypersensitivity

Reporting of side effects
If you get any side effects, talk to your doctor, pharmacist or nurse. This includes any possible side effects not listed in this leaflet. You can also report side effects directly via the national reporting system listed in Appendix V. By reporting side effects you can help provide more information on the safety of this medicine.

5. How to store Vaxzevria

Keep this medicine out of the sight and reach of children.

Your doctor, pharmacist or nurse is responsible for storing this vaccine and disposing of any unused product correctly. The following information about storage, expiry, use and handling as well as disposal is intended for healthcare professionals.

Do not use this vaccine after the expiry date which is stated on the label after EXP. The expiry date refers to the last day of that month.

Store in a refrigerator (2°C – 8°C).
Do not freeze.
Keep vials in outer carton in order to protect from light.

From the time of vial opening (first needle puncture) to administration store the vial for no more than 48 hours in a refrigerator (2°C–8°C). Within this time period the product may be kept and used at temperatures up to 30°C for a single period of up to 6 hours. After this time period, the product must be discarded. Do not return it to the refrigerator.

Discard the vial if the suspension is discoloured or particles are observed. Do not shake.

Vaxzevria contains genetically modified organisms (GMOs). Any unused vaccine or waste material should be disposed of in compliance with the local guidance for genetically modified organisms or biohazardous waste. Spills should be disinfected using agents with activity against adenovirus.

6. Contents of the pack and other information

What Vaxzevria contains
One dose (0.5 ml) contains:
Chimpanzee Adenovirus encoding the SARS-CoV-2 Spike glycoprotein ChAdOx1-S*, not less than 2.5×10^8 infectious units
*Produced in genetically modified human embryonic kidney (HEK) 293 cells and by recombinant DNA technology.

This product contains genetically modified organisms (GMOs).

The other excipients are L-histidine, L-histidine hydrochloride monohydrate, magnesium chloride hexahydrate, polysorbate 80 (E 433), sucrose, disodium edetate (dihydrate), water for injections (see section 2 “Vaxzevria contains sodium and alcohol”).

What Vaxzevria looks like and contents of the pack
Suspension for injection (injection). The suspension is colourless to slightly brown, clear to slightly opaque.

Pack sizes:
- 8-dose multidose vial (4 ml) with stopper (elastomeric with aluminium overseal) in a pack of 10 vials. Each vial contains 8 doses of 0.5 ml.

- 10-dose multidose vial (5 ml) with stopper (elastomeric with aluminium overseal) in a pack of 10 vials. Each vial contains 10 doses of 0.5 ml.

Not all pack sizes may be marketed.

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Manufacturer
AstraZeneca Nijmegen B.V.
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Nijmegen, 6545CG
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This leaflet was last revised in

This medicine has been given 'conditional approval'. This means that there is more evidence to come about this medicine.
The European Medicines Agency will review new information on this medicine at least every year and this leaflet will be updated as necessary.

Other sources of information

Scan the QR code with a mobile device to get **this information in different languages**.

www.azcovid-19.com

Detailed information on this medicine is available on the European Medicines Agency web site: http://www.ema.europa.eu

This leaflet is available in all EU/EEA languages on the European Medicines Agency website.

The following information is intended **for healthcare professionals only**:

For storage and disposal, see section 5 "How to store Vaxzevria".

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.

Handling instructions and administration

This vaccine should be handled by a healthcare professional using aseptic technique to ensure the sterility of each dose.

The vaccine should be inspected visually for particulate matter and discolouration prior to administration. Vaxzevria is a colourless to slightly brown, clear to slightly opaque suspension. Discard the vial if the suspension is discoloured or visible particles are observed. Do not shake. Do not dilute the suspension.

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

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 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 new needle for administration, when possible.

It is normal for liquid to remain in the vial after withdrawing the final dose. An additional overfill is included in each vial to ensure that 8 doses (vial of 4 ml) or 10 doses (vial of 5 ml) of 0.5 ml can be delivered. Do not pool excess vaccine from multiple vials. Discard any unused vaccine.