

**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

COVID-19 Vaccine AstraZeneca 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  $2.5 \times 10^8$  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

COVID-19 Vaccine AstraZeneca 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 COVID-19 Vaccine AstraZeneca 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 COVID-19 Vaccine AstraZeneca with other COVID-19 vaccines to complete the vaccination course. Individuals who have received the first dose

of COVID-19 Vaccine AstraZeneca should receive the second dose of COVID-19 Vaccine AstraZeneca to complete the vaccination course.

#### *Paediatric population*

The safety and efficacy of COVID-19 Vaccine AstraZeneca 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

COVID-19 Vaccine AstraZeneca 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

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 COVID-19 Vaccine AstraZeneca.

#### 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 COVID-19 Vaccine AstraZeneca. This includes

severe cases presenting as venous thrombosis, including unusual sites such as cerebral venous sinus thrombosis, mesenteric vein thrombosis, as well as arterial thrombosis, concomitant with thrombocytopenia. The majority of these cases occurred within the first seven to fourteen days following vaccination and occurred in women under 55 years of age, however this may reflect the increased use of the vaccine in this population. Some cases had a fatal outcome.

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 COVID-19 Vaccine AstraZeneca 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 COVID-19 Vaccine AstraZeneca. Individuals may not be fully protected until 15 days after the second dose is administered. As with all vaccines, vaccination with COVID-19 Vaccine AstraZeneca 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 COVID-19 Vaccine AstraZeneca with other vaccines has not been studied.

## **4.6 Fertility, pregnancy and lactation**

### Pregnancy

There is limited experience with use of COVID-19 Vaccine AstraZeneca 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 COVID-19 Vaccine AstraZeneca during pregnancy should only be considered when the potential benefits outweigh any potential risks for the mother and fetus.

### Breastfeeding

It is unknown whether COVID-19 Vaccine AstraZeneca 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**

COVID-19 Vaccine AstraZeneca 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 COVID-19 Vaccine AstraZeneca 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  $\geq 18$  years old had been randomised and received either COVID-19 Vaccine AstraZeneca or control. Out of these, 12,021 received at least one dose of COVID-19 Vaccine AstraZeneca 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  $>38^{\circ}\text{C}$  (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 ( $\geq 65$  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 ( $\geq 1/10$ ); common ( $\geq 1/100$  to  $< 1/10$ ); uncommon ( $\geq 1/1,000$  to  $< 1/100$ ); rare ( $\geq 1/10,000$  to  $< 1/1,000$ ); 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	Uncommon	Lymphadenopathy
Metabolism and nutrition disorders	Uncommon	Decreased appetite
Nervous system disorders	Very common	Headache
	Uncommon	Dizziness Somnolence
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 <sup>a</sup> Fatigue Malaise Feverishness Chills
	Common	Injection site swelling Injection site erythema Fever <sup>b</sup>

<sup>a</sup> Injection site bruising includes injection site haematoma (uncommon)

<sup>b</sup> Measured fever  $\geq 38^{\circ}\text{C}$

#### 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 COVID-19 Vaccine AstraZeneca. 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

COVID-19 Vaccine AstraZeneca 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 COVID-19 Vaccine AstraZeneca 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  $\geq 18$  years of age (including the elderly) in the UK; and a phase III study, COV003, in adults  $\geq 18$  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 COVID-19 Vaccine AstraZeneca. 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  $\geq 18$  years of age received two doses ( $5 \times 10^{10}$  viral particles per dose corresponding to not less than  $2.5 \times 10^8$  infectious units) of COVID-19 Vaccine AstraZeneca (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 COVID-19 Vaccine AstraZeneca and control treatment groups. In the pooled analysis, among the participants who received COVID-19 Vaccine AstraZeneca 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  $\geq 30$  kg/m<sup>2</sup>, 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  $\geq 15$  days post second dose 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. COVID-19 Vaccine AstraZeneca significantly decreased the incidence of COVID-19 compared to control (see Table 2).

**Table 2 COVID-19 Vaccine AstraZeneca efficacy against COVID-19<sup>a</sup>**

Population	COVID-19 Vaccine AstraZeneca		Control		Vaccine efficacy % (95% CI) <sup>b</sup>
	N	Number of COVID-19 cases, n (%)	N	Number of COVID-19 cases, n (%)	
<b><i>Licensing regimen</i></b>					
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;

<sup>a</sup> 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  $\geq 15$  days post second dose.

<sup>b</sup> 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  $\geq 4$ ) there were 0 (0.0%; N=5,258) cases of COVID-19 hospitalisation in participants who received two doses of COVID-19 Vaccine AstraZeneca ( $\geq 15$  days post dose 2) as compared to 8 (0.2%; N=5,210) for control, including one severe case (WHO Severity grading  $\geq 6$ ), 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 COVID-19 Vaccine AstraZeneca, 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 COVID-19 Vaccine AstraZeneca (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 COVID-19 Vaccine AstraZeneca ( $\geq 15$  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 COVID-19 Vaccine AstraZeneca ( $\geq 15$  days post dose 2) and control, respectively.

#### Paediatric population

The European Medicines Agency has deferred the obligation to submit the results of studies with COVID-19 Vaccine AstraZeneca 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. COVID-19 Vaccine AstraZeneca 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 COVID-19 Vaccine AstraZeneca 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 COVID-19 Vaccine AstraZeneca 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

COVID-19 Vaccine AstraZeneca 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

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

MedImmune Pharma B.V., Nijmegen  
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.

#### **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:

<b>Description</b>	<b>Due date</b>
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 COVID-19 Vaccine AstraZeneca, 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 COVID-19 Vaccine AstraZeneca, 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 COVID-19 Vaccine AstraZeneca 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**

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

**2. STATEMENT OF ACTIVE SUBSTANCE(S)**

One dose (0.5 ml) contains not less than  $2.5 \times 10^8$  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](http://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 additional 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**

COVID-19 Vaccine AstraZeneca 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**

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

**2. STATEMENT OF ACTIVE SUBSTANCE(S)**

One dose (0.5 ml) contains not less than  $2.5 \times 10^8$  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](http://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 additional 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**

COVID-19 Vaccine AstraZeneca 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

### COVID-19 Vaccine AstraZeneca 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 COVID-19 Vaccine AstraZeneca is and what it is used for
2. What you need to know before you are given COVID-19 Vaccine AstraZeneca
3. How COVID-19 Vaccine AstraZeneca is given
4. Possible side effects
5. How to store COVID-19 Vaccine AstraZeneca
6. Contents of the pack and other information

#### **1. What COVID-19 Vaccine AstraZeneca is and what it is used for**

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

COVID-19 Vaccine AstraZeneca 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 COVID-19 Vaccine AstraZeneca**

##### **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 COVID-19 Vaccine AstraZeneca:

- If you have ever had a severe allergic reaction after any other vaccine injection or after you were given COVID-19 Vaccine AstraZeneca 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.

#### **Blood disorders**

A combination of blood clots and low level of platelets, in some cases together with bleeding, has been observed very rarely following vaccination with COVID-19 Vaccine AstraZeneca. 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 seven to fourteen days following vaccination and mostly occurred in women under 55 years of age, however more women under 55 received the vaccine than other people. 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.

As with any vaccine, the 2-dose vaccination course of COVID-19 Vaccine AstraZeneca 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 COVID-19 Vaccine AstraZeneca in individuals aged 55 and older.

#### **Children and adolescents**

COVID-19 Vaccine AstraZeneca is not recommended for children aged below 18 years. Currently there is not enough information available on the use of COVID-19 Vaccine AstraZeneca in children and adolescents younger than 18 years of age.

#### **Other medicines and COVID-19 Vaccine AstraZeneca**

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 COVID-19 Vaccine AstraZeneca 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.

#### **COVID-19 Vaccine AstraZeneca 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 COVID-19 Vaccine AstraZeneca is given**

COVID-19 Vaccine AstraZeneca 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 COVID-19 Vaccine AstraZeneca. 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 COVID-19 Vaccine AstraZeneca is given for the first injection, the second injection to complete the vaccination course should also be with COVID-19 Vaccine AstraZeneca.

#### **If you miss an appointment for your second injection of COVID-19 Vaccine AstraZeneca**

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 COVID-19 Vaccine AstraZeneca. 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 COVID-19 Vaccine AstraZeneca:

##### 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

##### Uncommon (may affect up to 1 in 100 people)

- sleepiness or feeling dizzy
- decreased appetite
- enlarged lymph nodes
- excessive sweating, itchy skin or rash

#### **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 COVID-19 Vaccine AstraZeneca

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.

COVID-19 Vaccine AstraZeneca 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 COVID-19 Vaccine AstraZeneca contains

One dose (0.5 ml) contains:

Chimpanzee Adenovirus encoding the SARS-CoV-2 Spike glycoprotein ChAdOx1-S\*, not less than  $2.5 \times 10^8$  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 “COVID-19 Vaccine AstraZeneca contains sodium and alcohol”).

### What COVID-19 Vaccine AstraZeneca 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.

### Marketing Authorisation Holder

AstraZeneca AB  
SE-151 85 Södertälje

Sweden

**Manufacturer**

MedImmune Pharma B.V., Nijmegen  
Lagelandseweg 78  
Nijmegen, 6545CG  
Netherlands

For any information about this medicine, please contact the local representative of the Marketing Authorisation Holder:

**België/Belgique/Belgien**

AstraZeneca S.A./N.V.  
Tel: Tel: +32 2 808 53 06

**Lietuva**

UAB AstraZeneca Lietuva  
Tel: +370 5 2141423

**България**

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**Česká republika**

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**Magyarország**

AstraZeneca Kft.  
Tel.: +36 80 180 007

**Danmark**

AstraZeneca A/S  
Tlf: +45 89 87 04 78

**Malta**

Associated Drug Co. Ltd  
Tel: +356 2277 8134

**Deutschland**

AstraZeneca GmbH  
Tel: 0800 22 88 660 (gebührenfrei)

**Nederland**

AstraZeneca BV  
Tel: 0800 70 11 (gratis)  
+31 79 363 2222

**Eesti**

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**España**

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**Polska**

AstraZeneca Pharma Poland Sp. z o.o.  
Tel.: +48 22 104 60 80

**France**

AstraZeneca  
Tél: 0 800 08 92 44 (numéro vert)

**Portugal**

AstraZeneca Produtos Farmacêuticos, Lda.  
Tel: +351 30 880 17 68

**Hrvatska**

AstraZeneca d.o.o.  
Tel: +385 1 4628 000

**România**

AstraZeneca Pharma SRL  
Tel: +40 31 630 03 18

**Ireland**

AstraZeneca Pharmaceuticals (Ireland) DAC

**Slovenija**

AstraZeneca UK Limited

Tel: 1800 812456 (toll free)

Tel: +386 1 60 03 197

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Sími: +354 519 3643

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**Sverige**

AstraZeneca AB  
Tel: +46 3 130 11 892

**Latvija**

SIA AstraZeneca Latvija  
Tel: +371 68688132

**United Kingdom (Northern Ireland)**

AstraZeneca UK Ltd  
Tel: +44 8000 541 028

**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](http://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.

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

For storage and disposal, see section 5 “How to store COVID-19 Vaccine AstraZeneca”.

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. COVID-19 Vaccine AstraZeneca 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 COVID-19 Vaccine AstraZeneca 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 COVID-19 Vaccine AstraZeneca 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.

**ANNEX IV**  
**CONCLUSIONS ON THE GRANTING OF THE CONDITIONAL MARKETING**  
**AUTHORISATION PRESENTED BY THE EUROPEAN MEDICINES AGENCY**



**Conclusions presented by the European Medicines Agency on:**

- **Conditional marketing authorisation**

The CHMP having considered the application is of the opinion that the risk-benefit balance is favourable to recommend the granting of the conditional marketing authorisation as further explained in the European Public Assessment Report.