



**República Argentina - Poder Ejecutivo Nacional**  
2020 - Año del General Manuel Belgrano

**Disposición**

**Número:**

**Referencia:** 1-47-2002-532-20-1

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VISTO el Expediente N° 1-47-2002-532-20-1 del Registro de esta ADMINISTRACIÓN NACIONAL DE MEDICAMENTOS, ALIMENTOS Y TECNOLOGÍA MÉDICA y

**CONSIDERANDO:**

Que por las referidas actuaciones la firma AstraZeneca S.A solicita se autorice, en el contexto de la Pandemia COVID-19, la inscripción condicional en el Registro de Especialidades Medicinales (REM) de esta ADMINISTRACIÓN NACIONAL DE MEDICAMENTOS, ALIMENTOS Y TECNOLOGÍA MÉDICA de una nueva especialidad medicinal que será comercializada en la República Argentina.

Que las actividades de importación y comercialización de especialidades medicinales se encuentran contempladas en la Ley N° 16.463 y en los Decretos Nros. 9763/64 y 150/92 (t.o. 1993) y sus normas complementarias.

Que por las características que presenta el producto COVID-19 Vacuna AstraZeneca / VACUNA CONTRA COVID19 ChAdOx1-S recombinante, la solicitud presentada encuadra dentro de lo previsto en el Anexo I- Item 5 de la Disposición ANMAT Nro. 705/05 que prevé el registro de vacunas de interés sanitario en emergencias.

Que el Anexo antes citado establece que para el caso de emergencias o cuando las condiciones sanitarias hagan necesaria la disponibilidad de vacunas en desarrollo o de reducida disponibilidad de datos de seguridad y eficacia, la autoridad regulatoria establecerá un procedimiento que permita evaluar las condiciones de riesgo beneficio para la disponibilidad del biológico en el marco de la estrategia que fije el país

Que la solicitud presentada ha sido evaluada por la Dirección de Evaluación y Control de Biológicos y Radiofármacos de esta Administración Nacional, concluyéndose que la nueva especialidad medicinal cuya inscripción en el REM se solicita, presenta un aceptable balance beneficio-riesgo, permitiendo por lo tanto sustentar el otorgamiento de una inscripción y autorización condicional a los fines de su uso del producto para la indicación solicitada

Que, asimismo el área interviniente, sugiere las siguientes condiciones y requerimientos a los fines de otorgar la inscripción del producto: 1) que la condición de venta sea VENTA BAJO RECETA, 2) que en atención a que se trata de una autorización condicional de una vacuna deberá contar con el Plan de Gestión de Riesgos autorizado por esta Administración Nacional al momento de presentar la solicitud de autorización efectiva de comercialización, a los fines de que pueda realizarse un seguimiento estrecho de la seguridad y eficacia del medicamento, debiendo cumplir con el mismo y presentar los informes de avance, las modificaciones y las actualizaciones correspondientes ante el INAME; 3) incluir el producto dentro del Sistema de Trazabilidad de Medicamentos; 4) presentar informes de seguridad periódicos cada seis meses luego de la comercialización efectiva del producto ante el INAME; 5) todo cambio en el perfil de seguridad o de eficacia del producto deberá evidenciarse en la correspondiente modificación del prospecto.

Que asimismo, de acuerdo con lo informado, los proyectos de los rótulos, prospectos y la información para el paciente se consideran aceptables, y el/los establecimiento/s que realizarán la elaboración y el control de calidad de la especialidad medicinal en cuestión demuestran aptitud a esos efectos.

Que los datos identificatorios característicos del producto a ser transcritos en el Certificado han sido convalidados por el área técnica precedentemente citada.

Que en atención a lo sugerido en el informe técnico corresponde incluir el producto dentro del Sistema de Trazabilidad de Medicamentos, de conformidad con la Disposición ANMAT N° 3683/11, sus modificatorias y complementarias.

Que por lo expuesto corresponde autorizar la inscripción en el REM condicional a los fines de su uso de la especialidad medicinal solicitada.

Que la Dirección de Evaluación y Control de Biológicos y Radiofármacos y la Dirección de Asuntos Jurídicos han tomado la intervención de su competencia.

Que se actúa en ejercicio de las facultades conferidas por el Decreto N° 1490/92 y sus modificatorios.

Por ello,

EL ADMINISTRADOR NACIONAL DE LA ADMINISTRACIÓN NACIONAL DE  
MEDICAMENTOS, ALIMENTOS Y TECNOLOGÍA MÉDICA

DISPONE:

ARTÍCULO 1°.- Autorízase a la firma AstraZeneca S.A en el contexto de Pandemia Covid 19, la inscripción condicional a los fines de su uso en el Registro de Especialidades Medicinales (REM) y de la ADMINISTRACIÓN NACIONAL DE MEDICAMENTOS, ALIMENTOS Y TECNOLOGÍA MÉDICA de la especialidad medicinal de nombre comercial COVID-19 Vacuna AstraZeneca y nombre genérico VACUNA CONTRA COVID19 ChAdOx1-S recombinante, la que de acuerdo a lo solicitado en el tipo de Trámite N° 1.2. VAC, será comercializada en la República Argentina por ASTRAZENECA S.A de acuerdo con los datos identificatorios característicos del producto incluidos en el Certificado de inscripción.

ARTÍCULO 2°.- En virtud de tratarse de una autorización condicional, la vigencia del Certificado será de 1 (UN)

año a partir de la fecha de la presente Disposición.

ARTÍCULO 3º.- Autorizanse los textos de los proyectos rótulos y prospectos que constan como documentos IF-2020-91460576-APN-DECBR#ANMAT, IF-2020-91487526-APN-DECBR#ANMAT e IF-2020-91488480-APN-DECBR#ANMAT

ARTÍCULO 4º.- En los rótulos y prospectos autorizados deberá figurar la leyenda: “ESPECIALIDAD MEDICINAL AUTORIZADA POR EL MINISTERIO DE SALUD CERTIFICADO N°”, con exclusión de toda otra leyenda no contemplada en la norma legal vigente.

ARTÍCULO 5º.- Con carácter previo a la comercialización de la especialidad medicinal cuya inscripción se autoriza por la presente disposición, el titular deberá solicitar a esta Administración Nacional la autorización efectiva de comercialización notificando fecha de inicio de la importación del primer lote a comercializar a los fines de realizar la verificación técnica correspondiente.

ARTÍCULO 6º.- A los fines de la presentación de la solicitud de autorización efectiva de comercialización citada en el artículo precedente, el titular deberá contar con el Plan de Gestión de Riesgo autorizado por esta Administración Nacional.

ARTÍCULO 7º.- Establécese que el titular deberá cumplir con el Plan de Gestión de Riesgo aprobado por esta Administración Nacional.

ARTÍCULO 8º.- Hágase saber que el titular que deberá presentar los informes de avance, las modificaciones y las actualizaciones del Plan de Gestión de Riesgo ante el INAME.

ARTÍCULO 9º.- Hágase saber al titular que deberá presentar los informes de seguridad periódicos cada seis meses luego de la comercialización efectiva del producto ante el INAME.

ARTÍCULO 10º.- Hágase saber al titular que todo cambio en el perfil de seguridad o de eficacia del producto deberá evidenciarse en la correspondiente modificación del prospecto.

ARTÍCULO 11º. – Establécese que con relación a la especialidad medicinal cuya inscripción se autoriza por la presente Disposición, deberá cumplirse con los términos de la Disposición ANMAT N° 3683/11, sus modificatorias y complementarias.

ARTÍCULO 12º.- En caso de incumplimiento de las obligaciones previstas en los artículos precedentes, esta Administración Nacional podrá suspender la comercialización del producto aprobado por la presente disposición, cuando consideraciones de salud pública así lo ameriten.

ARTÍCULO 13º.- Regístrese. Inscríbase el nuevo producto en el Registro de Especialidades Medicinales. Notifíquese electrónicamente al interesado la presente disposición y los rótulos, prospectos e información para el paciente aprobados. Gírese al Departamento de Registro a los fines de confeccionar el legajo correspondiente. Cumplido, archívese.

Expediente N° 1-47-2002-532-20-1

Digitally signed by LIMERES Manuel Rodolfo  
Date: 2020.12.30 12:16:17 ART  
Location: Ciudad Autónoma de Buenos Aires

Digitally signed by Gestion Documental  
Electronica  
Date: 2020.12.30 12:16:32 -03:00

**PROYECTO DE RÓTULO  
(Etiqueta)**

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

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

4 mL

$1 \times 10^{11}$  vp/mL

Certificado N° XX.XXX  
Industria XX

Lot:  
Cad:

AstraZeneca 

**PROYECTO DE RÓTULO  
(Etiqueta)**

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

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

5mL

$1 \times 10^{11}$  vp/mL

Certificado N° XX.XXX  
Industria XX

Lot:  
Cad:

AstraZeneca 

**PROYECTO DE RÓTULO  
(Estuche)**

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

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

4mL

1 × 10<sup>11</sup> vp/mL

**BOX WITH 10 GLASS MULTIDOSE VIALS WITH 4ML OF  
SOLUTION**

Do not administer this medicine without reading the instructions (see QR code).

ROUTE OF ADMINISTRATION: Intramuscular.

Keep the box tightly closed in a refrigerator between 2 ° C to 8 ° C. Store in the original container to protect from light. Do not freeze

Keep out of reach of children.

Lot:

Cad:

Drug substance manufactured by:

Manufactured in



**PROYECTO DE RÓTULO  
(Estuche)**

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

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

5mL

$1 \times 10^{11}$  vp/mL

**BOX WITH 10 GLASS MULTIDOSE VIALS WITH 5ML OF  
SOLUTION**

Do not administer this medicine without reading the instructions (see QR code).

ROUTE OF ADMINISTRATION: Intramuscular.

Keep the box tightly closed in a refrigerator between 2 ° C to 8 ° C. Store in the original container to protect from light. Do not freeze

Keep out of reach of children.

Lot:

Cad:

Drug substance manufactured by:

Manufactured in









República Argentina - Poder Ejecutivo Nacional  
2020 - Año del General Manuel Belgrano

**Hoja Adicional de Firmas**  
**Informe gráfico**

**Número:**

**Referencia:** PROYECTO DE ROTULOS

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El documento fue importado por el sistema GEDO con un total de 5 pagina/s.

Digitally signed by Gestion Documental Electronica  
Date: 2020.12.30 08:08:51 -03:00

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Electronica  
Date: 2020.12.30 08:08:51 -03:00

This medicinal product has been given authorisation for temporary supply by the UK

Department of Health and Social Care and the Medicines & Healthcare products Regulatory Agency. It does not have a marketing authorisation, but this temporary authorisation grants permission for the medicine to be used for active immunisation of individuals aged 18 years and older for the prevention of coronavirus disease 2019 (COVID-19).

As with any new medicine in the UK, this product will be closely monitored to 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, solution for injection in multidose container  
COVID-19 Vaccine (ChAdOx1-S [recombinant])

2. QUALITATIVE AND QUANTITATIVE COMPOSITION

One dose (0.5 ml) contains:

COVID-19 Vaccine (ChAdOx1-S\* recombinant) 5 × 10<sup>10</sup> viral particles (vp)

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

This product contains genetically modified organisms (GMOs).

For the full list of excipients, see section 6.1.

3. PHARMACEUTICAL FORM

Solution for injection.

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

4. CLINICAL PARTICULARS

#### 4.1 Therapeutic indications

COVID-19 Vaccine AstraZeneca is indicated for active immunisation of individuals  $\geq 18$  years old for the prevention of coronavirus disease 2019 (COVID-19).

The use of COVID-19 Vaccine AstraZeneca should be in accordance with official guidance.

#### 4.2 Posology and method of administration

##### Posology

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 (see section 5.1).

It is recommended that individuals who receive a first dose of COVID-19 Vaccine AstraZeneca complete the vaccination course with COVID-19 Vaccine AstraZeneca (see section 4.4).

##### Elderly population

Efficacy and safety data are currently limited in individuals  $\geq 65$  years of age (see sections 4.8 and 5.1). No dosage adjustment is required.

##### Paediatric population

The safety and efficacy of COVID-19 Vaccine AstraZeneca in children and adolescents (aged  $< 18$  years old) have not yet been established. No data are available.

##### Method of administration

COVID-19 Vaccine AstraZeneca is for intramuscular (IM) injection only, preferably in the deltoid muscle.

For instructions on administration, 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

As with all injectable vaccines, appropriate medical treatment and supervision should always be readily available in case of an anaphylactic event following the administration of the vaccine.

### Concurrent illness

As with other vaccines, administration of COVID-19 Vaccine AstraZeneca should be postponed in individuals suffering from an acute severe febrile illness. However, the presence of a minor infection, such as cold, and/or low-grade fever should not delay vaccination.

### Thrombocytopenia and coagulation disorders

As with other intramuscular injections, COVID-19 Vaccine AstraZeneca should be given with caution to individuals with thrombocytopenia, any coagulation disorder or to persons on anticoagulation therapy, because bleeding or bruising may occur following an intramuscular administration in these individuals.

### Immunocompromised individuals

It is not known whether individuals with impaired immune responsiveness, including individuals receiving immunosuppressant therapy, will elicit the same response as immunocompetent individuals to the vaccine regimen.

### Duration and level of protection

The duration of protection has not yet been established.

As with any vaccine, vaccination with COVID-19 Vaccine AstraZeneca may not protect all vaccine recipients.

### Interchangeability

No data are available on the use of COVID-19 Vaccine AstraZeneca in persons that have previously received a full or partial vaccine series with another COVID-19 vaccine.

### Sodium

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

#### 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 (see section 5.1).

#### 4.6 Fertility, pregnancy and lactation

### Pregnancy

There is a limited experience with the use of COVID-19 Vaccine AstraZeneca in pregnant women.

Preliminary animal studies do not indicate direct or indirect harmful effects with respect to pregnancy, embryofetal development, parturition or post-natal development; definitive animal studies have not been completed yet. The full relevance of animal studies to human risk with vaccines for COVID-19 remains to be established.

Administration of COVID-19 Vaccine AstraZeneca in 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

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

## 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. The median duration of follow-up in the COVID-19 Vaccine AstraZeneca group was 105 days post-dose 1, and 62 days post-dose 2.

Demographic characteristics were generally similar among participants who received COVID-19

Vaccine AstraZeneca and those who received control. Overall, among the participants who received COVID-19 Vaccine AstraZeneca, 90.3% were aged 18 to 64 years and 9.7% were 65 years of age or older. The majority of recipients were White (75.5%), 10.1% were Black and 3.5% were Asian; 55.8% were female and 44.2% male.

The most frequently reported adverse reactions were injection site tenderness (>60%); injection site pain, headache, fatigue (>50%); myalgia, malaise (>40%); pyrexia, chills (>30%); and arthralgia, nausea (>20%). The majority of adverse reactions were mild to moderate in severity and usually resolved within a few days of vaccination. By day 7 the incidence of subjects with at least one local or systemic reaction was 4% and 13% respectively. When compared with the first dose, adverse reactions reported after the second dose were milder and reported less frequently.

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

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

#### Tabulated list of adverse reactions

Adverse drug reactions (ADRs) are organised by MedDRA System Organ Class (SOC). Within each SOC, preferred terms are arranged by decreasing frequency and then by decreasing seriousness.

Frequencies of occurrence of adverse reactions are defined as: very common (≥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).

Table 1 Adverse drug reactions

MedDRA SOC	Frequency	Adverse Reactions
Blood and lymphatic system disorders	Uncommon	Lymphadenopathy <sup>a</sup>
Metabolism and nutrition disorders	Uncommon	Decreased appetite <sup>a</sup>
Nervous system disorders	Very common	Headache
	Uncommon	Dizziness <sup>a</sup>
Gastrointestinal disorders	Very common	Nausea
	Common	Vomiting
	Uncommon	Abdominal pain <sup>a</sup>
Skin and subcutaneous tissue disorders	Uncommon	Hyperhidrosis <sup>a</sup> , pruritus <sup>a</sup> , rash <sup>a</sup>
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 erythema, injection site pruritus, injection site

		swelling, injection site bruising <sup>b</sup> , fatigue, malaise, pyrexia <sup>c</sup> , chills
	Common	Injection site induration, influenza-like illness <sup>a</sup>

<sup>a</sup> Unsolicited adverse reaction

<sup>b</sup> Injection site bruising includes injection site haematoma (uncommon, unsolicited adverse reaction) <sup>c</sup> Pyrexia includes feverishness (very common) and fever  $\geq 38^{\circ}\text{C}$  (common)

Very rare events of neuroinflammatory disorders have been reported following vaccination with COVID-19 Vaccine AstraZeneca. A causal relationship has not been established.

#### Reporting of suspected adverse reactions

If you are concerned about an adverse event, it should be reported on a Yellow Card. Reporting forms and information can be found at <https://coronavirus-yellowcard.mhra.gov.uk/> or search for MHRA Yellow Card in the Google Play or Apple App Store and include the vaccine brand and batch/Lot number if available.

Alternatively, adverse events of concern in association with COVID-19 Vaccine AstraZeneca can be reported to AstraZeneca on 08000541028 or via [www.azcovid-19.com](http://www.azcovid-19.com).

Please do not report the same adverse event(s) to both systems as all reports will be shared between AstraZeneca and MHRA (in an anonymised form) and dual reporting will create unnecessary duplicates.

#### 4.9 Overdose

Experience of overdose is limited.

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: Vaccine, 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. Following administration, the S



glycoprotein of SARS-CoV-2 is expressed locally stimulating neutralising antibody and cellular immune responses.

### Clinical efficacy

COVID-19 Vaccine AstraZeneca has been evaluated based on an interim analysis of pooled data from four on-going randomised, blinded, controlled trials: a Phase I/II Study, COV001, in healthy adults 18 to 55 years of age in the UK; a Phase II/III Study, COV002, in adults  $\geq 18$  years of age (including the elderly) in the UK; a Phase III Study, COV003, in adults  $\geq 18$  years of age (including the elderly) in Brazil; and a Phase I/II study, COV005, in adults aged 18 to 65 years of age in South Africa. The studies excluded participants with history of anaphylaxis or angioedema; participants with severe and/or uncontrolled cardiovascular, gastrointestinal, liver, renal, endocrine/metabolic disease, and neurological illnesses; as well as those with immunosuppression. In studies COV001 and COV002, licensed seasonal influenza and pneumococcal vaccinations were permitted (at least 7 days before or after their study vaccine).

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

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

In the pooled analysis for efficacy (COV002 and COV003), participants  $\geq 18$  years of age received two doses of COVID-19 Vaccine AstraZeneca (N=5,807) or control (meningococcal vaccine or saline) (N=5,829). Because of logistical constraints, the interval between dose 1 and dose 2 ranged from 4 to 26 weeks.

Baseline demographics were well balanced across COVID-19 Vaccine AstraZeneca and control treatment groups. Overall, among the participants who received COVID-19 Vaccine AstraZeneca, 94.1% of participants were 18 to 64 years old (with 5.9% aged 65 or older); 60.7% of subjects were female; 82.8% were White, 4.6% were Asian, and 4.4% were Black. A total of 2,070 (35.6%) participants had at least one pre-existing comorbidity (defined as a BMI  $\geq 30$  kg/m<sup>2</sup>, cardiovascular disorder, respiratory disease or diabetes). The median follow up time post-dose 1 and post-dose 2 was 132 days and 63 days, respectively.

Final determination of COVID-19 cases were made by an adjudication committee, who also assigned disease severity according to the WHO clinical progression scale. A total of 131 participants had SARS-CoV-2 virologically confirmed (by nucleic acid amplification tests) COVID-19 occurring  $\geq 15$  days post-dose 2 with at least one COVID-19 symptom (objective fever (defined as  $\geq 37.8^\circ\text{C}$ ), cough, shortness of breath, anosmia, or ageusia) and were

without evidence of previous SARS-CoV-2 infection. 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

Population	COVID-19 Vaccine AstraZeneca		Control		Vaccine efficacy % (CI)
	N	Number of COVID-19 cases, n (%)	N	Number of COVID-19 cases, n (%)	
Primary (see above)	5,807		5,829		
COVID-19 cases		30 (0.52)		101 (1.73)	70.42 (58.84, 80.63) <sup>a</sup>
Hospitalisations <sup>b</sup>		0		5 (0.09)	-
Severe disease <sup>c</sup>		0		1 (0.02)	-
Any dose	10,014		10,000		
COVID-19 cases after dose 1		108 (1.08)		227 (2.27)	52.69 (40.52, 62.37) <sup>d</sup>
Hospitalisations after dose 1 <sup>b</sup>		2 (0.02) <sup>e</sup>		16 (0.16)	-
Severe disease after dose 1 <sup>c</sup>		0		2 (0.02)	

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

CI = Confidence Interval; <sup>a</sup> 95.84% CI; <sup>b</sup> WHO severity grading  $\geq 4$ ; <sup>c</sup> WHO severity grading  $\geq 6$ ; <sup>d</sup> 95% CI; <sup>e</sup> Two cases of hospitalisation occurred on Days 1 and 10 post vaccination.

The level of protection gained from a single dose of COVID-19 Vaccine AstraZeneca was assessed in an exploratory analysis that included participants who had received one dose. Participants were censored from the analysis at the earliest time point of when they received a second dose or at 12 weeks post-dose 1. In this population, vaccine efficacy from 22 days post-dose 1 was 73.00% (95% CI: 48.79; 85.76 [COVID-19 Vaccine AstraZeneca 12/7,998 vs control 44/7,982]).

Exploratory analyses showed that increased immunogenicity was associated with a longer dose interval (see Immunogenicity Table 3). Efficacy is currently

demonstrated with more certainty for dose intervals from 8 to 12 weeks. Data for intervals longer than 12 weeks are limited.

Participants who had one or more comorbidities had a vaccine efficacy of 73.43% [95% CI: 48.49; 86.29]; 11 (0.53%) vs 43 (2.02%) for COVID-19 Vaccine AstraZeneca (N=2,070) and control (N=2,113), respectively; which was similar to the vaccine efficacy observed in the overall population.

The number of COVID-19 cases (2) in 660 participants  $\geq 65$  years old were too few to draw conclusions on efficacy. However, in this subpopulation, immunogenicity data are available, see below.

#### Immunogenicity

Following vaccination with COVID-19 Vaccine AstraZeneca, in participants who were seronegative at baseline, seroconversion (as measured by a  $\geq 4$  fold increase from baseline in S-binding antibodies) was demonstrated in  $\geq 98\%$  of participants at 28 days after the first dose and  $>99\%$  at 28 days after the second. Higher S-binding antibodies were observed with increasing dose interval (Table 3).

Generally similar trends were observed between analyses of neutralising antibodies and S-binding antibodies. An immunological correlate of protection has not been established; therefore the level of immune response that provides protection against COVID-19 is unknown.

Table 3 SARS CoV-2 S-binding antibody response to COVID-19 Vaccine AstraZeneca<sup>a, b</sup>

Population	Baseline	28 days after dose 1	28 days after dose 2
	GMT (95% CI)	GMT (95% CI)	GMT (95% CI)
Overall	(N=882) 57.18	(N=817) 8,386.46	(N=819) 29,034.74
Population	Baseline	28 days after dose 1	28 days after dose 2
	GMT (95% CI)	GMT (95% CI)	GMT (95% CI)
	(52.8; 62.0)	(7,758.6; 9,065.1)	(27,118.2; 31,086.7)
Dose Interval			
<6 weeks	(N=481) 60.51 (54.1; 67.7)	(N=479) 8,734.08 (7,883.1; 9,676.9)	(N=443) 22,222.73 (20,360.50; 24,255.3)

6-8 weeks	(N=137) 58.02 (46.3; 72.6)	(N=99) 7,295.54 (5,857.4; 9,086.7)	(N=116) 24,363.10 (20,088.5, 29547.3)
9-11 weeks	(N=110) 48.79 (39.6; 60.1)	(N=87) 7,492.98 (5,885.1; 9,540.2)	(N=106) 34,754.10 (30,287.2; 39,879.8)
≥12 weeks	(N=154) 52.98 (44.4; 63.2)	(N=152) 8,618.17 (7,195.4; 10,322.3)	(N=154) 63,181.59 (55,180.1; 72,343.4)

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

<sup>a</sup> Immune response evaluated using a multiplex immunoassay; <sup>b</sup> in individuals who received two recommended doses of vaccine.

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

High seroconversion rates were observed in older adults (≥65 years) after the first (97.8%; N=136) and the second recommended dose (100.0%; N=111). The increase in S-binding antibodies was lower for participants ≥65 years old (28 days after second dose: GMT=20,727.02 [N=116, 95% CI: 17,646.6; 24,345.2]) when compared to participants aged 18-64 years (28 days after second dose:

GMT=30,695.30 [N=703, 95% CI: 28,496.2; 33,064.1]). The majority of participants ≥65 years old had a dose interval of <6 weeks, which may have contributed to the lower titres observed.

In participants with serological evidence of prior SARS-CoV-2 infection at baseline (GMT=13,137.97 [N=29; 95% CI: 7,441.8; 23,194.1]), S-antibody titres peaked 28 days after dose 1 (GMT=175,120.84 [N=28; 95% CI: 120,096.9; 255,354.8]).

Spike-specific T cell responses as measured by IFN-γ enzyme-linked immunospot (ELISpot) assay were induced after a first dose of COVID-19 Vaccine AstraZeneca. These did not rise further after a second dose.

## 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. Animal studies into potential toxicity to reproduction and development have not yet been completed.

## 6. PHARMACEUTICAL PARTICULARS

### 6.1 List of excipients

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

### 6.2 Incompatibilities

In the absence of compatibility studies, this vaccine must not be mixed with other medicinal products.

### 6.3 Shelf life

Unopened multidose vial  
6 months

#### After first use

Use as soon as practically possible and within 6 hours.  
The vaccine may be stored between 2°C and 25°C during the in-use period.

### 6.4 Special precautions for storage

#### Unopened multidose vial

Store in a refrigerator (2 to 8°C).

Do not freeze.

Keep vials in outer carton to protect from light.

#### After first use

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

### 6.5 Nature and contents of container

### Multidose vial

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

Not all pack sizes may be marketed.

## 6.6 Special precautions for disposal and other handling

### Administration

COVID-19 Vaccine AstraZeneca is a colourless to slightly brown, clear to slightly opaque solution. The vaccine should be inspected visually prior to administration and discarded if particulate matter or differences in the described appearance are observed. Do not shake the vial.

Each vaccine dose of 0.5 ml is withdrawn into a syringe for injection to be administered intramuscularly. Use a separate sterile needle and syringe for each individual. It is normal for liquid to remain in the vial after withdrawing the final dose.

The vaccine does not contain any preservative. Aseptic technique should be used for withdrawing the dose for administration.

After first dose withdrawal, use the vial as soon as practically possible and within 6 hours (stored at 2°C to 25°C). Discard any unused vaccine.

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

### Disposal

COVID-19 Vaccine AstraZeneca contains genetically modified organisms (GMOs). Any unused vaccine or waste material should be disposed of in accordance with local requirements. Spills should be disinfected with an appropriate antiviral disinfectant.

## 7. MARKETING AUTHORISATION HOLDER

Not applicable.

## 8. MARKETING AUTHORISATION NUMBER(S)

Not applicable.

9. DATE OF FIRST AUTHORISATION/RENEWAL OF THE AUTHORISATION

Not applicable.

10. DATE OF REVISION OF THE TEXT

DD/MM/YYYY



República Argentina - Poder Ejecutivo Nacional  
2020 - Año del General Manuel Belgrano

**Hoja Adicional de Firmas**  
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**Número:**

**Referencia:** PROSPECTO PARA PRESCRIBIR

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Package leaflet: Information for the recipient

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

This medicinal product has been given authorisation for temporary supply by the UK

Department of Health and Social Care and the Medicines & Healthcare products Regulatory

Agency. It does not have a marketing authorisation, but this temporary authorisation grants permission for the medicine to be used for active immunisation of individuals aged 18 years and older for the prevention of coronavirus disease 2019 (COVID-19).

#### Reporting of side effects

As with any new medicine in the UK this product will be closely monitored to 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 receive 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 a vaccine used to protect people aged 18 years and older against COVID-19.

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

COVID-19 Vaccine AstraZeneca stimulates the body's natural defences (immune system). It causes the body to produce its own protection (antibodies) against the virus. This will help to protect you against COVID-19 in the future. None of the ingredients in this vaccine can cause COVID-19.

## 2. What you need to know before you receive COVID-19 Vaccine AstraZeneca

Do not have the vaccine:

- If you have ever had a severe allergic reaction to any of the active substances or any of the other ingredients listed in section 6. Signs of an allergic reaction may include itchy skin rash, shortness of breath and swelling of the face or tongue. Contact your doctor or healthcare professional immediately or go to the nearest hospital emergency room right away if you have an allergic reaction. It can be life-threatening.

If you are not sure, talk to your doctor, pharmacist or nurse.

Warnings and precautions

Tell your doctor, pharmacist or nurse before vaccination:

- If you have ever had a severe allergic reaction (anaphylaxis) after any other vaccine injection;  If you currently have a severe infection with a high temperature (over 38°C).  
However, a mild fever or infection, like a cold, are not reasons to delay vaccination;
- If you have a problem with bleeding or bruising, or if you are taking a blood thinning medicine (anticoagulant);
- 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, COVID-19 Vaccine AstraZeneca may not protect everyone who is vaccinated from COVID-19. It is not yet known how long people who receive the vaccine will be protected for. No data are currently available in individuals with a weakened immune system or who are taking chronic treatment that suppresses or prevents immune responses.

Children and adolescents

No data are currently 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, tell your doctor, pharmacist or nurse. There are limited data on the use of COVID-19 Vaccine AstraZeneca in pregnant or breastfeeding women. Your doctor, pharmacist or nurse will discuss with you whether you can be given the vaccine.

#### Driving and using machines

COVID-19 Vaccine AstraZeneca has no known effect on the ability to drive and use machines. However, side effects listed in section 4 may impact your ability to drive and use machines. If you feel unwell, do not drive or use machines.

#### COVID-19 Vaccine AstraZeneca contains sodium and alcohol (ethanol)

This medicine contains less than 1 mmol sodium (23 mg) per dose of 0.5 ml. This means that it is essentially 'sodium-free'.

This medicine contains a very small amount of alcohol (0.002 mg of alcohol (ethanol) per dose of 0.5 ml). This is not enough to cause any noticeable effects.

### 3. How COVID-19 Vaccine AstraZeneca is given

COVID-19 Vaccine AstraZeneca is injected into a muscle (usually in the upper arm).

You will receive 2 injections. You will be told when you need to return for your second injection of COVID-19 Vaccine AstraZeneca.

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

When COVID-19 Vaccine AstraZeneca is given for the first injection, COVID-19 Vaccine AstraZeneca (and not another vaccine against COVID-19) should be given for the second injection to complete vaccination course.

#### If you miss your second injection

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.

#### 4. Possible side effects

Like all medicines, this vaccine can cause side effects, although not everybody gets them. In clinical studies with the vaccine, most side effects were mild to moderate in nature and resolved within a few days with some still present a week after vaccination.

If side effects such as pain and/or fever are troublesome, medicines containing paracetamol can be taken.

Side effects that occurred during clinical trials with COVID-19 Vaccine AstraZeneca were as follows:

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

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

##### Common (may affect up to 1 in 10 people)

- a lump at the injection site
- fever
- being sick (vomiting)
- flu-like symptoms, such as high temperature, sore throat, runny nose, cough and chills

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

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

In clinical trials there were very rare reports of events associated with inflammation of the nervous system, which may cause numbness, pins and needles, and/or loss of feeling. However, it is not confirmed whether these events were due to the vaccine.

If you notice any side effects not mentioned in this leaflet, please inform your doctor, pharmacist or nurse.

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.

If you are concerned about a side-effect it can be reported directly via the Coronavirus Yellow Card reporting site <https://coronavirus-yellowcard.mhra.gov.uk/> or search for MHRA Yellow Card in the Google Play or Apple App Store and include the vaccine brand and batch/Lot number if available. By reporting side effects you can help provide more information on the safety of this vaccine.

## 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.

### Storage

Do not use COVID-19 Vaccine AstraZeneca after the expiry date which is stated on the carton. The expiry date refers to the last day of that month.

Store in a refrigerator (2°C to 8°C).

Do not freeze.

Keep vials in outer carton to protect from light.

The vaccine does not contain any preservative and should be administered by a healthcare professional. After the first dose is withdrawn, the vaccine should be used as soon as practically possible and within 6 hours. During use it can be stored from 2°C to 25°C.

### Disposal

COVID-19 Vaccine AstraZeneca contains genetically modified organisms (GMOs). Any unused vaccine or waste material should be disposed of in accordance with local requirements. Spills should be disinfected with an appropriate antiviral disinfectant.

## 6. Contents of the pack and other information

What COVID-19 Vaccine AstraZeneca

contains One dose (0.5 ml) contains:

COVID-19 Vaccine (ChAdOx1-S\* recombinant) 5 ×  
10<sup>10</sup> viral particles

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

This product contains genetically modified organisms (GMOs).

The other excipients are L-histidine, L-histidine hydrochloride monohydrate, magnesium chloride hexahydrate, polysorbate 80, ethanol, sucrose, sodium chloride, disodium edetate dihydrate, water for injections.

What COVID-19 Vaccine AstraZeneca looks like and contents of the pack  
Solution for injection. The solution is colourless to slightly brown, clear to slightly opaque and particle free.

Pack sizes (not all pack sizes may be marketed):

- 10 dose vial (5 ml) in packs of 10 vials.
- 8 dose vial (4 ml) in packs of 10 vials.

Manufacturer  
MedImmune UK Ltd  
6 Renaissance Way  
Liverpool, L24 9JW  
United Kingdom

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

For any information about this medicine, please contact:  
AstraZeneca UK Ltd  
Tel: 08000541028

This leaflet was last revised in

Other sources of information



[www.azcovid-19.com](http://www.azcovid-19.com)



República Argentina - Poder Ejecutivo Nacional  
2020 - Año del General Manuel Belgrano

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**Número:**

**Referencia:** FOLLETO PARA EL PACIENTE

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Date: 2020.12.30 09:27:49 -03:00

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**Referencia:** certificado 2002-532-20-1

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