PACKAGE LEAFLET

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

This medicinal product is under the conditional approval of modern medicine for human use in emergency situation during a pandemic crisis.

The prescribed physician is required to report any adverse reactions to the Food and Drug Administration.

Please read the information carefully.

COVID-19 Vaccine AstraZeneca

1. NAME OF THE MEDICINAL PRODUCT

COVID-19 Vaccine AstraZeneca

2. QUALITATIVE AND QUANTITATIVE COMPOSITION

One dose (0.5 ml) contains:

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

4. CLINICAL PARTICULARS

4.1 Therapeutic indications

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

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 Pharmacodynamic properties).

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 Special warnings and special precautions for use).

Elderly population
Efficacy and safety data are currently limited in individuals ≥65 years of age (see sections 4.8 Undesirable effects and 5.1 Pharmacodynamic properties). 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 Special precautions for disposal and other handling.

4.3 Contraindications
Do not use COVID-19 Vaccine AstraZeneca in individuals who have hypersensitivity to the active substance or to any of the excipients. (Please see section 2 QUALITATIVE AND QUANTITATIVE COMPOSITION and 6.1 List of excipients).

4.4 Special warnings and special 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
According to good medical practices, the individuals should be interviewed and reviewed all past history (especially the previous immunization and the potential of adverse reactions) before vaccination.

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 Pharmacodynamic properties).

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.

Breast feeding

It is unknown whether COVID-19 Vaccine AstraZeneca is excreted in human milk.

Administration of COVID-19 Vaccine AstraZeneca in breast feeding should only be considered when the potential benefits outweigh any potential risks for the mother and infant.

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 ≥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). 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[a]
Metabolism and nutrition disorders	Uncommon	Decreased appetite[a]
Nervous system disorders	Very common	Headache
	Uncommon	Dizziness[a]
Gastrointestinal disorders	Very common	Nausea
	Common	Vomiting
	Uncommon	Abdominal pain[a]
Skin and subcutaneous tissue disorders	Uncommon	Hyperhidrosis[a], pruritus[a], rash[a]
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[b], fatigue, malaise, pyrexia[c], chills
	Common	Injection site induration, influenza-like illness[a]

[a] Unsolicited adverse reaction

[b] Injection site bruising includes injection site haematoma (uncommon, unsolicited adverse reaction)

[c] Pyrexia includes feverishness (very common) and fever ≥38°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.

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 neutralizing 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 ≥18 years of age (including the elderly) in the UK; a Phase III Study, COV003, in adults ≥18 years of age (including the elderly) in Brazil; and a Phase I/II study, COV005, in adults aged 18 to 65 years of age in South Africa. The studies excluded participants with history of anaphylaxis or angioedema; participants with severe and/or uncontrolled cardiovascular, gastrointestinal, liver, renal, endocrine/metabolic disease, and neurological illnesses; as well as those with severe immunosuppression. In studies COV001 and COV002, licensed seasonal influenza and pneumococcal vaccinations were permitted (at least 7 days before or after their study vaccine).

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

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

In the pooled analysis for efficacy (COV002 and COV003), participants ≥18 years of age 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 ≥30 kg/m^2, cardiovascular disorder, respiratory disease or diabetes). The median follow up time post-dose 1 and post-dose 2 was 132 days and 63 days, respectively.

Final determination of COVID-19 cases were made by an adjudication committee, who also assigned disease severity according to the WHO clinical progression scale. A total of 131 participants had SARS-CoV-2 virologically confirmed (by nucleic acid amplification tests) COVID-19 occurring ≥15 days post-dose 2 with at least one COVID-19 symptom (objective fever (defined as ≥37.8°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)	**5807**		**5829**		
COVID-19 cases		30 (0.52)		101 (1.73)	70.42 (58.84, 80.63)[a]
Hospitalisations[b]		0		5 (0.09)	-
Severe disease[c]		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)[d]
Hospitalisations after dose 1[b]		2 (0.02)[e]		16 (0.16)	-
Severe disease after dose 1[c]		0		2 (0.02)	

N = Number of subjects included in each group; n = Number of subjects having a confirmed event; CI = Confidence Interval; [a] 95.84% CI; [b] WHO severity grading ≥4; [c] WHO severity grading ≥6; [d] 95% CI; [e] 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 ≥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 ≥4 fold increase from baseline in S-binding antibodies) was demonstrated in ≥98% of participants at 28 days after the first dose and >99% at 28 days after the second. Higher S-binding antibodies were observed with increasing dose interval (Table 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 (SDSD)[a,b]

Population	Baseline	28 days after dose 1	28 days after dose 2
	GMT (95% CI)	GMT (95% CI)	GMT (95% CI)
Overall	(N=882) 57.18 (52.8, 62.0)	(N=817) 8,386.46 (7,758.6, 9,065.1)	(N=819) 29,034.74 (27,118.2, 31,086.7)

Population	Baseline	28 days after dose 1	28 days after dose 2
	GMT (95% CI)	**GMT (95% CI)**	**GMT (95% CI)**
Dose Interval			
<6 weeks	(N=481) 60.51 (54.1, 67.7)	(N=479) 8734.08 (7883.1, 9676.9)	((N=443) 22222.73 (20360.50, 24,255.3)
6-8 weeks	(N=137) 58.02 (46.3, 72.6)	(N=99) 7295.54 (5857.4, 9086.7)	(N=116) 24363.10 (20088.5, 29547.3)
9-11 weeks	(N=110) 48.79 (39.6, 60.1)	(N=87) 7492.98 (5885.1, 9540.2)	(N=106) 34754.10 (30287.2, 39879.8)
≥12 weeks	(N=154) 52.98 (44.4, 63.2)	(N=152) 8618.17 (7195.4, 10322.3)	(N=154) 63181.59 (55180.1, 72343.4)

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

[a] Immune response evaluated using a multiplex immunoassay;

[b] in 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 do 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

Please see expiry date on the outer carton.

After first use

Use as soon as practically possible and within 6 hours.

The vaccine may be stored between 2℃ and 25℃ during the in-use period.

6.4 Special precautions for storage

Unopened multidose vial

Store in a refrigerator (2 to 8℃).

Do not freeze.

Keep vial in outer carton to protect from light.

After first use

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

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 an aluminium overseal with a plastic flip-off cap. Packs of 10 vials.

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 (store 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 AUTHORIZATION HOLDER

AstraZeneca (Thailand) Limited., Bangkok, Thailand.

8. MARKETING AUTHORIZATION NUMBER

1C 1/64 (NBC)

9. DATE OF AUTHORIZATION

20 January 2021

10. DATE OF REVISION OF THE TEXT

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LABELLING INFORMATION

EU PACK	KOREAN PACK	THAI PACK

COVID-19 Vaccine AstraZeneca

Solution for Injection

5 mL Vial

Each dose (0.5 mL) contains:-
COVID-19 Vaccine (ChAdOx1-S recombinant) 5×10^{10} viral particles (vp)

10 multidose vials
(10 doses per vial - 0.5 ml per dose)

ยาควบคุมพิเศษ

Reg. No. 1C 1/64 (NBC)

MFG.

EU PACK	KOREAN PACK	THAI PACK
PC 05000456064286 SN ############### LOT ABV#### EXP MM-YYYY	제조번호/LOT CTMAV### 유효기한/EXP YYYY.MM.DD (01)/PC 08806507011325 (21)/SN ###############	LOT A###### EXP MM YYYY MAN MM YYYY GTIN 0885########## SN ###############
Manufactured by: Catalent Anagni S.R.L. Località Fontana del Ceraso, S.P. Casilina, 4103012 Anagni (FR), Italy.	**Manufactured and Batch released by:** SK Bioscience Co Limited (No.97) 150, Saneopdanji-gil, Pungsan-eup, Andong-si, Gyeongsangbuk-do, Republic of Korea.	**Manufactured and Batch released by:** Siam Bioscience Co., Ltd. 99 Moo 4, Banmai, Bangyai, Nonthaburi 11140 Thailand.
Batch released by: **MedImmune Pharma BV** Lagelandseweg 78, 6545 CG Nijmegen, The Netherlands.		
Imported by: AstraZeneca (Thailand) Ltd., Bangkok, Thailand.		