▼This vaccine is subject to additional monitoring in Australia. This will allow quick identification of new safety information. Healthcare professionals are asked to report any suspected adverse events at www.tga.gov.au/reporting-problems.

AUSTRALIAN PRODUCT INFORMATION

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

1 NAME OF THE MEDICINE

ChAdOx1-S (provisional ABN)

2 QUALITATIVE AND QUANTITATIVE COMPOSITION

One dose (0.5 mL) contains $5x10^{10}$ viral particles (vp) of ChAdOx1-S [a, b].

[a] Recombinant, replication-deficient chimpanzee adenovirus vector encoding the SARS-CoV-2 Spike (S) glycoprotein (GP)

[b] The vaccine is manufactured using material originally sourced from a human embryo (Human Embryonic Kidney cells: HEK293)

There are two multi-dose vial presentations:

- 8 dose: $4x10^{11}$ vp of ChAdOx1-S in 4 mL.
- 10 dose: $5x10^{11}$ vp of ChAdOx1-S in 5 mL.

This product contains genetically modified organisms (GMOs).

For the full list of excipients, see Section 6.1 List of excipients.

3 PHARMACEUTICAL FORM

Solution for injection.

Clear to slightly opaque, colourless to slightly brown, particle free with a pH of 6.1 – 7.1.

4 CLINICAL PARTICULARS

4.1 THERAPEUTIC INDICATIONS

COVID-19 Vaccine AstraZeneca has **provisional approval** for the indication:

Active immunisation of individuals ≥18 years old for the prevention of coronavirus disease 2019 (COVID-19) caused by SARS-CoV-2.

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

The decision has been made on the basis of short term efficacy and safety data. Continued approval is dependent upon the evidence of longer-term efficacy and safety from ongoing clinical trials and post-market assessment.

4.2 DOSE AND METHOD OF ADMINISTRATION

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 precautions for use).

Special patient populations

Use in the elderly

No dosage adjustment is required in elderly individuals ≥65 years of age (see Section 4.4 Special warnings and precautions for use).

Paediatric use

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.

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

COVID-19 Vaccine AstraZeneca is a colourless to slightly brown, clear to slightly opaque solution. The vaccine should be inspected visually for particulate matter and discolouration prior to administration. Discard the vial if the solution is discoloured or visible particles are observed. Do not shake.

Using an aseptic technique, 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.

Each vial contains at least the number of doses stated. It is normal for liquid to remain in the vial after withdrawing the final dose. When low dead volume syringes and/or needles are used, the amount remaining in the vial may be sufficient for an additional dose. Care should be taken to ensure a full 0.5 mL dose is administered. Where a full 0.5 mL dose cannot be extracted, the remaining volume should be discarded. Do not pool excess vaccine from multiple vials.

The vaccine does not contain any preservative. After first opening, use the vial within:

- 6 hours when stored at room temperature (up to 30ºC), or
- 48 hours when stored in a refrigerator (2ºC to 8ºC).

The vial can be re-refrigerated, but after first opening the cumulative storage time at room temperature must not exceed 6 hours, and the total cumulative storage time must not exceed 48 hours. After this time, the vial must be discarded.

There is limited information available in relation to the storage of the vaccine in syringes. For practical reasons, if the contents of the vial are to be used within a short period of time, drawing up the content in multiple syringes at once may be considered. Vaccine in syringes may be kept for up to 6 hours when stored at room temperature (up to 30˚C). However, ensure that the cumulative storage time at room temperature from the first vial puncture to last dose administration does not exceed 6 hours. After this time, the syringe must be discarded. For more details in relation to administration, please refer to Department of Health Guidance Documents.

The vials, needles, syringes should be disposed of in the clinical waste bin (see Section 6.6 Special precautions for disposal).

4.3 CONTRAINDICATIONS

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

4.4 SPECIAL WARNINGS AND PRECAUTIONS FOR USE

As with any vaccine, vaccination with COVID-19 Vaccine AstraZeneca may not protect all vaccine recipients. Vaccination does not mitigate the need to follow other official recommendations to prevent the spread of COVID-19.

Hypersensitivity including anaphylaxis

Hypersensitivity reactions including anaphylaxis and angioedema have occurred following administration of COVID-19 Vaccine AstraZeneca.

Appropriate medical treatment and supervision should always be readily available in case of an anaphylactic event following the administration of the vaccine.

A second dose of the vaccine should not be given to those who have experienced a severe hypersensitivity reaction to the first dose of COVID-19 Vaccine AstraZeneca.

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.

Thrombosis and Thrombocytopenia

Very rare events of serious thrombosis with thrombocytopenia, including unusual sites such as cerebral venous sinus thrombosis and splanchnic vein thrombosis, some associated with arterial thrombosis, have been observed following vaccination with COVID-19 Vaccine AstraZeneca during post authorisation use. The majority of the events occurred within the first 14 days following vaccination and some events had a fatal outcome.

Healthcare professionals should be alert to the signs and symptoms of thromboembolism and thrombocytopenia as well as coagulopathies. Vaccinated individuals should be instructed to seek immediate medical attention if they develop symptoms such as a severe or persistent headache, blurred vision, shortness of breath, chest pain, leg swelling, persistent abdominal pain or unusual skin bruising and/or petechia a few days after vaccination.

Risk of bleeding with intramuscular administration

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.

Neurological events

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

As with other vaccines, the benefits and potential risks of vaccinating individuals with COVID-19 Vaccine AstraZeneca should be considered.

Immunocompromised individuals

The immunogenicity, efficacy and safety of COVID-19 Vaccine AstraZeneca has not been assessed in immunocompromised individuals, including those receiving immunosuppressive therapy. The immunogenicity of vaccines may be lower in immunosuppressed patients.

Duration of protection

The duration of protection has not yet been established. Studies are ongoing.

Interchangeability

There are no safety, immunogenicity or efficacy data to support interchangeability of COVID-19 Vaccine AstraZeneca with other COVID-19 vaccines.

Use in the elderly

There are currently limited data available for the efficacy and safety in individuals over 65 years of age. Further information will be collected from ongoing clinical studies and post-market monitoring. The decision to immunise an elderly patient should be decided on a case-by-case basis with consideration of age, co-morbidities, their environment, potential benefits and potential risks.

Use in individuals with significant co-morbidities

There are currently limited data available for the efficacy and safety in individuals with significant co-morbidities. The decision to immunise an individual should be made on the basis of potential benefits over risks to that individual.

Paediatric use

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.

Effects on laboratory tests

Vaccination with COVID-19 Vaccine AstraZeneca leads to the development of antibodies to the SARS-CoV-2 S protein. This does not interfere with results from SARS-CoV-2 PCR testing.

4.5 INTERACTIONS WITH OTHER MEDICINES AND OTHER FORMS OF INTERACTIONS

The safety, immunogenicity and efficacy of co-administration of COVID-19 Vaccine AstraZeneca with other vaccines have not been evaluated.

4.6 FERTILITY, PREGNANCY AND LACTATION

Effects on fertility

It is unknown whether COVID-19 Vaccine AstraZeneca may impact fertility. No data are available.

Use in pregnancy – Category B2

There are a limited amount of data from the use of COVID-19 Vaccine AstraZeneca in pregnant women, or women who became pregnant after receiving the vaccine. The data are insufficient to inform on vaccine-associated risk.

Animal reproductive toxicity studies have not been completed.

As a precautionary measure, vaccination with COVID-19 Vaccine AstraZeneca is not recommended during pregnancy. Use of COVID-19 Vaccine AstraZeneca in pregnant women should be based on an assessment of whether the benefits of vaccination outweigh the potential risks.

Use in lactation

There are no or limited data from the use of COVID-19 Vaccine AstraZeneca in lactating women. A risk to breastfed newborns/infants cannot be excluded.

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 Adverse effects (Undesirable effects) may temporarily affect the ability to drive or use machines.

4.8 ADVERSE EFFECTS (UNDESIRABLE EFFECTS)

Clinical trials

Overall summary of the safety profile

The overall safety of COVID-19 Vaccine AstraZeneca is based on an interim analysis (data lock: 4 November 2020) 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.

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.

Following vaccination, recipients may experience multiple adverse reactions occurring at the same time (for example, myalgia/arthralgia, headache, chills, pyrexia and malaise). If a recipient reports persistent symptoms, alternative causes should be considered.

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).

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

Safety in subgroups including the frail elderly, immunosuppressed, and pregnancy is unknown due to the low number of representative participants from these groups. Further information will become available from ongoing clinical studies and pharmacovigilance programmes.

Adverse drug 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 (ADR) interim analysis – pooled data set (safety analysis set[a])

MedDRA SOC	Adverse reaction[b]	COVID-19 Vaccine AstraZeneca (N= 10, 069)	Control[c] (N= 9, 902)
Nervous system disorders	Headache	Very common (52.6%)	Very common (39.0%)
Gastrointestinal disorders	Nausea	Very common (21.9%)	Very common (13.1%)
Musculoskeletal and connective tissue disorders	Muscle pain (Myalgia)	Very common (44.0%)	Very common (21.6%)
	Joint pain (Arthralgia)	Very common (26.4%)	Very common (12.4%)
General disorders and administration site conditions	**Local**		
	Injection site tenderness	Very common (63.7%)	Very common (39.5%)
	Injection site pain	Very common (54.2%)	Very common (36.7%)
	Injection site warmth	Very common (17.7%)	Very common (14.5%)
	Injection site itch (Injection site pruritus)	Very common (12.7%)	Common (7.5%)
	Injection site swelling	Common (3.4%)	Common (1.6%)
	Injection site redness (Injection site erythema)	Common (3.1%)	Common (1.4%)
	Systemic		
	Fatigue	Very common (53.1%)	Very common (38.2%)
	Malaise	Very common (44.2%)	Very common (20.2%)
	Feverishness[d] (Pyrexia)	Very common (33.6%)	Very common (10.7%)
	Chills	Very common (31.9%)	Common (8.3%)
	Fever[d] (Pyrexia)	Common (7.9%)	Common (1.2%)

[a] Frequencies of ADRs are reported from the safety analysis set where participants received the recommended dose (5×10^{10} vp) as their first dose.

[b] Solicited event reporting terms, where applicable MedDRA preferred terms are given in parentheses

[c] Control was either meningococcal vaccine or saline solution

[d] Defined as: Feverishness, (subjective) a self-reported feeling of having a fever; Fever, (objective) ≥38°C

The following table provides new ADR reported from the primary analysis of the pooled data from the four clinical trials (data lock: 7 December 2020; medium duration of follow-up of 4.5 months).

Table 2 New Adverse Drug Reactions (ADR) from the primary analysis – pooled data set (safety analysis set[a])

MedDRA SOC	Adverse reaction[b]	COVID-19 Vaccine AstraZeneca	Control [c]
Blood and lymphatic system disorders	Lymphadenopathy[d]	Uncommon	Uncommon
Nervous system disorders	Dizziness[d]	Uncommon	Uncommon
	Somnolence[d]	Uncommon	Uncommon
Gastrointestinal disorders	Vomiting	Common	Uncommon

MedDRA SOC	Adverse reaction[b]	COVID-19 Vaccine AstraZeneca	Control [c]
	Diarrhoea[d]	Common	Common
	Abdominal pain[d]	Uncommon	Uncommon
Skin and subcutaneous tissue disorders	Hyperhidrosis[d]	Uncommon	Uncommon
	Pruritus[d]	Uncommon	Uncommon
	Rash[d]	Uncommon	Uncommon
	Urticaria[d]	Uncommon	Uncommon
Musculoskeletal and connective tissue disorders	Pain in extremity[d]	Common	Uncommon
General disorders and administration site conditions	**Systemic**		
	Influenza-like illness[d]	Common	Uncommon

[a] Frequencies of ADRs are reported from the safety analysis set where participants received the recommended dose (5×10^{10} vp) as their first dose.

[b] Solicited event reporting terms, where applicable MedDRA preferred terms are given in parentheses

[c] Control was either meningococcal vaccine or saline solution

[d] Unsolicited adverse reactions

Post-marketing experience

The following adverse reactions were not observed during clinical trials and have been spontaneously reported during worldwide post-authorisation use of COVID-19 Vaccine AstraZeneca. The frequency of these adverse reactions is 'not known' (cannot be estimated from available data as the reports come from a population of unknown size).

Immune system disorders: Anaphylactic reaction

Skin and subcutaneous tissue disorders: Angioedema

Blood and lymphatic system disorders: Thrombosis and thrombocytopenia

Reporting suspected adverse effects

Reporting suspected adverse reactions after registration 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 at www.tga.gov.au/reporting-problems.

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.

For information on the management of overdose, contact the Poison Information Centre on 131126 (Australia).

5 PHARMACOLOGICAL PROPERTIES

5.1 PHARMACODYNAMIC PROPERTIES

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 trials

This section will be updated as evidence emerges from ongoing clinical studies.

Interim analysis of pooled data from COV001, COV002, COV003, and COV005

The efficacy and safety of COVID-19 Vaccine AstraZeneca has been evaluated based on an interim analysis (data lock: 4 November 2020) of pooled data from four on-going randomised, blinded, controlled trials: a Phase I/II Study, COV001 (NCT04324606), in healthy adults 18 to 55 years of age in the UK; a Phase II/III Study, COV002 (NCT04400838), in adults ≥18 years of age (including the elderly) in the UK; a Phase III Study, COV003 (ISRCTN89951424), in adults ≥18 years of age (including the elderly) in Brazil; and a Phase I/II study, COV005 (NCT04444674), in adults aged 18 to 65 years of age in South Africa. 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. 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. These studies are ongoing.

The interim efficacy analysis was based upon the results of COV002 and COV003, as at that time studies COV001 and COV005 had <5 virologically confirmed COVID-19 cases per study and therefore did not meet the predefined statistical threshold to be included in the efficacy analysis.

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). Participants randomised to COVID-19 Vaccine AstraZeneca received either two standard doses [SD] (5×10^{10} vp per dose) or one low dose [LD] (2.2×10^{10} vp) followed by one SD (5×10^{10}vp), administered via IM injection.

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. In the pooled analysis, 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 mild comorbidity (defined as a BMI ≥30 Kg/m^2, cardiovascular disorder, respiratory disease or diabetes). At the time of interim analysis the median follow up time post-dose 1 was 4.7 months and post-dose 2 was 2.2 months.

The primary efficacy endpoint was symptomatic COVID-19 infection, defined as objective fever (≥37.8°C), cough, shortness of breath, anosmia, or ageusia with virologically confirmed COVID-19 occurring ≥15 days post second dose, in participants without serological evidence of previous SARS-CoV-2 infection. 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 met the primary efficacy endpoint criteria. COVID-19 Vaccine AstraZeneca significantly decreased the incidence of COVID-19 compared to control (see Table 3).

Table 3 COVID-19 Vaccine AstraZeneca efficacy against COVID-19

Population	COVID-19 Vaccine AstraZeneca		Control		Vaccine efficacy % (95.84% CI)
	N	Number of COVID-19 cases, n (%)	N	Number of COVID-19 cases, n (%)	
Primary analysis population					
Participants who had 2 doses of COVID-19 AstraZeneca & were seronegative at baseline & followed ≥15 days after the 2nd dose [a]	5807	30 (0.52)	5829	101 (1.73)	70.42 (54.84, 80.63)
Licensing regimen					
Participants who had 2 doses of the standard dose & were followed for ≥15 days after the 2nd dose.	4440	27 (0.61)	4455	71 (1.59)	62.10 (39.96, 76.08)

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

[a] some of the participants in this group received an initial LD. These were included in the primary analysis as the immune response in this group was similar to that in the SD and efficacy would therefore be expected to be the same. However, when this subgroup was analysed, the efficacy was greater. There are many factors other than having a LD that may have influenced the results (including lower age, longer duration between doses), thus the use of a LD will not be considered further for regulatory purposes. Two doses of vaccine are required.

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]).

An exploratory analyses of the impact of duration between doses and efficacy demonstrated greater efficacy with increasing duration between vaccine doses (Table 4). This was supported by the immunogenicity data (see Immunogenicity Table 5).

Table 4 Vaccine efficacy for incidence of first SARS-CoV-2 virologically confirmed symptomatic COVID-19 occurring ≥15 days post second dose by dose interval (SDSD seronegative for efficacy analysis set)

Dose interval	Participants with events, n (%)				Vaccine efficacy (%)	95% CI (%)
	N	COVID-19 Vaccine AstraZeneca n (%)	N	Control n (%)		
< 6 weeks	1702	9 (0.53)	1698	19 (1.12)	53.28	(-3.21, 78.86)
6–8 weeks	562	5 (0.88)	521	9 (1.73)	51.08	(-45.57, 83.56)

Dose interval	Participants with events, n (%)				Vaccine efficacy (%)	95% CI (%)
	N	COVID-19 Vaccine AstraZeneca n (%)	N	Control n (%)		
9–11 weeks	1056	9 (0.85)	1110	24 (2.16)	60.55	(15.23, 81.64)
≥12 weeks	1120	4 (0.36)	1126	19 (1.69)	78.79	(37.63, 92.79)

Vaccine efficacy (VE) of COVID-19 Vaccine AstraZeneca versus control, the 95% CI and p value were estimated based on Poisson regression with robust variance including the term of treatment as well as the log of the follow-up time as an offset.

VE is defined as 1-(incidence from the COVID-19 Vaccine AstraZeneca arm / incidence from the control arm) expressed as a percentage, where the risk ratio is derived from Poisson regression with robust variance. The 95% CI for the VE is obtained by taking 1 minus the 95% CI of the risk ratio derived from the model.

The observation period for the endpoint was 15 days post second dose up to 1 year in study.

COVID-19 endpoints were based on adjudicated events.

COVID-19 Vaccine AstraZeneca reduced COVID-19 hospitalisation (WHO Severity grading ≥4). In all participants who received SD as a first dose, as from 22 days post dose 1, there were 0 (0.0%, N=6,307) cases of COVID-19 hospitalisation in participants who received COVID-19 Vaccine AstraZeneca (N=6,307), as compared to 9 (0.14%, N=6,297) reported for control.

Participants who had one or more mild 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 in the subgroup of participants ≥65 years old were too few to draw conclusions on efficacy. In this sub-population, efficacy has been inferred from immunogenicity data and efficacy demonstrated in the general population.

Limited data are available on the impact of emerging SARS-CoV-2 variants of concern on vaccine efficacy. Further information will be collected throughout the AZD1222 clinical development program by clinical and surveillance virology monitoring.

Immunogenicity

Interim analysis of pooled data from COV001, COV002, COV003, and COV005

An immunological correlate of protection has not been established; therefore the level of immune response that provides protection against COVID-19 is unknown.

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 (see Table 5).

Generally similar trends were observed between analyses of neutralising antibodies and S-binding antibodies.

Table 5 SARS-CoV-2 S-binding antibody response to COVID-19 Vaccine AstraZeneca (SDSD)[a]

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) 8386.46 (7758.6, 9065.1)	(N=819) 29034.74 (27118.2, 31086.7)
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, 24255.3)
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

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 SD (97.8% [N=136, 95% CI: 93.7; 99.5]) and the second SD (100.0% [N=111, 95% CI: 96.7; NE]). The increase in S-binding antibodies was numerically lower for participants ≥65 years old (28 days after second SD: Geometric mean titre (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 SD: 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 numerically 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-ɣ enzyme-linked immunospot (ELISpot) assay are induced 14 days 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

Toxicity and local tolerance studies

Non-clinical data obtained from toxicology and local tolerance studies with investigational vaccines utilising the same ChAdOx1 adenoviral vector vaccine technology as COVID-19 Vaccine AstraZeneca, concluded that the ChAdOx1 technology was well tolerated in mice and was not associated with any adverse effects.

Genotoxicity

COVID-19 Vaccine AstraZeneca is a vaccine, as such, genotoxicity (mutagenicity) studies have not been conducted.

Carcinogenicity

COVID-19 Vaccine AstraZeneca is a vaccine, as such, carcinogenicity studies have not been conducted.

6 PHARMACEUTICAL PARTICULARS

6.1 LIST OF EXCIPIENTS

COVID-19 Vaccine AstraZeneca contains the excipients histidine, histidine hydrochloride monohydrate, sodium chloride, magnesium chloride hexahydrate, disodium edetate (EDTA), sucrose, ethanol absolute, polysorbate 80 and water for injections.

COVID-19 Vaccine AstraZeneca does not contain any preservatives and the vial stopper is not made with natural rubber latex.

6.2 INCOMPATIBILITIES

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

6.3 SHELF LIFE

In Australia, information on the shelf life can be found on the public summary of the Australian Register of Therapeutic Goods (ARTG). The expiry date can be found on the packaging.

6.4 SPECIAL PRECAUTIONS FOR STORAGE

Unopened multidose vial

Store at 2°C to 8°C (Refrigerate. Do not freeze).

Store in outer carton in order to protect from light.

Opened multidose vial

After first opening, chemical and physical in-use stability has been demonstrated from the time of vial puncture to administration for no more than:

- 6 hours at room temperature up to 30°C, or
- 48 hours in a refrigerator (2°C to 8°C)

The vial can be re-refrigerated, but after first opening the cumulative storage time at room temperature must not exceed 6 hours, and the total cumulative storage time must not exceed 48 hours.

See Section 4.2 Dose and method of administration/Method of administration for details on the storage of the vaccine in syringes.

6.5 NATURE AND CONTENTS OF CONTAINER

- 4 mL of solution in a 8-dose vial (clear type I glass) with stopper (elastomeric with aluminium overseal). Packs of 10 multidose vials
- 5 mL of solution in a 10-dose vial (clear type I glass) with stopper (elastomeric with aluminium overseal). Packs of 10 multidose vials.

6.6 SPECIAL PRECAUTIONS FOR 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 in a clinical waste bin. Spills should be disinfected with an appropriate antiviral disinfectant.

6.7 PHYSICOCHEMICAL PROPERTIES

CAS number

2420395-83-9

7 MEDICINE SCHEDULE (POISONS STANDARD)

Prescription only medicine (Schedule 4)

8 SPONSOR

AstraZeneca Pty Ltd
ABN 54 009 682 311
66 Talavera Road
MACQUARIE PARK NSW 2113

For COVID-19 Vaccine AstraZeneca enquiries contact 1800 343 949 or visit azcovid-19.com

9 DATE OF FIRST APPROVAL

16 February 2021

10 DATE OF REVISION

8 April 2021

SUMMARY TABLE OF CHANGES

Section changed	Summary of new information
4.4	Inclusion of text relating to events of Thrombosis and Thrombocytopenia
4.8	Inclusion of text on Blood and lymphatic system disorders: Thrombosis and thrombocytopenia