SUMMARY OF PRODUCT CHARACTERISTICS
ChAdOx1 nCoV- 19 Corona Virus Vaccine (Recombinant)
COVISHIELD™

1 NAME OF THE MEDICINAL PRODUCT
COVISHIELD™
ChAdOx1 nCoV- 19 Corona Virus Vaccine (Recombinant)

2 QUALITATIVE AND QUANTITATIVE COMPOSITION
One dose (0.5 ml) contains:

ChAdOx1 nCoV- 19 Corona Virus Vaccine (Recombinant) \(5 \times 10^{10}\) 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.
Both COVISHIELD™ (manufactured by Serum Institute of India Pvt Ltd) and COVID-19 Vaccine AstraZeneca (manufactured by AstraZeneca) are ChAdOx1 nCoV- 19 Corona Virus Vaccines (Recombinant).

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

4.2 Posology and method of administration
Posology

COVISHIELD™ vaccination course consists of two separate doses of 0.5 ml each. The second dose should be administered between 4 to 6 weeks after the first dose. However, there is data available for administration of the second dose up to 12 weeks after the first dose from the overseas studies (see section 5.1).

It is recommended that individuals who receive a first dose of COVISHIELD™ complete the vaccination course with COVISHIELD™ (see section 4.4).
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Special populations

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 in elderly individuals $\geq 65$ years of age.

Paediatric population
The safety and efficacy of COVISHIELD™ in children and adolescents (aged $<18$ years old) have not yet been established. No data are available.

Method of administration
COVISHIELD™ 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 special precautions for use
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 COVISHIELD™ 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, COVISHIELD™ 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. Immunocompromised individuals may have relatively weaker immune response to the vaccine regimen.
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Duration and level of protection
The duration of protection has not yet been established.

As with any vaccine, vaccination with COVISHIELD™ may not protect all vaccine recipients (See section 5.1).

Interchangeability
No data are available on the use of ChAdOx1 nCoV-19 Corona Virus Vaccine (Recombinant) in persons that have previously received partial vaccine series with another COVID-19 vaccine.

4.5 Interaction with other medicinal products and other forms of interaction
No interaction studies have been performed.

Concomitant administration of COVISHIELD™ with other vaccines has not been studied (see section 5.1)

4.6 Fertility, pregnancy and lactation

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

Pregnancy
There is a limited experience with the use of ChAdOx1 nCoV-19 Corona Virus Vaccine (Recombinant) in pregnant women.

Preliminary animal studies do not indicate direct or indirect harmful effects with respect to pregnancy, embryofetal development, parturition or postnatal 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 COVISHIELD™ in pregnancy should only be considered when the potential benefits outweigh any potential risks for the mother and fetus.

Breastfeeding
It is unknown whether COVISHIELD™ is excreted in human milk.

4.7 Effects on ability to drive and use machines
ChAdOx1 nCoV-19 Corona Virus Vaccine (Recombinant) 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.
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4.8 Undesirable effects

Overall summary of the safety profile from the Overseas studies:

The overall safety of COVID-19 Vaccine AstraZeneca [ChAdOx1 nCoV-19 Corona Virus Vaccine (Recombinant)] 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.

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).
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Table 1 – Adverse drug reactions

<table>
<thead>
<tr>
<th>MedDRA SOC</th>
<th>Frequency</th>
<th>Adverse reactions</th>
</tr>
</thead>
<tbody>
<tr>
<td>Blood and lymphatic system disorders</td>
<td>Uncommon</td>
<td>Lymphadenopathy&lt;sup&gt;a&lt;/sup&gt;</td>
</tr>
<tr>
<td>Metabolism and nutrition disorders</td>
<td>Uncommon</td>
<td>Decreased appetite&lt;sup&gt;a&lt;/sup&gt;</td>
</tr>
<tr>
<td>Nervous system disorders</td>
<td>Very common</td>
<td>Headache</td>
</tr>
<tr>
<td></td>
<td>Uncommon</td>
<td>Dizziness&lt;sup&gt;a&lt;/sup&gt;</td>
</tr>
<tr>
<td>Gastrointestinal disorders</td>
<td>Very common</td>
<td>Nausea</td>
</tr>
<tr>
<td></td>
<td>Common</td>
<td>Vomiting</td>
</tr>
<tr>
<td></td>
<td>Uncommon</td>
<td>Abdominal pain&lt;sup&gt;a&lt;/sup&gt;</td>
</tr>
<tr>
<td>Skin and subcutaneous tissue disorders</td>
<td>Uncommon</td>
<td>Hyperhidrosis, pruritus, rash&lt;sup&gt;a&lt;/sup&gt;</td>
</tr>
<tr>
<td>Musculoskeletal and connective tissue disorders</td>
<td>Very common</td>
<td>Myalgia, arthralgia</td>
</tr>
<tr>
<td>General disorders and administration site conditions</td>
<td>Very common</td>
<td>Injection site tenderness, injection site pain, injection site warmth, injection site erythema, injection site swelling, injection site pruritus, injection site bruising&lt;sup&gt;b&lt;/sup&gt;, fatigue, malaise, pyrexia&lt;sup&gt;c&lt;/sup&gt;, chills</td>
</tr>
<tr>
<td></td>
<td>Common</td>
<td>Injection site induration, influenza like illness&lt;sup&gt;a&lt;/sup&gt;</td>
</tr>
</tbody>
</table>

<sup>a</sup> Unolicited 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 ≥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.

Overall summary of the safety profile from the Indian study:

COVISHIELD™ was also safe and well tolerated in the phase II/III clinical trial in India. An interim analysis included data of all 1600 participants who received first dose [1200 in COVISHIELD™ group, 100 in Oxford/AZ-ChAdOx1 nCoV-19 vaccine group and 300 in Placebo group]. This interim analysis includes data collected until 14 Dec 2020 of all 1600 participants who received first dose and 1577 participants who received second dose.
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Demographic characteristics were generally similar among participants across the three groups. Overall, among the participants who received COVISHIELD, 87.33% were aged 18 to 59 years and 12.67% were 60 years of age or older.

Overall, the incidence of solicited reactions (injection site reactions such as pain, tenderness, redness, warmth, itch, swelling and induration; and systemic reactions include fever, chills, fatigue, malaise, headache, arthralgia and myalgia), unsolicited adverse events and serious adverse events (SAEs) was comparable in the study and control groups. No causally related SAE was caused by the study vaccine.

**4.9 Overdose**

Experience of overdose is limited.

There is no specific treatment for an overdose with ChAdOx1 nCoV-19 Corona Virus Vaccine (Recombinant). 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**

**Mechanism of action**

**COVISHIELD™** 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.

**Efficacy and immunogenicity data from the Overseas studies:**

**Clinical efficacy**

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

COVID-19 Vaccine AstraZeneca [ChAdOx1 nCoV-19 Corona Virus Vaccine (Recombinant)] 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 (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 history of anaphylaxis or angioedema; 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 ≥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/m², cardiovascular disorder, respiratory disease or diabetes). At the time of interim analysis 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 second dose with at least one COVID-19 symptom (objective fever (defined as ≥37.8°C), cough, shortness of breath, anosmia, or ageusia) and were without evidence of previous SARS-CoV-2 infection. COVID-19 Vaccine AstraZeneca significantly decreased the incidence of COVID-19 compared to control (see Table 2a).

Table 2a – COVID-19 Vaccine AstraZeneca efficacy against COVID-19

<table>
<thead>
<tr>
<th>Population</th>
<th>COVID-19 Vaccine AstraZeneca</th>
<th>Control</th>
<th>Vaccine efficacy % (95.84% CI)</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>N</td>
<td>Number of COVID-19 casesb, n (%)</td>
<td>N</td>
</tr>
<tr>
<td>Primary (see above)</td>
<td>5807</td>
<td>30 (0.52)</td>
<td>5829</td>
</tr>
<tr>
<td>COVID-19 cases</td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>
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<table>
<thead>
<tr>
<th>Hospitalisations^b</th>
<th>0</th>
<th>5 (0.09)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Severe disease^c</td>
<td>0</td>
<td>1 (0.02)</td>
</tr>
<tr>
<td>Any dose</td>
<td>10,014</td>
<td>10,000</td>
</tr>
<tr>
<td>COVID-19 cases after dose 1</td>
<td>108 (1.08)</td>
<td>227 (2.27)</td>
</tr>
<tr>
<td>Hospitalisations after dose 1^b</td>
<td>2 (0.02)^c</td>
<td>16 (0.16)</td>
</tr>
<tr>
<td>Severe disease after dose 1^c</td>
<td>0</td>
<td>2 (0.02)</td>
</tr>
</tbody>
</table>

N = Number of subjects included in each group; n = Number of subjects having a confirmed event; CI = Confidence Interval; * This is a pooled data of LDSD + SDSD regimen with second dose given at dose intervals ranging from 4 to 12 weeks. LD = Low Dose, SD = Standard Dose.

^d 95.84% CI; ^b WHO severity grading ≥4; ^c WHO severity grading ≥6; ^d 95% CI; ^c Two cases of hospitalisation occurred on Days 1 and 10 post vaccination.

Table 2b – COVID-19 Vaccine AstraZeneca efficacy against COVID-19

<table>
<thead>
<tr>
<th>Population</th>
<th>COVID-19 Vaccine AstraZeneca</th>
<th>Control</th>
<th>Vaccine efficacy % (95.84% CI)</th>
</tr>
</thead>
<tbody>
<tr>
<td>N</td>
<td>Number of COVID-19 cases, n (%)</td>
<td>N</td>
<td>Number of COVID-19 cases, n (%)</td>
</tr>
<tr>
<td>Primary analysis population</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Overall (SDSD + LDSD)</td>
<td>5807</td>
<td>30 (0.52)</td>
<td>5829</td>
</tr>
<tr>
<td>Licensing regimen</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>SDSD</td>
<td>4440</td>
<td>27 (0.61)</td>
<td>4455</td>
</tr>
<tr>
<td>Exploratory analysis</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>LDSD</td>
<td>1367</td>
<td>3 (0.22)</td>
<td>1374</td>
</tr>
</tbody>
</table>

N = Number of subjects included in each group; n = Number of subjects having a confirmed event; CI = Confidence Interval; LD = Low dose; SD = Standard dose

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**Table 2c - COVID-19 Vaccine AstraZeneca efficacy against COVID-19 by Dose Interval (SDSD)**

<table>
<thead>
<tr>
<th>Dose interval</th>
<th>Participants with events, n (%)</th>
<th>Vaccine efficacy</th>
<th>95% CI (%)</th>
<th>P-value</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>AZD1222 n / N (%)</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>&lt; 6 weeks</td>
<td>9 / 1702 (0.53)</td>
<td>53.28</td>
<td>(-3.21, 8.86)</td>
<td>0.060</td>
</tr>
<tr>
<td>6-8 weeks</td>
<td>5 / 562 (0.88)</td>
<td>51.08</td>
<td>(-45.57, 3.56)</td>
<td>0.199</td>
</tr>
<tr>
<td>9-11 weeks</td>
<td>9 / 1056 (0.85)</td>
<td>60.55</td>
<td>(15.23, 81.64)</td>
<td>0.017</td>
</tr>
<tr>
<td>≥12 weeks</td>
<td>4 / 1120 (0.36)</td>
<td>78.79</td>
<td>(37.63, 92.79)</td>
<td>0.005</td>
</tr>
<tr>
<td></td>
<td>Control n / N (%)</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>&lt; 6 weeks</td>
<td>19 / 1698 (1.12)</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>6-8 weeks</td>
<td>9 / 521 (1.73)</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>9-11 weeks</td>
<td>24 / 1110 (2.16)</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>≥12 weeks</td>
<td>19 / 1126 (1.69)</td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

The level of protection gained from 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, and a similar trend for efficacy. 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.
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Table 3 – SARS CoV-2 S-binding antibody response to COVID-19 Vaccine AstraZeneca\(^{ab}\)

<table>
<thead>
<tr>
<th>Population</th>
<th>Baseline</th>
<th>28 days after dose 1</th>
<th>28 days after dose 2</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>GMT (95% CI)</td>
<td>GMT (95% CI)</td>
<td>GMT (95% CI)</td>
</tr>
<tr>
<td>Overall</td>
<td>(N=882)</td>
<td>(N=817)</td>
<td>(N=819)</td>
</tr>
<tr>
<td></td>
<td>57.18 (52.8, 62.0)</td>
<td>8386.46 (7758.6, 9065.1)</td>
<td>29034.74 (27118.2, 31086.7)</td>
</tr>
<tr>
<td>Dose Interval</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>&lt;6 weeks</td>
<td>(N=481)</td>
<td>(N=479)</td>
<td>(N=443)</td>
</tr>
<tr>
<td></td>
<td>60.51 (54.1, 67.7)</td>
<td>8734.08 (7883.1, 9676.9)</td>
<td>22222.73 (20360.5, 24255.3)</td>
</tr>
<tr>
<td>6-8 weeks</td>
<td>(N=137)</td>
<td>(N=99)</td>
<td>(N=116)</td>
</tr>
<tr>
<td></td>
<td>58.02 (46.3, 72.6)</td>
<td>7295.54 (5857.4, 9086.7)</td>
<td>24363.10 (20088.5, 29547.3)</td>
</tr>
<tr>
<td>9-11 weeks</td>
<td>(N=110)</td>
<td>(N=87)</td>
<td>(N=106)</td>
</tr>
<tr>
<td></td>
<td>48.79 (39.6, 60.1)</td>
<td>7492.98 (5885.1, 9540.2)</td>
<td>34754.10 (30287.2, 39879.8)</td>
</tr>
<tr>
<td>≥12 weeks</td>
<td>(N=154)</td>
<td>(N=152)</td>
<td>(N=154)</td>
</tr>
<tr>
<td></td>
<td>52.98 (44.4, 63.2)</td>
<td>8618.17 (7195.4, 10322.3)</td>
<td>63181.59 (55180.1, 72343.4)</td>
</tr>
</tbody>
</table>

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, 95% CI: 93.7; 99.5]) and the second recommended dose (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 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 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]).
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Spike-specific T cell responses as measured by IFN-γ enzyme-linked immunospot (ELISpot) assay are induced after a first dose of COVID-19 Vaccine AstraZeneca. These do not rise further after a second dose.

Immunogenicity data from the Indian study:

GMTs of IgG antibodies against spike (S) protein were comparable between the groups at baseline – Day 1. GMTs increased significantly after each dose of vaccine in both the groups and were comparable. There was 100% seroconversion in both the groups on Day 57. The immunogenicity data indicates that COVISHIELD is comparable in terms of anti-S IgG antibody titers and seroconversion rates to Oxford/AZ-ChAdOx1 nCoV-19 vaccine (see Tables 4 and 5).

Table 4 Summary of Anti-S IgG antibodies

<table>
<thead>
<tr>
<th>Timepoint</th>
<th>Statistic</th>
<th>COVISHIELD (N=291) n (%)</th>
<th>Oxford/AZ-ChAdOx1 nCoV-19 (N=97) n (%)</th>
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<tbody>
<tr>
<td>Baseline</td>
<td>N</td>
<td>291</td>
<td>97</td>
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<tr>
<td></td>
<td>GMT</td>
<td>95.4</td>
<td>80.7</td>
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<tr>
<td></td>
<td>95% CI</td>
<td>(77.8, 117.0)</td>
<td>(59.0, 110.4)</td>
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<tr>
<td>Visit 3 – Day 29 (+14)</td>
<td>N</td>
<td>289</td>
<td>97</td>
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<tr>
<td></td>
<td>GMT</td>
<td>9988.1</td>
<td>6738.5</td>
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<td>95% CI</td>
<td>(8395.0, 11883.7)</td>
<td>(4880.4, 9304.1)</td>
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<tr>
<td>Visit 4 – Day 57 (+14)</td>
<td>n</td>
<td>140</td>
<td>46</td>
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<tr>
<td></td>
<td>GMT</td>
<td>33331.6</td>
<td>33263.6</td>
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<tr>
<td></td>
<td>95% CI</td>
<td>(27756.0, 40027.2)</td>
<td>(24383.1, 45378.3)</td>
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Table 5 Summary of Proportion of Participants with Seroconversion for Anti-S IgG Antibodies

<table>
<thead>
<tr>
<th>Timepoint</th>
<th>COVISHIELD (N=291) n (%)</th>
<th>Oxford/AZ-ChAdOx1 nCoV-19 (N=97) n (%)</th>
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<tr>
<td></td>
<td>95(%) CI</td>
<td>95(%) CI</td>
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<tr>
<td>Visit 3 – Day 29 (+14)</td>
<td>279 (96.5)</td>
<td>89 (91.8)</td>
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<td></td>
<td>(93.7, 98.3)</td>
<td>(84.4, 96.4)</td>
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<tr>
<td>Visit 4 – Day 57 (+14)</td>
<td>140 (100.0)</td>
<td>46 (100.0)</td>
</tr>
<tr>
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<td>(97.4, 100.0)</td>
<td>(92.3, 100.0)</td>
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</tbody>
</table>

5.2 Pharmacokinetic properties

Not applicable.

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SUMMARY OF PRODUCT CHARACTERISTICS

ChAdOx1 nCoV- 19 Corona Virus Vaccine (Recombinant)

COVISHIELD™

5.3 Preclinical safety data

Toxicity and local tolerance studies

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 (EDTA)
Water for injection

(The names of inactive ingredients may vary according to geographical region)

6.2 Incompatibilities

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

6.3 Shelf-life

The expiry date of vaccine is indicated on the label and packaging.

Once opened, multi-dose vials should be used as soon as practically possible and within 6 hours when kept between +2°C and +25°C. All opened multidose vials of COVISHIELD™ should be discarded at the end of immunization session or within six hours whichever comes first.

6.4 Special precautions for storage

Store in a refrigerator (+2°C to +8°C).

Do not freeze. Protect from light.

Opened multidose vial

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

6.5 Nature and contents of container

COVISHIELD™ is supplied as ready for use liquid in rubber-stoppered multidose vial and single dose vial in below listed presentations

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SUMMARY OF PRODUCT CHARACTERISTICS

ChAdOx1 nCoV-19 Corona Virus Vaccine (Recombinant)

COVISHIELD™

1 dose – 0.5 mL per vial
2 dose – 1.0 mL per vial
5 dose – 2.5 mL per vial
10 dose – 5.0 mL per vial
20 dose – 10 mL per vial

6.6 Instructions for use, handling and disposal

Administration

COVISHIELD™ 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.

Once opened, multi-dose vials should be used as soon as practically possible and within 6 hours when kept between +2ºC and +25ºC. Discard any unused vaccine.

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

Disposal

COVISHIELD™ 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 (e.g. Hydrogen peroxide based disinfectants).

7 MARKETING AUTHORIZATION

Serum Institute of India Pvt. Ltd.
212/2, Hadapsar, Pune 411028, India.

Marketed by:

SERUM INSTITUTE LIFE SCIENCES PVT. LTD.
401, Sarosh Bhavan, 16-B/1, Dr. Ambedkar Road, Pune - 411 001, INDIA
### SUMMARY OF PRODUCT CHARACTERISTICS

ChAdOx1 nCoV-19 Corona Virus Vaccine (Recombinant)  
**COVISHIELD™**

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<th>MARKETING AUTHORISATION NUMBER (S)</th>
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<th>DATE OF FIRST AUTHORISATION/RENEWAL OF THE AUTHORISATION</th>
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Trademark under registration

Revised 01.01.2021, Version 3.0
### Annexure -3

**Title:** ChAdOx1 nCoV-19 Corona Virus Vaccine (Recombinant)

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#### Production Details

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#### Quality Control

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### Comments

- Any comments related to the production or quality control should be listed here.
- Ensure compliance with all regulatory and company standards.
- Regular checks and updates should be maintained for continuous improvement.

### References

- All relevant references and sources used in the production process should be cited.
- Include any patents or trademarks used.

### Conclusion

- Summary of the outcomes and conclusions from the production.
- Any further actions or recommendations should be outlined.

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**Reason for Issue:** Dimension and text revised

**Coatmark:**

**Product Code:** 200146021

**Specification:** Printed on rolls paper 40 gsm, 240 x 350 mm

**Subcedes Item Code:** 200146020

**Determination:** 20140320

**Contact:**

www.serumindia.com

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