1. NAME OF THE MEDICINAL PRODUCT

SARS-CoV-2 (Covid-19) Vaccine

2. QUALITATIVE AND QUANTITATIVE COMPOSITION

Each dose of 0.5 mL contains

RBD antigen of SARS-CoV-2 (Covid-19)[1]	25 µg
Aluminium Hydroxide gel as Al^{+++}	750 µg
CpG 1018	750 µg
Buffer (Tris and NaCl in WFI)	q.s to 0.5 mL

[1] Produced in *Pichia pastoris* (Yeast)

3. PHARMACEUTICAL FORM

SARS-CoV-2 (Covid-19) Vaccine (CORBEVAX®) is a whitish or almost white translucent liquid in which the mineral carrier tends to settle down slowly and should be free from particulate matter.

4. CLINICAL PARTICULARS

4.1 Therapeutic Indications

CORBEVAX® is indicated for active immunization against Covid-19 disease in individuals aged 5 years and above.

CORBEVAX® is also indicated as a booster dose at ≥6 months after completion of primary immunization with 2 doses of Covishield or Covaxin in individuals aged 18 years and above.

The vaccine is approved for restricted use in emergency situation.

4.2 Posology and Method of Administration

Posology: CORBEVAX® vaccination course consists of two separate doses of 0.5 mL. The second dose should be administered at least 4 weeks after the first dose. The vaccine should be administered intramuscularly in the deltoid muscle of upper arm.

4.3 Contraindications

Hypersensitivity to any constituents of the vaccine listed in the section 6.1

4.4 Special Warning and Precautions for Use

- Do not administer intravenously, intradermally, or subcutaneously.
- Like all other vaccines, supervision and appropriate medical treatment should always be available to treat any anaphylactic reactions following immunization

- **The vaccinee should remain under medical supervision for at least 30 minutes after vaccination**
- Concurrent illness: As with other vaccines, administration of CORBEVAX® should be postponed in individuals suffering from an acute severe febrile illness.
- Thrombocytopenia and coagulation disorders: As with any other intramuscular injection, CORBEVAX® should be given with caution in individuals with thrombocytopenia and coagulation disorders or to individuals on treatment with anticoagulation therapy, because of risk of bleeding or bruising following an intramuscular injection in these individuals.
- Immunocompromised individuals: it is not known if individuals with impaired immune responsiveness, including individuals receiving immunosuppressant therapy, will elicit the same response as immunocompetent individuals to CORBEVAX®. These individuals may have a weaker immune response to the vaccine.

CORBEVAX® should be shaken well to obtain a uniform, whitish translucent suspension before use. Prior to administration, the vaccine vial should be visually checked for complete suspension and presence of any particulate matter or other coloration, if any. If in doubt, do not use the contents of the vial. Sterile needle and syringe should be used for withdrawal of the vaccine.

4.5 Drug interactions

No interaction studies have been performed. Concomitant administration of CORBEVAX® with other vaccines has not been studied.

4.6 Use in Special Populations (such as pregnant women, lactating women)

Safety and effectiveness have not been established in pregnant women and nursing mothers. It is not known whether the vaccine is excreted in human milk.

4.7 Effect on Ability to Drive and Use Machines

No studies on the effect of CORBEVAX® on the ability to drive and use machines have been performed.

4.8 Undesirable Effects

Clinical Trial Experience: The safety of CORBEVAX® was established in a controlled clinical trials in individuals aged 5 years to 80 years. Within each system organ class (SOC) the adverse reactions were ranked under headings using the following convention:

Very common	≥ 10%
Common	≥ 1% and < 10%
Uncommon	≥ 0.1% and < 1%
Rare	≥ 0.01% and < 0.1%

Systemic:

Common (may affect up to 1 in 10 people)

- Fever/Pyrexia
- Headache
- Fatigue
- Body pain
- Myalgia
- Nausea

Uncommon (may affect up to 1 in 100 people)

- Arthralgia
- Urticaria
- Chills
- Lethargy

Local:

Very common (may affect up to ≥1 in 10 people)

- Injection site pain

Common (may affect up to 1 in 10 people)

- Injection site erythema

Uncommon (may affect up to 1 in 100 people)

- Injection site swelling
- Injection site rash
- Injection site pruritus

Rare (may affect up to 1 in 1000 people)

- Injection site irritation

Summary of Safety Profile:

In a phase I / II clinical study (BECT062) conducted in 360 subjects aged ≥18 to ≤65 years to assess the safety, reactogenicity and immunogenicity and to select the optimum formulation of BE's SARS-CoV-2 (Covid-19) Vaccine, all the four formulations were found to be safe and well tolerated.

In a phase II/III Clinical study (BECT069) conducted in 1268 subjects aged 18-80 years, a total of 51 adverse events were reported in 27 (27%) study subjects (phase II) and 532 adverse events were reported in 255 (21.8%) study subjects (phase III). In which 34 solicited adverse events were reported in 20 (20%) subjects and 455 solicited adverse events reported in 229 (19.6%) subjects in Phase II and phase III parts of the study respectively. Majority of adverse events

are mild to moderate in intensity and no severe AEs were reported in the study. No SAEs and AESI were reported in the study (See Table 1).

Table 1: Adverse Drug Reactions from Phase II & III study

MedDRA SOC	Frequency	Adverse reactions
General disorders and administration site conditions	Very common	Injection site pain
	Common	Fatigue, Pyrexia[b], Chills
	Uncommon	Injection site swelling, Pain, Injection site erythema
Nervous system disorders	Common	Headache
	Rare	Lethargy
Musculoskeletal and connective tissue disorders	Common	Myalgia, Arthralgia
	Uncommon	Pain in extremity[a]
	Rare	Back pain[a]
Respiratory, thoracic and mediastinal disorders	Uncommon	Cough[a], Dyspnoea[a], Oropharyngeal pain (Sore throat)[a]
Infections and infestations	Uncommon	Nasopharyngitis (Common cold)[a]
	Rare	Pharyngitis (Throat infection)[a]
Gastrointestinal disorders	Uncommon	Nausea, Diarrhoea
Metabolism and nutrition disorders	Rare	Decreased appetite[a]
Skin and subcutaneous tissue disorders	Rare	Urticaria[a]

[a] : Unsolicited event

[b] : Pyrexia includes feverishness (very common) and fever ≥100.4ºF (common)

All the unsolicited events were unrelated to the Vaccine.

In a phase III active comparator study (BECT074) conducted in 2140 subjects aged 18 to 80 years, the safety of the vaccine was found comparable to the comparator vaccine (Covishield™). All the adverse events were mild to moderate in intensity and no severe AEs which were related to study vaccine were reported in the study. No AESI were reported in the study. Most of the solicited adverse events were related to the study vaccine (See Table 2).

Table 2: Adverse Drug Reactions from Phase III Superiority Study

MedDRA SOC	Frequency	Adverse reactions
General disorders and administration site conditions	Very common	Injection site pain, Pyrexia[b]
	Common	Injection site erythema, Injection site pruritus, Headache, Injection site swelling, Fatigue
	Uncommon	Injection site warmth, Chills, Injection site rash, Pain
	Rare	Irritability, Injection site irritation
Nervous system disorders	Common	Headache
Musculoskeletal and connective tissue disorders	Very common	Myalgia
	Common	Arthralgia
	Rare	Back pain[a]
Respiratory, thoracic and mediastinal disorders	Uncommon	Cough[a], Oropharyngeal pain (Sore throat)[a]
	Rare	Rhinorrhoea (running nose), Throat irritation[a], Sneezes[a]

MedDRA SOC	Frequency	Adverse reactions
Infections and infestations	Uncommon	Nasopharyngitis (Common cold)[a]
Gastrointestinal disorders	Common	Nausea,
	Uncommon	Upper abdominal pain[a], Diarrhoea[a], Vomiting[a],
Skin and subcutaneous tissue disorders	Uncommon	Urticaria
	Rare	Acne[a], Rash

[a] : Unsolicited event [b] : Pyrexia includes feverishness (very common) and fever ≥100.4°F (common)

All the unsolicited events were unrelated to the vaccine.

In a phase II/III study (BECT072) conducted in 624 subjects aged ≥5 to <18 years in two age cohorts (≥5 to <12 and ≥12 to <18 years) to prove safety, tolerability and reactogenicity of the vaccine against placebo, the interim results from 312 subjects in ≥12 to <18 years (234 in vaccine arm and 78 in placebo arm) and 312 subjects ≥5 to <12 years (234 in vaccine arm and 78 in placebo arm) indicated that, there was no difference in the safety profile when compared to the data of earlier clinical trials conducted in adults (See Table 3).

Table 3: Adverse Drug Reactions from Phase II/III Pediatric Study

a) Adverse Drug Reactions from Phase II/III Pediatric Study (12-18 years age group)

MedDRA SOC	Frequency	Adverse reactions
General disorders and administration site conditions	Very common	Injection site pain, Pyrexia[a]
	Common	Injection site erythema, Chills, Injection site swelling
	Uncommon	Fatigue
Nervous system disorders	Common	Headache
	Uncommon	Somnolence
Musculoskeletal and connective tissue disorders	Common	Myalgia, Arthralgia
Gastrointestinal disorders	Common	Nausea
Skin and subcutaneous tissue disorders	Uncommon	Urticaria

[a] : Pyrexia includes feverishness (very common) and fever ≥100.4ºF (common)

b) Adverse Drug Reactions from Phase II/III Pediatric Study (5-12 years' age group)

MedDRA SOC	Frequency	Adverse reactions
General disorders and administration site conditions	Very common	Injection site pain,
	Common	Pyrexia[a], Injection site erythema, Chills, Injection site swelling, Fatigue
Nervous system disorders	Common	Headache
Musculoskeletal and connective tissue disorders	Uncommon	Myalgia
Infections and infestations	Uncommon	Nasopharyngitis (common cold), Rhinorrhea (running nose)
Gastrointestinal disorders	Common	Nausea

[a] : Pyrexia includes feverishness (very common) and fever ≥100.4ºF (common)

CORBEVAX as Booster dose: In a Phase III placebo controlled heterologous booster study (BECT070) conducted in 416 subjects aged 18 to 80 years who were previously vaccinated with 2 doses of either Covaxin or Covishield with the most recent dose at least 6 months prior to administration of CORBEVAX® as a booster dose to evaluate the immunogenicity and safety of single booster dose, the safety profile of CORBEVAX® found similar to that of the earlier clinical trials.

Out of 416 subjects randomized in 1:1 ratio between Covishield and Covaxin primed individuals, 312 subjects enrolled in CORBEVAX® arm and 104 subjects were enrolled under Placebo arm.

COVAXIN primed subjects (N=208): Of the 208 subjects primed with 2 doses of Covaxin; 156 subjects enrolled under CORBEVAX® arm and 52 subjects enrolled under PLACEBO arm. Out of 156 subjects in CORBEVAX® arm, 32 (20.5%) subjects reported 44 events. The most commonly reported adverse events were Injection site pain in 14 (8.9%) subjects, Pyrexia in 11 (7.1%) subjects, Headache in 8 (3.6%) subjects, Rhinorrhoea in 3 (1.9%) subjects, Arthralgia in 3 (1.9%) subjects. Out of the 52 subjects under Placebo arm, 7 (13.5%) subjects reported 10 events. The most commonly reported adverse events were Headache in 5 (9.6%) subjects, Injection site pain in 3 (5.8%) subjects.

COVISHIELD primed subjects (N=208): Of the 208 subjects; 156 subjects enrolled under CORBEVAX® arm and 52 subjects enrolled under PLACEBO arm. Out of 156 subjects in CORBEVAX® arm, 28 (17.9%) subjects reported 38 events. The most commonly reported adverse events were Injection site pain in 16 (10.3%) subjects, Headache in 3 (1.9%) subjects, Myalgia in 3 (1.9%) subjects, Fatigue in 3 (1.9%) subjects, Injection site swelling, Pyrexia & Arthralgia in 2 (1.3%) subjects each. Out of the 52 subjects under Placebo arm, 8 (15.4%) subjects reported 8 events. The most commonly reported adverse events were Injection site pain in 5 (9.6%) subjects, Pyrexia, Injection site erythema, Injection site itching in 1 (1.9%) subject each.

All reported adverse events were mild to moderate in intensity and no severe AEs reported in the study. No SAEs or AESI reported during weekly follow-up up to 3 months' after booster dose administration in any of the study subjects either in vaccine or placebo arms.

4.9 Overdose

No case of overdose has been reported. There is no specific treatment for an overdose with CORBEVAX®. In the event of an overdose, the individual should be monitored and provided with symptomatic treatment as appropriate.

5. PHARMACOLOGICAL PROPERTIES

5.1 Mechanism of Action

The receptor-binding domain (RBD) in the S1 subunit of the SARS-CoV-2 spike (S) protein binds to the ACE-2 receptor on human cells which initiates the virus infection and is the most important target for developing a Covid-19 vaccine. In particular, RBD of S protein contains the critical neutralizing domain (CND), which is able to induce highly potent neutralizing antibody response and cross-protection against divergent SARS-CoV-2 strains. RBD-based subunit vaccine is expected to be safer than other vaccines that may induce Th2-type immunopathology. CORBEVAX® targets the S1 subunit of the SARS-CoV-2 spike (S) protein leading to induction of protective immunity against severe Covid-19 infection.

5.2 Pharmacodynamic Properties

Covid-19 disease is caused due to SARS-CoV-2 virus infection. CORBEVAX® is based on classical vaccine technology of a protein antigen, SARS-CoV-2 Spike RBD, adsorbed to the adjuvants, has been studied in Phase I/II, II/III and III clinical studies for safety, reactogenicity and immunogenicity and found to be safe and immunogenic.

In a Phase I/II clinical study (BECT062) is conducted in 360 subjects aged ≥18 to ≤65 years to assess the safety, reactogenicity and immunogenicity and to select the optimum formulation of BE's SARS-CoV-2 (Covid-19) Vaccine. The immunogenicity testing indicated the optimum formulation elicited a significant humoral and cellular immune response.

In a Phase II/III Clinical study (BECT069) conducted in 1268 subjects aged 18-80 years, the immunogenicity was evaluated in 100 subjects in Phase II part in 18-55 year cohort and in a subset of population (elderly cohort aged >45 Year) in Phase III trial. Similar overall immune response was observed in both younger population (18-45 Year) and elderly population (45-80 Year) in terms of increase in anti-RBD IgG concentrations and Neutralizing Antibody Titers post-vaccination. Significant nAb titers were observed against Wuhan, Delta and Beta strains. The interim Wuhan-nAb GMT was indicative > 90% vaccine effectiveness in preventing symptomatic infection as shown by the Correlates of Protection evaluation from Covid-19 vaccine efficacy trial analysis. In the Phase III part of the study, pre-vaccination Anti-RBD IgG and nAb titers were higher than the Phase II study. However, significant increase in IgG and nAb titers were still observed post vaccination which indicates excellent immune response generated by CORBEVAX® (See Table 4). The sub-set of subjects assessed for immunogenicity also elicited a significant humoral and cellular immune response.

The median age in Phase II part (N=100) of the study was 33.5 years with a range of 18 to 52 years and median weight was 65.8 kg, while in Phase III part (N=1168) of the study, the median age was 34 years with a range of 18 to 78 years and median weight was 64.3 kg. Of these 1268 participants in the Phase II/III study, 26 participants (2.05%) had comorbidities at baseline. Comorbidities included diabetes, hypertension and hypothyroidism.

Table 4: Summary of Immunogenicity from Phase II/III Study

a)Summary of Anti-RBD IgG concentration

Time point	Statistic	CORBEVAX®	% SCR
Phase II part			
Base Line (Day 0)	N GMC (EU/mL) 95% CI	98 945 788-1134	NA
Day-42	N GMC (EU/mL) 95% CI	98 26448 19858-35223	95%
Phase III part			
Base Line (Day 0)	N GMC (EU/mL) 95% CI	65 4287 3137-5857	NA
Day-42	N GMC (EU/mL) 95% CI	65 61138 47485-78715	89 %

N: Number of subjects GMC: Geometric Mean Concentration
CI: Confidence Interval SCR: Seroconversion Rate NA: Not Applicable

b)Summary of Neutralizing Antibody (nAb) Titers against Wuhan

Time point	Statistic	CORBEVAX®
Phase II part		
Base Line (Day-0)	N GMT 95% CI	98 67 52-88
Day-42	N GMT 95% CI	98 1338 917-1954
Phase III part		
Base Line (Day-0)	N GMT 95% CI	65 470 330-670
Day-42	N GMT 95% CI % SCR	65 5166 3830-6967 86 %

N: Number of subjects GMT: Geometric Mean Titre
CI: Confidence Interval SCR: Seroconversion Rate

The sub-set of 20 subjects from Phase II part were tested for Neutralizing Antibody (nAb) Titers against Wuhan, Delta and Beta variants. The GMT was found to be 2351, 1487 and 511

respectively against Wuhan, Delta and Beta variants in this sub-set. The Sub-set of 65 subjects aged in elderly cohort (> 45 years age) from Phase III part were also tested for Neutralizing Antibody (nAb) Titers against Delta variant, in which the GMT was found to be 2341 (1614-3395).

In a Phase III superiority study (BECT074) conducted in 2140 subjects aged 18 to 80 years to prove the immunogenic superiority and safety, CORBEVAX® demonstrated superior immune response in comparison to Covishield™ when assessed for Neutralizing Antibody Titers against the Wuhan and Delta variants in terms of GMT's (See Table 5). The sub-set of subjects assessed for immunogenicity also elicited a significant humoral and cellular immune response. CORBEVAX® nAb GMT against Wuhan strain was indicative of vaccine effectiveness of >90% for prevention of symptomatic infections based on the Correlates of Protection assessment performed as part of Covid-19 vaccine efficacy trial analysis.

The median age of the study subjects in CORBEVAX® arm (N=1819) was 34 years with a range of 18 to 79 years and median BMI was 23.7 kg/m^2. Of these 1819 participants in the Phase III active comparator study, 16 participants had comorbidities at baseline. Comorbidities included diabetes, hypertension and hypothyroidism.

Table 5: Summary of Phase III Immunogenic Superiority Study

a) Summary of Anti-RBD IgG concentration

Time point	Statistic	CORBEVAX®	COVISHIELD™
Base Line (Day-0)	N GMC (EU/mL) 95% CI	304 1439 1268-1633	307 1503 1316-1716
Day-42	N GMC (EU/mL) 95 % CI % SCR	304 24478 21075-28431 91%	307 16203 14428-18196 88%

N: Number of subjects GMC: Geometric Mean Concentration
CI: Confidence Interval SCR: Seroconversion Rate

b) Summary of Neutralizing Antibody (nAb) Titers

Time point	Statistic	CORBEVAX®		COVISHIELD™	
		Wuhan	Delta	Wuhan	Delta
Base Line (Day-0)	N GMT 95% CI	303 85 75-96	ND	307 75 65-86	ND
Day-42	N GMT 95% CI % SCR	301 2123 1801-2514 95%	301 874 724-1055 NA	304 1833 1632-2089 94%	304 562 482-657 NA

N: Number of subjects GMT: Geometric Mean Titre ND: Not Done
CI: Confidence Interval SCR: Seroconversion Rate NA: Not Applicable

CORBEVAX® showed comparable seroconversion and higher anti-RBD IgG concentration in comparison to Covishield™ post vaccination.

In a Phase II/III placebo controlled clinical study (BECT072) conducted in 624 subjects aged ≥ 5 to < 18 years in two age cohorts (≥ 5 to < 12 and ≥ 12 to < 18 years) to prove the safety, tolerability and immunogenicity, the interim results from ≥ 5 to < 12 years and ≥ 12 to < 18 years age group showed significant increase in IgG and nAb titers post vaccination (at Day-42) against Wuhan and Delta variants, which indicates excellent immune response generated by CORBEVAX® and is inline with IgG and nAb titers observed in earlier clinical trials in Adults (See Table 6). The subjects were randomized in 3:1 ratio between CORBEVAX® and placebo groups.

The mean age in ≥12 to <18 years age group (N=312) was 14.7 years while the mean age in ≥5 to <12 years' age group (N=312) was 8.8 years. 51.9 % subjects are male and 48.1% subjects are female in ≥12 to <18 years' age group and 54.2 % subjects are male and 45.8% subjects are female in ≥5 to <12 years' age group.

Table 6: Summary of Interim study results of Phase II/III study

a) Summary of Anti-RBD IgG concentration

Time point	Statistic	CORBEVAX®
≥ 12 to < 18 years		
Base Line (Day-0)	N GMC (EU/mL)	229 939
Day-42	N GMC (EU/mL) % SCR	229 18049 91%
≥ 5 to < 12 years		
Base Line (Day-0)	N GMC (EU/mL)	229 964
Day-42	N GMC (EU/mL) % SCR	229 26802 96%

N: Number of subjects GMC: Geometric Mean Concentration SCR: Seroconversion Rate

b) Summary of Neutralizing Antibody (nAb) Titers

Time point	Statistic	CORBEVAX®	
		Wuhan	Delta
≥ 12 to < 18 years			
Base Line (Day-0)	N GMT	224 50	NA
Day-42	N GMT	224 1099	224 451
≥ 5 to < 12 years			
Base Line (Day-0)	N GMT	220 44	NA
Day-42	N GMT	220 1148	220 459

N: Number of subjects GMT: Geometric Mean Titre NA: Not Applicable

CORBEVAX® nAb titres in terms of GMT were indicative of vaccine effectiveness of > 90% based on the Correlates of Protection assessment performed as part of Covid-19 vaccine efficacy trial analysis.

CORBEVAX® as Booster dose: In a Phase III placebo controlled heterologous booster study (BECT070) conducted in 416 subjects aged 18 to 80 years who were previously vaccinated with 2 doses of either Covaxin or Covishield with the most recent dose at least 6 months (+28 days) or 9 months (+28 days) in two groups prior to administration of CORBEVAX® as a booster dose, the immunogenicity in terms of neutralizing antibodies ($PRNT_{50}$) showed significant boost after 28 days when compared with placebo cohort in both Covishield and Covaxin arms (See Table 7 and 8).

Table 7: Comparison of nAb titers in Covishield primed recipients:

Comparison Parameter	CORBEVAX	Placebo
≥2-fold increase in neutralizing antibodies		
% of Subjects that demonstrated ≥2-fold rise in nAb titers from Day-0 to Day-28	71%	20%
Geometric Mean Titers (GMTs) and Ratio of GMTs		
Day-0 GMT (Number of Subjects)	1143 (80)	1758 (25)
Day-28 GMT (Number of Subjects)	6317 (80)	1877 (25)
Ratio of Day-28 GMT's; CORBEVAX vs Placebo	3.365	

Table 8: Comparison of nAb titers in Covaxin primed recipients:

Comparison Parameter	CORBEVAX	Placebo
≥2-fold increase in neutralizing antibodies		
% of Subjects that demonstrated ≥2-fold rise in nAb titers from Day-0 to Day-28	68%	40%
Geometric Mean Titers (GMTs) and Ratio of GMTs		
Day-0 GMT (Number of Subjects)	834 (142)	1193 (48)
Day-28 GMT (Number of Subjects)	5622 (138)	2366 (48)
Ratio of Day-28 GMT's; CORBEVAX vs Placebo	2.376	

No significant difference in GMTs and ratio of GMTs between 6 months (+28 days) and 9 months (+28 days) groups.

Significant boost in immunogenicity in terms of Anti-RBD IgG concentration was observed in both Covishield and Covaxin primed recipients at 28 days after CORBEVAX booster dose administration in both 6 months (+28 days) and 9 months (+28 days) groups.

The CORBEVAX® booster dose effect in terms of increase in neutralizing antibodies ($PRNT_{50}$) and Anti-RBD IgG concentration in both Covishield and Covaxin vaccinated groups was comparable in subjects that were boosted either at 6 months (+28 days) or 9 months (+28 days) after completion of primary vaccination.

Neutralizing antibodies against Omicron: A sub-set of 39 subjects from Phase III part of Phase II/III study in Adults (BECT069) were tested for Neutralizing Antibody (nAb) titers against Omicron variant in comparison with Wuhan and Delta variants. The response rate of 87% (34 out of 39 subjects) and the nAb GMT of 126 against Omicron with CORBEVAX® is among the highest observed when compared with published data for other marketed COVID19 vaccines developed based on mRNA, adenovector and inactivated platforms post two dose regimen. The GMT of 126 against Omicron is indicative of high vaccine effectiveness against symptomatic infection based on the Phase III efficacy study analysis of marketed vaccines.

A sub-set of subjects (n=82) from Phase III heterologous booster study (BECT070) in adults were tested for the neutralizing antibodies against Omicron variant by Pseudovirus Neutralization Assay (PNA) and a significant increase in nAb titer GMTs as well as % responders were observed after CORBEVAX® administration for both Covishield (91%) and Covaxin (75%) recipient arms.

Antibody Persistence: As part of the long term immunogenicity, the study subjects in Phase II part of Phase II/III study (BECT069) were tested for anti-RBD IgG concentrations at Day-0, Day-28, Day-42, Day-56 and Day-208 time-points. The GMC's, GMFR's and % Seroconversion shows excellent anti-RBD antibody immune response persistence till 6 months after the completion of two dose regimen.

Similar immunological persistence in terms of Anti-RBD IgG and Neutralizing antibodies was observed with formulations evaluated in Phase I/II study (BECT062) at 6 months post second dose.

5.3 Pharmacokinetic Properties

Evaluation of pharmacokinetic properties is not required for vaccines.

5.4 Preclinical Safety Data

Single dose toxicity studies in Rats and repeat dose toxicity studies in Rats and Rabbits were conducted. Based on the toxicity studies conducted, it is concluded that the vaccine formulation did not produce any adverse effects at dose level of 0.5 mL.

Immunogenicity studies are also conducted with the vaccine in Rats and Mice. Based on the immunogenicity studies, the vaccine shown higher antibody titre (IgG and NT_{50}) when compared to Pre immune sera group and Placebo's groups. CORBEVAX® efficacy in prevention of SARS-CoV-2 infection was also demonstrated in virus challenge studies conducted in Non-Human Primates which showed absence or significant reduction of viral RNA in lung tissue or nasal/throat swabs in vaccinated animals in comparison to unvaccinated controls.

6. PHARMACEUTICAL PARTICULARS

6.1 List of Excipients

The vaccine contains RBD antigen of SARS-CoV-2 (Covid-19) and is produced in *Pichia pastoris (Yeast).*

List of excipients:

- Aluminium Hydroxide gel as Al^{+++}
- CpG 1018
- Buffer (Tris and NaCl in WFI)

6.2 Incompatibilities

The product should not be mixed with any other medicinal products or active immunizing agents.

6.3 Shelf Life

Shelf life of CORBEVAX® is 12 months from the date of manufacturing. The manufacturing date of the vaccine is indicated on the label and carton of the product.

6.4 Special Precautions for Storage

Store at +2°C to +8°C. DO NOT FREEZE. Discard if found frozen. Shake well before use. Keep out of reach of children. Multi dose vials should be used within 6 hours once opened. All opened multidose vials of CORBEVAX® should be discarded at the end of immunization session or six hours after the first opening, whichever comes first. Do not use the vaccine after the expiry date as mentioned in the label.

6.5 Nature and Contents of Container

The CORBEVAX® is supplied as liquid and is filled in USP type I glass vials, closed using bromobutyl rubber stoppers and sealed with aluminium flip-off seals. The vaccine is offered in the following presentations:

- Single dose vial (0.5 mL)
- Ten dose vial (5 mL)
- Twenty dose vial (10 mL)

6.6 Special Precautions for Disposal

Any unused product or waste material should be disposed as per local regulatory requirements

7. MARKETING AUTHORISATION HOLDER

Biological E. Limited

Regd. office: 18/1 & 3, Azamabad, Hyderabad, Telangana - 500 020, INDIA.

Manufacturing Site Address:

BE's Shameerpet site.	**BE's Azamabad site:**
M/s. Biological E. Limited Plot No. 1, Biotech Park, Phase II, Kolthur Village - 500 078, Shameerpet, Medchal-Malkajgiri District, Telangana, INDIA. Web site: www.biologicale.com	M/s. Biological E. Limited 18/1&3, Azamabad, Hyderabad, Telangana -500020 Tel: 91-40-3021 3999; Fax: 91-40-2761 5309

8. MARKETING AUTHORISATION NUMBER(S)

Permission No: MF/BIO/21/000136

28-Dec-2021 for individuals aged 18 years and above

21-Feb-2022 for individuals aged ≥12 years to <18 years

26-Apr-2022 for individuals aged ≥5 years to <12 years

9. DATE OF FIRST AUTHORISATION

28-Dec-2021 (for individuals aged 18 years and above)

® Registered Trade Mark

FACT SHEET FOR VACCINE RECIPIENTS AND CARE GIVERS APPROVED FOR RESTRICTED USE IN EMERGENCY SITUATION IN PUBLIC INTEREST
THE BIOLOGICAL E. LIMITED, SARS-CoV-2 (Covid-19) Vaccine
CORBEVAX®

IN PREVENTION OF COVID-19 DISEASE IN INDIVIDUALS AGED 5 YEARS AND ABOVE

This vaccine has been approved for restricted use in emergency situation. It does not have a marketing authorization, however, this approval for the restricted use in emergency situation grants permission for the vaccine to be used for active immunization in individuals aged 5 years and above for the prevention of coronavirus disease 2019 (COVID-19). CORBEVAX® is also indicated as a booster dose at ≥6 months after completion of primary immunization with 2 doses of Covishield or Covaxin in individuals aged 18 years and above.

Reporting of Side Effects

As with any new medicine, this vaccine will be closely monitored to allow quick identification of new safety information. You can help by reporting any side effects, you may get after vaccination to the Biological E. Limited (BE) who is the manufacturer of **CORBEVAX®** on 24x7 Toll-free Number: 1800 309 0150 or at pharmacovigilance@biologicale.com.
For more information, read this fact sheet carefully.

You are being offered the SARS-CoV-2 (Covid-19) Vaccine [**CORBEVAX®**] of Biological E. Limited to prevent Coronavirus Disease 2019 (COVID-19) caused by SARS-CoV-2. This Fact Sheet contains information to help you understand the risks and benefits of the **CORBEVAX®**.

The **CORBEVAX®** is a vaccine and may prevent you from getting COVID-19 disease.

Read this Fact Sheet for information about the **CORBEVAX®** Talk to the vaccinator / healthcare provider if you have questions. It is your choice to receive the Biological E. Limited Covid-19 Vaccine [**CORBEVAX®]**

The **CORBEVAX®** vaccination course consists of two separate doses of 0.5 mL each. The second dose should be administered at least 4 weeks after the first dose.

CORBEVAX® can also be administered as a booster dose in individuals aged 18 years and above at ≥6 months after completion of primary immunization with 2 doses of Covishield or Covaxin.

After the vaccine is administered, **the vaccinee should be monitored by a healthcare professional for 30 minutes.** The vaccine should be administered by intramuscular (IM) injection only. The **CORBEVAX®** may not protect everyone.

WHAT YOU NEED TO KNOW BEFORE YOU GET THIS VACCINE

WHAT IS COVID-19?

COVID-19 disease is caused by a coronavirus called SARS-CoV-2. This type of coronavirus has not been seen before. You can get COVID-19 through contact with another person who has the virus. It is predominantly a respiratory illness that can affect other organs. People with COVID-19 have had a wide range of symptoms reported, ranging from mild symptoms to severe illness. Symptoms may appear 2 to 14 days after exposure to the virus. Symptoms may include: fever or chills; cough; shortness of breath; fatigue; muscle or body aches; headache; new loss of taste or smell; sore throat; congestion or runny nose; nausea or vomiting; diarrhoea.

WHAT IS THE BE's CORBEVAX® VACCINE?

CORBEVAX® is a protein sub-unit vaccine, developed from a component of the spike protein on the virus's surface, which helps the body build the immune response against the virus.

The vaccine has the Receptor Binding Domain (RBD) protein as an antigen, CpG 1018 and Aluminium hydroxide as adjuvants formulated in Tris buffer.

WHAT SHOULD YOU MENTION TO YOUR HEALTHCARE PROVIDER BEFORE YOU GET CORBEVAX® VACCINE?

- Tell the healthcare provider/Doctor about all of your medical conditions, including:
- If you have ever had a severe allergic reaction (anaphylaxis) after any drug, food, any vaccine or any ingredients of **CORBEVAX®**
- If you have fever or severe infection
- If you have a bleeding disorder or are on a blood thinner
- If you are immunocompromised or are on a medicine that affects your immune system
- If you are pregnant or plan to become pregnant and lactating women
- If you have received another COVID-19 vaccine

If you have any of the above conditions, you should consult your healthcare provider/Doctor before deciding to take the vaccine.

WHO SHOULD GET THE CORBEVAX® VACCINE?

CORBEVAX® has been approved for restricted use in emergency situation in individuals aged 5 years and above. CORBEVAX® can also be administered as a booster dose in individuals aged 18 years and above at ≥6 months after completion of primary immunization with 2 doses of Covishield or Covaxin.

WHO SHOULD NOT GET THE CORBEVAX® VACCINE?

You should not get the **CORBEVAX®** if you:

- Had a severe allergic reaction after a previous dose of this vaccine
- Hypersensitivity to any component of a vaccine or a vaccine containing similar components
- History of severe allergic reactions
- If you are suffering from common cold, runny nose, fever, cough, body ache or loose motions etc
- Pregnancy and the period of lactation
- Individuals aged below 5 years

WHAT ARE THE INGREDIENTS IN THE CORBEVAX® VACCINE?

The **CORBEVAX®** includes the following ingredients:

- Aluminium Hydroxide gel as Al^{+++}
- CpG 1018
- Buffer (Tris and NaCl in WFI)

HOW IS THE CORBEVAX® GIVEN?

The **CORBEVAX®** will be given to you as an intramuscular (IM) injection only, preferably in the deltoid muscle. The **CORBEVAX®** vaccination course consists of two separate doses of 0.5 mL each.

If you receive one dose of the **CORBEVAX®** then the second dose should be administered at least 4 weeks after the first dose. **After the vaccine is administered, you will be monitored by a healthcare professional for 30 minutes.**

If you miss your second dose;

If you forget to go back at the scheduled time, ask your healthcare provider/doctor for advice.

It is important that you return for your second dose of **CORBEVAX®.**

CORBEVAX® can also be administered as a booster dose in individuals aged 18 years and above at ≥6 months after completion of primary immunization with 2 doses of Covishield or Covaxin.

HAS THE CORBEVAX® BEEN USED BEFORE?

The **CORBEVAX®** is used in clinical trials, a number of participants received one or two doses in Indian trials. The vaccine is also being used in individuals aged 12 years to 14 years as part of immunization in India.

WHAT ARE THE BENEFITS OF THE CORBEVAX® VACCINE?

In clinical trials, the **CORBEVAX®** has been shown to prevent COVID-19 disease following 2 doses given at 4 weeks' interval. The duration of protection against COVID-19 disease is currently unknown. You may get protective immune response 2 weeks after the second dose of **CORBEVAX®**.

It is important to appreciate that receiving the vaccine does not mean that other precautions related to COVID-19 need not be followed. All Covid-19 precautions such as maintaining physical distance from others, wearing mask in public and cleaning your hands frequently with alcohol-based hand rub or soap and water need to followed even after receiving the vaccine dose.

WHAT ARE THE RISKS OF THE CORBEVAX® VACCINE?

Side effects that have been reported with the **CORBEVAX®** include:

Systemic:

Common (may affect up to 1 in 10 people)

- Fever/Pyrexia
- Headache
- Fatigue
- Body pain
- Myalgia
- Nausea

Uncommon (may affect up to 1 in 100 people)

- Arthralgia
- Urticaria
- Chills
- Lethargy

Local:

Very common (may affect up to ≥1 in 10 people)

- Injection site pain

Common (may affect up to 1 in 10 people)

- Injection site erythema

Uncommon (may affect up to 1 in 100 people)

- Injection site swelling
- Injection site rash
- Injection site pruritus

Rare (may affect up to 1 in 1000 people)

- Injection site irritation

These may not be all the possible side effects of the **CORBEVAX®** Serious and unexpected side effects may occur. If you notice any side effects not mentioned in this leaflet, please inform your healthcare provider / doctor.

WHAT SHOULD I DO ABOUT SIDE EFFECTS?

If you experience a severe allergic reaction, call or go to the nearest hospital. Call the healthcare provider if you have any side effects that bother you or do not go away.

In addition, you can report side effects after vaccination to Biological E. Limited, who is the manufacturer of **CORBEVAX®** as below.

- 24x7 Toll-free Number (For Medical and Adverse Event Related Queries Only): 1800 309 0150 or pharmacovigilance@biologicale.com.

All adverse events reported will be entered in COWIN App by the health care provider.

WHAT IF I DECIDE NOT TO GET THE CORBEVAX® VACCINE?

It is your choice to receive or not receive the **CORBEVAX®**. You may prefer to consult your healthcare provider.

CAN I RECEIVE THE CORBEVAX® VACCINE WITH OTHER VACCINES?

There is no information on the use of the **CORBEVAX®** with other vaccines.

CAN CORBEVAX® VACCINE BE GIVEN AS A BOOSTER DOSE?

Yes. The CORBEVAX® can be administered as a booster dose in individuals aged 18 years and above at ≥6 months after completion of primary immunization with 2 doses of Covishield or Covaxin.

The Phase III clinical trials conducted with CORBEVAX as a booster dose showed significant increase in neutralizing antibodies ($PRNT_{50}$) in individuals who completed primary immunization with 2 doses of Covishield or Covaxin.

WHAT IF I AM PREGNANT OR BREASTFEEDING?

You may discuss your options with the healthcare provider/Doctor.

WILL THE CORBEVAX® VACCINE GIVE ME COVID-19 INFECTION?

No. The **CORBEVAX®** COVID-19 Vaccine does not contain SARS-CoV-2 and cannot give you COVID-19 infection.

KEEP YOUR VACCINATION CARD

When you get your dose, please discuss with your healthcare provider regarding the option of your vaccination record on digital platform, if available.

HOW CAN I LEARN MORE?

- Ask the healthcare provider/Doctor.
- Consult your local or state public health department.

Manufactured by:
Biological E. Limited

Registered office:
18/1 & 3, Azamabad, Hyderabad,
Telangana - 500 020, INDIA.
Tel: 91-40-3021 3999;
Fax: 91-40-2761 5309
Email: info@biologicale.com

® Registered Trademark

Corporate Office Address:
Road No. 35, Jubilee Hills,
Hyderabad, Telangana -500033
Tel: 91-40-7121 6000;
Fax: 91-40-7121 6128/ 6030
Email: info@biologicale.com