For use only of a Registered Medical Practitioner or Hospital or Laboratory

COVID-19 Vaccine [ChAd36-SARS-CoV-2-S (Recombinant)]

iNCOVACC®

1. NAME AND DESCRIPTION OF THE MEDICINAL PRODUCT:

COVID-19 Vaccine [ChAd36-SARS-CoV-2-S (Recombinant)] is a colourless to pinkish liquid, free from extraneous particles, containing NLT $5x10^{10}$ virus particles per mL.

2. QUALITATIVE AND QUANTITATIVE COMPOSITION:

Each Dose of 0.5 mL, total of 8 drops contains:

ChAd36-SARS-CoV-2-S COVID-19 virus (recombinant)	NLT $5x10^{10}$ particles per mL
Tris (pH 7.4)	20 mM
Sodium Chloride	25 mM
Magnesium Chloride	2 mM
Glycerol	NLT 2.5 %
Polysorbate- 80	0.1%

For excipients see section 6.1.

3. PHARMACEUTICAL FORM:

Vaccine (Liquid)

4. CLINICAL PARTICULARS:

4.1 Therapeutic indication

COVID-19 Vaccine [ChAd36-SARS-CoV-2-S (Recombinant)] is indicated for active immunization against SARS-CoV-2 infection.

iNCOVACC® is indicated for active immunization against SARS-CoV-2 virus infection for age ≥ 18 years for **restricted use in emergency situation in public interest**.

4.2 Posology and method of administration.

iNCOVACC® is an Adenoviral vector-based (expressing a stabilized spike protein) COVID-19 vaccine for nasal administration only.

Primary Series: iNCOVACC® is administered as 0.5mL per dose in 8 drops, (4 drops in each nostril). The vaccination course consists of two doses administered 28 days apart.

Booster Dose: iNCOVACC® - iNCOVACC® is also indicated as a booster dose to individuals aged 18 years and above, at ≥6 months after completion of primary schedule of COVISHIELD or COVAXIN®

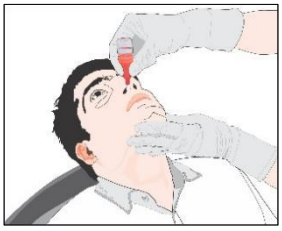


Fig. 1

Method of administration for Vial (2 Dose)

1. Blow nose gently to clear.
2. Tilt head back as far as comfortable (Refer Fig 1 and Sec 8.1).
3. Close one nostril with fore-finger. Insert dropper a little away into another nostril. Squeeze the dropper to release 4 drops and inhale gently. Keep the head back for 30 seconds.
4. Repeat step 3 for another nostril.

In case **iNCOVACC®** partially or completely does not enter the nostril, you may re-administer into the same nostril. In case the recipient prematurely gets up, and the **iNCOVACC®** liquid is seen running from any nostril, you may re-administer to that nostril.

Once opened, Multi-Dose vials should be used within 6 hours and stored at 2 to 8ºC between administrations. Post 6 hours after opening, the vials should be discarded.

iNCOVACC® is presented as a two-dose presentation per vial and for nasal use only. Care should be taken not to contaminate the dropper of the vaccine while administration. Post administration of 8 drops to the recipient, the dropper should be discarded and new dropper should be affixed prior administration to the next recipient. In case, the vaccine is not used immediately for administration to the second recipient, the open vial should be closed with rubber stopper. A new dropper should be placed for the administration of vaccine to the second recipient. The vaccine should not be used beyond 6 hours after the vial is opened.

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

4.3 Contraindications

Hypersensitivity to any constituents of the vaccine.

4.4 Special warnings and precautions for use

- Do not administer intramuscularly, intravenously, intradermally, or subcutaneously.
- Like all other vaccines, supervision and appropriate medical treatment should always be available to treat any anaphylactic reactions following immunization. Vaccinees should remain under medical supervision for at least 30 minutes after vaccination.

- Concurrent illness: As with other vaccines, administration of **iNCOVACC®** should be postponed in individuals suffering from an acute severe febrile illness/acute infection.
- Thrombocytopenia and coagulation disorders**: iNCOVACC®** should be given with caution to individuals with thrombocytopenia, coagulation disorder or to persons on anticoagulation therapy.
- **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.
- **Paediatric population:** Data not available for the use of **iNCOVACC®** in paediatric population.

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

4.6 Pregnancy and Lactation
No data available.

4.7 Effects on ability to drive and use machine
No studies for the effect of **iNCOVACC®** on the ability to drive and use machines have been performed.

4.8 Undesirable effects
Safety of iNCOVACC® is established in a controlled clinical trial in individuals aged 18 and above. Within the clinical trial of heterologous booster dose, the adverse events reported after iNCOVACC® are 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)

- Fatigue
- Fever
- Headache

Uncommon (may affect up to 1 in 100 people)

- Joint pain
- Weakness
- Cough
- Cold
- Itching in eyes
- Redness in eyes
- Breathlessness

Local:

Common (may affect up to 1 in 10 people)

- Runny Nose

Uncommon (may affect up to 1 in 100 people)

- Nasal Pain
- Sneezing

Safety of the **iNCOVACC®** vaccine was evaluated in the Phase 1, Phase 2 and Phase 3 trials of adults age ≥18 years

Summary of safety profile:

Phase 1 clinical trial: Homologous

The phase 1 study was conducted in India with a total of 175 subjects, 70 in group A (Single dose), 70 in group B (Double dose) and 35 in group C (Placebo). Among 70 subjects in group A, 57 (81.43%) were males and 13 (18.57%) were females. In group B, among 70 subjects, 57 (81.43%) were males and 13 (18.57%) were females. In group C, among 35 subjects, 30 (85.71%) were males and 5 (14.29%) were females.

A total of 8 solicited adverse events were reported during the study. 3 adverse events were reported from group. In group A, 3 solicited adverse events (2 events of headache and 1 event of Fever) were reported in 3 subjects (4.29%). In group B, 5 solicited adverse events (3

events of Fever and 2 events of sneezing) were reported in 5 subjects (7.14%). No serious adverse event was reported in the study.

	Total number of subject N= 175		
	Group A (Single dose N=70)	Group B (double dose N=70)	Group C (placebo N=35)
Total Solicited Adverse events reported 8	Total 3 (4.29%) events were reported of which 2 events of headache, 1 event of fever	Total 5 (7.14%) events were reported of which 3 events of fever, 2 events of sneezing	No adverse events

Phase 2 clinical trial: **Homologous**

A Phase 2, Randomized, Double Blinded, Multi-centric Study to evaluate the Immunogenicity, Reactogenicity and Safety of an Intranasal COVID-19 Vaccine (ChAd36-SARS-CoV-2-S (Recombinant)) was conducted in 200 Healthy Volunteers of ages 18 to 60., of which 148 (74.00%) were male and 52 (26.0%) were female.

A total of six solicited adverse events were reported during the study. 5 solicited adverse events were reported in group-1 (2 events of running nose and 3 events of hheadache) were reported in 5 subjects (3.12%).one adverse event (Headache) was reported in 1 subject (2.5%) in group-2. **w**hich were mild in severity and resolved within 24 hours

No serious adverse event was reported in the study.

Phase 3 clinical trial: Homologous

A Phase 3 randomized open label multi-centric study to compare immunogenicity and safety of iNCOVACC® with COVAXIN®, and to assess Lot to Lot Consistency of iNCOVACC® in Healthy Volunteers is ongoing in 3160 subjects of 18 years and above. The data is analysed till day 90 for a total of 3141 subjects. Percentages of male and female subjects enrolled in the study are 69.24% and 30.76% respectively.

A total of 248 adverse events, 197 in iNCOVACC® group and 51 in COVAXIN® group were reported in the study till day 90.

Total 248 adverse event till day 90	iNCOVACC®	COVAXIN®
	197 subjects	51 subjects
Solicited local adverse events	3.28% running nose, sneezing, nasal congestion, nasal pain, sore throat, lacrimation.	21.73% Injection site pain, injection site swelling and injection site redness.
Common solicited systemic events reported	Fever, headache, myalgia, fatigue, nausea and vomiting.	Fever, headache, nausea
No Serious Adverse Events were seen in both groups		

Phase 2 Clinical trial: Heterologous

A total of 608 subjects participated in the Phase 2 randomized, multi-centric, Clinical Trial of Heterologous Prime-Boost Combination of SARS-CoV-2 Vaccines to evaluate the immunogenicity and safety of **COVAXIN®** with **iNCOVACC®** (Adenoviral Intranasal COVID-19 vaccine) in Healthy Volunteers of which 470 (77.3%) were male and 138 (22.70%) were female with 152 subjects in each group:

Total 54 Solicited local adverse events and 172 Solicited systemic adverse events were seen in 144 subjects. Total 45 Unsolicited adverse events were seen in 31 subjects. All the adverse events were mild and resolved within 24 hours

	Group1 (COVAXIN®+ COVAXIN®)	Group2 (COVAXIN®+ iNCOVACC®)	Group3 (iNCOVACC® + COVAXIN®)	Group4 (iNCOVACC® + iNCOVACC®)
Solicited Systemic adverse events	Fever, headache, nausea, vomiting, body pain	Fever, headache, body pain, fatigue	Cough, fever, headache, body pain,	Fever, headache, fatigue, vomiting
Solicited Local adverse events	Injection site pain, injection site redness	Injection site pain, injection site swelling, Running nose	Nasal pain, Injection site pain	Nasal pain, nose irritation, running nose
Unsolicited adverse events	Dizziness, fever, malaise, oral ulcer, rashes, reduced appetite, cold, cough, ASOM, syncope	Cough, dizziness, fever, headache, haematochezia, stomach pain, right rib pain	malaise, rashes, watery eyes, dengue fever, cold, cough	Fever, ASOM, cold, cough, headache, malaise, reduced hearing, body pains
No SAEs were reported				

Phase 3 Clinical trial: Heterologous

A total of 875 subjects participated in the Phase 3, Randomized, Multi-Centric, Open-labelled Study to Evaluate Immunogenicity and safety of **iNCOVACC®** Booster Dose in Participants Previously Vaccinated with EUA Vaccines of which 565 (64.57%) were male and 310 (35.43%) were female.

A total of 138 adverse events were reported in 107 subjects which is 12.23% of the total population. Among the 138 adverse events, 113 events were solicited and 25 events were unsolicited in 6 months (180 days).

In group 1, 17 solicited adverse events and 8 unsolicited events were reported. In group 2, 25 solicited adverse events and 2 unsolicited events were reported. In group 3, 21 solicited adverse events and 8 unsolicited events were reported. In group 4, 18 solicited adverse events and 3 unsolicited events were reported. In group 5, 32 solicited adverse events and 4 unsolicited events were reported.All the adverse events were mild and resolved within 24 hours and No SAEs were reported during the study

Parent Vaccine	**COVAXIN®**		**COVISHIELD**		
Booster Vaccine	**Group-1 iNCOVACC®**	**Group-2 COVAXIN®**	**Group-3 iNCOVACC®**	**Group-4 COVAXIN®**	**Group-5 COVISHIELD**
Solicited Systemic adverse events	Fever, headache, fatigue	Fever, headache, fatigue, nausea, sneezing, vomiting	Fever, headache, fatigue, joint pain, weakness	Fever, fatigue, joint pain, muscle pain, body pain	Body pain, chills, headache, fever, fatigue, vomiting
Solicited Local adverse events	Nasal pain, sneezing	Injection site pain, injection site redness, injection site swelling, injection site induration	Running nose	Injection site pain	Injection site pain
Unsolicited adverse events	Chest pain. cold, fatigue, fever, itching in eyes	weakness	Breathlessness cough, fatigue	Runny nose, sore throat	Cold, weakness
No SAEs were reported					

4.9 Overdose

No case of overdose has been reported.

5. PHARMACOLOGICAL PROPERTIES

5.1 Pharmacodynamic properties: Immune Response and Efficacy

Phase 1 clinical trial (GMTs of MNT_{50}**): Homologous**

Days	Statistics	Group A	Group B	Group C
Day 0	**GMT -95 % CI**	17.97(11.73,27.51)	16.75(11.6, 24.19)	15.05(9.84, 23.02)
Day 28	**GMT -95 % CI**	47.9(30.44,75.38)	44.01(28.3, 68.44)	17.36(10.68, 28.21)
Day 42	**GMT -95 % CI**	65.58(41.27,97.94)	150.7(108.6, 209.1)	23.89(13.44, 42.46)

Phase 2 clinical trial (GMTs of $PRNT_{50}$**): Homologous**

Drug	Statistic	Day 0	Day 42	Day 90	Day 180
iNCOVACC® (n=160)	GMT 95 % CI	3.1 (1.65,5.67)	286.8 (32,432.09)	43.92 (24.71,78.04)	364.69 (241.95,549.68)
Placebo (n=40)	GMT 95 % CI	3.7 (1.01,13.73)	47.112.34,179.58	24.51(6.8,88.37)	178.24(54.58,582.05)

Spike specific mucosal (Saliva) IgA

Drug	Statistic	Day 0	Day 9	Day 28	Day 42
iNCOVACC® (n=32)	GMT 95 % CI	16.00 (16.00,16.00	16.78 (11.27,24.99)	17.19 (11.37,25.98)	22.63 (15.00,34.14))
Placebo (n=8)	GMT 95 % CI	16.00 (16.00,16.00)	16.00 (16.00,16.00)	19.50 (5.81,65.50)	32.00 (10.04,101.97)

Increase in the mucosal IgA titers is significant in subjects, who received iNCOVACC®

Phase 3 clinical trial (GMTs of $PRNT_{50}$**): Homologous**

Drug	Statistics	Day 0	Day 42	Day 90
INCOVACC® / iNCOVACC®(n=481)	GMT 95 % CI	26.1(18.7,36.6)	768.5(665.1,888.0)	843.20(746.30,952.70)
BBV152/ COVAXIN®(n=159)	GMT 95 % CI	37.0(21.0,65.4)	531.0(425.9,662.1)	712.70(587.70,864.50)

iNCOVACC® nasal vaccine has been evaluated and shown satisfactory immune response against several variants of Omicron including the recent variant BA.5. Cell mediated immune response, both T and B cell phenotype distribution is evaluated against SARS-CoV-2 variants including omicron variants found the response is persistent across variants.

Variant		BA.1		BA.2		BA.2.12		BA.5	
Group		iNCOVACC®	COVAXIN®	iNCOVACC®	COVAXIN®	iNCOVACC®	COVAXIN®	iNCOVACC®	COVAXIN®
Day 0	GMT	10.67	21.97	17.97	7.29	0.49	334.59	10.19	4.22
	95% CI	(1.41, 80.66)	(0.31, 1563.82)	(2.57, 125.87)	(0.03, 1708.74)	(0.12, 2.02)	(238.39, 469.62)	(6.07, 17.10)	(1.41, 12.61)
Day 42	GMT	219.97	458.66	355.74	197.10	524.87	92.28	170.80	82.36
	95% CI	(62.07, 779.59)	(215.18, 977.68)	(215.58, 587.03)	(62.35, 623.09)	(336.09, 819.67)	(53.72, 158.51)	(136.80, 213.20)	(48.91, 38.70)

Heterologous Clinical Trial

Phase 2 clinical trial (GMTs of $PRNT_{50}$)**:Heterologous**

	Statistics	Group-1 (N=152)	Group-2 (N=152)	Group-3 (N=152)	Group-4 (N=152)
		COVAXIN® + COVAXIN®	COVAXIN® + iNCOVACC®	iNCOVACC® + COVAXIN®	iNCOVACC®+ iNCOVACC®
Day 0	GMT (95% CI)	20.34(13.0,31.7)	19.31(11.9,31.2)	19.72(12.6,30.6)	25.95(15.6,43.1)
Day 56	GMT (95% CI)	285.11(199.3,407.7)	464.54(335.12,643.9)	303.6(226.7,406.5)	430.2(286.7,645.3)
Day 90	GMT (95% CI)	188.58(120.7,294.6)	253.47(170.3,377.2)	365.24(273.8,487.0)	298.91(206.6,432.2)
Day 180	GMT (95% CI)	493.38(346.2,703.1)	577.65(437.4,762.8)	511.74(366.1,715.8)	405.64(272.8,603.1)

Effectiveness against SARS-CoV-2 Variants

iNCOVACC® nasal vaccine has been evaluated and shown satisfactory immune response against several variants of such as Delta and Beta. Cell mediated immune response, both T and B cell phenotype distribution is evaluated against SARS-CoV-2 variants including omicron variants found the response is persistent across variants.

Delta					
Days	Statistics	(COVAXIN® + COVAXIN®	(COVAXIN® + iNCOVACC®)	(iNCOVACC® + COVAXIN®	(iNCOVACC® + iNCOVACC®)
Day 0	GMT (95% CI)	2.4 (0.6,9.5)	0.7 (0.2,2.1)	1.4(0.4,5.0)	2.3 (0.7,7.1)
Day 37	GMT (95% CI)	55.8(19.3,161.5)	107.3(39.2,293.3)	59.5(18.3,193.9)	40.3(12.4,130.8)
Day 56	GMT (95% CI)	166.3 (80.3,344.3)	323.5(199.8,524.0)	280.8(144.9,544.4)	216.4(113.0,414.1)

Beta					
Days	**Statistics**	**(COVAXIN® + COVAXIN®**	**(COVAXIN® + iNCOVACC®)**	**(iNCOVACC® + COVAXIN®**	**(iNCOVACC® + iNCOVACC®)**
Day 0	**GMT(95% CI)**	6.81 (2.0,23.0)	2.0(0.6,6.8)	3.7(1.1,12.5)	4.8(1.6,14.2)
Day 37	**GMT(95% CI)**	16.5(4.1,65.9)	36.1(9.6,136.0)	20.1(4.8,83.6)	29.0(9.4,89.3)
Day 56	**GMT(95% CI)**	101.7(42.9,240.9)	201.9(107.8,377.9)	209.0(111.7,391.0)	159.5(82.0,310.0)

Phase 3 clinical trial (GMTs of $PRNT_{50}$**) Heterologous**

Day	**Statistics**	**COVAXIN® (n=300)**		**COVISHIELD (n=500)**		
Day 0	**GMT (95%CI)**	319.55 (242.13,421.72)		376.4 (296.95,477.12)		
		iNCOVACC® (n=250)	**COVAXIN® (n=125)**	**iNCOVACC® (n=250)**	**COVAXIN® (n=125)**	**COVISHIELD (n=125)**
Day 0	**GMT (95%CI)**	289.63 (204.84,409.53)	388.65 (243.83,619.5)	372.19 (270.15,512.76)	320.88 (185.08,556.31)	451.56 (289.71,703.83)
Day 28	**GMT (95%CI)**	365.47 (272.01,491.05)	409.11 (287.58,581.99)	518.09 (403.35,665.46)	368.84 (238.91,569.43)	363.25 (227.04,581.16)
Day 56	**GMT (95%CI)**	564.06 (479.09,664.11)	578.05 (436.86,764.89)	655.49 (533.25,805.75)	625.39 (474.68,823.96)	650.07 (519.74,813.09)

Spike specific mucosal (Saliva) IgA Titers

Increase in the mucosal IgA titers is significant in subjects, who received iNCOVACC® as booster dose, compared to the other booster vaccines.

Day 0	**COVAXIN®**		**COVISHIELD**		
n	18		38		
GMT*	16.63		33.80		
95%CI	(8.85-31.25)		(21.15-54.02)		
BOOSTER	**INCOVACC®**	**BBV152**	**INCOVACC®**	**BBV152**	**COVISHIELD**
	iNCOVACC®	**COVAXIN®**	**iNCOVACC®**	**COVAXIN®**	**COVISHIELD**
Day 0 (n)	12	6	20	8	10
GMT*	14.25	22.63	22.63	53.82	51.98
95%CI	(5.81-34.97)	(8.3-61.67)	(11.68-43.84)	(15.74-184.0)	(20.38-132.6)
Day 28 (n)	12	6	20	8	10
GMT*	32	20.16	25.99	41.5	22.63
95%CI	(11.85-86.44)	(3.92-103.6)	(13.24-51.04)	(14.9-115.6)	(5.88-87.1)
GMT Ratio	2.25	0.89	1.15	0.77	0.44

Effectiveness against SARS-CoV-2 Variants

iNCOVACC® nasal vaccine has been evaluated and shown satisfactory immune response against several variants of Omicron including the recent variant BA.5. Cell mediated immune response, both T and B cell phenotype distribution is evaluated against SARS-CoV-2 variants including omicron variants found the response is persistent across variants.

Day 0	COVAXIN®		COVISHIELD		
BA.1	3430.23		1689.05		
BA.2	484.79		232.71		
BA.5	256.32		298.26		
Ancestral	247.61		439.36		
BOOSTER	**iNCOVACC®**	**COVAXIN®**	**iNCOVACC®**	**COVAXIN®**	**COVISHIELD**
Day 56	**Group 1**	**Group II**	**Group III**	**Group IV**	**Group V**
BA.1	1166.78	1337.99	1140.61	1173.79	1179.71
BA.2	119.64	133.27	128.19	155.06	163.10
BA.5	164.87	267.71	170.74	67.33	79.36
Ancestral	344.38	475.12	185.96	164.62	206.95

5.2 Pharmacokinetic properties

Evaluation of pharmacokinetic properties is not required for vaccines.

5.3 Preclinical safety data

Safety and immunogenicity in Mice, Rats, Hamsters and Rabbits

Repeated dose toxicity study conducted with **iNCOVACC®** in laboratory animals (BALB/c mice, Swiss Albino mice, Wister rats, Syrian Hamsters and New Zealand Rabbits), based on the New Drugs and Clinical Trials Rules, 2019 and WHO guidelines on Nonclinical Evaluation of Vaccines.

Treatment with **iNCOVACC®** did not show treatment related changes in clinical signs, body weights, feed consumption, body temperature, clinical pathology, terminal fasting body weights, organ weights and gross pathology in both sexes. There was no treatment related microscopic findings observed in animals treated with **iNCOVACC®**.

No mortality was observed throughout the study period. No clinical signs of toxicity were observed in all the treated animals.

Local reactogenicity was assessed Prior to study, on day of each dosing and followed by 24 hours as per Draize scoring system. No skins reactions were observed.

There were no treatment related changes observed in clinical pathology parameters, terminal fasting body weights and organ weights in any of the groups in both sexes.

Animals immunized through intranasal route with **iNCOVACC®**, at a given antigen concentrations found to be immunogenic, eliciting high levels of IgG and IgA antibodies specific to SARS-CoV-2 S1 antigen. High Neutralization antibody titers were observed in sera collected from vaccinated animals.

In conclusion, treatment with **iNCOVACC®** even at high dose (5 x 10^{11} VP/animal) did not produce any treatment related changes when administered with full Human Single Dose (HSD) of multiple doses (n+1).

iNCOVACC® and COVAXIN® Heterologous vaccination in laboratory animal models: Heterologous vaccination study was conducted in rabbits; wherein, a group of animals primed with COVAXIN® (Whole-Virion Inactivated vaccine) intramuscularly (IM) followed by intranasal (IN) booster dose with iNCOVACC®. Animals received two doses of either COVAXIN® or iNCOVACC® were used as controls to compare the immunogenicity results. Heterologous vaccination elicited significantly high levels of spike-specific IgG and IgA titers, compared with the homologous vaccination.

Challenge Studies of ChAd36-SARS-CoV-2-S Carried out at Washington University.

Introduction: ChAd36-SARS-CoV-2-S is an adenoviral based SARS-CoV-2 intranasal vaccine (ChAd36-SARS-CoV-2-S) expressing a prefusion stabilized spike (S) protein developed by Michael Diamond's group (Washington University, Saint Louis, USA).

Brief summary of challenge studies

Challenge studies were performed in three different animal models, K18-hACE2 transgenic mice, Syrian hamster and non-human primates.

(i) K18-hACE2 transgenic mice: Mice were immunized with ChAd36-SARS-CoV-2-S, in two different routes. Both, Intranasal or intramuscular administration of ChAd36-SARS-CoV-2-S, prevents SARS-CoV-2 lung infection and pneumonia in mice. In particular, intranasal delivered ChAd36-SARS-CoV-2-S uniquely prevents both upper and lower respiratory tract infections, potentially protecting against SARS-CoV-2 infection and transmission (*Hassan et al. 2020*).

(ii) Syrian Hamsters: Similarly, intranasal administration of ChAd36-SARS-CoV-2-S in Syrian hamster showed superiority over intramuscular vaccination, in terms of neutralizing antibodies and in preventing SARS-CoV-2 infection in both the upper and lower respiratory tracts (*Bricker et al. 2020*).

(iii) Rhesus macaques: Single-dose intranasal immunization of ChAd36-SARS-CoV-2-S, in Rhesus macaques induces neutralizing antibodies and T cell responses against SARS-CoV-2. ChAd36-SARS-CoV-2-S vaccine protected Rhesus monkeys against SARS-CoV-2 infection (Hassan et a*l. 2021*).

Protection against SARS-CoV-2 Variants: Further, assessment of durability, dose response, and cross-protective activity of ChAd36-SARS-CoV-2-S against SARS-CoV-2 variants following single intranasal dose induced durable high neutralizing antibodies along with S-specific IgG and IgA secreting long-lived plasma cells in the bone marrow. Protection against a historical SARS-CoV-2 strain was observed across a 100-fold vaccine dose range and over a 200-day period. At 6 weeks or 9 months after vaccination, serum antibodies neutralized SARS-CoV-2 strains, B.1.351, B.1.1.28, and B.1.617.1 spike protein and conferred almost complete protection in the upper and lower respiratory tracts after challenge with variant viruses. Thus, in mice, intranasal immunization with ChAd36-SARS-CoV-2-S provides durable protection against historical and emerging SARS-CoV-2 strains (Hassan *et al. 2021b*).

6. PHARMACEUTICAL PARTICULARS

6.1 List of excipients

Tris (pH 7.4), Sodium Chloride, Magnesium Chloride, Glycerol and Polysorbate- 80.

6.2 Incompatibilities

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

6.3 Shelf life

The expiry date of **iNCOVACC®**COVID-19 Vaccine [ChAd36-SARS-CoV-2-S (Recombinant)] is indicated on the label and carton of the vaccine. Do not use the vaccine after the expiration date shown on the label and carton of the vaccine. Once opened, Multi dose vial should be used as soon as practically possible and within 6 hours when kept between +2 to +8°C.

iNCOVACC® should be discarded at the end of the immunization session or within 6 hours whichever comes first.

6.4 Special precautions for storage

Store at +2° to +8 °C, do not freeze. Discard if frozen.

Shake gently before use.

Keep out of reach of children.

Protect from light. Store vials in the original carton till the vial is used.

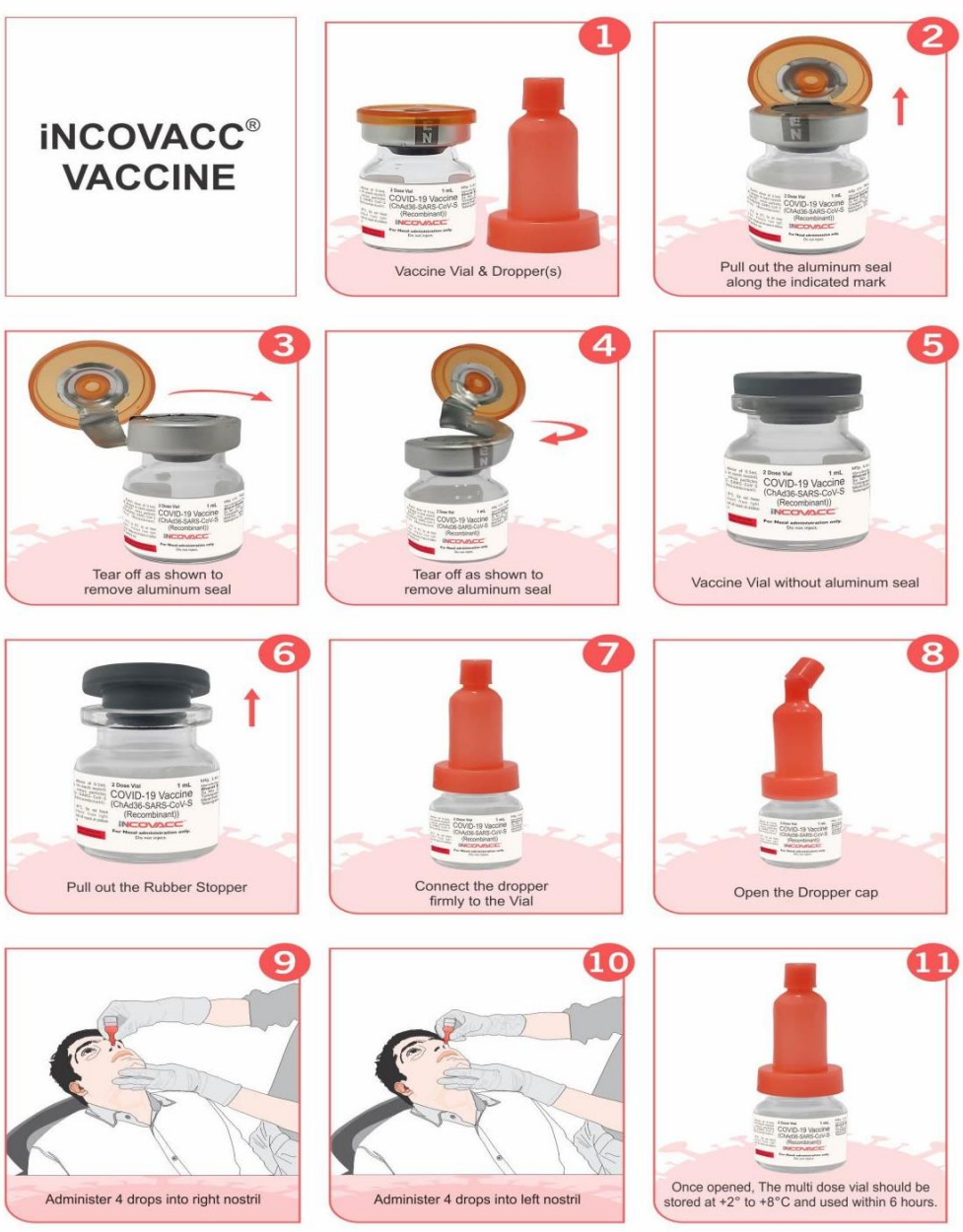
7. PRESENTATION

iNCOVACC® COVID-19 Vaccine [ChAd36-SARS-CoV-2-S(Recombinant)] is presented in USP type 1-glass vials.

- Multi dose vial - 1mL (2 dose)

8. INSTRUCTIONS FOR USE, HANDLING AND DISPOSAL

8.1 Vial (2Dose) Administration procedure:



Note - Dropper should be replaced for the administration of vaccine to the second recipient.

iNCOVACC® 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).

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Manufactured and Marketed by:

Bharat Biotech International Ltd.
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please email feedback@bharatbiotech.com or call on **Toll-free number 1800 102 2245**