V4.0

Package Insert

First Approval Date: 16-06-2021

Revision date: 26-12-2022

Convidecia (Trade Mark) Recombinant Novel Coronavirus Vaccine (Adenovirus Type 5 Vector) Solution for Injection

Convidecia™

DISCLAIMER: THIS PRODUCT IS APPROVED UNDER MALAYSIA CONDITIONAL REGISTRATION FOR PHARMACEUTICAL PRODUCTS DURING DISASTER GUIDELINE. THE ADMINISTRATION OF THE PRODUCT IS PURELY BASED ON INDIVIDUAL'S PREFERENCE

This medicinal product is subject to additional monitoring. This will allow quick identification of new safety information. Healthcare professionals are asked to report any suspected new or serious adverse events. This product information will be updated on a regular basis as further data and safety reports become available

1. DRUG NAME

Proprietary Name: Recombinant Novel Coronavirus Vaccine (Adenovirus Type 5 Vector)
Trade Name: Convidecia or CONVIDECIA

2. DESCRIPTION

The final product is sterile liquid injection in 2 ml glass vial of single dose (0.5 ml per dose) or three doses per vial (1.5 ml per vial, 0.5 ml per dose). The vaccine is colorless or slightly white liquid injection.

Active Ingredient: Each 0.5mL contains $\geq 4\times10^{10}$ viral particles of replication-defective recombinant human type 5 Adenovirus expressing S protein of SARS-CoV-2.

Excipients: Mannitol, sucrose, sodium chloride, magnesium chloride, polysorbate 80, glycerin, and N-(2-Hydroxyethyl) piperazine-N'-(2-ethanesulfonic acid) (HEPES) and Water-For-Injection as solvent.

3. INDICATIONS AND USAGE

Convidecia is indicated for active immunization to prevent COVID-19 caused by SARS-CoV-2, in individuals 18 years of age and older.
The use of this vaccine should be in accordance with official recommendations.

4. RECOMMENDED DOSAGE

Individuals 18 years of age and older:

Single dose. Each dose contains 0.5 mL liquid injection, supplied in a single-dose glass vial or three-dose glass vial.

A booster dose (0.5ml) may be administered at least 3-6 months after the first single dose when the potential benefits outweigh any potential risks.

The decision when and for whom to implement a booster dose of the vaccine should be made based on available vaccine effectiveness data, taking into account limited safety data (see clinical section).

Pediatric Population:

The safety and efficacy data in children and adolescent (less than 18 years old) have not yet established. No data available.

Elderly Population (>60 years and above):

The safety and efficacy data of people aged 60 years and above are limited in the clinical trials.

Women in childbearing age:

The data collected in clinical trials for women who have unintended pregnancy after Recombinant Novel Coronavirus Vaccine (Adenovirus Type 5 Vector) vaccination is very limited. It is not enough to assess the risk of adverse pregnancy outcomes (including spontaneous abortion) after vaccination with Recombinant Novel Coronavirus Vaccine (Adenovirus Type 5 Vector).

Method of administration

A single dose for intramuscular injection in the deltoid muscle of the upper arm.

Instruction for use

1) A disposable medical grade syringe is used to extract the liquid in the vial. After emptying air bubbles, the vaccine can be injected in the deltoid muscle of the upper arm.
2) The vaccine should be checked if the packaging container, label, appearance and expiry date meet the requirements before injection. It should not be used under following circumstances: crack on the vaccine vial or syringe, presence of visible particles, discoloration, falling off label or expired vaccine.
3) Once the vaccine is opened, it should be used immediately. Each dose of vaccine should be used up at one time and not divided into multiple uses.

5. ADVERSE REACTIONS

The safety of Ad5-nCoV vaccine has been evaluated in three clinical trials carried out in China and internationally:

1) A non-randomized, opened phase I clinical trial in adults aged 18-60 years in China;
2) A randomized, double-blind, placebo-controlled phase II clinical trial in people aged 18 years and older in China;
3) A randomized, double-blind, placebo-controlled, multi-center phase III efficacy clinical trial in people aged 18 years and older in Pakistan, Mexico, Russia, Chile and Argentina.

In the Phase I and Phase II clinical trials, adverse events within 28 days after vaccination and severe adverse events (SAE) within 6 months after vaccination were collected for all subjects. In the phase III clinical trial, all subjects were regularly followed up by the investigator to collect Medically Attended Adverse Events (MAE) and SAE within 12 months. Adverse events within 28 days after vaccination were systematically collected in the safety extended cohort (3000 people), which has not yet been completed currently.

In the clinical trials of Ad5-nCoV vaccine in China and internationally, a total of 17,355 subjects aged 18 years and older were vaccinated with one dose of Ad5-nCoV vaccine. Among them, 500 subjects have completed the systematic safety follow-up for at least 28 days after vaccination. The long-term safety follow-up is still in progress.

According to the classification of the incidence of adverse reactions recommended by the Council for International Organizations of Medical Sciences (CIOMS): very common (≥10%), common (1%~10%, including 1%), uncommon (0.1%~1%, including 0.1%), rare (0.01%~0.1%, including 0.01%), very rare (<0.01%), the safety data from clinical trials and the experience of emergency use of Ad5-nCoV are summarized as follows:

(1) Local adverse reaction at injection site

Very common: pain;

Common: swelling, itch, redness, induration;

Uncommon: bleeding, rash, cellulitis.

(2) Systemic adverse reactions

Very common: fever, headache, fatigue, myalgia, drowsiness, nausea, diarrhea;

Common: joint pain, cough, oropharyngeal pain, vomiting, loss of appetite, dizziness, mucosal disease, pruritus;

Uncommon: hypoesthesia, gastrointestinal dysfunction, joint swelling, syncope, difficulty in breathing, acute bronchospasm, itching (non-vaccination site), acute allergic reaction.

(3) Severity of adverse reactions

The severity of adverse reactions observed in clinical trials of Ad5-nCoV is mainly grade 1 (mild), and the incidence of grade 3 and above adverse reactions is 7.40%.

The adverse reactions at the injection site of grade 3 and above are pain, swelling, and redness; the systemic adverse reactions of grade 3 and above are fever, headache, drowsiness, nausea, and myalgia.

(4) Serious adverse event

Investigators have judged all the serious adverse events (SAE) observed in clinical trials as unrelated or possible unrelated to vaccination till January 10, 2021.

Based on data from Phase I (NCT04568811) and Phase IIb (NCT04566770) clinical trials, the overall incidence of adverse reactions after booster vaccination is found to be similar to that of the first dose, but the severity is better than that of the first dose.

6. CONTRAINDICATIONS

1) Allergic reaction to any component of this vaccine or similar vaccines.
2) People who have experienced severe allergic reactions to vaccines in the past (such as acute allergic reactions, angioedema, dyspnea, etc.).
3) People with uncontrolled epilepsy and other progressive neurological diseases, and the history of Guillain-Barré syndrome.
4) Pregnant and lactating women.

7. WARNINGS AND PRECAUTIONS

1) The protection persistency data of Recombinant Novel Coronavirus Vaccine (Adenovirus Type 5 Vector) has not yet been obtained. Necessary self-protection measures against COVID- 19 still should be taken after vaccination.

2) This vaccine is strictly prohibited by intravascular injection. There are no data on the safety and efficacy of this vaccine by subcutaneous or intradermal injection.

3) Before use, check whether the packaging container, label, appearance, and expiration date meet the requirements. It should not be used under following circumstances: damage or crack, spots, stains, scratches on the outer surface of the vaccine container, unclear label, expired vaccine, or abnormal appearance.

4) Keep the product out of reach of children.

5) People who are vaccinated should be observed on site according to the local general vaccination practice (at least 30 minutes). The vaccination clinic should be equipped with first- aid drugs and equipment such as epinephrine to deal with the emergency such as severe acute allergic reaction.

6) Recombinant Novel Coronavirus Vaccine (Adenovirus Type 5 Vector) cannot be mixed with other vaccines in the same syringe.

7) Recombinant Novel Coronavirus Vaccine (Adenovirus Type 5 Vector) should be used immediately after opening.

8) People suffering from acute diseases, acute-outbreak period of chronic diseases, severe chronic diseases, allergies and fever should be used with caution. If necessary, the vaccination shall be delayed after the doctor's evaluation.

9) Cautionary use for diabetic patients and those with history of convulsions, epilepsy, encephalopathy or mental illness or family history.

10) Cautionary use for those with a history of asthma.

11) Cautionary use for patients with thrombocytopenia or any coagulation dysfunction since intramuscular injection of this vaccine may cause bleeding.

12) The safety and efficacy data for people with impaired immune function (such as malignant tumors, nephrotic syndrome) is limited. Those people should be vaccinated based on individualized considerations.

13) Those who have been injected with immune globulin should vaccinate Recombinant Novel Coronavirus Vaccine (Adenovirus Type 5 Vector) at an interval of more than 1 month to avoid decreasing the immune effect.

14) There is no evidence of the efficacy of Recombinant Novel Coronavirus Vaccine (Adenovirus Type 5 Vector) for people with SARS-CoV-2 infection history at this point.

15) People with positive HIV infection. There is very limited data available for this vaccine in HIV-positive population. It is recommended that the use of this vaccine in people with positive HIV infection should be strictly under physicians' guidance.

16) Same as other vaccines, Recombinant Novel Coronavirus Vaccine (Adenovirus Type 5 Vector) may not produce 100% efficacy in the vaccinated population.

17) This is a CONTROLLED MEDICINE in Malaysia.

8. SYMPTOMS AND TREATMENT OF OVERDOSE

In the event of overdose, monitoring of vital functions and possible symptomatic treatment is recommended. Only one single dose is used for administration for each person. No overdose should occur.

9. AFFECTS ON ABILITY TO DRIVE AND OPERATE MACHINERY

Based on available clinical trial results, no effect on ability to drive and operate machinery caused by Recombinant Novel Coronavirus Vaccine (Adenovirus Type 5 Vector) has been found. However, some of the adverse effects may temporarily affect the ability to drive or use machines.

10. SPECIAL POPULATION

1) Women of childbearing age: The data collected in clinical trials for women who have unintended pregnancy after Recombinant Novel Coronavirus Vaccine (Adenovirus Type 5 Vector) vaccination is very limited. It is not enough to assess the risk of adverse pregnancy outcomes (including spontaneous abortion) after vaccination with Recombinant Novel Coronavirus Vaccine (Adenovirus Type 5 Vector).

2) Pregnant or lactating women: Convidecia is contraindicated in pregnant and lactating women. There is limited information on the use of Convidecia in pregnant and lactating women.

3) Fertility: Animal studies on Reproductive and Developmental toxicity found that the vaccine does not suppress fertility.

4) People age 60 years and older: The safety and efficacy data of people aged 60 years and above are limited in the clinical trials.

11. DRUG INTERACTIONS

1) Simultaneous vaccination with other vaccines: No undergone clinical trial for simultaneous vaccination with other vaccines.

2) Concomitant use with other drugs: no relevant data is available for immunosuppressants, chemotherapeutics, antimetabolites, alkylating agents, cytotoxic drugs, corticosteroids, etc., which may reduce the immune response of Recombinant Novel Coronavirus Vaccine (Adenovirus Type 5 Vector).

3) For people received or is receiving drug therapy, the consultancy of professional physician is required to avoid possible drug interactions.

12. STORAGE AND HANDLING

1. Unopened vial (single-dose and multi-dose)
It should be stored and transported in refrigerated conditions at 2-8 degrees Celcius. Do not freeze.

2. Opened multi-dose vial
Opened multi-dose vial should be used as soon as practically possible and within 6 hours of opening. The vaccine (vial) should be stored between 2°C and 8°C during in-use period. Discard any unused vaccine if is not kept within the recommended conditions.

13. SHELF-LIFE

1. Unopened vial (single-dose and multi-dose)
18 months.

2. Opened multi-dose vial
Opened multi-dose vial should be used as soon as practically possible and within 6 hours of opening. The vaccine (vial) should be stored between 2°C and 8°C during in-use period. Discard any unused vaccine if is not kept within the recommended conditions.

14. PACKAGE

Single-dose (0.5ml/vial) in 2ml glass vial;
Multi-dose (3 doses/1.5ml/vial) in 2ml glass vial.

15. PRE-CLINICAL SAFETYDATA

Non-clinical data reveal no special hazard for humans based on conventional studies of single dose toxicity, repeat dose toxicity and local tolerance.

Genotoxicity/Carcinogenicity

Neither genotoxicity nor carcinogenicity studies were performed. The components of Recombinant Novel Coronavirus Vaccine (Adenovirus Type 5 Vector) are not expected to have genotoxic potential.

Reproductive toxicity

The reproductive toxicity study in rats show no toxicity in dams or foetuses.

16. PHARMACODYNAMIC

Mechanism of actions

Recombinant Novel Coronavirus Vaccine (Adenovirus Type 5 Vector) has been developed based on gene sequence of SARS-CoV-2. The target gene sequence of S protein was synthesized and packaged into a replication-deficient recombinant adenovirus to express S protein of SARS-CoV-2. One dose contains ≥ 4×10^{10}vp recombinant replication-defective human type 5 adenovirus expressing the S protein of SARS-CoV-2. No adjuvant and no preservative is used in the formulation. No component from animal sources is used in the manufacturing of the Recombinant Novel Coronavirus Vaccine (Adenovirus Type 5 Vector). Following administration, the S protein of SARS-CoV-2 is expressed locally stimulating neutralising antibody and cellular immune responses. The vaccine successfully induced a high level of cellular and humoral immune response on 28 days after vaccination. The cellular immune response peaked on 14 days.

Clinical results of immunogenicity

The immunogenicity endpoint of this Recombinant Novel Coronavirus Vaccine (Adenovirus Type 5 Vector) mainly included the geometric mean titer (GMT) of neutralizing antibody and the response level of cellular immune index (IFN-γ). Some subjects in the phase I clinical trial completed a booster immunization study 6 months after the primary immunization. Neutralizing antibody was determined by micro cytophysiologic method, IFN-γ was determined by ELISpot method.

Determination criteria of Ad5 neutralizing antibody level: high level of Ad5 neutralizing antibody titer is >1:200; low level of Ad5 neutralizing antibody titer is ≤1:200. The high level of Ad5 antibody could weaken the specific antibody response and T cell response induced by the inoculation of this Recombinant Novel Coronavirus Vaccine (Adenovirus Type 5 Vector). See below for details.

Table 1. Analysis results of neutralizing antibody and IFN-γ response level in I,II clinical trials and Phase I booster, Phase IIb Clinical trial(PPS)

Time after immunization	Low-dose group in I phase (After primary immunization N=35, after booster immunization N=28)		Low-dose group in II phase（N=124）		Low-dose group in I phase（N=35）	Low-dose group inII phase (N=124)
	Live virus GMT（95%CI）	Pseudovirus GMT（95%CI）	Live virus GMT（95%CI）	Pseudovirus GMT（95%CI）	Response level of IFN-γ（95%CI）	
Day 0	4.000	5.000	4.000	5.450	0.0	0.3

Day 14 after primary immunization	7.827 (5.580, 10.979)	17.853 (10.540, 30.242)	/	/	53.4 (22.3,84.5)	/
Ad5≤200	15.213 (8.219, 28.160)	44.852 (17.383,115.728)	/	/	72.2 (4.3,140.1)	/
Ad5>200	4.754 (3.826,5.909)	8.947 (5.766,13.883)	/	/	39.4 (13.4,65.3)	/
Day 28 after primary immunization	14.155 (9.334,21.464)	29.049 (17.780,47.462)	18.436 (14.508,23.427)	55.800 (45.818,67.957)	34.8 (14.8,54.8)	18.4 (14.5,22.3)
Ad5≤200	30.471 (16.058,57.820)	60.509 (29.538,123.955)	27.315 (19.022,39.223)	72.041 (56.536,91.798)	59.5 (15.2,103.9)	22.4 (15.1,29.7)
Ad5>200	7.964 (5.199,12.201)	16.754 (9.142,30.705)	13.748 (10.090,18.731)	46.112 (34.509,61.617)	16.2 (5.9,26.5)	15.4 (11.3,19.4)
Month 3 after primary immunization	11.955 (7.230,19.765)	33.885 (21.078,54.473)	/	/	/	/
Ad5≤200	39.329 (17.032,90.815)	91.163 (43.140,192.646)	/	/	/	/
Ad5>200	4.894 (3.986,6.008)	16.130 (10.845,23.992)	/	/	/	/
Month 6 after primary immunization	10.059 (6.748,14.994)	21.579 (13.497,34.500)	/	32.607 (26.718,39.794)	6.5 (1.0,7.0)	/
Ad5≤200	24.394 (12.383,48.057)	60.982 (28.315,131.338)	/	55.883 (41.874,74.579)	10.7 (-2.0,23.3)	/
Ad5>200	5.176 (4.140,6.472)	9.901 (7.274,13.475)	/	21.810 (17.196,27.661)	3.4 (1.5,5.2)	/
	Phase I booster		**Phase IIb**		**Phase I booster**	**Phase IIb**
Day 14 after booster immunization	74.354 (46.843,118.021)	519.471 (344.780,782.674)	/	125.714 (79.336,199.202)	41.6 (-0.5,83.7)	8.1 (4.2,12.0)
Day 28 after booster immunization	101.810 (65.720,157.717)	426.067 (298.158,608.850)	/	76.806 (52.361,112.663)	/	9.2 (5.6,12.8)
Month 6 after booster immunization	16.114 (11.697,22.199)	58.574 42.247,81.211		/	/	/

The booster immunization of the Ad5-based COVID-19 vaccine is safe and immunogenic on healthy adults. The booster immunization can stimulate much higher level of immuneresponse when given at 3-6 months later compared with that of the primary vaccination.

Efficacy

This overseas pivotal phase III clinical trial was carried out in a multi-center, randomized, double blind, placebo-controlled design in five countries, including Pakistan, Mexico, Russia, Chile, and Argentina, to evaluate the protective efficacy of this Recombinant Novel Coronavirus Vaccine (Adenovirus Type 5 Vector).

The primary study hypothesis of protective efficacy is that the lower limit of the 95%confidence interval (95% CI) for protective efficacy is greater than 30% in the 1-dose

vaccination for 28 days and later compared with placebo group. The main analysis method of protective efficacy is to calculate the protection rate based on incidence rate. The secondary study hypothesis is that the lower limit of 95%CI for protection is greater than 30% in the 1-dose vaccination for 14 days and later compared with placebo group. All valid endpoint cases were confirmed by the Endpoint Determination Committee. At the time of the interim analysis of the phase Ⅲ clinical trial, a total of 34,385 subjects were randomly enrolled, 9.90% of whom were subjects aged 60 years and above.

In the interim analysis, 100 cases of valid endpoint cases to be primarily studied (28 days after vaccination) were obtained. Protective efficacy against COVID-19 at28 days and later after 1 dose immunization: The protective efficacy in all symptomatic cases was 65.28% (95%CI: 45.73, 77.79), meeting the primary study hypothesis; The protective efficacy in severe cases was 90.07% (95%CI: 22.41, 98.73). In the interim analysis, 205 cases of valid endpoint cases to be secondly studied (14 days after vaccination) were obtained. Protective efficacy against COVID-19 14 days and later after 1 dose immunization: Protection in all symptomatic cases was 68.83% (95%CI: 57.03, 77.39), meeting the secondary study hypothesis; The protective efficacy in severe cases was 95.47% (95%CI: 66.39, 99.39).

17. PHARMACOKINETIC

Not applicable

18. REGISTRATION NUMBER(S)

MAL21066050AZ

19. HEADQUARTERS

CANSINO BIOLOGICS INC.

185 South Ave., TEDA West District, Tianjin, China, 300462

20. MANUFACTURED AND RELEASED BY

CANSINO BIOLOGICS INC.

Building 020, 6 Xinpeng Road, TEDA West District, Binhai New Area,
Tianjin, China, 300462

21. PRODUCT REGISTRATION HOLDER

Solution Biologics Sdn. Bhd.

PT 13796Jalan Tekno Usahawan 2, Technology Park Malaysia, 57000 Kuala Lumpur,
Wilayah Persekutuan, Malaysia