เอกสารกำกับยาภาษาอังกฤษ

Summary of Product Characteristic

CoronaVac

โปรดสแกน QR Code
เพื่ออ่านคู่มือและเอกสารกำกับยา

CoronaVac is indicated for active immunization of individuals 6-59 years old for the prevention of coronavirus disease 2019 (COVID-19).

This medicinal product is under the conditional approval of modern medicine for human use in emergency situation during a pandemic crisis.

The prescribed physician is required to report any adverse reactions to the Food and Drug Administration.

Please read the information carefully.

1. NAME OF THE MEDICINAL PRODUCT

CoronaVac

2. QUALITATIVE AND QUANTITATIVE COMPOSITION

Each dose (0.5 ml) contains inactivated SARS-CoV-2 as an antigen of 600 SU.

The adsorbed vaccine COVID-19 (inactivated) is derived from the new coronavirus SARS-CoV-2 (strain CZ02) and grown in an African green monkey kidney cell (Vero Cell), followed by culture, harvesting, inactivation, concentration, purification and adsorption with aluminum hydroxide.

For full list of excipients, see section 6.1.

3. PHARMACEUTICAL FORM

Suspension for Injection.

CoronaVac is a milky-white suspension. Stratified precipitate may form which can be dispersed by shaking.

4. CLINICAL PARTICULARS

4.1 Therapeutic indications

CoronaVac is indicated for active immunization of individuals 6-59 years old for the prevention of coronavirus disease 2019 (COVID-19).

For elderly population, see section Elderly population.

For Paediatric population, see section Paediatric population.

4.2 Posology and method of administration

Posology

CoronaVac consists of two separate doses of 0.5 ml each. The second dose should be administered at 2 weeks after the first dose (See 5.1 Pharmacodynamic Properties).

The results of phase 1 / 2 clinical studies conducted in mainland China revealed that administration of CoronaVac at a 4-week interval after the first dose demonstrated a relatively better immunogenicity profile. Please see section 5.1 Pharmacodynamic Properties.

It is recommended that individuals who received the first dose of CoronaVac complete the vaccination course with CoronaVac (see section Special Warnings and Precautions for Use).

Elderly population

Efficacy and safety data are currently limited in individuals ≥60 years old. Administration of CoronaVac should only be carefully considered when the potential benefits outweigh any potential risks for elderly individuals. No dosage adjustment is required.

Paediatric population

Administration and schedule: Two doses should be administered for primary immunization. The second dose is preferably given 28 days after the first dose. 0.5 mL/dose. The vaccination depends on the physician decision.

Method of administration

CoronaVac is for intramuscular (IM) injection only in the deltoid muscle.

For instructions on administration, see section 6.6 Special precautions for disposal and other handling.

4.3 Contraindications

Do not use CoronaVac in individuals who have hypersensitivity to the active substance or to any of the excipients. (Please see section 2. QUALITATIVE AND QUANTITATIVE COMPOSITION and 6.1 List of excipients).

4.4 Special warnings and special precautions for use

Traceability

In order to improve the traceability of CoronaVac, the name and the batch number of the administered product should be clearly recorded.

Hypersensitivity

As per good medical practices, individuals should be interviewed and reviewed all past history (especially the previous immunization and the potential of adverse reactions) before vaccination. 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 CoronaVac should be postponed in individuals suffering from an acute severe febrile illness and/or temperature >37.5°C. However, the presence of a minor illness, such as cold, and/or low-grade fever should not delay vaccination.

Thrombocytopenia and coagulation disorders

As with other intramuscular injections (IM), CoronaVac 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.

Duration and level of protection

The duration of protection has not yet been established. As with any vaccine, vaccination with CoronaVac may not protect all vaccine recipients.

Interchangeability

No data are available on the use of CoronaVac in persons that have previously received a full or partial vaccine series with another COVID-19 vaccine.

4.5 Interaction with other medicinal products and other forms of interaction

No drug interaction studies have been conducted.

Concomitant administration of CoronaVac with other vaccines has not been studied.

4.6 Fertility, Pregnancy, and Lactation

Pregnancy

No data are available for the use of CoronaVac in pregnant women.

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

Breast feeding

It is unknown whether CoronaVac is excreted in human milk.

Administration of CoronaVac in breast feeding should only be considered when the potential benefits outweigh

any potential risks for the mother and infant.

Fertility

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

4.7 Effects on ability to drive and use machines

No data are available regarding the effects of CoronaVac on the ability to drive or use machines.

4.8 Undesirable effects

Summary of Safety Profile in population aged 18-59 old

There are two (2) phase 1 / 2 clinical studies conducted in mainland China and three (3) phase III clinical studies performed in Brazil, Turkey, and Indonesia. However, no summary of the safety profiles were systematically presented in the interim reports of the phase III clinical studies in Brazil and Turkey.
This section is based on the interim report of the phase III clinical trial conducted in Indonesia.
A phase III clinical study conducted in Indonesia involved 1620 participants with 810 participants in each vaccine and placebo groups. In this study, the subjects were vaccinated with two doses of SARS-CoV-2 vaccine or placebo with 14 days interval of immunization schedule. All participants were included in safety population (ITT). The safety data set in this interim report includes the solicited and unsolicited adverse event within 28 days after second dose in the subset immunogenicity subjects and the SAE occurred at all subjects since beginning of study until December 31, 2020.

It was found that the overall incidence of AEs was 71.5% in the period from beginning of vaccination to 28 days after the whole-schedule immunization. The incidence rate of AEs in vaccinated group and placebo group were 71.6% and 71.1%, respectively. Most of the adverse events were solicited and the incidence rate of solicited adverse events was 60.7%. The incidence in vaccine and placebo groups were 63.0% and 54.0%, respectively. The incidence of unsolicited adverse events in each group was only 45.0% and 43.7%, respectively. There was no significant difference in the incidence of local reactions from both solicited and

unsolicited adverse events between the treatment groups, while there was a significant difference in the incidence of systemic events from solicited adverse events.

The most frequently reported adverse events by preferred term were local pain in injection site and myalgia. In the vaccine group, local pain was reported by 33.3% subjects and 30.5% subjects after first and second injection, respectively. In the placebo group, local pain was reported by 22.2% subjects and 30.1% subjects after first and second injection, respectively. In the vaccine group, myalgia was reported by 25.2% subjects and 19.6% subjects after first and second injection, respectively. In the placebo group, myalgia was reported by 12.6% subjects and 9.0% subjects after first and second injection, respectively.

Most of the adverse events' intensity were mild in both vaccine and placebo groups. Only one subject had Grade 3 hypersensitivity (urticaria) which occurred at Day 2 after vaccination and recovered at Day 6 after treatment. After the first injection, the percentage of mild adverse events in the vaccine and placebo groups were 54.3 and 46.7, respectively. After the second injection, the percentage of mild adverse events in the vaccine and placebo groups were 47.9 and 42.1, respectively. There was significant difference for distribution of severe local reactions between the vaccine and placebo groups, with higher proportion in the placebo group.

In the vaccine group, during the 14-days follow up period after first vaccination, there were 158 (39.0%) participants experiencing local reactions and 185 (45.7%) participants experiencing systemic events. During the 28-days follow up period after second vaccination, there were 137 (34.5%) participants experiencing local reactions and 148 (37.3%) experiencing systemic events. The most common local reaction was pain, while the most common systemic event was myalgia. There were nine serious adverse events (SAE) occurred at all subjects with classification as not related to study vaccine products (five SAEs), one SAE was very unlikely and three SAE reported as less likely to study vaccine products as assessed by the DSMB.

The most common adverse events were pain and myalgia, which were reported in small number of vaccine recipients and with no significant difference in proportion with placebo group. Most adverse events were mild or moderate in severity.

In the vaccine group, fever was reported in 2.5% participants after first dose and 1.8% participants after second dose of vaccines, no significant difference in proportion between the vaccine and placebo groups.

Tabulated list of adverse reactions

Table 1: Grading Adverse Events after First and Second Injection

Category	Severity	First vaccination							Second vaccination						
		Vaccine (n=405)		Placebo (n=135)		Total (n=540)		p-value	Vaccine (n=397)		Placebo (n=133)		Total (n=530)		p-value
		No. of events	No. of subjects (%)	No. of events	No. of subjects (%)	No. of events	No. of subjects (%)		No. of events	No. of subjects (%)	No. of events	No. of subjects (%)	No. of events	No. of subjects (%)	
Total adverse events	Mild	475	220 (54.3)	105	63 (46.7)	580	283 (52.4)	0.123	401	190 (47.9)	92	57 (42.9)	493	247 (46.6)	0.317
	Moderate	100	68 (16.8)	21	12 (8.9)	121	80 (14.8)	0.025	79	43 (10.8)	25	14 (10.5)	104	57 (10.8)	0.922
	Severe	25	19 (4.7)	8	8 (5.9)	33	27 (5.0)	0.569	19	14 (3.5)	12	11 (8.3)	31	25 (4.7)	0.026
Total Solicited Adverse Events	Mild	346	186 (45.9)	61	44 (32.6)	407	230 (42.6)	0.007	284	164 (41.3)	58	45 (33.8)	342	209 (39.4)	0.127
	Moderate	51	40 (9.9)	11	7 (5.2)	62	47 (8.7)	0.094	42	30 (7.6)	14	10 (7.5)	56	40 (7.5)	0.988
	Severe	11	8 (2.0)	3	3 (2.2)	14	11 (2.0)	0.860	7	6 (1.5)	4	4 (3.0)	11	10 (1.9)	0.279
Local reactions															
Local pain	Mild	116	114 (28.1)	26	25 (18.5)	142	139 (25.7)	0.027	108	104 (26.2)	31	31 (23.3)	139	135 (25.5)	0.508
	Moderate	19	19 (4.7)	4	4 (3.0)	23	23 (4.3)	0.389	16	16 (4.0)	5	5 (3.8)	21	21 (4.0)	0.890
	Severe	3	3 (0.7)	3	3 (2.2)	6	6 (1.1)	0.168	1	1 (0.3)	4	4 (3.0)	5	5 (0.9)	0.015
Redness	Mild	23	23 (5.7)	5	5 (3.7)	28	28 (5.2)	0.278	16	16 (4.0)	3	3 (2.3)	19	19 (3.6)	0.341
	Moderate	2	2 (0.5)	0	0 (0.0)	2	2 (0.4)	1.000	1	1 (0.3)	0	0 (0.0)	1	1 (0.2)	1.000
	Severe	0	0 (0.0)	0	0 (0.0)	0	0 (0.0)	1.000	0	0 (0.0)	0	0 (0.0)	0	0 (0.0)	-
Induration	Mild	34	34 (8.4)	5	5 (3.7)	39	39 (7.2)	0.068	28	28 (7.1)	6	6 (4.5)	34	34 (6.4)	0.300
	Moderate	0	0 (0.0)	1	1 (0.7)	1	1 (0.2)	0.250	1	1 (0.3)	0	0 (0.0)	1	1 (0.2)	1.000
	Severe	0	0 (0.0)	0	0 (0.0)	0	0 (0.0)	-	0	0 (0.0)	0	0 (0.0)	0	0 (0.0)	-
Swelling	Mild	9	9 (2.2)	1	1 (0.7)	10	10 (1.9)	0.464	12	12 (3.0)	1	1 (0.8)	13	13 (2.5)	0.201
	Moderate	0	0 (0.0)	0	0 (0.0)	0	0 (0.0)	-	1	1 (0.3)	0	0 (0.0)	1	1 (0.2)	1.000
	Severe	0	0 (0.0)	0	0 (0.0)	0	0 (0.0)	-	1	1 (0.3)	0	0 (0.0)	1	1 (0.2)	1.000
Systemic events															
Fever	Mild	4	4 (1.0)	0	0 (0.0)	4	4 (0.7)	0.576	4	4 (1.0)	2	2 (1.5)	6	6 (1.1)	0.640
	Moderate	3	3 (0.7)	0	0 (0.0)	3	3 (0.6)	0.577	0	0 (0.0)	1	1 (0.8)	1	1 (0.2)	0.251
	Severe	3	3 (0.7)	0	0 (0.0)	3	3 (0.6)	0.577	3	3 (0.8)	0	0 (0.0)	3	3 (0.56)	0.577
Fatigue	Mild	63	59 (14.6)	10	10 (7.4)	73	69 (12.8)	0.031	44	43 (10.8)	7	7 (5.3)	51	14 (2.6)	0.057
	Moderate	9	8 (2.0)	2	2 (1.5)	11	10 (1.9)	1.000	12	12 (3.0)	3	2 (1.5)	15	14 (2.6)	0.534
	Severe	3	3 (0.7)	0	0 (0.0)	3	3 (0.6)	0.577	0	0 (0.0)	0	0 (0.0)	0	0 (0.0)	-
Myalgia	Mild	97	84 (20.7)	14	13 (9.6)	111	97 (18.0)	0.003	72	66	8	8 (6.0)	80	74	0.002
	Moderate	18	18 (4.4)	4	4 (3.0)	22	22 (4.1)	0.450	11	11 (2.8)	5	4 (3.0)	16	15 (2.8)	1.000
	Severe	2	2 (0.5)	0	0 (0.0)	2	2 (0.4)	1.000	2	2 (0.5)	0	0 (0.0)	2	2 (0.4)	1.000
Total Unsolicited Adverse Events	Mild	129	93 (23.0)	44	35 (25.9)	173	128 (23.7)	0.483	117	86 (21.7)	34	22 (16.5)	151	108 (20.4)	0.204
	Moderate	49	40 (9.9)	10	7 (5.2)	59	47 (8.7)	0.094	37	26 (6.5)	11	7 (5.3)	48	33 (6.2)	0.595
	Severe	14	13 (3.2)	5	5 (3.7)	19	18 (3.3)	0.782	12	9 (2.3)	8	7 (5.3)	20	16 (3.0)	0.081
Respiratory, thoracic and mediastinal disorders	Mild	32	26 (6.4)	3	3 (2.2)	35	29 (5.4)	0.061	21	17 (4.3)	9	6 (4.5)	29	23 (4.3)	0.911
	Moderate	7	5 (1.2)	1	1 (0.7)	8	6 (1.1)	1.000	3	2 (0.5)	3	3 (2.3)	6	5 (0.9)	0.104
	Severe	1	1 (0.2)	0	0 (0.0)	1	1 (0.2)	1.000	2	2 (0.5)	0	0 (0.0)	2	2 (0.4)	1.000

Infection and infestations	Mild	9	9 (2.2)	1	1 (0.7)	10	10 (1.9)	0.464	8	8 (2.0)	1	1 (0.8)	9	9 (1.7)	0.461
	Moderate	1	1 (0.2)	1	1 (0.7)	2	2 (0.4)	0.438	4	4 (1.0)	1	1 (0.8)	5	5 (0.9)	1.000
	Severe	1	1 (0.2)	0	0 (0.0)	1	1 (0.2)	1.000	0	0 (0.0)	0	0 (0.0)	0	0 (0.0)	-
Gastrointestinal disorders	Mild	17	16 (4.0)	15	12 (9.0)	32	28 (5.2)	0.022	15	13 (3.3)	2	2 (1.5)	17	15 (2.8)	0.377
	Moderate	13	12 (3.0)	2	2 (1.5)	15	14 (2.6)	0.348	8	8 (2.0)	1	1 (0.8)	9	9 (1.7)	0.461
	Severe	4	4 (1.0)	0	0 (0.0)	4	4 (0.7)	0.576	3	2 (0.5)	2	2 (1.5)	5	4 (0.8)	0.263
Musculoskeletal and connective tissue diseases	Mild	7	7 (1.7)	2	2 (1.5)	9	9 (1.7)	1.000	9	9 (2.3)	2	2 (1.5)	11	11 (2.1)	0.739
	Moderate	2	2 (0.5)	1	1 (0.7)	3	3 (0.6)	1.000	4	2 (0.5)	2	1 (0.8)	6	3 (0.6)	1.000
	Severe	1	1 (0.2)	1	1 (0.7)	2	2 (0.4)	0.438	1	1 (0.3)	1	1 (0.8)	2	2 (0.4)	0.439
Ear and labyrinth disorders	Mild	2	2 (0.5)	0	0 (0.0)	2	2 (0.4)	1.000	0	0 (0.0)	1	1 (0.8)	1	1 (0.2)	0.251
	Moderate	0	0 (0.0)	0	0 (0.0)	0	0 (0.0)	-	0	0 (0.0)	0	0 (0.0)	0	0 (0.0)	-
	Severe	0	0 (0.0)	0	0 (0.0)	0	0 (0.0)	-	0	0 (0.0)	0	0 (0.0)	0	0 (0.0)	-
Eye disorders	Mild	1	1 (0.2)	0	0 (0.0)	1	1 (0.2)	1.000	2	2 (0.5)	0	0 (0.0)	2	2 (0.4)	0.263
	Moderate	0	0 (0.0)	0	0 (0.0)	0	0 (0.0)	-	0	0 (0.0)	0	0 (0.0)	0	0 (0.0)	-
	Severe	1	1 (0.2)	0	0 (0.0)	1	1 (0.2)	1.000	0	0 (0.0)	0	0 (0.0)	0	0 (0.0)	-
Vascular disorders	Mild	0	0 (0.0)	1	1 (0.7)	1	1 (0.2)	0.250	0	0 (0.0)	0	0 (0.0)	0	0 (0.0)	-
	Moderate	0	0 (0.0)	0	0 (0.0)	0	0 (0.0)	-	0	0 (0.0)	0	0 (0.0)	0	0 (0.0)	-
	Severe	0	0 (0.0)	0	0 (0.0)	0	0 (0.0)	-	0	0 (0.0)	1	1 (0.8)	1	1 (0.2)	0.439
Injury, poisoning and procedure complications	Mild	0	0 (0.0)	0	0 (0.0)	0	0 (0.0)	-	0	0 (0.0)	0	0 (0.0)	0	0 (0.0)	-
	Moderate	1	1 (0.2)	0	0 (0.0)	1	1 (0.2)	1.000	0	0 (0.0)	0	0 (0.0)	0	0 (0.0)	-
	Severe	0	0 (0.0)	0	0 (0.0)	0	0 (0.0)	-	1	1 (0.3)	0	0 (0.0)	1	1 (0.2)	0.251
Immune system disorders	Mild	0	0 (0.0)	0	0 (0.0)	0	0 (0.0)	-	1	1 (0.3)	0	0 (0.0)	1	1 (0.2)	1.000
	Moderate	1	1 (0.2)	0	0 (0.0)	1	1 (0.2)	1.000	0	0 (0.0)	1	1 (0.8)	1	1 (0.2)	0.439
	Severe	0	0 (0.0)	0	0 (0.0)	0	0 (0.0)	-	1	1 (0.3)	0	0 (0.0)	1	1 (0.2)	0.251
Cardiac disorders	Mild	1	1 (0.2)	0	0 (0.0)	1	1 (0.2)	1.000	0	0 (0.0)	0	0 (0.0)	0	0 (0.0)	-
	Moderate	1	1 (0.2)	0	0 (0.0)	1	1 (0.2)	1.000	0	0 (0.0)	0	0 (0.0)	0	0 (0.0)	-
	Severe	0	0 (0.0)	0	0 (0.0)	0	0 (0.0)	-	0	0 (0.0)	0	0 (0.0)	0	0 (0.0)	-
Skin and subcutaneous tissue	Mild	10	9 (2.2)	1	1 (0.7)	11	10 (2.0)	0.306	10	10 (2.5)	4	3 (2.3)	14	13 (2.5)	1.000
	Moderate	1	1 (0.2)	0	0 (0.0)	1	1 (0.2)	1.000	0	0 (0.0)	0	0 (0.0)	0	0 (0.0)	-
	Severe	0	0 (0.0)	1	1 (0.7)	1	1 (0.2)	0.250	1	1 (0.3)	0	0 (0.0)	1	1 (0.2)	0.439
Renal and urinary disorders	Mild	0	0 (0.0)	1	1 (0.7)	1	1 (0.2)	0.250	0	0 (0.0)	0	0 (0.0)	0	0 (0.0)	-
	Moderate	0	0 (0.0)	0	0 (0.0)	0	0 (0.0)	-	0	0 (0.0)	0	0 (0.0)	0	0 (0.0)	-
	Severe	0	0 (0.0)	0	0 (0.0)	0	0 (0.0)	-	0	0 (0.0)	0	0 (0.0)	0	0 (0.0)	-
Nervous system diseases	Mild	34	31 (7.7)	15	15 (11.1)	49	46 (8.5)	0.213	34	31 (7.8)	12	11 (8.3)	47	42 (7.9)	0.864
	Moderate	18	16 (4.0)	4	3 (2.2)	22	19 (3.5)	0.345	12	11 (2.8)	3	3 (2.3)	15	14 (2.6)	1.000
	Severe	4	4 (1.0)	2	2 (1.5)	6	6 (1.11)	0.643	2	2 (0.5)	4	3 (2.3)	6	5 (0.9)	0.105
Neoplasms benign, malignant and unspecified (incl. cysts and polyps)	Mild	0	0 (0.0)	0	0 (0.0)	0	0 (0.0)	-	1	1 (0.3)	0	0 (0.0)	1	1 (0.2)	0.251
	Moderate	0	0 (0.0)	0	0 (0.0)	0	0 (0.0)	-	0	0 (0.0)	0	0 (0.0)	0	0 (0.0)	-
	Severe	0	0 (0.0)	0	0 (0.0)	0	0 (0.0)	-	0	0 (0.0)	0	0 (0.0)	0	0 (0.0)	-
Reproductive system and	Mild	0	0 (0.0)	0	0 (0.0)	0	0 (0.0)	-	3	3 (0.8)	1	1 (0.8)	4	4 (0.8)	1.000
	Moderate	0	0 (0.0)	0	0 (0.0)	0	0 (0.0)	-	1	1 (0.3)	0	0 (0.0)	1	1 (0.2)	0.439

breast disorders	Severe	0	0 (0.0)	0	0 (0.0)	0	0 (0.0)	-	0	0 (0.0)	0	0 (0.0)	0	0 (0.0)	-
Other general disorders	Mild	16	15 (3.7)	5	5 (3.7)	21	20 (3.7)	1.000	13	12 (3.0)	2	2 (1.5)	15	14 (2.6)	0.534
	Moderate	4	4 (1.0)	1	1 (0.7)	5	5 (0.9)	1.000	5	5 (1.3)	0	0 (0.0)	5	5 (0.9)	0.338
	Severe	2	2 (0.5)	1	1 (0.7)	3	3 (0.6)	1.000	1	1 (0.3)	0	0 (0.0)	1	1 (0.2)	0.439

*p-value is calculated using Chi-square test or Fisher's exact test for expectation cell <5

Table 2: Comparison of Overall Solicited AEs between Vaccine and Placebo.

Adverse events	After first vaccination, n(%)			After second vaccination, n(%)		
	Vaccine (n=405)	Placebo (n=135)	p-value*	Vaccine (n=397)	Placebo (n=133)	p-value*
Local reactions	155 (38.3)	37 (27.4)	0.022	136 (34.3)	44 (33.1)	0.804
Local pain	135 (33.3)	30 (22.2)	0.015	121 (30.5)	40 (3.1)	0.930
Redness	25 (6.2)	5 (3.7)	0.278	17 (4.3)	3 (2.3)	0.288
Induration	34 (8.4)	6 (4.4)	0.129	29 (7.3)	6 (4.5)	0.262
Swelling	9 (2.2)	1 (0.7)	0.269	14 (3.5)	1 (0.8)	0.095
Systemic events	128 (31.6)	24 (17.8)	0.002	98 (24.7)	18 (13.5)	0.007
Fever	10 (2.5)	0 (0.0)	0.065	7 (1.8)	2 (1.5)	0.841
Fatigue	70 (17.0)	12 (8.9)	0.018	54 (13.6)	9 (6.8)	0.035
Myalgia	102 (25.2)	17 (12.6)	0.002	78 (19.6)	12 (9.0)	0.005

* p-value is calculated using Chi-square test.

Summary of Safety Profile in population aged 3-17 years old

Phase I/II clinical studies in china

A total of 550 subjects aged 3-17 years old received at least one dose of investigational vaccine or placebo in phase I/II clinical trial of Study Corona 03. In the combined safety profile of phase I and phase II,

any adverse reactions within 28 days after vaccination occurred in 56 (25.57%) of 219 subjects in low-dosage group (300 SU/0.5 ml dose), 63 (29.03%) of 217 in medium dosage group (600 SU/0.5 ml dose) and 27 (23.68%) of 114 in the placebo group, without significant difference.

Most adverse reactions were mild (grade 1) to moderate (grade 2) in severity and transient, and only 2 (0.36%) of 550 subjected reported grade 3 reactions. The incidence of adverse reactions was comparable in low-dosage group after the first dose and the second dose, and the incidence of adverse reaction after the first dose were slightly higher than that after the second dose in medium-dosage groups and placebo group.

Vaccination site pain was the most frequently reported adverse events, with the incidence of 16.44% in the low-dosage group, 16.13% in the medium dosage group and 1.75% in the placebo group, and the difference mainly due to grade 1 vaccination site pain. The incidences of all other symptoms were lower than 5%, without significant difference.

From the beginning of vaccination to 6 months after the second dose , only one subjects in placebo group reported serious adverse events (pneumonia), which was considered unrelated to vaccination.

Biochemical, hematological and urine routine evaluations were conducted before and 3 days after each dose of vaccination in phase I. The incidence of clinically significant laboratory index abnormalties after vaccination was low, with 2.82% after first dose and 2.90% after dose vaccination.

All laboratory abnormalties were grade 1 in severity.

These safety results demonstrate that the safety of low-dosage and medium dosage vaccines are favorable in children and adolescents aged 3-17 years.

Report Date: July 2021

Table 3: Overview of adverse events combined Phase 1 and 2 Clinical studies in China

Category	Low-dosage group (N=219)		Medium-dosage group (N=217)		Placebo Group(N=114)		Total (N=550)		P*
	No. of events	No. of subjects (%)	No. of events	No. of subjects (%)	No. of events	No. of subjects (%)	No. of events	No. of subjects (%)	
Total	185	85(38.81)	167	87(40.09)	82	46(40.35)	434	218(39.64)	0.9543
AEs unrelated to vaccination	67	47(21.46)	55	40(18.43)	43	27(23.68)	165	114(20.73)	0.4973
AEs related tovaccination (adverse reactions)	118	56(25.57)	112	63(29.03)	39	27(23.68)	269	146(26.55)	0.5498
Local	51	36(16.44)	53	38(17.51)	3	3(2.63)	107	77(14.00)	**<0.0001**
Systemic	67	28(12.79)	59	34(15.67)	36	25(21.93)	162	87(15.82)	0.0952
Solicited	103	51(23.29)	92	59(27.19)	29	22(19.30)	224	132(24.00)	0.2758
Unsolicited	15	11(5.02)	19	15(6.91)	10	9(7.89)	44	35(6.36)	0.5148
30 minutes	1	1(0.46)	1	1(0.46)	0	0(0.00)	2	2(0.36)	1.0000
0~ 7 days	118	56(25.57)	111	63(29.03)	39	27(23.68)	268	146(26.55)	0.5498
First dose¶	60	33(15.07)	74	46(21.20)	28	19(16.67)	162	98(17.82)	0.2388
Second dose¶	58	35(16.36)	38	26(12.32)	11	11(9.91)	107	72(13.43)	0.2404

* P value was calculated using Fisher's exact probability method

The incidence of adverse events in low-dosage group (300 SU), medium dosage group (600 SU) and placebo group were 38.81% (85/219), 40.09 % (87/217) and 40.35% (46/114) respectively, and there was no significant difference in incidence among the three groups (P=0.9543).

The overall incidence of adverse events related to vaccination (adverse reactions) was 26.55% (146/550), and the incidence of low-dosage group, medium-dosage group and placebo group were 25.57% (56/219), 29.03% (63/217) and 23.68% (27/114) respectively, and there was no significant difference among the three groups (P=0.5498).

Phase IIb Children in China

A total of 500 adolescents and children aged 3-17 (including 100 subjects aged 3-5, 200 subjects aged 6-11 and 200 subjects aged 12-17 respectively) were selected. Each age group was randomly divided into 2 groups according to the ratio of 3:1. According to the D0/28 immunization schedule, they were vaccinated with 2 doses of medium-dosage vaccine (600SU) or placebo respectively.

The immediate reactions of all subjects within 30 min after each dose of inoculation were observed; the

local and systemic solicited adverse events on Days 0-7 and the non-solicited adverse events on Days 0~28 were collected; and the SAE monitoring from the inoculation to 6 months after full-course inoculation was completed to evaluate the safety of vaccines

Adverse events within 28 days after full-course immunization have been collected from all subjects. Analysis on the safety data of all subjects: the incidence of adverse reaction in the vaccine group was 19.20% and that in the placebo group was 15.20%, the difference between the groups was not statistically significant.

The adverse reaction was mainly Grade 1, and the incidence was 14.93% and 12.80% respectively in vaccine group and placebo group, and the difference between the groups was not statistically significant. Adverse reactions were mainly systemic diseases and reactions at the administration site. The incidence of the vaccine group and placebo group was 16.00% and 7.20% respectively, and the difference between groups was statistically significant.

The symptoms with higher incidence (>5%) in vaccine group were pain at the vaccination site (10.4%) and fever (5.87%), the incidence of corresponding symptoms in placebo group was 4.00% and 4.00% respectively. The difference in the incidence of the adverse reaction symptoms other than pain at the vaccination site between two groups was not statistically significant. Adverse reactions mainly occurred within 7 days after vaccination, and only one subject of the placebo group had adverse reactions within 30 minutes. During the study, 3 participants (including 2 participants in vaccine group and 1 participant in placebo group) had Grade 3 adverse reactions, all of which were fever. Further analysis of age groups showed that the incidence of adverse reactions in subjects aged 3-5 years, 6-11 years and 12-17 years was 28.00%, 16.00% and 15.50% respectively. The incidence of adverse reactions in subjects aged 3-5 years was higher than that in subjects of other two age groups. The main reason was that the incidence of fever and pain at the vaccination site in this age group of subjects was higher after the inoculation of test vaccine, which was 18.67% and 13.33% respectively, but the main adverse reactions were Grades 1-2, and there was no statistical difference between the incidence of vaccine group and placebo group.

Phase 3 studies is ongoing

This study will enroll 14,000 healthy children and adolescents aged from 6 months to 17 years old. Participants will be randomly divided into 2 groups according to a 1:1 ratio and vaccinated with 2 doses of vaccine (600SU) or placebo at 28-day intervals. Target countries include South Africa, Chile, Malaysia and Philippines.

Post-marketing Data

As of December 19, 2021, a total of 19,094 cases of AEFIs had been received from Chinese Center for Disease Control and Prevention AEFI monitoring system and Marketing Department at Sinovac. Collected AEFIs among the population aged 3-17 years are classified according to causes. See the Table 4 for details

Table 4 : Classification of AEFI by age group among the population aged 3-17 years on the Chinese mainland

Classification*	No. of cases	Proportion (%)	Age groups (Years)				Reporting rate among 3-17 population (/100,000 doses)	Causality Assessment*	Reporting rate among whole population (/100,000 doses)
			3-5	6-11	12-17	Unknown			
General reaction	17068	89.39	5126	7847	4094	1	7.25	Related	5.10
Abnormal reaction	623	3.26	97	271	255	--	0.26	Related	0.42
Coincidental event	532	2.79	119	220	193	--	0.23	Not related	0.67
Psychogenic reaction	341	1.79	6	101	234	--	0.14	Not related	0.21
Suspected Immunization error-related reaction	1	0.01	--	1	--	--	0.00	Related	0.00
To be determined	529	2.77	106	308	115	--	0.22	Unknown	0.12
Total	19094	100.00	5454	8748	4891	1	8.11	/	6.51

***Classification:** All Classification is made by China CDC according to their internal guideline which is not the same as that of WHO.

Table 5 : Top 10 AEFI symptoms distribution among the population aged 3-17 years on the Chinese mainland

AEFI symptoms	New		Known		No. of cases	Reporting rate (/100,000 doses)
	Serious	Non-serious	Serious	Non-serious		
Pyrexia	--	--	7	9574	9581	4.068
Dizziness	--	--	1	2289	2290	0.972
Asthenia	--	--	1	2270	2271	0.964
Vaccination site swelling	--	--	--	1684	1684	0.715
Vaccination site erythema	--	--	--	1675	1675	0.711
Headache	--	--	3	1622	1625	0.690
Nausea	--	--	2	1336	1338	0.568
Vomiting	--	--	--	1322	1322	0.561
Injection site induration	--	--	--	1053	1053	0.447
Dermatitis allergic	1	987	--	--	988	0.419
Total	1	987	14	22825	23827	10.117

The top 10 symptoms accounted for 71.35% of the total number of AEFI cases among the population aged 3-17 on the Chinese mainland.

As is shown in the table above, pyrexiaaccounted for the highest proportion of all AEFI symptoms, with a total of 9,581 cases (reporting rate 4.068 cases/100,000 doses), followed by dizziness with a total of 2,290 cases (reporting rate 0.972 cases/100,000 doses), asthenia with 2,271 cases (reporting rate 0.964 cases/100,000 doses), vaccination site swelling with 1,684 cases (reporting rate 0.715 cases/100,000 doses), vaccination site erythema with 1,675 cases (reporting 0.711 cases/100,000 doses)

4.9 Overdose

No data are available with overdose of CoronaVac.

There is no specific treatment for an overdose with CoronaVac. 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

CoronaVac is derived from the new coronavirus SARS-CoV-2 (strain CZ02) and grown in an African green monkey kidney cell (Vero Cell), followed by culture, harvesting, inactivation, concentration, purification and adsorption with aluminum hydroxide. Following administration, the inactivated SARS-CoV-2 as an antigen stimulates immunity against SAR-CoV-2 and prevent COVID-19.

Clinical efficacy

Efficacy of CoronaVac has been evaluated based on an interim analysis of data from three (3) ongoing randomized, blinded, and controlled phase III clinical studies performed in Brazil, Turkey, and Indonesia. However, due to methodological and sample size issues, the CoronaVac efficacy cannot be informatively concluded based on the data made available from the Turkey and Indonesia phase III studies. Only the phase III study in Brazil was currently used for the critical review and evaluation for the vaccine efficacy.

A phase 3 placebo-controlled study has been conducted in Brazil involving around 12,000 subjects who were healthcare professionals, with the data cut-off date of 17 December 2020 and demonstrating that CoronaVac was effective at preventing COVID-19 in adults of 18-59 years (efficacy in elderly subjects of $\geq$60 years old is inconclusive because of insufficient data) with a 0, 14 days vaccination schedule.

The primary efficacy endpoint of vaccine efficacy against symptomatic COVID-19 cases was evaluated in nearly 10,000 healthcare professionals who worked in direct contact of people with possible or confirmed COVID-19 cases and had no history of possible or confirmed cases of COVID-19. The subjects had been followed up for at least two weeks after completion of two doses of vaccination at 0, 14 days interval. The vaccine efficacy was 50.39% (95% CI: 35.26 – 61.91), (85 cases out of 4 653 vaccinated subjects got symptomatic COVID-19) compared with subjects who received the placebo (167 cases out of 4589 non-vaccinated subjects got symptomatic COVID-19).

Immunogenicity

Two phase 1/2 clinical studies were conducted in mainland China to evaluate the safety and immunogenicity of CoronaVac in adults of 18 to 59 years of age (around 700 subjects) and 60 years of age or above (around 400 subjects), respectively. Both Phase 1/ 2 clinical studies concluded a high seroconversion rate of neutralizing antibodies of CoronaVac when compared to those not vaccinated. The seroconversion rate of CoronaVac for either 0, 14 days schedule and 0, 28 days schedule in adults aged 18 to 59 years, and 0, 28 days schedule in adults of 60 years or older were demonstrated to be well above 90% after completion of the two-dose regimen, while the 0, 28 days schedule demonstrated a relatively better immunogenicity profile. There was also preliminary information showing that the CoronaVac might induce mixed Th1 (initial) and Th2 (subsequent) type of cell-mediated immune response.

CoronaVac in pediatric population

Immunogenicity results in population aged 3-17 years old

Phase I/II clinical studies in china

Immunogenicity results 28 days after the second dose

None of the subjects had any detectable neutralizing antibody response with a positive threshold of 1:8, which indicate the population aged 3-17 years old are generally susceptible to the SARS-CoV-2.

In phase I, 28 days after the second dose, the seroconversion rates of neutralizing antibody were 100.00%, 100.00%, 0.00% respectively, with the GMTs (1:) of 55.0, 117.4, 2.0, respectively.

In phase II, the seroconversion rates were 96.77%, 100.00%, 0.00% respectively, with the GMTs (1:) of 86.4, 142.2, 2.1 respectively. These results showed that seroconversion rates were higher than 96% in both low-dosage and medium-dosage groups, and GMT in medium-dosage group was obviously higher than that in low-dosage group.

In an exploratory analysis stratified by age, the seroconversion rates after the second dose reached more than 92% after receiving the low dosage vaccine or medium dosage vaccine in all age groups (3-5 years, 6-11 years and 12-17 years). In phase I, GMTs (1:) after the second dose of low-dosage vaccine were 71.9, 50.5 and 45.9 in three age groups (3-5 years, 6-11 years and 12-17 years) and were 212.6, 101.6 and 70.8, respectively, after the second dose of medium-dosage vaccine;

in phase II, GMTs (1:) after the second dose of low-dosage vaccine were 94.1, 90.3 and 78.3 in three age groups and were 140.5, 139.7 and 146.0 respectively, after the second dose of medium-dosage vaccine. GMTs in phase I decreased with age in recipients of the same vaccine, whereas they were similar in phase II. Small sample size might account for the change trends of GMT in phase I. In each age group, there were statistically significant differences in GMTs between the low-dosage groups

and medium-dosage groups after the second dose, except in the group aged 12-17 years old in phase 1. Taking together, the medium dosage vaccine could induce higher immune responses in all age groups compared with the low-dosage vaccine.

Immune persistence 3 months after the second dose

In phase II, 227 subjects were included in the analysis of immune persistence 3 months after the second dose. The seropositive rates of neutralizing antibody were 98.91% in low-dosage group and 100.00% in medium-dosage group 3 months after the second dose, and the GMTs were 67.8 and 110.5, respectively. Compared with 28 days after the second dose, the seropositive rates did not decrease, and there was no significant downward trend in GMTs.

In an exploratory analysis stratified by age, the seropositive rates 3 months after the second dose exceeded 97% after receiving the low-dosage vaccine or medium-dosage vaccine in all age groups (3-5 years, 6-11 years and 12-17 years). GMTs did not show significant downward trends in all age groups. Especially for children aged 3-5 years old, the GMTs were similar at 28 days and 3 months after the second dose. Neutralizing antibodied still remained at high levels 3 months after the second dose.

5.2 Pharmacokinetic properties

Not applicable

5.3 Pre-clinical safety data

Non-clinical data reveal no special hazard for humans based on a conventional study of repeated dose toxicity in Cynomolgus monkeys. Animal studies into potential toxicity to reproduction and development have not yet been completed.

6. PHARMACEUTICAL PARTICULARS

6.1 List of excipients

Aluminum hydroxide, disodium hydrogen phosphate, sodium dihydrogen phosphate, sodium chloride, sodium hydroxide. This product contains no preservatives.

6.2 Incompatibilities

No compatibility studies are performed, this vaccine must not be mixed with other medicinal products or any vaccine.

6.3 Shelf-life

The expiry date CoronaVac is 12 months from the date of manufacturing.

Please see expiry date on the outer carton and box.

6.4 Special precautions for storage

Store and transport between +2 to +8 ºC and protect from light.

Do not freeze.

Do not use after expiration date.

6.5 Nature and contents of container

0.5 mL of suspension in a single dose vial (clear type I) with a rubber stopper, an aluminum overseal with a plastic flip-off cap. Box of 40 vials.

6.6 Special precautions for disposal and other handling

Administration

CoronaVac is a milky-white suspension intended for a single use. Stratified precipitate may form which can be dispersed by shaking.

Shake vial well before use.

This product contains no preservatives. Aseptic technique should be used for withdrawing the dose for administration.

Do not re-use or save un-used of CoronaVac.

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

Disposal

Open and broken vials, and vaccine pre-drawn by providers - these cannot be returned and should be discarded according to your state requirements.

Any unused vaccine or waste material should be disposed of in accordance with local requirements.

7. MARKETING AUTHORIZATION HOLDER

The Government Pharmaceutical Organization 75/1 Rama VI Road, Ratchathewi, Bangkok, Thailand 10400.

8. MARKETING AUTHORIZATION NUMBER

1C 3/64 (NBC)

9. DATE OF AUTHORIZATION

22 February 2021

10. DATE OF REVISION OF THE TEXT

23 March 2022

LABELLING INFORMATION

2 mL Vial

CoronaVac

Suspension for Injection

Each dose (0.5 mL) contains:-

inactivated SARS-CoV-2 as an antigen 600 SU

Intramuscular use

40 Single dose vials

(1 dose per vial - 0.5 ml per dose)

ยาควบคุมพิเศษ

Reg. No. 1C 3/64 (NBC)

MFG.

LOT **##########**

EXP **YYYYMMDD**

Manufactured and batch released by:

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