Revised: 17 February, 2023

COVID-19 Vaccine (Vero Cell), Inactivated

This is the Conditional Marketing Authorization, please refer to the instruction and use under the doctor guidance.

【NAME OF THE MEDICAL PRODUCT】

Generic Name: COVID-19 Vaccine (Vero Cell), Inactivated
Trade Name: CoronaVac
Chinese Phonetic Alphabet: Xinxing Guanzhuang Bingdu Miehuoyimiao (Vero Xibao)

【COMPOSITION】

The product is derived from SARS-CoV-2 virus (CZ02 strain) cultured inoculated in African green monkey kidney cells (Vero cells), followed by cultivation, harvest, inactivation, concentration, purification and aluminum hydroxide adsorption. Free of preservative.
Active ingredient: Inactivated SARS-CoV-2 Virus (CZ02 strain)
Adjuvant: Aluminum hydroxide
Excipients: disodium hydrogen phosphate, monosodium dihydrogen phosphate, sodium chloride, water for injection.

【DESCRIPTION】

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

【TARGET GROUPS FOR VACCINATION】

Susceptible people aged 3 and above.
In Brazil phase III clinical trial, only 5.10% participants enrolled was 60 years and above, hence, the efficacy evidence of people aged 60 and above is insufficient. Besides, the efficacy results of children less than 18 years are not yet available.
The subsequent clinical trials will be carried out for further evaluation of efficacy in this population. Data from conducted clinical trials showed that neutralizing antibodies would be induced after vaccination. When use CoronaVac among people aged 60 and above by relevant institutions, the health status and exposure risk of people aged 60 and above shall be considered.

【THERAPEUTIC INDICATION】

CoronaVac is indicated for active immunization against diseases caused by SARS-CoV-2 virus.
Based on the efficacy results for two months from overseas phase III clinical trial, a conditional marketing authorization (CMA) for CoronaVac has been issued. The final efficacy data are not yet available; hence, the efficacy and safety results need to be further confirmed.

【PRESENTATION】

Each vial (syringe) contains 0.5 mL. Single dose of 0.5 mL contains 600SU of inactivated SARS-CoV-2 virus as antigen.

【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 per dose. Additional dose is recommended to be administered at least one month after primary immunization in immunocompromised individuals, and at least 6 months after primary immunization in adults of 18 years or above.
CoronaVac should be administered by intramuscular injection in the deltoid region of the upper arm. Shake well before use.

【ADVERSE REACTIONS】

- **Adult**

The safety of CoronaVac was evaluated in 5 clinical trials conducted domestic and overseas, including randomized, double-blind, placebo-controlled phase I/II clinical trials in people aged 18-59 years and in elderly aged 60 years and above, a phase III clinical efficacy trial in Brazilian health professionals aged 18 years and above, and a phase IIIb bridging trial in different production scales and different populations, and a lots consistency study. Systematic safety follow-up observation was carried out within 7 days after each dose vaccination, and adverse events were collected by voluntary report of subjects and regular follow-up of investigators on 8-14/28 days, long-term of serious adverse events within 12 months after the full vaccination is still ongoing.

1. General description of adverse reactions in clinical trials of this product

A total of 15,679 subjects aged 18 and above were enrolled in a series of clinical trials conducted domestic and overseas, of which 14,405 subjects received at least one dose. All subjects have completed at least 28 days of follow-up after full immunization, and long-term safety visits are ongoing.

According to the grading standard of adverse reaction incidence from Council for International Organizations of Medical Sciences (CIOMS), i.e. very common (≥10%), common (1%-10%, 1% was inclusive), uncommon (0.1%-1%, 0.1% was inclusive), rare (⩾ 0.01% and <0.1%) and very rare (<0.01%), all adverse reactions were summarized and described as follows.

1) Adverse reactions at inoculation site

Very common: pain

Common: swelling, pruritus, erythema, induration

Uncommon: burn at injection site

Rare: rash/papule

2) Systemic adverse reaction

Very common: Headache, fatigue

Common: myalgia, nausea, diarrhea, arthralgia, cough, chills, pruritus, loss of appetite, rhinorrhea, oropharyngeal pain, nasal congestion, abdominal pain

Uncommon: vomit, hypersensitivity(containing acute allergic reaction), abnormal skin and mucosa, fever, tremor, flushing, edema, dizziness, drowsiness, discomfort, sneezing, odynophagia

Rare: muscle spasms, eyelid edema, periorbital swelling, nose bleeds/epistaxis, abdominal distension, constipation, hyposmia/anosmia, ocular congestion, hot flashes, hiccups, conjunctival hyperaemia, larynx irritation, hyperhidrosis, skin warm, pain in extremity, back pain, myopathy, colitis ulcerative, appendicitis, seizure

Very rare: *Bell's palsy**

** Adverse reaction observed post-authorisation in Hong Kong*

3) Severity of adverse reactions

The severity of adverse reactions observed in these clinical trials is mainly Grade 1 (mild), no Grade 3 adverse reactions were observed in phase I/II clinical trials. The incidence rate of solicited adverse reactions in phase III clinical trial in Brazil for Grade 3 and above was 1.10%, and unsolicited adverse reactions for Grade 3 and above was 0.69%. The incidence of Grade 4 adverse reactions was 0.05%. The incidence of Grade 3 adverse reactions in phase IIIb trial was 0.19% (one subject).

4) Serious adverse reaction

Eight serious adverse reactions were identified in clinical trials, including myopathy, colitis ulcerative, hypersensitivity, urticaria, fever, appendicitis, seizure and rash.

2. General description of adverse reactions domestic and overseas in clinical trials of this product

1) Domestic clinical trials

A total of 3,283 subjects aged 18 and above were enrolled in domestic phase I/II, phase IIIb bridging clinical trials and lots consistency study, of which 2,532 subjects received at least one dose (medium dosage in phase I/II trials) including 2,147 subjects aged 18-59 (84.79%) and 385 subjects aged 60 and above (15.21%). All subjects have completed at least 28 days of follow-up after full immunization, and long-term safety visits are ongoing.

The main adverse reactions were solicited reactions within 28 days after full immunization. The incidence of unsolicited adverse reactions in adult was 1.50%. The incidence of unsolicited adverse reactions in the aged subjects was 1.30%. Grade 3 adverse reactions occurred in 2 subjects. The incidence of Grade 3 adverse reactions was 0.08%. The symptoms were fever and headache.

The safety data of the study population for phase I/II and phase IIIb bridging clinical trials are shown in Table 1.

Table 1 Incidence of Adverse Reactions in domestic Phase I/II and Phase IIIb Bridging Clinical Trials n (%)

Age Group	**18-59 Years**				**≥60 Years**		
Administration Schedule	**0, 14 days**		**0,28 days**		**0,14 days**	**0,28 days**	
Groups	**Vaccine (N=923) n (%)**	**Placebo (N=84) n (%)**	**Vaccine (N=144) n (%)**	**Placebo (N=83) n (%)**	**Vaccine (N=260) n (%)**	**Vaccine (N=125) n (%)**	**Placebo (N=73) n (%)**
Overall adverse reactions	**159(17.23)**	**15(17.86)**	**26(18.06)**	**14(16.87)**	**15(5.77)**	**25(20.00)**	**15(20.55)**
Solicited adverse reactions	**152(16.47)**	**15(17.86)**	**26(18.06)**	**13(15.66)**	**13(5.00)**	**24(19.20)**	**12(16.44)**
Systemic adverse reaction	93(10.08)	10(11.90)	16(11.11)	7(8.43)	8(3.08)	12(9.60)	9(12.33)
Fatigue	25(2.71)	7(8.33)	10(6.94)	2(2.41)	2(0.77)	4(3.20)	1(1.37)
Fever	28(3.03)	1(1.19)	4(2.78)	2(2.41)	3(1.15)	4(3.20)	1(1.37)
Myalgia	14(1.52)	1(1.19)	2(1.39)	3(3.61)	0(0.00)	2(1.60)	2(2.74)
Diarrhea	19(2.06)	1(1.19)	2(1.39)	1(1.20)	4(1.54)	1(0.80)	1(1.37)
Headache	13(1.41)	1(1.19)	3(2.08)	0(0.00)	1(0.38)	0(0.00)	0(0.00)
Cough	11(1.19)	0(0.00)	3(2.08)	0(0.00)	1(0.38)	1(0.80)	1(1.37)
Nausea	7(0.76)	0(0.00)	2(1.39)	0(0.00)	0(0.00)	1(0.80)	3(4.11)
Abnormal skin and mucous membrane	4(0.43)	0(0.00)	0(0.00)	0(0.00)	0(0.00)	0(0.00)	0(0.00)
Anorexia	2(0.22)	0(0.00)	0(0.00)	0(0.00)	2(0.77)	1(0.80)	0(0.00)
Vomiting	2(0.22)	0(0.00)	0(0.00)	0(0.00)	0(0.00)	0(0.00)	0(0.00)
Acute allergic reaction	0(0.00)	0(0.00)	1(0.69)	0(0.00)	0(0.00)	1(0.80)	0(0.00)
Local adverse reactions	**77(8.34)**	**7(8.33)**	**15(10.42)**	**9(10.84)**	**7(2.69)**	**15(12.00)**	**3(4.11)**
Pain	71(7.69)	7(8.33)	15(10.42)	9(10.84)	6(2.31)	15(12.00)	3(4.11)
Pruritus	6(0.65)	0(0.00)	0(0.00)	0(0.00)	1(0.38)	0(0.00)	0(0.00)
Swelling	6(0.65)	0(0.00)	0(0.00)	1(1.20)	0(0.00)	1(0.80)	0(0.00)
Redness	2(0.22)	0(0.00)	0(0.00)	0(0.00)	0(0.00)	0(0.00)	1(1.37)
Induration	1(0.11)	0(0.00)	0(0.00)	0(0.00)	0(0.00)	0(0.00)	0(0.00)

Age Group	18-59 Years				≥60 Years		
Administration Schedule	0, 14 days		0,28 days		0,14 days	0,28 days	
Groups	Vaccine (N=923) n (%)	Placebo (N=84) n (%)	Vaccine (N=144) n (%)	Placebo (N=83) n (%)	Vaccine (N=260) n (%)	Vaccine (N=125) n (%)	Placebo (N=73) n (%)
Unsolicited adverse reactions	16(1.73)	0(0.00)	0(0.00)	2(2.41)	2(0.77)	3(2.40)	5(6.85)

2) Brazil clinical trial

A total of 12,396 subjects aged 18 years and above were enrolled in phase III clinical trials, of which 6202 subjects received at least one dose vaccination (600SU/0.5ml), including 316 subjects aged 60 years and above (5.10%). All subjects have completed at least 28 days of follow-up after whole immunization, and long-term safety monitoring is ongoing.

The results of solicited adverse reactions in phase III clinical trial are shown in Table 2. The incidence rate of unsolicited adverse reactions was 36.83%, the symptoms were mainly runny nose (7.01%), sore throat (6.93%), nasal congestion (2.74%), abdominal pain (1.34%) and dizziness (0.66%).

The severity of adverse reactions was mainly grade 1 and grade 2, the incidence of grade 3 adverse reactions was 1.58%. Among the unsolicited adverse reactions, the grade 3 symptoms compared with solicited adverse reactions were sore throat (0.03%), abdominal pain (0.03%), dizziness (0.02%) and drowsiness (0.02%).

Table 2 Incidence of Solicited Adverse Reactions in Phase III Clinical Trials in Brazil n (%)

Name of adverse reactions	Vaccine (N=6202) n (%)	Placebo (N=6194) n (%)
Solicited adverse reactions	4536(73.14)	3714(59.96)
Grade 3	66(1.06)	69(1.11)
Local adverse reactions	3815(61.51)	2143(34.6)
Grade 3	4(0.06)	1(0.02)
Pain	3742(60.34)	2014(32.52)
Grade 3	4(0.06)	1(0.02)
Swelling	359(5.79)	130(2.1)
Grade 3	0(0.00)	0(0.00)
Pruritus	263(4.24)	181(2.92)
Grade 3	0(0.00)	0(0.00)
Redness	241(3.89)	89(1.44)
Grade 3	0(0.00)	0(0.00)
Induration	235(3.79)	67(1.08)
Grade 3	0(0.00)	0(0.00)
Systemic adverse reaction	2999(48.36)	2947(47.58)
Grade 3	64(1.03)	69(1.11)
Headache	2128(34.31)	2157(34.82)
Grade 3	34(0.55)	46(0.74)
Fatigue	989(15.95)	922(14.89)
Grade 3	12(0.19)	13(0.21)
Myalgia	727(11.72)	648(10.46)
Grade 3	5(0.08)	10(0.16)
Nausea	490(7.9)	522(8.43)
Grade 3	6(0.10)	6(0.10)

Diarrhea	492(7.93)	501(8.09)
Grade 3	8(0.13)	7(0.11)
Arthralgia	353(5.69)	321(5.18)
Grade 3	8(0.13)	3(0.05)
Cough	343(5.53)	322(5.2)
Grade 3	0(0.00)	0(0.00)
Chills	309(4.98)	313(5.05)
Grade 3	1(0.02)	1(0.02)
Pruritus	263(4.24)	225(3.63)
Grade 3	1(0.02)	0(0.00)
Appetite impaired	217(3.5)	243(3.92)
Grade 3	0(0.00)	0(0.00)
Vomiting	61(0.98)	61(0.98)
Grade 3	3(0.05)	3(0.05)
Hypersensitivity	58(0.94)	58(0.94)
Grade 3	2(0.03)	2(0.03)
Abnormal skin and mucous membrane	49(0.79)	42(0.68)
Grade 3	1(0.02)	0(0.00)
Fever	9(0.15)	4(0.06)
Grade 3	0(0.00)	0(0.00)

3. Post Authorization Experience of Primary Immunization

According to a case series and nested case-control study reported in the period between February 23, 2021 and May 4, 2021 conducted in Hong Kong, 28 cases of clinically confirmed Bell's palsy following CoronaVac was reported voluntarily to the Department of Health of Hong Kong. The age-standardized incidence rate was 66.9 (95% confidence interval (CI): 37.2-96.6) per 100,000 person-years for CoronaVac vaccination. The age-standardized rate ratios were 2.64- times higher than the background population rate equivalent to an additional 4.8 cases for CoronaVac per 100,000 people vaccinated. In the nested case-control analysis, 298 cases were matched to 1181 controls, the adjusted odds ratios were 2.39 (1.42-4.02) for CoronaVac. The findings in Hong Kong described a signal of risk of Bell's palsy who received CoronaVac vaccine, and additional studies are needed in other regions to confirm the risk.

4. Adverse reactions of additional immunization in phase I/II clinical trials in adults and elderly

The proportion of subjects aged 18-59 years reporting adverse reactions was 16.82% (18/107), and the proportion of subjects aged 60 years and above reporting adverse reactions was 5.56% (5/90) of CoronaVac. All adverse reactions were grade 1 and grade 2 in intensity. Table 3 presents the number and percentage of subjects reported adverse reactions within 28 days after the additional dose.

Table 3 Incidence of Adverse Reactions of Additional Immunization in Phase I/II Clinical Trials n (%)

Adverse Reactions	**18-59 Years**	**≥60 Years**
	N=107	**N=90**
Any adverse reactions	18(16.82)	5(5.56)

Local adverse reactions		
Vaccination site pain	14(13.08)	2(2.22)
Vaccination site pruritus	1(0.93)	0(0.00)
Vaccination site erythema	0(0.00)	1(1.11)
Vaccination site swelling	1(0.93)	0(0.00)
Systemic adverse reaction		
Headache	2(1.87)	0(0.00)
Fever	1(0.93)	0(0.00)
Fatigue	1(0.93)	0(0.00)
Asthenia	0(0.00)	1(1.11)
Dizziness	0(0.00)	1(1.11)
Throat irritation	1(0.93)	0(0.00)
Oropharyngeal pain	1(0.93)	0(0.00)

- **Children**

The safety of CoronaVac in children was evaluated in 2 clinical trials conducted in China, including the phase I/II and phase IIb clinical trial in children aged 3-17 years. Immunization schedule of day 0,28 was adopted in both studies. Systematic safety observation was carried out within 7 days after each vaccination, and adverse events were collected by voluntary report of subjects and regular follow-up of investigators on 8-28 days, long-term of serious adverse events within 12 months after the full vaccination is still ongoing.

1. General description of adverse reactions in clinical trials

A total of 1052 subjects aged 3-17 years were enrolled in the above-mentioned clinical trials, of which 592 subjects received at least one dose of CoronaVac (600SU/0.5ml). All subjects have completed at least 28 days follow-up after full immunization, and long-term safety visits are ongoing. According to the grading standard of adverse reaction incidence from CIOMS, all adverse reactions were summarized and described as follows.

1) Adverse reactions at injection site

Very common: pain
Common: induration, swelling
Uncommon: pruritus, erythema

2) Systemic adverse reactions

Very common: N/A
Common: fever, abnormal skin and mucous membrane, decreased appetite, nausea, headache, cough, fatigue, rhinorrhea, oropharyngeal pain
Uncommon: hypersensitivity, diarrhea, vomiting, myalgia, laryngeal pain, pharyngeal erythema, upper respiratory tract infection, abdominal pain, upper abdominal pain, abdominal distention, dizziness, lymphadenitis, chest discomfort, blepharitis

3) Severity of adverse reactions

The severity of adverse reactions observed in these clinical trials is mainly grade 1 (mild), the incidence rate of adverse reactions for grade 3 was 0.34% and no grade 4 was reported. Symptom of grade 3 and above adverse reactions is fever.

4) Serious adverse event (SAE)

No serious adverse event related to vaccination was identified up to November, 2021.

2. Adverse reactions in clinical trials

A total of 1052 subjects aged 3-17 years old were enrolled into phase I/II and phase IIb clinical trials, of which 592 subjects received at least one dose of vaccination (600SU/0.5ml). All subjects have completed at least 28 days of follow-up after whole immunization, and long-term safety monitoring is ongoing.

Solicited adverse reactions were mainly reported within 28 days after immunization. The incidence rates of unsolicited adverse reactions were merely 4.39%. Only two episode of grade 3 adverse reaction (fever) was reported with an incidence of 0.34%. The pooled safety data of phase I/II and phase IIb clinical trials among children aged 3-17 years were shown in Table 4.

Table 4 Incidence of Solicited Adverse Reactions in Phase I/II and Phase IIb Clinical Trials in Children Aged 3-17 Years Old, n (%)

Name of adverse reactions	Vaccine(N=592)	Placebo(N=239)
Overall adverse reactions	135(22.80)	46(19.25)
Solicited adverse reactions	128(21.62)	39(16.32)
Systemic adverse reactions	66(11.15)	35(14.64)
Fever	33(5.57)	10(4.18)
Hypersensitivity	2(0.34)	1(0.42)
Abnormal skin and mucous membrane	6(1.01)	2(0.84)
Diarrhea	5(0.84)	5(2.09)
Decreased appetite	7(1.18)	3(1.26)
Vomiting	4(0.68)	1(0.42)
Nausea	9(1.52)	5(2.09)
Myalgia	1(0.17)	1(0.42)
Headache	11(1.86)	6(2.51)
Cough	9(1.52)	7(2.93)
Fatigue	8(1.35)	2(0.84)
Local adverse reactions	78(13.18)	8(3.35)
Pain	74(12.50)	7(2.93)
Induration	6(1.01)	0(0)
Swelling	9(1.52)	1(0.42)
Erythema	2(0.34)	0(0)
Pruritus	3(0.51)	0(0)

- **Post-marketing clinical trials on safety**

Besides the adverse reactions reported in clinical trials, the following adverse reactions have been observed in the postmarketing safety evaluation trial, including vocal cord polyp, herpes zoster, palpitations, cardiac fibrillation, rhinitis.

- **Post-marketing surveillance**

1) Domestic safety surveillance among population aged 18 and above

The following adverse reactions have been identified during postmarketing use of CoronaVac. Because these reactions are reported voluntarily from a population of uncertain size, it is not always possible to reliably estimate their frequency or establish a causal relationship to vaccine exposure.

Eye and labyrinth disorders: vertigo, tinnitus

Nervous system disorders: hypoesthesia, syncope, Guillain-Barre syndrome, Bell's palsy, cerebral infarction

Musculoskeletal and connective tissue disorders: muscular weakness

Respiratory, thoracic and mediastinal disorders: pharyngeal erythema, dyspnoea
Immune system disorders: anaphylactic shock
Skin and subcutaneous tissue disorders: dermatitis allergic, rash maculo-papular, angioedema, Henoch-Schonlein purpura
General disorders and administration site conditions: chest discomfort, chest pain
Gastrointestinal disorders: gastrointestinal disorder
Cardiac disorders: palpitations
Vascular disorders: pallor
Blood and lymphatic disorders: thrombocytopenic purpura
Investigations: blood pressure increased

2) Overseas safety surveillance

The following adverse reactions have been identified during post-marketing use overseas of CoronaVac. Because these reactions are reported voluntarily from a population of uncertain size, it is not always possible to reliably estimate their frequency or establish a causal relationship to vaccine exposure.
Respiratory, thoracic and mediastinal disorders: dysphonia
Psychiatric disorders: acute stress disorder
General disorders and administration site conditions: malaise
Cardiac disorders: tachycardia

【CONTRAINDICATION】

1. People with history of allergic reaction to CoronaVac or other inactivated vaccine, or any component of CoronaVac (active or inactive ingredients, or any material used in the process);
2. Previous severe allergic reactions to the vaccine (eg, acute anaphylaxis, angioedema, dyspnea, etc.);
3. People with severe neurological conditions (eg, transverse myelitis, Guillain-Barré syndrome, demyelinating diseases, etc.);
4. Patients with uncontrolled severe chronic diseases.

【PRECAUTIONS】

1. Due to the insufficient data of protection persistence, necessary protective measures should be taken in line with the COVID-19 epidemic.
2. Due to the insufficient data of efficacy in people aged 60 and above, when use CoronaVac among people aged 60 and above by relevant institutions, the health status and exposure risk of people aged 60 and above shall be considered.
3. This vaccine is strictly prohibited for intravenous injection. There is no safety and efficacy data of subcutaneous or intradermal injection.
4. Before use, check whether the packaging container, label, appearance and validity period meet the requirements or not. Do not use if there are cracks in the vial, spots, stains and scratches on the outer surface of the vial, label is not clear or more than the expiration date and abnormal appearance.
5. Avoid expose CoronaVac to the disinfectant during use.
6. This product should be stored at places out of reach of children.
7. Adequate treatment provisions, including epinephrine injection and emergency treatment, should be available for immediate use. Individuals should be observed for at least 15 minutes on site after vaccination.
8. Do not mix with other vaccines in the same syringe.
9. Do not freeze. It shall be administered immediately after open.
10. Patients with acute diseases, acute exacerbation of chronic diseases, severe chronic diseases, atopy and fever should be used with caution; if necessary, delay vaccination after doctor's evaluation.

11. Patients with diabetes, or history of convulsions, epilepsy, encephalopathy or mental illness, or family history of those diseases should be used with caution.
12. Patients with thrombocytopenia or hemorrhagic diseases, intramuscular injection of this product may cause bleeding, so it should be used with caution.
13. The safety and efficacy data of this product on people with impaired immune function (such as malignant tumor, nephrotic syndrome, AIDS patients) have not been obtained, and the vaccination of this product should be based on individual considerations.
14. The injection of human immunoglobulin should be given at least one month interval to avoid affecting the immune effect.
15. No clinical study has been carried out on the evaluation of immune response with other vaccines on the immunogenicity at the same time (before, after or at the same time). Professionals should be consulted when concomitant use.
16. Do not use if there is any adverse reaction of nervous system after inoculation.
17. Like other vaccines, the protective effect may not reach 100% for all recipients.
18. Based on the findings of "False COVID-19 cases due to contamination by inactivated virus vaccine" published in the *Clinical Infectious Diseases*, and the immunogenicity study conducted by Sinovac, the adaptive deletions (as showed by whole-genome sequencing) on the spike protein of Inactivated SARS-CoV-2 Virus (CZ02 strain) of CoronaVac do not change its safety, antigenicity and efficacy.

【SPECIAL POPULATION MEDICATION】

1. Women of childbearing age: the data collected of women with unexpected pregnancy after vaccination from clinical trials are very limited, which is not enough to decide the risk of adverse pregnancy outcomes after vaccination.
2. Pregnant or lactating women: the clinical data of pregnant and lactating women are not available at present.
3. People aged 60 and above: the immunogenicity and safety data from conducted clinical trials have been obtained, while the efficacy data from phase III clinical trial is insufficient.

【DRUG-DRUG INTERACTIONS】

1. Concomitant use with other vaccines: no clinical study has been carried out on the evaluation of immune response with other vaccines on the immunogenicity at the same time (before, after or at the same time).
2. Concomitant use with other drugs: immunosuppressive drugs, such as immunosuppressive drugs, chemotherapy drugs, antimetabolic drugs, alkylating agents, cytotoxic drugs, corticosteroid drugs, etc., may reduce the immune response to this product.
3. Patients undergoing treatment: for patients undergoing treatment, please consult the professional doctors before use CoronaVac to avoid possible drug interactions.

【CLINICAL TRIALS】

1. Efficacy

A multicenter, randomized, double-blind, placebo-controlled design was adopted in the pivotal phase III clinical trial, which was carried out among healthcare professionals aged 18 years and above in Brazil and healthy adults aged 18-59 years in Turkey, to evaluate the efficacy in high-risk populations and regular population. The primary study hypotheses is that the lower limit of 95% confidence interval of vaccine efficacy (VE) is greater than 30% compared with the placebo group after 14 days of the whole vaccination. The primary analysis of the efficacy in Brazilian clinical trial is based on person-year incidence, and the efficacy of the vaccine in Turkish clinical trial is based

on incidence rate. All valid COVID-19 cases were confirmed by the Clinical Endpoint Adjudication Committee.

1) Phase III clinical trial in Brazil

The target population in Brazil was healthcare professionals who work in direct contact with COVID-19 cases. A total of 12,396 subjects were enrolled, a total of 253 cases of symptomatic COVID-19 were reported in the case monitoring period in the primary efficacy analysis. The efficacy against hospitalized, severe and dead COVID-19 cases was 100.00% (95% CI: 56.37-100.00). And the efficacy against symptomatic COVID-19 cases who need medical treatment was 83.70% (95% CI: 57.99-93.67). The efficacy against symptomatic COVID-19 cases was 50.65% (95% CI: 35.66-62.15). The average follow-up time was 70.3 ± 25.6 days, and the median follow-up duration was 73.0 days.

Table 5 Efficacy against COVID-19, 14 Days after 2 Doses of Vaccination in Phase III Clinical Trial in Brazil

Group	The Vaccine (N=4953)			Placebo (N=4870)			VE(%) (95% CI)
	Number of cases	Person-year of exposure	Person-year incidence (%)	Number of cases	Person-year of exposure	Person-year incidence (%)	
COVID-19 cases	85	754.6	11.03	168	736.5	22.34	50.65 (35.66, 62.15)
WHO-Grade 3 and above*	5	755.6	0.66	30	737.9	4.07	83.70 (57.99, 93.67)
WHO-Grade 4 and above#	0	755.6	0.00	10	738.2	1.35	100.00 (56.37, 100.00)

*WHO-Grade 3 and above: COVID-19 cases requiring medical treatment;

#WHO-Grade 4 and above: hospitalized, severe and dead COVID-19 cases, including 5 severe cases and 1 death case;

VE: vaccine efficacy.

2) Phase III clinical trial in Turkey

The target population in Turkey contains high-risk healthcare professionals (K-1) and regular population (K-2). As of December 23, 2020, a total of 7,371 subjects were enrolled, including 918 subjects in K-1 and 6,453 subjects in K-2. Among which, 1,322 subjects completed two doses vaccination and entered the monitoring period of 14 days after the second vaccination. Based on the analysis result of 29 cases, the efficacy against symptomatic COVID-19 cases was 91.25% (95% CI: 71.25- 97.34). See more details in Table 6.

Table 6 Efficacy against COVID-19, 14 Days after 2 Doses of Vaccination in Phase III Clinical Trial in Turkey

Group Index	The Vaccine (N=752)		Placebo (N=570)		VE (%) (95%CI)
	Number of cases	Incidence rate (%)	Number of cases	Incidence rate (%)	
COVID-19	3	0.40	26	4.56	91.25 (71.25,97.34)

2. Immunogenicity

The seroconversion rate and geometric mean titer (GMT) of neutralizing antibody were used to evaluate the immunogenicity of CoronaVac. Seroconversion was defined by a titer of less than 1:8 before any injections with a titer of 1:8 or more after any injections, or by an increase in the antibody titer by a factor of four or more. Neutralizing antibody was determined by cell culture microneutralization test (cytopathic inhibition method).

Table 7 Seroconversion Rate and GMT of Neutralizing Antibody in Different

Immunization Schedules (95%CI)(PPS)

Group	0,14 days schedule			0,28 days schedule		
	N	Seroconversion % (95% CI)	GMT (95% CI)	N	Seroconversion % (95% CI)	GMT (95% CI)
Adult aged 18-59 years						
Primary immunization	118	92.37 (86.01, 96.45)	27.6 (22.7, 33.5)	117	97.44 (92.69, 99.47)	44.1 (37.2, 52.2)
Additional immunization	53	98.11 (89.93, 99.95)	137.9 (99.9, 190.4)	49	95.92 (86.02, 99.50)	143.1 (110.8, 184.7)
Elderly aged 60 years and above						
Primary immunization	--	--	--	98	97.96 (92.82, 99.75)	42.2 (35.2, 50.6)
Additional immunization	--	--	--	86	98.84 (93.69, 99.97)	342.8 (266.4, 441.1)
Children aged 3-17 years						
Primary immunization	--	--	--	180	100.00 (97.97, 100.00)	142.2 (124.7, 162.1)

3. Cross-neutralization

Based on the serum of domestic 80 subjects aged 26-45 years and 100 oversea adult subjects using 0,14 days schedule, the cross-neutralizing immunogenicity was carried out for 15 SARS-CoV-2 strains (CZ02, WZL, WGF, ZJY, SSH, JWL, ZYF, HAC, HJL, ZXZ, QHF, NOOR, BETA, GAMMA and DELTA). Neutralizing antibody was determined by cell culture micro neutralization test (cytopathic inhibition method). The results showed that the seroconversion rate of neutralizing antibody after vaccination range in 20.00% to 100.00%, GMT (1:) range in 5.3 to 46.7. The seroconversion rates of neutralizing antibody against BETA, GAMMA and DELTA were 20.00%, 34.74% and 23.96%, respectively; the GMT were 5.26, 6.13 and 5.72, respectively.

【STORAGE】

Store and transport between +2 and +8℃, and protect from light. Do not freeze.

【SHELF LIFE】

The shelf life of the vaccine is scheduled as 24 months.

【PACKAGE】

This product is packaged into vial, 40 vials per box.

【SPECIFICATION IMPLEMENTED】

YBS00152021

【MARKETING AUTHORIZATION HOLDER】

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