Revised: 17 February, 2023

COVID-19 Vaccine (Vero Cell), Inactivated (Brief Edition)

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】

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】

- **Adults**

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.

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 reactions

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, hiccup, 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.

For detailed information of adverse reactions among these clinical trials, please refer to the complete version of the leaflet.

- **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 trials 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.

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.

For detailed information of adverse reactions among these clinical trials, please refer to the

complete version of the leaflet.

【CONTRAINDICATIONS】

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.

【STORAGE】

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

【SHELF LIFE】

The shelf life of the vaccine is tentatively 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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