This package insert was last revised in 03/2022.

# COVID-19 Vaccine (Vero Cell), Inactivated

This product is conditional approval. Please read the instructions carefully and use under the guidance of a physician

## 【Drug Name】

Common Name: 新型冠状病毒灭活疫苗（Vero 细胞）
Trade Name: COVILO
English Name: COVID-19 Vaccine (Vero Cell), Inactivated
Chinese Phonetic Alphabet: Xinxing Guanzhuang Bingdu Miehuoyimiao (Vero Xibao)

## 【Composition】

The COVID-19 Vaccine (Vero Cell), Inactivated is made from the SARS-CoV-2, 19nCoV-CDC-Tan-HB02 strain which is inoculated on the Vero cells for culturing, harvesting, β-propiolactone-inactivation, concentration and purification, then followed by adsorption with aluminium hydroxide adjuvant to form the liquid vaccine. The vaccine is free of antibiotics and preservatives.
Active Composition: SARS-CoV-2, 19nCoV-CDC-Tan-HB02 strain (inactivated)
Adjuvant: Aluminium hydroxide
Excipients: Disodium hydrogen phosphate, Sodium chloride, Sodium dihydrogen phosphate

## 【Appearance】

The product is a semi-transparent suspension with slight white color, which could be layered due to precipitation, and the precipitation can be easily dispersed by shaking.

## 【Therapeutic Indication】

This product is for active immunization to prevent COVID-19 caused by SARS-CoV-2 virus in individuals from 18 to 59 years of age.
The vaccine efficacy of this product for adults in 18-59-year-old cohort have been shown based on the interim report of the international Phase III clinical trial, in which, the proportion of older adults (≥60 years old) was low (2.01%).

## 【Pharmacodynamic Properties】

The antibodies against the SARS-CoV-2 can be produced after vaccination, to prevent the COVID-19 disease caused by SARS-CoV-2 virus.
This product is conditionally approved based on the results of protective efficacy reported in interim analysis of the international Phase III clinical trial.
The present experience with the vaccine from a Phase I/II trial up to 90 days post last

vaccination and the second interim data in approximately 30,000 healthy adults aged 18 years and older in UAE.

**【Presentation】**

Each non-auto disable pre-filled syringe/vial contains 0.5mL of product for each administration, each dose contains 3.9-10.4 units of inactivated SARS-CoV-2 antigen and 0.3-0.6 mg/mL aluminium hydroxide adjuvant.

**【Immunization Regimen and Dosage】**

Two dose regimen at an interval of 21~28 days, each dose is 0.5mL.
The recommended administration is through intramuscular route, the injection into a muscle will be preferably performed in the upper part of the arm.
The need for booster immunization with this product has not been determined.

**【Adverse Reactions】**

The safety of this product is evaluated through the China and international clinical trials. The China Phase I/II clinical trials are randomized, double-blinded and placebo parallel controlled to preliminarily evaluate the safety and immunogenicity of this product for adults 18 years and older. The international Phase III clinical trial is an international multi-center, randomized, double-blinded, placebo parallel controlled to evaluate the protective efficacy, safety and immunogenicity of this product. Investigators actively follow up the safety data of 0~21/28 days after each vaccination to observe the occurrence of adverse events, and pay attention to the serious adverse events occurred within 12 months after full-course vaccination at the same time.

The incidence for Adverse Reactions (ARs) (CIOMS recommendation) can be presented as: 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%). Summarize the safety data of this product in the Phase I/II and Phase III clinical trials:

**1. ARs at the Injection Site**

Very common: Pain;
Uncommon: Redness, swelling, induration, rash, pruritus;
Rare: Erythema

**2. Systemic ARs**

Very common: Headache
Common: Fever, fatigue, myalgia, arthralgia, cough, dyspnea, nausea, diarrhea, pruritus;
Uncommon: Dizziness, anorexia, vomiting, oropharyngeal pain, dysphagia, running nose, constipation, hypersensitivity;
Rare: Acute allergic reaction, lethargy, drowsiness, difficulty falling asleep, sneezing, nasopharyngitis, nasal congestion, dry throat, influenza, hypoesthesia, limb pain, palpitations, abdominal pain, rash, abnormal skin mucosa, acne, ophthalmodynia, ear

discomfort, lymphadenopathy;
Very rare: Chills, taste dysfunction, loss of taste, paresthesia, tremor, attention disorder, epistaxis, asthma, throat irritation, tonsillitis, physical discomfort, neck pain, jaw pain, neck lump, mouth ulcers, toothache, esophagus disorders, gastritis, fecal discoloration, blurred vision, eye irritation, earache, tension, hypertension, hypotension, urinary incontinence, delayed menstruation.

**3. Severity of ARs**

The severity of ARs for this product observed in clinical trials is mainly grade 1 (mild), and the incidence of grade 3 and above solicited ARs is 0.54%, no grade 4 ARs related to this product are reported. The grade 3 ARs at the injection site reported in clinical trials include: pain, rash, pruritus; the grade 3 systemic ARs include: fever, fatigue, headache, myalgia, arthralgia, cough, dyspnea, nausea, vomiting, diarrhea, constipation, dysphagia.

**4. Serious Adverse Event (SAE)**

As the date of December 31st, 2020, among all observed SAEs during the international Phase Ⅲ clinical trials, one subject with serious nausea, vomiting and other symptoms was confirmed to be related to the vaccination of this product, this subject was hospitalized and cured. Another subject with 'right upper limb weakness and cannot speak clearly' was diagnosed as 'inflammatory demyelination syndrome, multiple sclerosis (MS), clinical isolated syndrome (CIS), and acute disseminated encephalomyelitis (ADEM)' by hospital. Whether this case is related to the vaccination could not be determined.

## 【Contraindications】

1. Individuals who are allergic to any component (including excipients) of this product.
2. Individuals who have allergic reactions with vaccines before (acute allergic reaction, angioneurotic edema, dyspnea, etc.).
3. Individuals with uncontrolled epilepsy or other progressive nervous system diseases, and with a history of Guillain-Barre syndrome.

## 【Special Warnings and Precautions for Use】

1. Long-term persistence of protection study is still ongoing, no data in this regard is available at present, the recommendations are based on interim data.
2. At present, the evidence of the protective efficacy of this product on people aged ≥ 60 has not been obtained.
3. Before use, carefully check the vaccine container, label, appearance and expiration date. If there are cracks, spots, stains, scratches, blurred label on the container, vaccine expired, or abnormal appearance observed, the vaccine shall not be used.

4. Intravascular injection is strictly prohibited. There is no safety and efficacy data of the vaccine through subcutaneous and intradermal injection.
5. Drugs and equipment such as epinephrine should be available for emergency treatment in the event of an occasional severe allergic reaction. The vaccinee should be observed for at least 15 minutes after vaccination.
6. Use with caution in patients with acute diseases, acute onset of chronic diseases and fever; Delay the vaccination after the doctor's evaluation if necessary.
7. Use with caution in patients who have diabetes and those with a history or family history of convulsions, epilepsy, encephalopathy or mental illness.
8. Use with caution in patients who have decrease in platelets or clotting disorders because of the risk of bleeding which may occur during intramuscular administration of the vaccine.
9. Use with caution in patients with impaired immune function (such as malignant tumor, nephrotic syndrome, AIDS patients, etc.) because safety and efficacy data have not been obtained in these individuals.
10. People injected with immunoglobulin should be vaccinated with this product at least 1 month apart, so as not to affect the immune efficacy.
11. Clinical trials of this vaccine used in combination with other vaccines have not yet been conducted.
12. It is prohibited to use this product again if any adverse nervous system reaction occurred after vaccination.
13. There is no evidence of protective efficacy of this product for SARS-CoV-2 infected persons.
14. Like all vaccines, this product may not have 100% preventive efficacy for the vaccinee.

**【Vaccination for Special Population】**

- Pregnancy

  Limited experience exists with use of COVID-19 Vaccine (Vero Cell), Inactivated in pregnant women. Animal studies do not indicate direct or indirect harmful effects with respect to pregnancy, embryo/foetal development, parturition or post-natal development. Administration of COVID-19 Vaccine (Vero Cell), Inactivated in pregnancy should only be considered when the potential benefits outweigh any potential risks for the mother and foetus.
- Breastfeeding

  Unknown is whether COVID-19 Vaccine (Vero Cell), Inactivated is excreted in human milk.
- Fertility

Animal studies do not indicate direct or indirect harmful effects with respect to reproductive toxicity.

**【Drug Interaction】**

1. The concomitant clinical trials on this vaccine in combination with other vaccines have not yet been conducted, therefore no data regarding the interaction between this vaccine with other vaccines are available.
2. Combination use with other drugs: Combination use with immunosuppressive drugs, such as immunosuppressive agents, chemotherapy drugs, anti-metabolic drugs, alkylating agents, cytotoxic drugs, corticosteroids, etc. may reduce the body's immune response to this product.

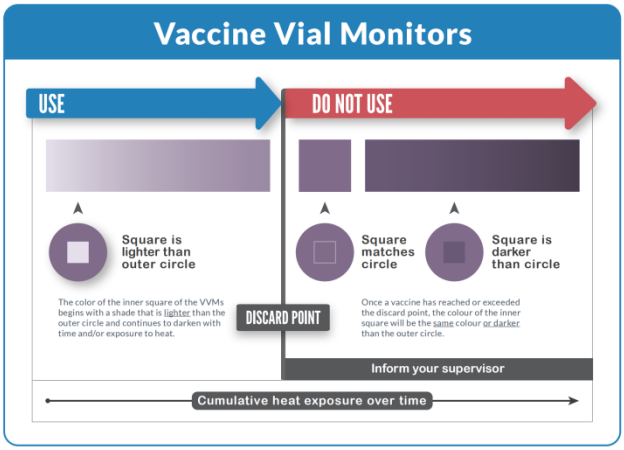
If any vaccines or drugs are being taken or recently taken, please inform the physician in time to avoid drug interaction.

**【Clinical Trials】**

The Phase III clinical trial is a multi-center, randomized, double-blinded, and placebo parallel controlled design and it was conducted in the United Arab Emirates (Abu Dhabi, Sharjah), Kingdom of Bahrain, and many other countries/regions. At least 45,000 healthy subjects aged 18 years and above were randomized to receive candidate vaccine 1 (this product), candidate vaccine 2 or placebo with two-dose regimen (0, 21 (+7) days) to evaluate the vaccine efficacy, safety and immunogenicity. The primary study hypothesis was that the lower limit of the 95% confidence interval (95%CI) of the vaccine efficacy (VE) calculated from 14 days after of the 2$^{nd}$ immunization of this product was greater than 30% in healthy individuals aged 18 years and above. The interim analysis results of the international Phase III clinical trials are as following.

The primary endpoint of the Phase III clinical trial is the incidence of COVID-19 case calculated from 14 days after 2 doses, and the calculation method for vaccine efficacy based on person-year incidence is the main analysis method for vaccine efficacy. During the interim analysis, all effective endpoint cases (114 cases) of infection during the monitoring period were confirmed by the Endpoint Assessment Committee (EAC). The interim analysis data showed that following the two-dose vaccination regimen with 21 (+7) days apart, the vaccine efficacy against COVID-19 was 78.89% (95%CI: 65.79%~86.97%) from 14 days after full-course vaccination, which achieved the hypothesis of the vaccine efficacy for second interim analysis. The median duration of participants follow-up at the time of data lock was 112 days.

**【Storage】** Store and transport in a refrigerated (2℃-8℃) condition, protect from light. Do not freeze.




The Vaccine Vial Monitors (VVM) are on the label of Beijing Institute of Biological Products Co., Ltd. The colour dot which appears on the label of the vial is a VVM. This is a time-temperature sensitive dot that provides an indication of the cumulative heat to which the vial has been exposed. It warns the end user when exposure to heat is likely to have degraded the vaccine beyond an acceptable level. The interpretation of the VVM is simple. Focus on the central square. Its colour will change progressively. As long as the colour of this square is lighter than the colour of the ring, then the vaccine can be used. As soon as the colour of the central square is the same colour as the ring or of a darker colour than the ring, then the vial should be discarded. As indicated in the VVM graphic above.

**【Shelf-life】** 24 months

**【Packaging Configuration】** Non-auto disable pre-filled syringe assembly (with syringe needle), 1 syringe/box; middle borosilicate glass vial, film-coated halogenated butyl rubber stopper, 1 vial/box, 3 vials/box, 10 vials/box.

**【Executed Standard】** YBS00352021, YBS01092021

**【Authorization Number】** GYZZ S20200029; GYZZ S20200030

**【Marketing Authorization Holder】**

Name: Beijing Institute of Biological Products Co., Ltd.

Address: Room 205, Second Floor, Building 4, No.9 Bo'xing 2nd Road, Economic-Technological Development Area, Beijing, P.R. China.

**【Manufacturer】**

Name: Beijing Institute of Biological Products Co., Ltd.

Address: No. 6&9 Bo'xing 2nd Road, Economic-Technological Development Area, Beijing, P.R. China

Post Code: 100176

Telephone: 0086 10 87220568

Fax: 0086 10 87220568