Approval Date:

Revision Date: June 3, 2025

Recombinant COVID-19 Trivalent (XBB.1.5+BA.5+Delta) Trimer Protein Vaccine (Sf9 Cell) Package Insert

Please read this instruction carefully and use under the guidance of a physician.

[NAME OF THE MEDICAL PRODUCT]

Generic Name: Recombinant COVID-19 Trivalent (XBB.1.5+BA.5+Delta) Trimer Protein Vaccine (Sf9 Cell)

Trade Name: Coviccine® Trivalent XBB.1.5

English Name: Recombinant COVID-19 Trivalent (XBB.1.5+BA.5+Delta) Trimer Protein Vaccine (Sf9 Cell)

Chinese Phonetic Alphabet: Chongzu Sanjia Xinguan Bingdu (XBB.1.5+BA.5+Delta Bianyizhu) Sanjuti Danbai Yimiao (Sf9 Xibao)

[COMPOSITION]

This vaccine is produced by the spike receptor-binding domain (S-RBD) of the XBB.1.5, BA.5, and Delta variants of the severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) and heptad repeat (HR) trimeric fusion protein, which is expressed and secreted by using a recombinant baculovirus vector in Sf9 cells, followed by purification, and mixed with a squalene-based oil-in-water emulsion adjuvant in the appropriate proportions. The vaccine does not contain any preservatives or antibiotics.

Active Ingredients: Recombinant trimeric S-RBD-HR protein derived from XBB.1.5, BA.5, and Delta variants of SARS-CoV-2.

Adjuvant: Squalene-based oil-in-water emulsion adjuvant.

Excipients: Disodium hydrogen phosphate, sodium dihydrogen phosphate, sodium chloride.

[DESCRIPTION]

This vaccine is a homogeneous milky-white liquid.

[TARGET GROUPS FOR VACCINATION]

Individuals aged 18 and above.

[THERAPEUTIC INDICATION]

This vaccine is indicated for active immunization to prevent COVID-19 caused by SARS-CoV-2 variants.

[STRENGTH]

Each vial contains 0.5 mL, with a total of 60 μg of recombinant S-RBD-HR trimeric protein (2 doses for human use). A single human dose is 0.25 mL containing 30 μg of recombinant S-RBD-HR trimeric protein.

[ADMINISTRATION AND DOSAGE]

1. Primary series: This vaccine is to be administered as a series of 3 doses (30 μg, 0.25

mL per dose) 3-4 weeks apart.

2. Booster doses: A booster dose of 30 μg (0.25 mL) may be administrated at least 3 months after the last of ≥2 previous COVID-19 vaccine doses.
3. Or adhere to recommended schedule.of the National Administration of Disease Control and Prevention.
4. Coviccine® Trivalent XBB.1.5 is for intramuscular injection only, preferably in the deltoid muscle of the upper arm. Shake well before injection.

[ADVERSE REACTIONS]

The safety of Coviccine® Trivalent XBB.1.5 was based on an analysis of data from a clinical trial conducted in China. Safety follow-up was conducted within 7 days after a single booster dose. Adverse events from day 8 to day 30 collection were conducted by active and passive safety monitoring. SAE within 6 month was also collected.

1. General description of adverse reactions in the clinical trial

A total of 1565 subjects have completed safety follow-up for more than 7 days after booster dose. The long-term safety follow-up is ongoing.

Adverse reactions were classified according to the frequency of adverse reactions recommended by the Council for International Organizations of Medical Sciences (CIOMS): very common (≥10%), common (≥1% and <10%), uncommon (≥0.1% and <1%), rare (≥0.01% and <0.1%), and very rare (<0.01%). Adverse reactions to this vaccine were described as per the CIOMS criteria as follows:

(1) Injection site adverse reactions

Very common: injection site pain.

Common: injection site swelling, injection site induration, injection site pruritus.

(2) Systemic adverse reactions

Common: headache, fatigue/weakness, muscle pain.

(3) Severity of adverse reactions

The reported adverse reactions were mainly grade 1 (mild) with an incidence rate of 12.50%; grade 2 with an incidence rate of 1.25%. No adverse reactions of grade 3 or above reported.

(4) Related serious adverse events (SAEs)

As of May 15, 2023, no vaccine-related serious adverse events have been reported.

2. Adverse reactions in the clinical trial

The clinical data available on safety indicate that this vaccine has a good safety profile.

Among participants 18 years of age and older, the overall incidence rate of adverse reactions following administration of a booster dose of Coviccine® Trivalent XBB.1.5 was 13.75%, the majority of which were solicited adverse reactions, with an incidence rate of 12.50%. The incidence rate of solicited local adverse reactions was 10.00%, with symptoms mainly including injection site pain (10.00%), injection site swelling (2.50%), and injection

site induration (1.25%). The incidence rate of solicited systemic adverse reactions was 5.00%, with symptoms mainly including headache (2.50%), fatigue/weakness (1.25%), and muscle pain (1.25%). The solicited adverse reactions were mainly grade 1, with an incidence rate of 11.25%; grade 2 with an incidence rate of 1.25%. No systemic adverse reactions of Grade 3 or above.

The incidence rate of unsolicited adverse reactions was 1.25%, with the symptom being injection site pruritus. There were no adverse reactions leading to withdrawal/ death. No vaccine-related serious adverse events occurred.

[CONTRAINDICATIONS]

1. People with history of allergic reaction to any component, or any material used in the manufacturing process, or people who have developed allergic reaction to vaccines of the same type.
2. Previous severe allergic reactions (e.g., acute anaphylaxis, angioneurotic edema, dyspnea, etc.)
3. Patients with severe neurological disorders (e.g., transverse myelitis, Guillain-Barre Syndrome, demyelination disease, etc.).
4. Pregnant and breastfeeding women.

[WARNINGS AND PRECAUTIONS]

1. This vaccine is packaged in 2 doses with each vial containing enough vaccine for 2 individuals, each dose for human use is 0.25 mL. Use immediately after opening. The recommended practice is simultaneous vaccination of 2 individuals. In cases where simultaneous vaccinations are not possible, only a single dose should be drawn for the first vaccination, and the remaining vaccine should be kept in the vial and stored refrigerated at 2°C to 8°C, discard the vial after 8 hours., Shake well before use.
2. Check the packaging container, label, appearance and expiry date before use. Do not use it in case of any abnormal condition, including cracks in the vial, spots, stains, scratches on the outer surface, unclear label, expired product, or turbid product. Shake well before use. Do not use the vaccine if the vial shows abnormities such as crack, foreign matters, clumps that can't disappear after shaking, or illegible label.
3. Freezing is strictly prohibited.
4. Keep out of the reach of children.
5. Do not mix with other vaccine in the same syringe.
6. Coviccine® Trivalent XBB.1.5 must not be administered by intravascular, intravenous, subcutaneous or intradermal injection. Safety and efficacy of this vaccine have not been assessed through subcutaneous and intradermal injection.
7. The recipients should be observed for at least 30 minutes on site after injection. Adrenaline and other necessary medications and monitoring equipment should be available for first aid in case of severe anaphylactic reactions.
8. A second dose should not be given to those who have experienced allergic reactions or

other abnormal circumstances after the first dose.

9. Patients with diabetes, or history of convulsions, epilepsy, encephalopathy or mental illness, or family history of those diseases should be used with caution.
10. Patients with acute diseases, atopy and fever should be used with caution; if necessary, delay vaccination after doctor's evaluation.
11. Patients with thrombocytopenia or hemorrhagic diseases, intramuscular injection of this vaccine may cause bleeding, so it should be used with caution.
12. The injection of immunoglobulin should be given at least one month interval to avoid affecting the immune effect.
13. The safety and efficacy of this vaccine on immunocompromised individuals (such as patients with malignant tumors, nephrotic syndrome and HIV/AIDS) have not been assessed. Individualized vaccination programs are recommended.
14. The duration of protection of this vaccine is temporarily unknown by ongoing clinical trials. Necessary protective measures are needed after vaccination.
15. Like other vaccines, vaccination with this vaccine may not protect all vaccine recipients.

[DRUG INTERACTIONS]

1. Concomitant administration of Coviccine® Trivalent XBB.1.5 with other vaccines has not been studied.
2. Concomitant use with other drugs: Drugs with immunosuppressive effects, including immunosuppressive drugs/agents, chemotherapy drugs, antimetabolites, alkylating agents, cytotoxic drugs, corticosteroids, etc., may lead to suppression of immune response to this vaccine.
3. Patients undergoing treatment: In order to avoid possible drug interactions in patients who are taking medication, it is recommended to ask a doctor before use.

[USE IN SPECIFIC POPULATIONS]

Data from clinical studies on the use of this vaccine in specific populations are not available.

[NON-CLINICAL STUDIES]

1. Pharmacodynamics study:

Pharmacodynamics study showed that primary immunization with this vaccine produced high levels of cross-neutralizing antibodies in mice, the geometric mean titer (GMT) of neutralizing antibodies against the XBB.1.5 variant was greater than 50,000, the GMTs against other variants such as BA.4/5 ranged from 5,000 to 25,000. Sequential immunization with this vaccine can produce high levels of cross-neutralizing antibodies in mice, the GMT against the XBB.1.5 variant was greater than 40,000, which was more than 1000-fold increase compared to that of sequential immunization with inactivated vaccines. The GMTs against the prototype strain and other variants ranged from 7,600 to 20,000, indicating good broad-spectrum activity.

2. Toxicology study:

Local tolerance study was conducted under Good Laboratory Practice (GLP) conditions,

including active systemic anaphylaxis test in British-bred guinea pigs and muscle irritation test in Japanese big-eared white rabbits. Negative results were shown in the active systemic anaphylaxis test in British-bred guinea pigs after intramuscular injection with this vaccine. The muscle irritation test in Japanese big-eared white rabbits, with a single intramuscular injection of 0.5 mL/rabbit showed only mild irritation to the muscle at the injection site. Study results indicate a good safety profile.

[CLINICAL STUDY]

The safety, immunogenicity, and efficacy of Coviccine® Trivalent XBB.1.5 was evaluated in a clinical study: A total of 2905 subjects received a booster vaccination in population aged 18 years and older who had previously received 2 or 3 doses of COVID-19 vaccine. Data available indicate that this vaccine (30 μg/0.25 mL) has good safety, immunogenicity, and efficacy.

A booster vaccination with Coviccine® Trivalent XBB.1.5 (30 μg/0.25 mL) could elicit high titer of neutralizing antibodies against XBB.1, XBB.1.5, XBB.1.16, XBB.1.9.1, XBB.2.3, BQ.1, BF.7, BA.4/5, BA.2.75 and other SARS-CoV-2 Omicron variants after 14 days. The geometric mean titers (GMT) of neutralizing antibodies ranged from 900 to 3,500, an increase of 6.9 to 39 folds compared to that before vaccination, demonstrating a good broad-spectrum activity. The GMT of neutralizing antibodies against the SARS-CoV-2 Omicron XBB.1.5 variant was 1728.26, 39.19 folds higher than that before vaccination; the GMT of neutralizing antibodies against the SARS-CoV-2 Omicron XBB.1.16 variant was 1093.67, 8.8 folds higher than that before vaccination; the GMT of neutralizing antibodies against the SARS-CoV-2 Omicron XBB.1.9.1 variant was 616.03, 12.87 folds higher than that before vaccination; the GMT of neutralizing antibodies against the SARS-CoV-2 Omicron XBB.2.3 variant was 1112.53, 12.42 folds higher than that before vaccination; the GMT of neutralizing antibodies against the SARS-CoV-2 Omicron BA.4/5 variant was 3235.68, 15.52 folds higher than that before vaccination; the GMTs of neutralizing antibodies against other SARS-CoV-2 Omicron variants, including BQ.1, BF.7, and BA.2.75, were 1329.77, 2052.24, and 3681.23, which were 12.65, 14.14, and 23.63 folds higher than that before vaccination, respectively. This vaccine has good immune persistence, with neutralizing antibody levels against a wide range of XBB variants remaining at approximately 50% of peak levels 6 months after vaccination.

The efficacy against symptomatic COVID-19 caused by SARS-CoV-2 was 93.28% (95% CI: 92.76%, 93.81%) more than 14 days after vaccination. Preliminary results of gene sequencing suggested that this vaccine has a good broad-spectrum efficacy against symptomatic COVID-19 caused by SARS-CoV-2 Omicron XBB.1, XBB.1.5, and XBB.1.9 variants. Long-term efficacy (6 months): 86.18% (95% CI: 84.24%, 88.12%) against symptomatic COVID-19 caused by SARS-CoV-2 after vaccination with this product.

Another investigator-initiated trial (IIT) evaluated the protective efficacy of this vaccine against emerging subvariants, including KP.3, XDV, XEC, and LP.8.1, by measuring serum

neutralizing antibody titers in 64 subjects. Pseudovirus neutralization assays demonstrated that the GMTs of neutralizing antibodies against the KP.3, XDV, XEC, and LP.8.1 subvariants before vaccination were 77, 87, 78, and 86, respectively. At 14 days post-vaccination, the GMT levels increased to 903, 668, 704, and 816, respectively, demonstrating significant elevation compared to the level before vaccination, with GMT fold increases of 11.73, 7.67, 9.02, and 9.49, respectively.

[STORAGE]

Store and transport refrigerated at 2°C to 8°C. Protect vials from light. Do not freeze. Discard if the vaccine has been frozen.

After the first dose has been withdrawn, the vial should be held at 2°C to 8°C. Discard vial after 8 hours.

[PACKAGE]

Packaged in injection vials made of middle borosilicate glass tubing, and covered with a bromobutyl rubber stopper for injection (brominated), which does not contain natural latex. 0.5 mL/vial, 1 vial/box.

[SHELF-LIFE]

24 months tentatively.

[SPECIFICATION IMPLEMENTED]

Manufacturing and Verification Procedures for Recombinant COVID-19 Trivalent (XBB.1.5+BA.5+Delta) Trimer Protein Vaccine (Sf9 Cell).

[AUTHORIZATION NUMBER]

To be determined. Emergency Use Authorization.

[MARKETING AUTHORIZATION HOLDER]

Name: WestVac Biopharma Co., Ltd.

Address: No.552, Fenghuang Road, Shuangliu District, Chengdu, Sichuan Province, P.R. China

Zip Code: 610200

Tel.:+86 400-996-6969

Fax: +86 28-60651111

Email: westvac@westvacpharma.com

Website: http://www.westvacpharma.com

[MANUFACTURER]

Name: WestVac Biopharma Co., Ltd.

Address: No.552, Fenghuang Road, Shuangliu District, Chengdu, Sichuan Province, P.R. China

Zip Code: 610200

Tel.: 400-996-6969

Fax: +86 28-60651111

Email: westvac@westvacpharma.com

Website: http://www.westvacpharma.com